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## NON-INVASIVE POSITRON DETECTOR FOR THE MONITORING OF THE ARTERIAL INPUT FUNCTION IN PET

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**Purpose:** To extract quantitative data from dynamic positron emission tomography (PET) scans, the concentration of the radiotracer in the arteries, known as the arterial input function (AIF), is required. Currently, manual blood sampling at different time intervals is considered the gold standard, despite limitations such as invasiveness due to arterial cannulation causing discomfort for the patient and lacking time resolution to accurately determine the AIF's peak. Our proposed detector system based on scintillating optical fibers wrapped around the patient's wrist will eliminate the need for invasive blood sampling and overcome the limitations noted with other alternatives for measuring the AIF.

**Materials and Methods:** Before the clinical use of the detector system, we verified the robustness of its set-up with attenuation measurements. Our scintillating fiber was excited by UV light and gamma rays (Cs-137 186.5 kBq). The excitation sources were placed at different positions along the scintillating fibre axis.

The prototype is developed using a 1.5 m scintillating fiber with a polystyrene core (BCF-12, Saint-Gobain) coupled at both ends to an 11 m transmission fiber with a core of PMMA (Eska, Mitsubishi). The coupling was performed using a UV cured optical adhesive (NOA 68, Norlands) after all fibre ends were carefully polished. Each end of the transmission fibres is connected to a photomultiplier tube (PMT) (H6779, Hamamatsu). The ratio of the PMTs' output at both ends will be fitted with a decreasing mono exponential as a function of the distance. In addition, since the detector is wrapped around the patient's wrist, the loss of signal for different bending radius needs to be evaluated. The ratio of the PMT's output was taken for loops of different size with the excitation source fixed at one end and compared to the ratio when the fibre is straight. The outputs from the PMTs are read simultaneously by an oscilloscope, without amplification. The oscilloscope signal is recorded with an instrument driver directly in Matlab.

**Results:** The attenuation length of the UV and Cs-137 sources in the scintillating fibre was  $146 \pm 6$  cm and  $169 \pm 9$  cm respectively. One possible explanation for this difference is that the attenuation depends on the wavelength and both sources do not necessarily result in the same spectrum of light. The bending losses with the Cs-137 were smaller than the measurements' uncertainty, but for the UV, measured losses ranged from 0.82% with radius of 15 cm to 2.20% at 6 cm.

**Conclusions:** The first tests demonstrated the feasibility and robustness of the detector set-up. The next step will be phantom measurement resembling a clinical case with 18F-FDG before moving on to testing the detector on patients.

2

## INTRA-ARC BINARY COLLIMATION ALGORITHM FOR THE OPTIMIZATION OF STEREOTACTIC RADIOTHERAPY TREATMENT OF MULTIPLE METASTASES WITH MULTIPLE PRESCRIPTIONS

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**Purpose:** A novel system of algorithms has been developed that allows for the automated generation of dynamic conformal arc (DCA) radiotherapy plans for the treatment of multiple metastases with multiple prescription doses. This study uses simulated annealing to optimize the collimation of subsets of targets at specified control points, along with control point-specific MU weighting, to achieve prescription target coverage and normal tissue sparing.

**Materials and Methods:** At each control point (CP), the system aims to optimize the number of targets treated, the rotation angle of the collimator, the MLC positions, and the number of MU delivered. A novel optimization objective function (OF) was designed for this study using a linear-quadratic metric penalty function, with a generic form applied to OAR maximum doses and clinical target metrics. This OF is used as a minimization metric in a simulated annealing procedure to define the intra-arc binary collimation

(iABC) pattern. In iABC, each target can either be conformally treated or entirely shielded by the MLC at each CP. At every iteration in the simulation, a new pattern is generated for which targets to treat at a given CP. Using a collimator optimization method, the collimator rotation angle was optimized at each CP to generate a dynamic collimator rotation trajectory. A final optimization was applied, using the same objective function to define a CP-specific MU distribution (MUD), which specifies the relative contribution of dose at each of the 175 fields. Seven multiple metastases cases previously treated at the Nova Scotia Health Authority were anonymized and re-planned with VMAT, DCA, and iABC using consistent planning methods. All plans were normalized such that the prescription dose to the coldest target, with reference to its prescription, was covering 99% of said target volume. Target coverage accuracy was quantified by the ratio of the dose covering 99% of the volume to the prescription dose.

**Results:** Treatment plans generated with iABC used an average of 3044 (37%) fewer MU in the total plan than VMAT ( $p = 0.026$ ). All normal tissue metrics for all plans and all patients were within clinical acceptability. No statistically significant difference was observed for any normal tissue metrics. Normalized prescription target coverage accuracy for all targets was 4.0% better on average for VMAT plans when compared to iABC ( $p = 0.016$ ), and 14.8% better on average for iABC when compared to DCA ( $p = 0.041$ ).

**Conclusions:** Intra-arc binary collimation has the potential to improve treatment delivery to multiple metastases treatment plans with multiple unique prescriptions with a statistically significant improvement to target coverage accuracy when compared to conventional DCA. Additionally, this method retains the majority of MU sparing inherent in DCA (37% when compared to VMAT) without a statistical significant difference in normal tissue dose when compared to VMAT.

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## CAN DOSE PROXIMAL TO THE PTV INFLUENCE THE RISK OF DISTANT METASTASES IN EARLY STAGE LUNG CANCER PATIENTS TREATED WITH SBRT?

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**Purpose:** In an era where little is known about the "abscopal" (out-of-the-field) effects of lung SBRT, we investigated correlations between the radiation dose proximally outside the PTV and the risk of cancer recurrence after SBRT in patients with primary Stage I non-small cell lung cancer (NSCLC).

**Materials and Methods:** This study included 217 Stage I NSCLC patients across two institutions who received SBRT. Correlations between clinical and dosimetric factors were investigated. The clinical factors considered were distant metastasis (DM), loco-regional control (LRC) and radiation pneumonitis (RP). The dose (converted to EQD2) in regions of varying size directly outside of the PTV were computed. For each feature, area under the curve (AUC) and odds ratios with respect to the outcome parameters DM, LRC and RP were estimated; Kaplan-Meier (KM) analysis was also performed.

**Results:** Thirty-seven (17%) patients developed DM after a median follow-up of 24 months. It was found that the mean dose, delivered to a shell-shaped region of thickness 30 mm outside the PTV had an AUC of 0.82. Two years after treatment completion, the rate of DM in patients where the mean dose delivered to this region was higher than 20.8 Gy2 was 5% compared to 60% in those who received a dose lower than 20.8 Gy2. KM analysis resulted in a hazard ratio of 24.2 (95% CI: 10.7, 54.4);  $p < 10^{-5}$ . No correlations were found between any factor and either LRC or RP.

**Conclusions:** The results of this study suggest that the dose received by the region outside but close to the PTV has a significant impact on the risk of distant metastases in Stage I NSCLC patients treated with SBRT. If these results are independently confirmed, caution should be taken, particularly when a treatment plan results in a steep dose gradient extending outwards from the PTV.

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### SYNTHETIC-CT FROM 3D GRADIENT-ECHO MRI

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**Purpose:** MRI-based treatment planning in radiotherapy benefits from increased soft-tissue contrast and functional imaging. This approach is limited by the lack of electron density information and the difficulty to differentiate air and bone. Magnetic susceptibility can be mapped using MRI and used to separate bone from air. We propose a method to produce synthetic-CT through automatic voxel-wise assignment of Hounsfield units (HU) from an MRI dataset that includes a susceptibility map and fat-water separation.

**Materials and Methods:** Three-dimensional datasets were acquired with a multi-echo gradient-echo sequence in four healthy volunteers in a 3T MRI, under informed consent approved by our institution. Magnitude and phase data were reconstructed. Fat and water images were calculated, and susceptibility mapping was performed using the iterative phase replacement algorithm, with a streaking correction to reduce artifacts from structures with large susceptibility. The synthetic-CT was produced using a segmentation algorithm based on fuzzy c-means clustering and adaptive thresholding. Voxels classified as air were assigned a HU of -1000. HU assignment in bone and soft tissue was performed using a probability-weighted sum. The algorithm was tested in the head of three volunteers and in the lower leg of one volunteer.

**Results:** The skull, spine, frontal sinus, maxillary sinus, mastoid sinus, ethmoid sinus, sphenoid sinus and teeth were clearly distinguished in the synthetic-CT of the head. Observations were consistent across the three volunteers. The cortical bone of the tibia and fibula was properly mapped in the lower leg result.

**Conclusions:** Susceptibility mapping informs the differentiation of air and bone. The feasibility of the proposed technique was demonstrated in volunteers. The proposed method allows HU variations in each tissue class, as opposed to bulk HU assignment. It is automated, fast, and based on a commercially available pulse sequence. The method avoids registration errors typical of multi-sequence techniques and does not rely on a priori information, making it suitable for nonstandard geometry. Evaluation and validation in phantoms and in patients is ongoing.

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### INTRAOPERATIVE VERIFICATION OF NEEDLE PLACEMENT USING 360-DEGREE 3D TRANSVAGINAL ULTRASOUND DURING HIGH-DOSE-RATE INTERSTITIAL GYNECOLOGIC BRACHYTHERAPY

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**Purpose:** Treatment of vaginal tumours may include high-dose-rate (HDR) interstitial brachytherapy with a perineal template. To optimize treatment and avoid overexposure of organs-at-risk (OAR), precise needle placement is necessary; however, there is no standard approach to intraoperative imaging during needle insertion with only a post-insertion x-ray computed tomography (CT) image to verify all needle positions and perform dose planning. The introduction of intraoperative needle position verification would allow OAR to be avoided, enable deviations in needle placements from intended positions to be immediately corrected, and allow the clinical acceptability of the implant to be assessed intraoperatively. We have designed a 360° 3D transvaginal ultrasound (TVUS) system and report on needle visualization and localization in three patients.

**Materials and Methods:** Three patients were imaged using the 3D US system, which uses a 2D side-fire transrectal ultrasound (US) probe rotated by a motor to generate a ring-shaped 360° 3D image, available immediately after the 20s scan. Prior to image acquisition the probe is placed in the hollow centre of a sonolucent vaginal cylinder, which is compatible with the template. In all cases, a 3D TVUS image was acquired after most needles had been inserted and then the US probe and hollow vaginal cylinder were removed and replaced with the clinical cylinder.

The 3D TVUS images were rigidly registered to the post-insertion CT image and for each needle the entrance and exit point visible along the needle path were selected. Corresponding points between the modalities were established by projecting the 3D US points onto the needle path in CT. The distance between these sets of points was used to evaluate each needle's position difference and the maximum distance (entrance or exit) was used to assess the maximum difference in the needle positions. Angular errors between the needle paths were also evaluated.

**Results:** In addition to needles being clearly visualized in the 3D US images, OAR, including bladder (with Foley catheter in the bladder), rectum, and bowel were identifiable in the images. Twenty-eight needles were inserted with a mean entrance and exit point differences of  $1.98 \pm 0.92$  mm and  $1.91 \pm 0.81$  mm, respectively, with a mean maximum distance of  $2.33 \pm 0.78$  mm. The mean angular difference was  $1.67 \pm 0.75^\circ$ . In the approximate anterior/posterior and left/right planes, the mean angular differences were  $-0.09 \pm 1.25^\circ$  and  $0.23 \pm 1.09^\circ$ , respectively, indicating a lack of systematic angular differences relative to the imaging planes.

**Conclusions:** We developed a 360° 3D TVUS system for use during interstitial brachytherapy needle insertion for gynecologic malignancies. Based on initial results, this approach may be feasible to provide 3D intraoperative imaging to verify needle positions and allow for clear visualization of key OAR.

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### STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR SPINAL METASTASES AT THE EXTREMES OF THE SPINE: IMAGING-BASED OUTCOMES FOR CERVICAL AND SACRAL METASTASES

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**Purpose:** Most of the data following spine stereotactic body radiotherapy (SBRT) are specific to thoracic and lumbar metastases. The unique anatomy and biomechanical features of the cervical spine and sacrum may impact treatment outcomes following SBRT. The purpose of this study was to report our imaging-based outcomes following SBRT specific to cervical and sacral metastases.

**Materials and Methods:** From our institutional prospectively maintained spine SBRT database, we retrospectively reviewed only cervical and sacral metastases. All patients were followed at two- to three-month intervals with a clinical visit and full spine MRI. Outcomes of interest were imaging-based local control (LC), overall survival (OS), vertebral compression fracture (VCF) and other serious adverse effects.

**Results:** A total of 52 patients and 93 spinal segments were identified consisting of 56 treated segments within the cervical spine and 37 within the sacrum. The median follow-up was 14.4 months and 19.5 months, respectively, and the median total dose and number of fractions was 24 Gy in 2, respectively, in both cohorts. Cumulative LC rates at one- and two-years were lower for the sacral cohort (86.5% and 78.7%) compared to the cervical spine cohort (94.5% and 92.7%). Lack of posterior spinal element involvement was predictive of LC in the cervical spine cohort (no local failures,  $p < 0.0001$ ) cohort, and absence of epidural disease (HR 0.275, 95% CI 0.076-0.989,  $p = 0.048$ ) predicted LC in the sacral cohort. Median OS was 16.3 months and 28.5 months in the cervical spine and sacrum cohorts, respectively. In the cervical spine group, presence versus absence of liver and/or lung metastases was prognostic with a median survival of 10.8 months versus not reached even after 48 months ( $p = 0.0494$ ), respectively. In the sacral cohort, patients with oligometastatic disease (HR 0.139, 95% CI 0.031-0.616,  $p = 0.0094$ ) and breast primary (HR 0.136, 95% CI 0.026-0.697,  $p = 0.0168$ ) had longer OS. Two cases of VCF in the sacrum, one brachial plexopathy and one lumbar-sacral plexopathy were observed.

**Conclusions:** Although high rates of LC were observed following SBRT to the cervical spine and sacrum, strategies specific to the sacrum may require further investigation to optimize results. Serious sequelae after SBRT to cervical spine and sacrum were rare.

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### FEASIBILITY AND CONSISTENCY OF ON-TREATMENT CONE BEAM CT FEATURE EXTRACTION USING AN AUTOMATED DEFORMABLE REGISTRATION RADIOMICS PIPELINE

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**Purpose:** To evaluate a novel automated pipeline (AP) with an alternate deformable image registration algorithm compared to semi-automated deformable registration (SADR) to derive CBCT imaging markers (CBCTM) previously correlated to radiation pneumonitis (RP).

**Materials and Methods:** NSCLC patients treated between 2011-2014 with curative radiation with  $\geq 12$  months follow-up without tumour recurrence prior to development of toxicity were included. RP (CTCAE G2+) was obtained from a prospectively collected database. Treatment plan and CBCT registrations for all treatment fractions was attempted via: (SADR) an intensity-based algorithm using the Elastix toolbox and custom pre-processing, or (AP) an intensity-based algorithm in RayStation with the CBCTM extracted in a custom image processing module. The SADR dataset was the training dataset, and extra patients extracted via AP were the validation dataset. Patient characteristics in the training/validation and correlations between CBCTM values (SADR and AP) were compared. Associations between RP, CBCTM at fractions 10 and 20 (CBCTM10, CBCTM20), average CBCTM of 5 consecutive fractions around fractions 10 and 20 (CBCTM10avg, CBCTM20avg), and dosimetric factors were evaluated using logistic regression. Model performance was evaluated using area under the receiver operating characteristic curve (AUC) analysis. Models derived from the training dataset were evaluated independently in the testing dataset.

**Results:** One hundred and twenty-nine patients were included, with 36 patients (27.9%) having RP. Eighty-three of 129 (64.3%) were successfully registered using both SADR and AP (training set). Failures were due to inconsistent data formats, convergence failure, and grossly incorrect registrations. The remaining 46 patients were successfully processed using AP (validation set). Patient characteristics including the rates of pneumonitis (26.5% versus 31.1%) in the training and validation datasets were similar. In the training dataset: CBCTM values extracted using SADR and AP were highly correlated for both F10 and F20 ( $\rho = 0.81, 0.92, p < 0.005$ ); using either SADR or AP, mean lung dose (MLD) and CBCTM20 were associated with RP on multivariable analysis ( $p < 0.05$ ); CBCTM10avg and CBCTM20 avg were both correlated with RP ( $p < 0.05$ ) on univariable and multivariable analysis; and the best performing model (CBCTM20+MLD) had an AUC of 0.679. In the validation dataset, the CBCTM20+MLD model had an AUC of 0.678.

**Conclusions:** A previously validated CBCT marker of lung toxicity can be automatically derived using a different deformable image registration method, and remains correlated with RP, in addition to high correlation of marker values between the two methods. The CBCTM20 + MLD model was predictive of RP in an independent validation dataset.

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### A POPULATION-BASED STUDY OF MELANOMA BRAIN METASTASIS TREATMENT: HAVE ADVANCES IN RADIOTHERAPY AND SYSTEMIC THERAPY IMPROVED OUTCOMES?

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**Purpose:** Outcomes for patients with melanoma brain metastasis (MBM) are poor. New radiotherapy techniques and systemic agents have improved outcomes in trials. Outcomes have rarely been studied at the population level. We undertook a population-based study investigating changes in management and outcome for MBM.

**Materials and Methods:** This was a retrospective cohort study of MBM patients in the Ontario Cancer Registry treated 2007-2016. Treatment, covariates and outcomes were defined using administrative data. Treatments

and outcomes were described by era (2007-2009, 2010-2012, 2013-2016). Outcomes were adjusted using Cox regression.

**Results:** One thousand and ninety-six MBM patients were treated 2007-2016 (326 in 2007-2009, 310 in 2010-2012, 460 in 2013-2016). Patient factors and time from melanoma diagnosis to the first palliative treatment were similar between eras, though case numbers increased. The first brain-directed treatment (i.e. surgery, whole brain radiation therapy [WBRT] or conformal RT) was WBRT in 75.5% 2007-2009, dropping to 52.0% 2013-2016. Stereotactic radiation or other conformal techniques increased: 3.4% 2007-2009; 21.3% 2013-2016. Intracranial resection also increased: 21.2% in 2007-2009; 26.7% in 2013-2016. Use of BRAF/MEK inhibitors and/or immunotherapy increased:  $< 2.0\%$  2007-2009; 40.9% 2013-2016. In 2013-2016, one- and two-year overall survival (OS) was 21.8% and 13.8%. This compared to 12.3% and 6.4% 2007-2009, and 10.7% and 5.5% 2010-2012 ( $p = 0.001$ ). In adjusted analysis the OS difference remained (adjusted hazard ratio [AHR] 2013-2016 versus 2007-2009: 0.65 (95% CI 0.56-0.77). Analysis included adjustment for temporal and regional variation in pre-diagnosis surveillance with brain MRI or CT. In 2007-2009 more WBRT was prescribed (AHR 2013-2016 versus 2007-2009: 0.32 [0.22-0.46]). The time from first to second brain-directed treatment was shorter in later eras (e.g. AHR 2013-2016 versus 2007-2009: 2.16 [1.48-3.14]).

**Conclusions:** The uptake of new radiotherapy techniques and systemic treatments for MBM was associated with increased survival and less WBRT. The time between brain-directed courses decreased as stereotactic treatments increased. However, many still received WBRT.

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### ANALYSIS OF RADIOTHERAPY PEER REVIEW: COSTING HUMAN RESOURCE SUPPORTS

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**Purpose:** Radiotherapy peer review (RTPR), if properly planned and implemented, can further quality of care. In a systematic review of the literature, multidisciplinary RTPR found changes in one in nine plans, with major changes in one of 40 cases. However, it is essential with the implementation and expansion of RTPR that there exist: clear definitions and objectives; an implementation plan; uniformity of data to ensure meaningful comparisons; and alignment of objectives with definitions to ensure quality of care. In the era of cost-containment, alignment of resource support required for quality RTPR is crucial. The objective of this study was thus to analyze the yield of RTPR relative to the human resources support and costs required for it.

**Materials and Methods:** A model dataset of patients receiving RT (curative and palliative) over one calendar year at a tertiary care centre was compiled. Institutionally, our RTPR rounds are conducted weekly/bi-weekly for each disease site and attended by staff and students of radiation oncology (RO), therapy, and physics. Resource time requirements of PR were modeled using internal data by treatment site, interviews with participants and CCO data on PR rates. Literature review revealed major plan change rates. Requirements to meet future targets of 100% PR rates were modeled in three PR scenarios: 1) Gold-standard (GS) multi-disciplinary PR; 2) Minimum standard, two RO staff supported by RT and Physics; 3) Sign-off, RO staff review cases independently, without support. Hourly staff costs were sourced from publicly available documents, adjusted for vacation and benefits.

**Results:** Model data included 4904 unique treatment plans (69% radical, 31% palliative) within 12 disease sites. Annually, multidisciplinary PR requires an estimated 850 hours of RO time and 1180 hours from others to achieve PR rates above 85% for radical plans and 35% for palliative. This represents an opportunity cost of more than \$280,000(k)/year to identify a projected 93 major changes (~\$3k/change). Targeting 100% review rate with GS model projects to cost \$395k. Alternative peer review models were analyzed. Scenario 2 revealed costs of \$192k, and 530 RO hours to achieve 100% radical and palliative peer review, assuming similar throughput rate to the base case (GS). Scenario 3 revealed a cost of \$135k, and 440 RO hours of single RO sign off assuming a 50% reduction in throughput rate.

**Conclusions:** The use of comprehensive RTPR is feasible and the support costs for detecting a major change are approximately \$3,000. While GS method aligns with most literature and a major plan change rate of 2%, its

supports exceed those in which RTPR consists of treatment plan by a second RO. It remains unclear if major event detection rates are as high in reduced intensity PR models and opportunities to measure and increase actionable event detection, reduce the resource support burden or improve throughput of RTPR while enhancing efficiency should be explored.

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### PRIMARY ORGAN PRESERVATION VERSUS TOTAL LARYNGECTOMY FOR T4 LARYNX CANCER

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**Purpose:** The optimal treatment for patients with T4 larynx is unknown. This study evaluates population-based outcomes of organ preservation with radiation (RT) +/- chemotherapy (chemo) versus upfront total laryngectomy (SX) for T4 larynx cancer.

**Materials and Methods:** Patient characteristics, treatments, and outcomes were retrospectively analyzed for patients with T4 larynx cancer treated in our province from 1984 to 2014. Patients who had metastatic disease or who were treated with palliative intent were excluded. The Kaplan-Meier method was used to assess loco-regional recurrence-free survival (LRRFS) and cancer-specific survival (CSS). Multivariable analysis was performed using Cox regression analysis.

**Results:** Preliminary results are based on 223 patients. The median age at diagnosis was 64 years (Interquartile Range [IQR] 57-70 years) and 86% of patients were male. Most were current (64%) or former (29%) smokers, with a mean 43 pack year smoking history and 41% consumed daily alcohol. Two thirds (66%) were ECOG status 0-1 at diagnosis at 33% were 2-4. Most (96%) had T4A disease, 4% had 4B disease and 72% had thyroid cartilage invasion. Over half (54%) were N0, 16% N1, 23% N2 and 2% N3. The majority (94%) were evaluated by a surgeon at diagnosis. Forty per cent had SX, 25% were offered SX as an option and chose RT, 12% had inoperable disease, 12% were medically inoperable and 5% were recommended to have SX but refused. Initial treatment was as follows: 13% SX alone, 27% with SX + post-op RT and 4% with SX + post-op chemoRT, 44% treated with RT and 14% with chemoRT. The median RT dose was 60 Gy (IQR 50-66 Gy). The most common concurrent chemotherapy regimens included every 3 weeks Cisplatin, (55%) Cetuximab (17%) and every week Cisplatin (15%). Of the patients receiving upfront RT; 21% underwent salvage laryngectomy. At one year after RT, 36% were G-tube dependent and 35% were tracheostomy dependent.

Five-year LRRFS was 14% (95% CI 8-20%) for patients treated with SX alone, 45% (95% CI 39-51%) for SX + RT (+/- chemo), 28% (95% CI 23-33%) for RT alone and 33% (95% CI 24-42%) for chemoRT ( $p = 0.002$ ). Five-year CSS was 29% (95% CI 18-38%) for patients treated with SX alone, 52% (95% CI 46-58%) for SX + RT +/- chemo, 42% (95% CI 37-47%) for RT alone and 46% (95% CI 36-56%) for chemoRT ( $p = 0.03$ ). On multivariate analysis increasing age (HR 1.02, 95% CI 1.0-0.04,  $p = 0.03$ ) and N2/3 disease (HR 2.0, 95% CI 1.4-3.0,  $p = 0.001$ ) were associated with decreased LRRFS. RT (HR 1.6, 95% CI 1.1-2.4,  $p = 0.01$ ) and SX alone (HR 2.6, 95% CI 1.6-4.5,  $p < 0.0001$ ) were associated with decreased LRRFS relative to SX + RT. ChemoRT was not associated with decreased LRRFS relative to SX + RT (HR 0.9, 95% CI 0.5-1.6,  $p = 0.72$ ). Gender, thyroid cartilage invasion, T4b disease, ECOG status, and year of diagnosis were not associated with LRRFS ( $p > 0.05$ ).

**Conclusions:** In this population-based analysis, organ preservation with chemoRT was not associated with inferior LRRFS relative to upfront laryngectomy + adjuvant RT (+/- chemo). Of those who underwent upfront organ preservation, one fifth required salvage laryngectomy and over a third were either G-tube or tracheostomy dependent at one year post-RT. ChemoRT may be considered as a treatment option for patients with T4 larynx cancer after a careful discussion of the risks and benefits of this approach.

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### RESULTS OF A PROSPECTIVE COHORT TRIAL: STEREOTACTIC IMAGE-GUIDED NEOADJUVANT ABLATIVE RADIATION THEN LUMPECTOMY (SIGNAL) FOR EARLY-STAGE BREAST CANCER

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**Purpose:** For certain low-risk patients, recurrences after lumpectomy tend to be localized to the resection cavity, suggesting a role for partial-breast irradiation. Neoadjuvant single-fraction radiation therapy (SFRT) is a novel approach in which unresected disease is irradiated prior to surgery. SFRT has been associated with favourable local control, survival and toxicity. However, because most large-scale studies of SFRT employed specialized treatment delivery platforms that were not widely available, its implementation has been limited. For such reasons, we developed SIGNAL, a single-arm, single-institution Phase 2 study examining neoadjuvant SFRT followed by surgery. We report the dosimetry and outcomes of a cohort of 27 patients treated according to this novel regimen.

**Materials and Methods:** SIGNAL was open to postmenopausal women, with biopsy-proven ductal carcinoma, any grade, unifocal,  $\leq 3$  cm, ER-positive, without axillary involvement. All patients received contrast-enhanced prone breast MR and prone CT simulation. The GTV was delineated on T2 diffusion MR. CTV and PTV were delineated by successive 5 mm expansions of the GTV. A prescription dose of 21 Gy was delivered in a single fraction to the PTV via an opposed, 2-beam volumetric modulated arc therapy (VMAT) technique. Relevant dosimetric constraints were defined via review of the published literature and from basic radiobiological principles. Patients went for lumpectomy and sentinel node dissection (SND) one week after surgery and were seen at regular intervals after that for clinical follow-up and toxicity assessment using both visual toxicity scales and validated QOL questionnaires.

**Results:** We enrolled 52 patients. Of these, 13 were excluded at the time of MR, leaving 39 patients who were scanned and eligible for planning. Over the course of the study, we applied two different sets of dosimetric constraints. Using our original constraints, acceptable treatment plans were attainable for only 16 of 28 (57%) patients. After implementation of revised dosimetric constraints, acceptable treatment plans were attainable for 11 of 11 (100%) patients. In total, 27 patients were treated with SFRT. All 27 patients went on to lumpectomy: 25 patients had T1 disease; one patient had T2 disease; one patient had Tis. Only 23 patients received SND: 20 patients had N0 disease; three patients had axillary nodal spread (one macroscopic; one microscopic; one seen on IHC); four patients did not receive SND. All 27 patients were ER-positive; 15 patients received hormonal therapy; four patients received chemotherapy. At a median follow-up of 487 days from radiotherapy, all 27 patients were alive and free of recurrence. At six months post-surgery, toxicity, patient-rated cosmesis and QOL were not significantly different from baseline. **Conclusions:** SIGNAL represents a feasible method of implementing single-dose radiotherapy for neoadjuvant treatment of low-risk breast cancer. It appears to be clinically effective, practicable and without significant toxicity. Randomized studies to corroborate these findings are ongoing.

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### CANCER-SPECIFIC OUTCOMES OF HYPOFRACTIONATED LOCO-REGIONAL RADIOTHERAPY FOR PATIENTS WITH STAGE I-III BREAST CANCER

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**Purpose:** Hypofractionated (HypoF) radiotherapy (RT) is well established following breast conserving surgery for breast cancer but many centres continue to use conventional fractionation (CF;  $\leq 2$  Gy/day) if regional lymph nodes are included in the target volume. At our institution, HypoF regional nodal RT (15-16 fractions of  $>2$  Gy/day) has been used for over 30 years, with published data reporting no additional toxicity. This study evaluated long-term, population-based cancer-specific outcomes of HypoF versus CF for breast/chest wall plus regional nodal RT for patients with breast cancer. **Materials and Methods:** A prospective provincial database was used to

identify 6,247 newly diagnosed patients with Stage I-III breast cancer treated with curative intent breast/chest wall + regional nodal RT from 1998 to 2010. Loco-regional relapse-free survival (LRRFS) distant relapse-free survival (DRFS) and breast cancer-specific survival (BCSS) were compared using Kaplan Meier (KM) analyses of HypoF versus CF, for the entire cohort and for high-risk subgroups: Grade 3, ER-negative, HER2+, and  $\geq 4$  positive nodes. Multivariable Cox regression analysis (MVA) was performed to assess the effect of RT fractionation on LRRFS.

**Results:** Overall, 70% (4384) received HypoF and 30% (1863) received CF. Median follow up was 12.2 years and was similar between the two groups (HypoF: 12.8 years versus CF: 11.2 years). Patients treated with HypoF were significantly older, more likely to be post-menopausal, HER2+, not receive chemotherapy, and less likely to have Stage III disease. Ten-year outcomes in the HypoF versus CF cohorts were: LRRFS 94.5% versus 94.1% ( $p = 0.91$ ), DRFS 73.5% versus 74.4%, ( $p = 0.31$ ), and BCSS 76.9% versus 78.6% ( $p = 0.18$ ). On subgroup analysis, LRRFS and DRFS were not different between HypoF and CF cohorts with Grade 3, ER-, or  $\geq 4$  positive nodes (all  $p > 0.05$ ). On MVA, HypoF was not associated with inferior LRRFS (HR 1.0, 95% CI 0.8 – 1.2,  $p = 0.83$ ), DRFS (HR 1.0, 95% CI 0.9 – 1.1,  $p = 0.996$ ) or BCSS (HR 1.0, 95% CI 0.8 – 1.1,  $p = 0.92$ ) compared to CF.

**Conclusions:** This large, population-based analysis with long-term follow-up demonstrates that modest hypofractionation provides similar local and distant control and breast cancer-specific survival outcomes compared to conventional fractionation when the RT volume included the breast/chest wall plus regional lymph nodes. Hypofractionation is an effective alternative for patients with Stage I-III breast cancer receiving nodal RT.

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#### LOCAL RELAPSE AFTER BREAST CONSERVING THERAPY VERSUS MASTECTOMY FOR EXTENSIVE PURE DUCTAL CARCINOMA IN-SITU $>4$ CM

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**Purpose:** The optimal treatment for patients with extensive pure DCIS  $>4$  cm is controversial. Mastectomy (MX) has been historically recommended but whether this provides improved outcomes compared to breast conserving therapy is unclear. This study evaluates local relapse (LR) outcomes according to type of local therapy: MX, breast conserving surgery (BCS) alone, and BCS + radiation therapy (RT) with or without boost.

**Materials and Methods:** Subjects were 720 female patients diagnosed between 1989 and 2010 with pure DCIS  $> 4$  cm and referred to our institution. Clinicopathologic and treatment characteristics were compared between cohorts treated with BCS and MX. Ten-year LR were estimated using Kaplan-Meier estimator and Sidak's method was used to adjust for multiple comparisons. Multivariable analysis (MVA) was performed using Cox regression analysis.

**Results:** Overall, 490 patients had MX and 230 patients had breast conserving treatment with BCS alone ( $n = 38$ ), BCS + whole breast RT ( $n = 192$ ), with boost ( $n = 83$ ) and with no-boost ( $n = 109$ ). Median follow-up was 12.9 years for BCS and 13.2 years for MX patients ( $p = 0.7$ ). Patients treated with MX were younger (median age 52 versus 58 years,  $p < 0.0001$ ) and more likely to be premenopausal (48 versus 28%,  $p < 0.0001$ ). Patients treated with MX had larger tumours (median 5.5 versus 4.6 cm,  $p < 0.0001$ ), were more likely to have negative margins  $\geq 2$ mm (88% versus 80%,  $p = 0.006$ ) and less likely to receive adjuvant endocrine therapy (9% versus 21%,  $p < 0.0001$ ). Ten-year LR risks were 17% (95% CI 8-33%) for BCS alone, 8% (95% CI 4-16 %) for BCS+RT no-boost, 7% (95% CI 3-16%) for BCS+RT+boost and 2% (95% CI 1-3%) for MX. Pairwise comparisons between the local treatment subgroups were: BCS alone versus MX,  $p = < 0.0001$ , BCS+RT no-boost versus MX  $p = 0.0007$  and BCS+RT+boost versus MX,  $p = < 0.0001$ . On MVA, factors associated with increased LR were positive margins (HR 4.3, 95% CI 1.9-9.7,  $p = 0.0005$ ) and ER negative disease (HR 3.5, 95% CI 1.2-10.8,  $p = 0.03$ ). Compared to MX, increased LR was observed with BCS alone (HR 9.1, 95% CI 2.3-9.5,  $p < 0.0001$ ) and with BCS + RT (HR 4.7, 95% CI 2.3-9.5,  $p < 0.0001$ ). Age, grade, close margins ( $< 2$ mm), comedonecrosis, tumour size and endocrine therapy were not associated with LR risk.

**Conclusions:** Outcomes in this population-based analysis are consistent with data from randomized DCIS trials. Local recurrence is low (2%) with MX and high ( $>15\%$ ) with BCS alone. Adjuvant RT after BCS reduces LR risk by one-half (7-8%). Mastectomy remains a standard local treatment for extensive DCIS, while BCS + RT may be reasonably considered in selected patients with a careful discussion of the benefits and side effects.

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#### A SINGLE PRE-OPERATIVE RADIATION THERAPY (SPORT) PHASE I TRIAL FOR LOW RISK BREAST CANCER

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**Purpose:** A single-arm Phase 1 feasibility trial offering a preoperative 20 Gy fraction for low-risk breast cancer in the post-menopausal setting. We report on our primary objective; feasibility, early surgical complications and cosmetic toxicity at three months.

**Materials and Methods:** Eligibility criteria for low-risk disease included, age 60 years, unifocal invasive ductal carcinomas  $< 2$  cm, clinically node negative, ER positive and HER2 negative. The gross tumour volume (GTV) was defined using mammography, ultrasonography and MRI and grown by 5 mm to form the clinical target volume (CTV) and a further 10 mm for the planning target volume (PTV). Patients were treated with a single 20 Gy fraction to the PTV using volumetric arc therapy up to 72 hours prior to partial mastectomy and sentinel node biopsy. Toxicity was assessed, both subjectively and objectively, using the RTOG-EORTC radiation toxicity scale, NCIC CTCAE and EORTC cosmetic scale at baseline, 48 hours, 14 days and three, six, nine and 12 months.

**Results:** A total of nine patients with clinical T1N0 invasive ductal carcinomas with a median age of 69 were treated between October 2016 and February 2017. All patients were planned and treated successfully using pre-defined constraints to a mean PTV of 46.8 cc. Pathological review demonstrated an increase in tumour size by a mean of 2.06 mm; all patients were pathologically node negative however four patients had close ( $< 1$ mm) margins to in-situ or invasive malignancy. One patient required margin revision and three required whole breast radiotherapy (42.56 Gy in 16 fractions). There were no surgical complications. All patients had Grade 1 surgical scar pain and oedema seven days following the surgery but no delays in wound healing were demonstrated. At three months, seven patients reported good ( $n = 6$ ) to excellent ( $n = 1$ ) cosmesis (two further patients are awaiting endpoint), five reported Grade 1 hyperpigmentation and one patient had Grade 3 breast oedema.

**Conclusions:** The preliminary results demonstrate feasibility and tolerability following a single pre-operative 20 Gy fraction for early stage breast cancer. Continued follow-up is required to meet the secondary objectives, including cosmesis at 12 months and ipsilateral breast recurrence.

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#### CORRELATION OF PATHOLOGIC RESPONSE FOR BREAST CANCER AFTER NEOADJUVANT CHEMOTHERAPY ASSESSED BY MULTIPLE METHODS AND OUTCOMES FOLLOWING ADJUVANT RADIOTHERAPY

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**Purpose:** Several methods have been developed to classify pathological response of breast cancer to neoadjuvant chemotherapy (NAC). We report correlation between survival and pathologic assessment after NAC using available synoptic pathology reports (generally using the Residual Cancer Burden method), Miller-Payne, and Chevallier assessment systems as well as recurrence and survival for a cohort of patients treated with NAC, surgery and adjuvant radiotherapy (ART). We hypothesized that recurrence and

survival outcomes will correlate with response to NAC as scored by all three methods.

**Materials and Methods:** All breast cancer patients treated at our centre with NAC, surgery, and ART from 2009 to 2014 were included. Radiotherapy consisted of 50 Gy to the breast/chest wall and regional lymph nodes. Response to NAC was first extracted from synoptic pathology reports in our centre's electronic medical record which indicated whether a response to NAC was noted and whether there was any residual tumour in the specimen; the Residual Cancer Burden method is predominantly used at our centre. Miller-Payne score was determined by the cellularity present in the pathologic specimen. Chevallier score was determined by the presence or absence of invasive and in situ carcinoma. Loco-regional control (LC), recurrence-free survival (RFS) and overall survival (OS) were measured from the start date of NAC.

**Results:** One hundred and three patients were included, divided between Stage II (49%) and Stage III (51%). Median follow up was 45.6 months. NAC included both an anthracycline and a taxane in > 95% of patients. Recurrence occurred in 23 patients (21.3%) of which seven (6.8%) were loco-regional. Fourteen deaths (13.6%) were recorded. Survival outcomes were calculated using the Kaplan-Meier method. Actuarial rates of LC, RFS, and OS were 99%, 98%, and 100% at one year and 89%, 69%, and 77% at five years, respectively. Better response to NAC as assessed by each method did not correlate with LC ( $p > 0.05$ ). Better response predicted for improved RFS and OS ( $p < 0.05$ ), except Chevallier score which showed only a trend toward predictive ability for RFS ( $p = 0.06$ ). Using bivariate Cox modeling tumour size, pretreatment stage group, and response as assessed by all three methods significantly predicted for RFS ( $p \leq 0.05$ ). No factors were identified that predicted for LC.

**Conclusions:** Recurrence rates after NAC, surgery, and radiotherapy are low. Pathologic complete response assessed by synoptic pathology reports, Miller-Payne and Chevallier methods correlate with improved survival but are not associated with decreased local recurrence rates.

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#### WHAT TARGET VOLUME SHOULD BE CONSIDERED WHEN IRRADIATING THE REGIONAL NODES IN BREAST CANCER? RESULTS OF A NETWORK - META-ANALYSIS

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**Purpose:** Radiation treatment to the regional nodes results in an improvement in survival in breast cancer according to a meta-analysis of randomized trials. However different volumes were targeted in these studies (breast or chest wall only (WBI/CWI), inclusion of the medial supraclavicular region and axillary apex (MS+WBI/CWI), additional inclusion of the internal mammary chain (IM+MS+WBI/CWI). The benefit of treating the medial supraclavicular region and axillary apex compared to tangential breast or chest wall irradiation remains unclear

**Materials and Methods:** A literature search was conducted identifying trials for adjuvant radiation volumes in nodal irradiation after breast surgery and axillary treatment. Events and effect sizes were extracted from the publications for the endpoints of overall survival (OS), breast cancer-specific survival (BCSS), disease-free survival (DFS), distant metastasis-free survival (DMFS) and loco-regional control (LRC). A network meta-analysis was performed using MetaXL V5.3 with the inverse variance heterogeneity model

**Results:** We found two randomized studies ( $n = 5836$ ) comparing comprehensive nodal irradiation to sole breast treatment as well as one randomized ( $n = 1407$ ) and one prospective cohort study ( $n = 3377$ ) analyzing the additional treatment of the internal mammary chain against sole local and supraclavicular and axillary apex radiation. Compared to WBI/CWI alone the treatment of IM+MS+WBI/CWI (HR = 0.88; CI:0.78-0.99;  $p = 0.036$ ) results in improved OS unlike MS+WBI/CWI (HR = 0.99; CI:0.86-1.14;  $p = 0.89$ ). These results are confirmed in BCSS: IM+MS+WBI/CWI (HR=0.82; CI:0.72-0.92;  $p = 0.002$ ) and MS+WBI/CWI (HR=0.96; CI:0.79-1.18;  $p = 0.69$ ). PFS is significantly improved with the treatment of MS+WBI/CWI (OR=0.83; CI:0.71-0.97;  $p = 0.019$ ). Both nodal treatment volumes improve LRC (MS+WBI/CWI OR=0.74; CI:0.62-0.87;  $p = 0.004$  and IM+MS+WBI/CWI OR = 0.60; CI:0.43-0.86;  $p < 0.001$ ). Yet only the internal mammary

nodes provide a benefit in DMFS (MS+WBI/CWI HR = 0.97; CI:0.81-1.16;  $p = 0.74$  and IM+MS+WBI/CWI HR=0.84; CI:0.75-0.94;  $p = 0.002$ ).

**Conclusions:** Expanding the radiation field to the axillary apex and supraclavicular nodes after axillary node dissection reduced loco-regional recurrences without improvement in overall and cancer-specific survival. A prolongation in survival due to regional nodal irradiation is achieved when the internal mammary chain is included. One explanation could be the reduction of distant metastasis.

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#### CANCER SURVIVAL OUTCOMES IN ONTARIO: SIGNIFICANT UNEXPLAINED VARIATIONS

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**Purpose:** Cancer-specific outcomes are critical for assessing quality of care, and are among the key quality indicators for Canadian radiotherapy programs. Cancer-specific survival rates are known to vary among developed countries, but little information is available regarding differences in cancer survival outcomes in Canada. We sought to describe: five-year cancer-specific survival (5Y-CSS) rates among Ontario's 14 Local Health Integration Networks (LHINs) and the impact of adjusting these rates for known patient factors or of stratifying by stage. 5Y-CSS rates among patients diagnosed at Ontario's 50 largest cancer-diagnosing hospitals were also investigated to further elucidate possible reasons for variation.

**Materials and Methods:** Newly diagnosed cases (colorectal, lung, breast, or prostate cancer) were identified in the Ontario Cancer Registry. Records were linked to data from CIHI and Statistics Canada, thereby identifying date of diagnosis, cause-specific vital status, diagnosing hospital, and other reported variables. Cox regression models were used, and all models were adjusted for age and sex.

**Results:**  $N = 498,382$  incident cases (2007-2013) were included. 5Y-CSS varied across the 14 regional LHINs for all patients combined (range 62%-72%;  $p < 0.0001$ ). Further, 5Y-CSS significantly varied across LHINs for patients diagnosed with lung (range 16%-21%), breast (83%-89%), prostate (87%-93%), or colorectal cancers (58%-66%) (all  $p < 0.0001$ ). Considering colorectal cancer cases as illustrative ( $n = 57,927$ ), adjusting for socioeconomic and urban-rural status minimally reduced the 5Y-CSS variation. Collaborative staging data were available for a subset of patients; 5Y-CSS for Stage III patients ( $n = 5,360$ ) ranged from 72% to 87%. Limiting the analysis cohort to patients diagnosed at one of Ontario's 50 largest hospitals ( $n = 43,245$ ), 5Y-CSS ranged from 52% to 72% ( $p < 0.0001$ ) among hospitals, and from 55% to 63% ( $p < 0.0001$ ) among the hospitals affiliated with regional cancer centres. Comparable findings were seen for patients diagnosed with lung, breast, or prostate cancer.

**Conclusions:** Important, highly significant differences in survival outcomes exist across Ontario, including within cancer stage. These are of great interest to patients, healthcare providers, system administrators, and policy makers, and are not explained by adjusting for the variables included in these analyses.

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#### A MULTICENTRE PROSPECTIVE COHORT STUDY EVALUATING QUALITY OF LIFE AFTER RADIATION OR SURGERY FOR POTENTIALLY UNSTABLE SPINAL METASTASES

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**Purpose:** The purpose of this study was to compare health related quality of life (HRQOL) outcomes for surgery and/or radiotherapy in patients with potentially unstable spinal metastases.

**Materials and Methods:** A multicentre prospective observational study specific to patients undergoing radiation and/or surgical intervention for the treatment of symptomatic spinal metastases was conducted. Patients with potentially unstable spinal metastases, defined as a Spinal Instability Neoplastic Score (SINS) between 7 and 12, were included. HRQOL scores were modeled and compared between treatment groups using mixed effect models with adjustment for baseline differences.

**Results:** In total, 120 patients were treated with surgery +/- radiotherapy and 82 with radiotherapy alone. At baseline, surgically treated patients presented with worse performance status, HRQOL, numeric rating scale (NRS) pain scores, and a greater median SINS score [10 versus 8 in those treated with radiotherapy alone ( $p < 0.001$ )]. Significant differences in the distribution of individual SINS factors were also observed between both treatment groups. From baseline to 12 weeks post-treatment, surgically treated patients experienced a greater improvement in HRQOL with a 12-point increase in adjusted mean SOSGOQ2.0 score (95%CI 5.1 – 19.0,  $p < 0.001$ ) as compared to a 6.2-point gain in those treated with radiotherapy alone (95%CI -2.2 – 14.6,  $p = 0.352$ ). In addition, the gain in the SOSGOQ2.0 score exceeded the minimal clinically important difference threshold in 63% of the surgical cohort as compared to 44% in the radiotherapy alone cohort ( $p = 0.017$ ).

**Conclusions:** For patients presenting with potentially unstable spinal metastases, treatment with surgery +/- radiotherapy resulted in greater and clinically meaningful changes in HRQOL as compared to patients treated with radiotherapy alone. However, these results must be taken into context according to differences in individual SINS factors and grouping of SINS factors that comprise the individual cohorts.

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#### RADIOTHERAPY AT THE END-OF-LIFE: EXAMINING PRACTICE PATTERNS IN A CANADIAN PROVINCE

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**Purpose:** Radiotherapy (RT) is a resource intensive cancer treatment where benefits are often realized weeks afterwards and side effects are noted more immediately. Palliative RT is commonly delivered at the end of life (EOL). In patients with limited life expectancy, single fraction treatments may substitute for more complicated multi-fraction treatments. Our objective was to document the RT prescriptions given to patients with cancer at EOL, with the goal of informing treatment practices, reducing potentially futile treatment and unnecessary side effects for patients.

**Materials and Methods:** Cancer Registry data was examined with REB approval. Patient and treatment data were collected and analyzed to determine the number of RT prescriptions among those with cancer diagnoses who died between January 1 2016 and July 31 2017, starting within 14 days, 30 days, 60 days, and 90 days of death. Data was stratified by patient demographics, disease factors, tertiary treatment centre and prescription factors including number of fractions prescribed and delivered. Results are reported in aggregate and explored using tests of association using Stata 11.1.

**Results:** 2448 RT prescriptions across 1874 patients were identified. Of those who were prescribed RT within 90 days of death, there were 442 single fraction courses 100% completed, 1267 2-5 fraction courses 90% completed, 552 6-10 fraction courses 77% completed, and 187 11+ fraction courses 57% completed. Of those who were prescribed RT 14 days prior to death, 24% of patients had been prescribed a single fraction of treatment compared to 18% of those within 90 days of death ( $\text{Chi}^2 17.92$ ,  $p < 0.001$ ). Of those who were prescribed RT 90 days prior to death, 25% of patients in Centre A were prescribed a single fraction compared to 13% of patients in Centre B ( $\text{Chi}^2 121.90$ ,  $p < 0.001$ ). Patients were 47% as likely to complete

a multi-fraction treatment within 14 days of their death as compared to within 90 days. Patients who had a diagnosis to death interval of under a year were 69% as likely to complete radiation therapy than those who had a two-year interval or more. Gender was not an independent factor for RT patterns across any time frame prior to death.

**Conclusions:** RT prescription patterns vary across the province. Multi-fraction treatments are often not completed prior to death. There is the possibility that a large proportion of EOL RT courses may be futile.

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#### A PERSON-CENTRED MODEL OF CARE FOR RADIATION THERAPY SERVICES: PROOF-OF-CONCEPT STUDY

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**Purpose:** Patient experiences over the course of radiotherapy are fragmented by the many technical and supportive care sessions performed by different Radiation Therapists (RT). Aligning RTs with individual patients rather than procedures would improve continuity of care, patient satisfaction and treatment quality. The aim was to demonstrate the proof-of-concept of a person-centred model of care with patients partnered with a primary RT over the course of therapy.

**Materials and Methods:** The model was prospectively piloted over four months for new breast cancer patients and limited to one treatment linac with four RTs. Patients were triaged based on complexity of technique (e.g. breath hold immobilization) or a perceived need for added support (e.g. self-reporting high anxiety at consult), and partnered with a primary RT. This RT aimed to perform, at a minimum, all point-of-care activities identified as priorities for their patients as often as scheduling permitted. The priorities were: all education sessions, CT-simulation procedures, dosimetry review, peer review rounds, treatment delivery (first three and last fractions), providing all routine supportive care and a newly developed follow-up call at two weeks (coinciding with the probability of highest-grade skin toxicity). RT activity was recorded to assess feasibility of the model. Patient satisfaction surveys were offered at the final appointment for those treated in the pilot or with standard practice on other linacs. The RTs in the pilot evaluated both the proposed model and standard practice using validated inventories on work satisfaction and burnout. Electronic surveys were offered to multi-disciplinary staff to assess stakeholder insights.

**Results:** Sixty-seven patients were triaged to the new model, limited by the linac capacity. The primary RTs performed 80% of the priority points of care for their patients on average, equal to 40% fewer "handoffs" versus standard practice. Patient uptake of the new follow-up call with their RT was high (77%), suggesting an unmet need for access to post-treatment care. Overall, 98% of patients ( $n = 77$  surveys) were satisfied with their experience. For those partnered with a primary RT ( $n = 54$ ), approximately 20% more agreed their information needs were met upfront and RT staff were consistent, and 30% fewer reported accessing "drop-in" nursing support clinics. Multi-disciplinary stakeholders ( $n = 36$  surveys) perceived improvements in patient support, with resource needs and workflow impact as potential barriers. RTs partnered with individual patients ( $n = 4$ ) were significantly more satisfied and had lower burnout measures driven by the improved relationships, intrinsic work values, use of existing skills and personal accomplishment.

**Conclusions:** Reconfiguring how services are delivered by RTs facilitates a person-centred approach in radiotherapy. Early experience suggests meaningful improvements for patients, including enhanced continuity of care and support, within the existing RT scope of practice and without advanced technologies. Efforts are underway to develop the model for patients with higher care needs (e.g. head and neck cancers). Personalizing patient experiences in radiotherapy, coupled with improvements in treatment quality and supportive care, may improve clinical outcomes.

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### THE IMPACT OF THE ASCO CHOOSING WISELY CAMPAIGN FOR BREAST AND PROSTATE CANCER ON PHYSICIAN BEHAVIOUR

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**Purpose:** In April 2012, the American Society of Clinical Oncology (ASCO) published its Choosing Wisely (CW) list of low-value services not supported by clinical evidence. The effectiveness of this campaign in changing physician behavior in oncology remains unknown.

**Materials and Methods:** Retrospective analysis of breast and prostate cancer patients diagnosed from 2010-2013 and contained in the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database and the population-based health system administrative databases from Ontario, Canada. Quarterly rates of imaging tests (positron emission tomography, computed tomography, bone scans) for staging in low-risk prostate cancer (T1-2a, Gleason <7, PSA<10 ng/mL) and for staging and post-treatment surveillance in early-stage breast cancer (AJCC I and II, N0, no neoadjuvant chemotherapy) was determined. Change in the proportion of patients receiving low-value tests before and after publication of the CW recommendations was evaluated using interrupted time series analysis. Tests were attributed to the specialty of the referring provider associated with the claim. Differences in utilization between Ontario and SEER-Medicare were compared using regression analyses.

**Results:** The SEER-Medicare cohorts consisted of 14,596 prostate, 43,591 breast staging, and 32,548 breast surveillance patients. Use of staging tests for prostate cancer was declining pre-CW (-0.52% per quarter) and experienced a small, but significant increase in the rate of decline post-CW to -0.79% per quarter,  $p = 0.0013$ ; average utilization was 26.5% of patients pre-CW and 20.7% post. Use of surveillance imaging for breast cancer was stable pre-CW at 25.2%; it decreased post-publication to -0.61 percentage points per quarter ( $p < 0.001$ ) to 21.3% post. No significant change in use of breast cancer staging was observed (-0.05% per quarter,  $p = 0.37$ ), with an average rate of 10%. Surgeons were responsible for 63.9% of prostate staging, 44.7% of breast staging, and 8.3% of breast surveillance tests. Medical oncologists were responsible for 1.6% of prostate staging, 17.8% of breast staging, and 25% of breast surveillance tests. Radiation Oncologists were responsible for <5% of tests overall. Primary care and other providers were responsible for 30.1% of prostate staging, 37% of breast staging, and 61.7% of breast surveillance tests. Ontario analysis and geographic comparisons ongoing.

**Conclusions:** Following CW, there was a modest change in some physician behaviors toward recommendations. Further multidisciplinary efforts coupled with incentives may be needed to educate providers on judicious use of imaging.

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### COMPARISON OF PATIENT REPORTED OUTCOMES BY EGFR AND ALK MUTATION STATUS IN LUNG CANCER PATIENTS TREATED WITH PALLIATIVE RADIOTHERAPY FOR BONE METASTASES

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**Purpose:** Pre-clinical studies on clonogenic cell lines suggest that epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) over-expression confer a relative radioresistance. The impact of driver mutations in EGFR and ALK on the clinical response to radiotherapy is not well known. We examined the significance of EGFR and ALK mutation status on subjective response to palliative radiotherapy for bone metastases in patients with metastatic non-small cell lung cancer (NSCLC) hypothesizing a decreased pain response in EGFR and ALK mutants.

**Materials and Methods:** We performed an analysis of prospectively collected patient reported outcomes for patients with metastatic NSCLC treated with palliative radiotherapy for bone metastases between 2013 and 2016. Patient reported pain scores, on a scale from 0-4, were collected at baseline and at

three weeks after palliative radiation. We included any patient treated with palliative radiotherapy for bone pain from metastatic NSCLC who had pain scores collected. The cohort was divided into four groups: EGFR/ALK wild-type (WT), EGFR+, ALK+, and EGFR/ALK unknown.

**Results:** There were 388 bone metastases treated in 329 patients. The patient cohort comprised: 185 WT, 57 EGFR+, eight ALK+, and 79 EGFR/ALK unknown. Patients with ALK rearrangements tended to have lower baseline pain scores, with mean baseline score 2.73, 2.24, 1.78, and 2.58 for WT, EGFR+, ALK+, and EGFR/ALK unknown respectively ( $p < 0.01$ ). The proportion of patients who had at least a partial response in bone pain following radiotherapy was 67%, 87%, 100%, and 73% for WT, EGFR+, ALK+, and EGFR/ALK unknown respectively ( $p < 0.01$ ). The proportion of patients who had a complete response in bone pain following palliative radiotherapy was 17%, 26%, 57%, and 19% for WT, EGFR+, ALK+, and EGFR/ALK unknown respectively ( $p < 0.04$ ).

**Conclusions:** NSCLC patients with EGFR mutations or ALK gene rearrangements had better subjective responses to palliative radiotherapy for bone pain when compared to non-mutants. This may impact clinical decision making in an era of evolving molecular markers.

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### MOTION MANAGEMENT FOR LIVER STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR) - SINGLE INSTITUTIONAL EXPERIENCE WITH RESPIRATORY GATING VERSUS DYNAMIC TUMOUR TRACKING VERSUS MOTION-ENCOMPASSING (ITV) TECHNIQUES

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**Purpose:** Patient and technical factors determine which motion management strategy provides an optimal balance between benefit to the patient and efficiency/complexity of treatment for liver Stereotactic Ablative Radiotherapy (SABR). This study describes options for motion-management at a single institution and determines what patient/technical factors contribute to the multidisciplinary decision-making process when choosing between motion-encompassing ITV (internal target volume) method, respiratory-gating with VMAT (Varian TrueBeam), or dynamic-tumour-tracking with 3DCRT (BrainLab VERO).

**Materials and Methods:** Forty-five patients had fluoroscopic assessment and liver SABR treatment between July 1 2017 and March 1 2018. The decision making-process was reviewed to identify patient-specific and technical (planning/delivery) characteristics that contributed to the selection of treatment modality. All patients had implanted fiducials (FIDs), an imaging surrogate for tumour location and motion.

**Results:** Thirty-three of the 45 patients (73%) received ITV-SABR, eight (18%) VMAT-Gating, and four (9%) 3DCRT Dynamic-Tracking. The four categories of patient-specific factors influencing choice of treatment were 1) Tumour: volume and proximity to organs-at-risk, 2) FIDs: shape, location, number, radio-opacity, 3) Respiration: amplitude, regularity and correlation of internal/external motion (with/without abdominal compression), exhale phase in gating window of > 2 sec, and ability to breath-hold in exhale for > 20s, 4) Physical/Social: comfort with holding the immobilized position, MRSA+ status, and language barriers. Machine-specific factors were: compatible planning/delivery techniques (ITV Method=VMAT, static-field IMRT, 3DCRT, dynamic conformal arcs (DCA) / Gating=VMAT / Dynamic-Tracking=3DCRT), and the ability to detect/monitor FID position during treatment. A decision tree was created to guide the healthcare team during a pre-simulation fluoroscopy to select the most appropriate treatment for liver SABR.

**Conclusions:** All motion-management methods are utilized at this clinic and are necessary to maximize the number of patients eligible for liver SABR. The decision-making process is multidisciplinary. Each method has specific benefits and limitations and a decision tree can help ensure that patients receive the most appropriate treatment.

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### A FEASIBILITY STUDY OF A NOVEL BREAST SUPPORT TO REDUCE TOXICITY FROM SUPINE ADJUVANT WHOLE BREAST RADIOTHERAPY

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**Purpose:** Breast patients having large, pendulous or ptotic breasts pose challenges for treatment planning and positioning for radiotherapy and experience higher rates of moist desquamation compared with other patients. We present results of feasibility testing of a novel carbon-fibre breast support designed to improve breast positioning, reduce treatment toxicity and facilitate reproducible and efficient patient set-up for whole breast radiotherapy in the supine position.

**Materials and Methods:** A carbon-fibre breast support was designed and fabricated to be cleanable, reusable, universal and indexed for individual patients, as well as being compatible with the deep inspiration breath hold technique. We report here on a research ethics board-approved, 10 patient study for women with a brassiere size of D cup or greater or any skin fold > 1 cm with the patient in the supine treatment position. The attending radiation oncologists re-planned the breast tangents on planning CTs with the breast supported using the carbon-fibre device. These plans were compared to the actual delivered clinical plans without the device. Electronic portal imaging verification images with and without the device were compared to assess set-up reproducibility.

**Results:** Elimination of infra-mammary skin folds up to 5 cm deep, and concomitant reduction in superior-inferior tangential field length was achieved in all patients supported with the device. The medial-lateral breast separation decreased by up to 30% with better breast positioning using the support, allowing a reduction in the relative weight of 10 MV versus 6 MV beams required to meet dose constraints. An average reduction of 87.5 cc in absolute volume of lung receiving 20 Gy or more was observed. The volume of body receiving 50% or more and 105% or more of the prescribed dose was reduced by up to 782 cc and 163 cc respectively. The breast support set-up took an average of less than 2 minutes at CT sim and at the treatment unit. The carbon-fibre support increased the entrance dose of the lateral beam by up to 30% in areas of tangential incidence. The combined entrance and exit dose to the skin at all points on the breast surface remained below 80% of the prescription dose when the breast was supported. Without the support, dose to inframammary skin folds was greater or equal to the prescription dose. No collisions with radiotherapy equipment were encountered and no image artefacts were observed with the support device in place.

**Conclusions:** This device offers a promising solution to the challenge of supine breast positioning for women with large or pendulous breasts. The results from this feasibility study support the testing of this device in a clinical trial to determine whether it is able to reduce acute toxicity from breast radiotherapy.

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### INDEPENDENT VALIDATION OF THE ALBI (ALBUMIN-BILIRUBIN) GRADE IN HEPATIC CANCER PATIENTS TREATED WITH RADIATION THERAPY

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**Purpose:** External beam radiotherapy (RT) is increasingly utilized for treatment of cancer within the liver. Currently, it is unclear which patients are most likely to benefit from this treatment. Patients' performance and different liver status scores have been previously correlated with overall survival (OS) and therefore may be used to predict the benefit of undergoing radiotherapy. The purpose of this study was to compare the predictive power of the Child-Pugh score (CP) with the newer, more objective, Albumin-Bilirubin (ALBI) score for radiation induced liver disease (RILD), liver toxicity, and

OS prediction in patients with hepatocellular carcinoma (HCC) and hepatic metastases (METS) treated using radiation therapy (RT).

**Materials and Methods:** This retrospective study evaluated patients who underwent RT between 2004 and 2017. CP and ALBI correlation with and prediction of OS, RILD, and liver toxicity were analyzed. Liver toxicity was defined as at least 150% elevation of the baseline levels in alkaline phosphatase (ALP), aspartate aminotransferase (AST), or alanine aminotransferase (ALT) at follow-up (categorized into having elevation in 1 to 3 of the biological markers). RILD was defined as worsening of ALBI scores by more than 40% post-RT.

**Results:** This study included 188 patients of whom 59 were HCC and 129 were METS patients. The CP and ALBI grades and scores were both significantly associated with OS ( $p < 0.01$ ) and displayed a strong, significant ( $p < 0.01$ ) inter-correlation; while ALBI scores significantly complemented CP class in predicting OS based on multivariate analysis. Furthermore, both ALBI and CP scores were independent and highly concordant predictors of early death (four months). However, only baseline ALBI scores were predictive of liver toxicity and early RILD at follow-up post-RT with a significant model ( $p < 0.01$ ), with good concordance ( $> 0.7$ ) statistics. Incidentally, the data suggested low-risk (low ALBI and CP scores) HCC and METS patients displayed a significant effect of the biologically effective dose (BED) on OS, which remained significant when accounting for other covariates.

**Conclusions:** This is the first paper to validate the value of ALBI for prediction of OS, RILD and toxicity following radiation of both HCC and METS patients by helical tomotherapy (HT), linac-based intensity-modulated radiation therapy (IMRT), volumetric-modulated arc therapy (VMAT), and 3-D conformal radiotherapy (3D-CRT) techniques. While both CP and ALBI predicted OS, only ALBI predicted RILD and liver toxicity significantly in both HCC and METS. ALBI may be superior to CP for providing prognostic survival and toxicity information, and for selecting which patients may benefit the most from RT and HCC or METS. Further prospective studies are necessary to allow the use of ALBI as a prognostic tool.

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### SMALL TARGET VOLUME DELIVERY LIMITATIONS FOR LUNG SBRT

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**Purpose:** Mechanical uncertainties can limit the accuracy of delivery for small field lung stereotactic body radiation therapy (SBRT) treatments. This study quantifies limitations in small field delivery relating to multi-leaf collimator (MLC) positioning errors, determining the relationship with target volume, and assesses the impact on dosimetry to define target size limits.

**Materials and Methods:** Five small lung target treatments, planned to deliver 48 Gy in 4 fractions, were retrospectively evaluated. Treatment planning target volumes (PTVs) were shrunk to generate PTVs with equivalent spherical diameters of 1.0, 1.5, 2.0, 2.5, and 3.0 cm for each of the five patients. Clinically relevant SBRT treatment plans were optimized independently based on each target volume, resulting in 25 SBRT plans. Plans were delivered on a single Varian Clinac iX linear accelerator. Dynalog files captured during delivery were used to assess the actual gaps between leaf pairs every 50 ms throughout the delivery, quantified by the percentage of gaps greater than 0.5 mm from their planned values, using in-house software. Treatment plans were reconstructed using the actual delivery leaf positions acquired from the Dynalogs, and calculated dose distributions were compared to the original plan dose-volume histogram (DVH) to assess the clinical impact of leaf positioning errors.

**Results:** Median treatment PTV equivalent sphere diameter was 3.7 cm (range 2.5-4.7 cm). During clinical delivery, mean (SD) 0.5 mm gap error was 3.5% (1.5%), with inter-fraction deviations < 0.1% in all cases. Mean 0.5 mm gap errors were 1.9% (2.2%), 1.5% (.8%), 2.4% (1.3%), 3.4% (1.2%), 3.4% (1.7%) for the 1, 1.5, 2, 2.5, and 3 cm targets, respectively. A strong correlation was observed between the target diameter and the gap error percentage ( $r = 0.9$ ). Dose calculations using the Dynalog reconstructed plans had mean PTV V100 coverage 0.2% (0.2%) greater than the optimized plans, and max dose 0.5% (0.1%) greater. No significant trends were observed between the target size or gap error and the changes in the PTV DVH.

**Conclusions:** Actual leaf gap sizes do not correlate significantly with target

size. Greater percentage of gap errors were observed for the larger targets, potentially related to the increased modulation present in these plans. Based on the assessed metrics, the leaf positioning variations during delivery are not clinically significant and machine delivery accuracy is not limited by target sizes as small as 1 cm diameter for lung SBRT treatments.

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#### INTRAFRACTION TRACKING FOR SPINAL SBRT AND MOTION ASSESSMENT ON AN ELEKTA LINAC

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**Purpose:** Spine stereotactic body radiation therapy (SBRT) uses ablative levels of radiation to treat tumours and high-risk post-operative regions. Due to the large doses and dose gradients surrounding the spinal cord, tight positioning tolerances of 1 mm and 1° are used for these patients, however movement during treatment remains unaccounted for. Recent development on the Elekta linac/XVI platform allows for the acquisition of an intra-fraction CBCT dataset during arc treatment delivery. The overall purpose of this work is to develop a framework for real-time vertebrae tracking using the intra-fraction CBCT projections to assess intra-fraction motion for SBRT treatments at our centre. Our framework involves in-plane tracking of spinal vertebrae during SBRT treatment through registration of intra-fraction CBCT projections compared to simulated projections created from the planning CT. Initial phantom results to assess the accuracy of our framework is presented here.

**Materials and Methods:** Simulated projections were created using the SimpleRTK software using a pre-treatment CT acquired with a GE CT scanner. In order to study the efficacy of our framework a custom solid water anthropomorphic torso phantom was used to evaluate registration of spinal vertebrae. Comparison was made with projections acquired using an XVI intra-fraction protocol during the delivery of a 12 Gy VMAT plan. This was acquired using 40 and 160 mA currents and exposure times of 40 ms per projection acquired every 1°. Registration was performed with SimpleITK using a mutual information metric and a regular gradient descent optimizer. Patient set-up errors were introduced by applying known shifts to the planning CT in 3D along the X and Y axes of the kV panel. This shifted volume was then re-projected and the resulting registration accuracy with the acquired intra-fraction projections was quantified as a function of angle and displacement.

**Results:** Registration accuracy for the 40 mA and 40 ms data set using the anatomical phantom at isocenter was found to be  $0.82 \pm 0.29$  mm up to 3.2 mm and  $1.3 \pm 1.5$  mm up to 8.2 mm simulated shifts in the X direction. Accuracy in the Y axis was found to be  $0.51 \pm 0.21$  mm up to 1 cm in displacement. The use of the 160 mA current to improve image quality only improved mean registration accuracy by 0.02 mm and 0.04 mm in the X and Y directions respectively. Due to the effects on accuracy, angle that included unaccounted for portions of the couch were excluded. The registration time was found to be 0.7 seconds per projection and 1.7 seconds to simulate a single projection which can be pre-calculated.

**Conclusions:** The proposed frame work demonstrates feasibility in terms of accuracy and speed for real-time tracking of vertebrae. Additional improvement involving further post-processing and isolation of the spine are ongoing. Furthermore, a prospective study of para-spinal patient data is planned.

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#### BRINGING RELIEF TO THE PRAIRIES: A SINGLE CENTRE'S EXPERIENCE IN IMPLEMENTING VOLUMETRIC MODULATED ARC THERAPY FOR LUNG SBRT USING FLATTENING FILTER-FREE BEAMS

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**Purpose:** Stereotactic body radiation therapy (SBRT) has demonstrated high rates of local control in lung cancer patients with low associated toxicities. SBRT requires the delivery of a large radiation dose in a few fractions with high accuracy. At our centre, cone beam CT is used to precisely localize the

target volume, adjust and confirm patient positioning prior to treatment. A remaining concern is the risk of patient intra-fraction motion as treatment delivery currently lasts 5-7 minutes. Flattening filter-free (FFF) beams offer the possibility of reducing treatment time to less than 1.5 minutes, thus minimizing the risk of patient intra-fraction motion. A review of the literature offered conflicting views regarding plan quality and deliverability for FFF beams. We thus performed a comprehensive evaluation of FFF beams in the context of lung SBRT, where we compared the quality of treatment plans and dose delivery for beams with and without flattening filters to alleviate these concerns.

**Materials and Methods:** A retrospective study of five lung SBRT patients enrolled in the LUSTRE trial was performed, where the original volumetric modulated arc therapy (VMAT) plans using 6MV beams were re-optimized with FFF beams. Plan quality was assessed in terms of target coverage, dose conformity, and sparing of normal tissues. Treatment deliverability was evaluated by irradiating a cylindrical diode array, as well as an acrylic phantom with a lung-equivalent insert, where dose was recorded using films or ion chambers. Interplay effects were investigated by acquiring film measurements with simulated breathing motion.

**Results:** No clinically significant differences were found between the plans generated with flattened and FFF beams. Gamma analyses using a 2%/2mm criterion and 10% threshold yielded pass rates > 97% for all treatment plans verified with high-density diode-array measurements. Ion-chamber measurements showed absolute dose delivery to within 1% with and without breathing motion. Gamma analyses of film measurements with and without breathing motion led to pass rates > 95% for all plans, indicating that interplay effects were small.

**Conclusions:** FFF beams were shown to be an effective way to minimize treatment time and thus reduce the risk of intra-fraction motion for lung SBRT patients, while preserving the quality of treatment delivery.

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#### TOTAL BODY IRRADIATION ON A LINAC COUCH? A TREATMENT PLANNING STUDY OF MOVING COUCH GANTRY AND JAWS

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**Purpose:** Total body irradiation (TBI) in combination with chemotherapy is a common preconditioning regimen prior to bone marrow transplantation for treating hematological malignancies. Numerous linac-based TBI techniques exist with the patient either on a dedicated floor-level couch below the linac at ~200 cm SSD, or lateral to the linac at very extended SSDs (~400 cm). Treatment at floor level can involve a translating couch moving through a stationary beam or a stationary couch with an arc beam delivery. Some disadvantages of these methods are the requirement for an additional patient support system and the time required for set-up. We present a preliminary feasibility study of a novel method of TBI with the patient positioned on a standard linac couch.

**Materials and Methods:** Our approach aims to take advantage of the current "Developer Mode" research tool on Varian Truebeam linacs that permits computer control of all mechanical components during beam delivery. Our proposed method has the patient lie either feet or head first on the couch at 90°. The delivery consists of a dynamic sequence of jaw motion, gantry rotation and longitudinal couch translation; repeated for a prone and supine patient. The coordinated jaw and gantry motion overcome the limited 1.4 m range of couch translation. The modelling of dose delivery was carried out on a Varian treatment planning system (TPS) running Eclipse v13.6 AAA algorithm. Each dynamic sequence was modelled as a summation of static fields stepped 1 cm in jaw position, 1.5° gantry angle and 1 cm isocenter translation. We evaluated the feasibility of this new method by comparing it against the published translating couch method, also simulated on the Eclipse TPS. Dose coverage, dose uniformity and treatment times are compared for both rectangular and human like phantoms.

**Results:** It is possible to encompass a 200 cm long patient with this technique using a dynamic controlled 20 x 40 cm<sup>2</sup> field and the linac couch near its lowest vertical position (165 cm source to couch). This requires the full 1.4 m translation of the couch together with up to a 45 degree gantry arc. The moving jaw sequence at each end of the patient permits the field edges to

pass through without the need for a larger gantry arc. The treatment SSD in this technique does limit the width of patient being treated to ~ 59 cm. Acceptable dose uniformity of +/- 10% can be achieved provided that the MUs are optimized throughout each couch, gantry or jaw motion sequence. At an average of 300 MU/min, the treatment time is estimated to be less than 10 min for each supine and prone position.

**Conclusions:** We present preliminary proof of principle for an efficient TBI delivery technique where a hybrid dynamic jaw, gantry and couch sequence provides the capability to span a field over a patient lying directly on a linac couch. One unique advantage of our technique is the ability to perform on board imaging for lung shielding verification.

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#### DEVELOPMENT OF A DVH REGISTRY FOR PLAN EVALUATION, DOSE ACCUMULATION, AND COHORT ANALYSIS

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**Purpose:** To develop a flexible user-friendly tool for the evaluation of organ-at-risk contours, planned dose, and accumulated dose using historical cohorts and treatment outcomes.

**Materials and Methods:** Our DVH Registry is an interactive web-app constructed using a Django framework with a Bootstrap and Javascript front end. Patient DVHs and treatment data are transferred from the Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA) to the registry using the Eclipse API. Within the registry, patient data may be grouped into user-specified cohorts. Individual patient DVHs, along with structure volumes, structure lengths, and the mean, median and standard deviation of each cohort are plotted as interactive graphs using the Highcharts API (highcharts.com). In addition to planning-DVHs, the Registry can track structure changes and accumulated dose over the course of treatment using contours drawn on daily CBCT images. Finally, statistical and survival analysis functions are incorporated using Python statistics modules (Python Software Foundation, python.org) to allow the user to investigate relationships between treatment outcomes and dose-volume parameters.

**Results:** Time to prepare retrospective patient cohorts for analysis is greatly reduced by the automation provided by the DVH Registry. The tool's ability to categorize DVHs by toxicity type and grade and to overlay new DVHs onto those of an existing cohort provides a facility to compare current DVHs to those previously treated, with outcomes data incorporated. We are currently using the tool to perform a retrospective analysis of rectal toxicity in prostate cancer patients, examining the level of correlation between toxicity and dose-volume parameters extracted from planning and accumulated DVHs. The DVH Registry has proven useful as a QA tool for contour quality on daily CBCTs, identifying several fractions in patients where the retrospectively-drawn rectum contour was not complete. Preliminary data have also shown that the volume and DVH of the rectum changes on a daily basis and can lead to differences in the planned and accumulated doses in some patients.

**Conclusions:** We have developed and implemented a useful tool in our clinic for the visualization of DVHs and associated treatment outcomes, including accumulated dose.

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#### ICONE-SRS: DEVELOPMENT OF SIMULATED ANNEALING INVERSE PLANNING FOR CONE-BASED STEREOTACTIC RADIOSURGERY

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**Purpose:** Effective stereotactic radiosurgery (SRS) can be delivered on conventional linear accelerators equipped with a set of small conical collimators. At present, commercially available treatment planning systems (TPS) only offer forward planning functionality for cone-based deliveries and so planning can be labour intensive. The objective of this study was to develop and test a simple inverse TPS for rapid generation of high quality cone-based SRS plans.

**Materials and Methods:** iCONE-SRS was developed using MATLAB r2015a. A simple correction-based dose engine was implemented based

on commissioning data collected at our centre for the Brainlab iPlan TPS (v4.5). To generate a plan, structures segmented in Brainlab are imported by iCONE-SRS and then the user must specify the number of arcs, maximum number of cone sizes, and optimization priorities for the target and organs-at-risk (OARs). Simulated annealing is used to determine the optimal table angle, gantry start and stop positions, cone-size and weighting for each arc. To investigate preliminary efficacy, iCONE-SRS was retrospectively applied to data from 15 patients previously treated with SRS for brain metastases. Five arcs and a maximum of two cone sizes were used for all optimizations. The user was permitted a maximum of 15 minutes of planning time per patient and was blind to the clinical plan. The best plan produced within this time limit was then manually input into Brainlab and compared to the clinical plan.

**Results:** The median planning target volume was 3.5 cc [0.5-10.7 cc]. Target and OAR constraints were met by all iCONE-SRS plans except one case where there was an unacceptably high target dose. iCONE-SRS plans exhibited a median increase in conformity index of 9.9% [0%-20%] ( $p < 0.001$ ) relative to the clinical plans and no statistically significant difference in the target or OAR maximum doses.

**Conclusions:** iCONE-SRS shows potential for significantly reducing treatment planning time for cone-based SRS. Future work will characterize efficacy in a larger patient population, determine if longer planning time or the addition of some manual optimization can reproduce or exceed clinical plan quality, and establishing best practices for integration into the clinical workflow.

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#### IMPORTANCE OF INITIAL PLAN PARAMETERS AS PREDICTORS OF INTER-FRACTIONAL PLAN QUALITY DEGRADATION

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**Purpose:** Adaptive radiation therapy (ART) protocols that exclusively use pre-treatment characteristics as predictors of inter-fractional plan quality degradation may allow for replan consults to be scheduled weeks in advance. From a practical view, this aids in clinical resource allocation, as not all patients will benefit from a replan, and may lead to quicker initiation of replans when required. This study compares the prediction error of replan-candidate identification models developed using only pre-treatment characteristics versus those including during-treatment parameters.

**Materials and Methods:** Supervised machine learning methods (lasso logistic regression, random forests, bagged/boosted trees) are used in this study to develop predictive models of replan need in head and neck cancer patients. Feasibility-based replan capacity (e.g. replanning 15% of patients) provides ground-truth binary replan/no-replan responses: patient dose deviations are ranked according to structure priority and deviation magnitude and weighted by the number of remaining fractions. Pre-treatment characteristics considered include patient stage, initial weight, p16 status and planned dose parameter values; during-treatment characteristics include measured morphological changes, such as change in external body contour, as well as changes in inter-fractional dose parameter values.

**Results:** Preliminary analysis of 105 sample fractions corresponding to a 15 patient cohort indicates that pre-scheduling ART consults based on a subset of pre-treatment characteristics (planned dose parameter values) gives similar results to inter-fractional replan-candidate identification (adding inter-fractional dose parameter values and measured morphological changes). Respectively, cross-validated lasso logistic regression accuracy was 62.2% and 64.5%; bagging out-of-bag accuracy was 74.2% and 80.0%; random forest out-of-bag accuracy was 73.3% and 78.1%; boosting test set accuracy was 80% and 82.9%. In comparison, assuming that no patients required a replan resulted in an accuracy of 56.2%; previous assessment of a during-treatment body contour-based ART protocol revealed an accuracy of 44.3%. Planned brainstem PRV D1%, contralateral parotid gland D50% and fraction number were of high predictive importance in multiple models. Patients continue to be accrued to the retrospective cohort; we anticipate the accuracy of pre-treatment-based predictive models to increase with sample size and inclusion of additional pre-treatment features.

**Conclusions:** Challenges of ART implementation largely stem from clinical feasibility considerations and inherent difficulties in identifying patients most

in need of a replanned treatment. Preliminary results of this study suggest that ART replan-candidates may be identified prior to treatment start with comparable accuracy to during-treatment monitoring.

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### DOSE RECONSTRUCTION FOR LUNG CANCER PATIENTS WITH GROSS ANATOMICAL CHANGES DURING RADIOTHERAPY

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**Purpose:** To assess the dosimetric effect of gross anatomical changes (e.g. atelectasis, pleural effusion) occurring during radiation treatment (RT) of locally advanced lung cancer using dose reconstruction with the goal of informing future decision making around replanning. Our secondary objective was to investigate the impact of replanning on the agreement between planned and delivered doses.

**Materials and Methods:** We retrospectively identified 11 patients with gross changes identified on treatment, six of which were replanned. To estimate the dose delivered, we performed dose reconstruction in RayStation (v6, RaySearch Laboratories, Stockholm, Sweden). This involved dose calculation on daily CBCTs and deformable image registration (DIR) to map the reconstructed dose onto the corresponding plan or replan CT. For each fraction, we compared DVH metrics between the planned and reconstructed delivered dose. Key OAR dose statistics compared included maximum dose for the spinal canal, V40 for heart, V20 for lung and the mean lung dose. For patients that were replanned, we assessed whether the replan impacted the agreement between planned and delivered OAR doses. We also compared the agreement between planned and delivered doses between the cohorts with and without replanning. Statistical tests were performed with Student's two-tailed t-test ( $p < 0.05$  considered significant).

**Results:** We successfully reconstructed dose for all patients except for one replanned case with large changes that could not be recovered using deformable registration. We qualitatively assessed DIR accuracy and excluded fractions with gross registration errors. Across all patients and fractions, the mean differences between the planned and delivered dose metrics were  $0.9 \pm 2.4\%$  (mean  $\pm$  STD error) for spinal canal maximum dose,  $-0.4 \pm 0.7\%$  for heart V40,  $-1.3 \pm 0.5\%$  for lung V20 and  $-1.5 \pm 0.5\%$  for mean lung dose. Within treatment courses replanned, no significant differences existed before and after the new plan with regards to the agreement between planned and delivered doses. Moreover, no significant differences in this agreement existed between treatment courses replanned versus those that were not.

**Conclusions:** We demonstrated the value of dose reconstruction for lung patients with gross anatomical changes. We found that the agreement between planned and delivered dose metrics for the spinal canal, heart and lung did not vary considerably throughout treatment, even in the presence of large anatomical changes, or whether the cases were replanned or not. We are currently exploring quantification of inherent uncertainties in accumulating dose in this challenging cohort, including impact of DIR quality, CBCT dose calculation and lung tissue deformation.

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### THE INTRABEAM DOSIMETRIC INTERREGNUM: ARE THE BREAST TARGIT PROTOCOL DOSES DELIVERED BY INTRABEAM ACCURATE?

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**Purpose:** The INTRABEAM system (Carl Zeiss Meditec AG) is a miniature 50 kVp x-ray source for use in intraoperative radiotherapy. The manufacturer provides a calibration depth-dose curve which is used for planning INTRABEAM treatments. To validate the calibration data, users are offered a water phantom to independently measure their INTRABEAM source depth-dose curve, calculated with a recommended formula. However, to compare the water phantom dose measurements with the calibration data, a depth-dependent conversion function is required. The necessity for a

dose conversion function is troubling, as by definition the absorbed dose to water should be independent of measurement technique. In this work we investigated the INTRABEAM system dosimetry by performing ionization chamber and EBT3 Gafchromic film measurements of absorbed dose in a water phantom.

**Materials and Methods:** The absorbed dose from an INTRABEAM source was measured at various depths in water (5 mm to 30 mm) using a PTW 34013 soft x-ray ionization chamber and EBT3 Gafchromic films. From the ionization chamber measurements, the absorbed dose to water was calculated using three methods: i) the formula recommended by the water phantom manual (Zeiss), ii) the Zeiss formula with depth-dependent correction function to compare with the calibration data (TARGIT), and iii) our own dose formalism which relies on monte carlo calculations of the chamber response (CQ). For the EBT3 film measurements, the film energy dependence was accounted for by interpolating between multiple net optical density to dose calibration curves across a range of photon beam qualities relevant to the INTRABEAM spectrum in water (HVL = 0.12 to 2.18 mm Al).

**Results:** The doses calculated by the TARGIT method agreed with the calibration data to 5%, within measurement uncertainty. However, at all depths investigated, the TARGIT dose was significantly lower than that measured by the Zeiss and CQ methods, as well as EBT3 film. These dose differences ranged from 14% to as large as 80%, with the discrepancy increasing with decreasing depth in water. In general, the doses measured by EBT3 film, and the Zeiss and CQ methods were in good agreement within measurement uncertainties (5-6%).

**Conclusions:** These results suggest that the TARGIT dose, which is consistent with the manufacturer calibration dose, severely underestimates the physical dose to water. The depth dependence of this discrepancy also means that the delivered dose varies wildly with the depth of prescription (e.g. TARGIT dose of 20 Gy @ 30 mm corresponds to 23-26 Gy, while 20 Gy @ 5 mm corresponds to 31-36 Gy). Understanding this relationship between the calibration and physical dose is important for any studies wishing to make meaningful dosimetric comparisons between the INTRABEAM and other radiation emitting devices.

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### OUTCOMES OF STEREOTACTIC BODY RADIOTHERAPY FOR ABDOMINOPELVIC OLIGOMETASTASES

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**Purpose:** Stereotactic body radiotherapy (SBRT) allows for the delivery of highly conformal, locally ablative doses of radiation to extracranial targets. Limited data exists in the management of oligometastases (OMs) in the abdominopelvic (AP) space, where the delivery of SBRT poses challenges given the proximity of radiosensitive organs-at-risk, particularly luminal GI structures. We conducted a retrospective chart review to assess clinical outcomes in patients with AP OMs treated with SBRT at our centre.

**Materials and Methods:** Eligible patients were those with OMs (defined as disease in  $\leq 3$  involved organs and  $\leq 3$  total sites) in the AP soft tissues (excluding the liver) treated with SBRT. All primary tumour histologies were included. Minimum follow-up of three months was required. Clinical endpoints assessed included progression-free survival (PFS), local control (LC), chemotherapy-free survival (CFS), overall survival (OS) and toxicity (CTCAEv5.0). Descriptive statistical analyses and Kaplan-Meier estimates of LC, PFS, CFS and OS (from date of SBRT completion) were then conducted.

**Results:** Fifty-one eligible patients with 58 AP OMs were treated with SBRT between January 2011 and December 2015. Median follow-up was 21.9 months. Primary tumours were predominately gynecologic (39%), gastrointestinal (31%), or genitourinary (16%). Eighty-eight percent of patients had a solitary OM. Eighty-three percent of treated OMs were AP lymph nodes (48/58). Median maximal lesion size was 22 mm (range 7-74 mm). All treatments were delivered in 5 fractions with a median dose of 35 Gy (25-40 Gy; BED10 31.25-72 Gy). Initial progression post-SBRT occurred in 38/51 patients (75%) mostly due to distant failures alone (33/38; 87%). Median initial PFS was five months (95%CI 2.5-7.5), with a two-year rate of 29%. Oligometastatic progression occurred in more than half of patients (21/37)

who progressed at any time point during follow-up. Of these patients, 48% (10/21) received further SBRT. Resulting two- and four-year CFS were 47% and 37%, respectively (median CFS 15 months). Rates of two- and four-year LC were 74% and 69%. Median OS was 43 months (95%CI 31-55). Nineteen patients (37%) experienced acute toxicity, predominately Grade 1/2, with only one Grade 3 toxicity observed. One late non-GI toxicity occurred. No Grade 4 or 5 acute or late toxicities were seen.

**Conclusions:** Despite concerns regarding initial distant PFS, modest BED SBRT for AP OMs was associated with sustained LC without significant toxicity. In this population, excellent OS and CFS were also observed, yet no definitive conclusions can be made if this is solely due to treatment. Oligometastatic disease may behave more indolently and allow for the opportunity to salvage limited-burden local and distant failures and delay chemotherapy; however, prospective validation of our findings is warranted.

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### DOSE TOLERANCE OF THE BRACHIAL PLEXUS: A SYSTEMATIC REVIEW OF THE LITERATURE

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**Purpose:** The dose tolerance of the brachial plexus is not well established. Emami et al first described the dose tolerance of the brachial plexus, amongst other organs, from a compilation of early cohort studies. Current RTOG trial recommendations restrict the dose received by the brachial plexus to 60-66 Gy. However, radiation technology has advanced dramatically with the introduction of image guided radiation therapy (IGRT) and techniques such as 3D-CRT, IMRT, VMAT, and stereotactic radiotherapy. The introduction of these methods and changes in dose fractionation schedules further obscures the dose tolerance of the brachial plexus.

**Materials and Methods:** A systematic literature search was conducted utilizing MEDLINE, EMBASE, CINAHL, and Northern Lights without language restriction through February 2018. Eligible studies included clinical trials and cohort studies. Case reports were excluded. Studies reporting no radiation induced brachial plexopathy (RIBP) cases, that did not define absorbed plexus doses, or contained groups receiving heterogeneous radiotherapy treatments were excluded. Search results were compiled and data were abstracted using Covidence. Main outcome measures of brachial plexus biological effective dose (BED) absorbed and RIBP incidence were analyzed for correlation using a linear regression model.

**Results:** We retrieved 2061 abstracts of which 25 studies with 40 unique patient cohorts met the inclusion criteria. Study publication date ranged from 1966 to 2017. A total of 13 patient cohorts were treated with conventional fractionation, five with SBRT, and 22 with hypofractionated dose fractionations (defined as >2 Gy/fraction). Sixteen patient cohorts were reported in studies utilizing IGRT. RIBP incidence ranged from 0.7-85.7% amongst the cohorts. No incidences of RIBP were seen under BED3 of 83 (EQD2 = 50 Gy). In non-SBRT patients, the incidence of RIBP did not exceed 5% for BED3 under 118 (EQD2 = 70.9 Gy) with the exception of one outlier. For patients treated with IGRT plans using conventional or conventional and hypofractionated (but not ablative) dose fractionations, a correlation was found on linear regression between BED3 and RIBP incidence ( $R^2 = 0.60$  and  $0.66$  respectively).

**Conclusions:** The incidence of RIBP ranged from 0.7% to 85.7% in the studies. No incidences of RIBP were seen with a BED3 under 83, and no more than 5% seen with a BED3 under 118. With IGRT guided non-stereotactic treatments, there was a linear correlation between BED3 and RIBP incidence ( $R^2 = 0.66$ ). The literature appears to define safe thresholds for both conventional and hypofractionated dose schedules to the brachial plexus.

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### EFFECT OF FEEDING TUBE STRATEGY ON HOSPITALIZATION RATES AND OUTCOMES IN HEAD AND NECK CANCER PATIENTS TREATED WITH CHEMORADIOTHERAPY

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**Purpose:** Patients receiving definitive chemoradiation for head and neck cancers remain at risk for hospital admission often owing to poor oral intake and frequent underlying dehydration. The objective of this study was to determine potential differences between those receiving prophylactic versus emergent enteral nutrition with regards to hospitalization rates and survival outcomes.

**Materials and Methods:** A retrospective chart review of adult head and neck cancer patients receiving radical radiation therapy +/- chemotherapy (CRT) at our tertiary care cancer centre was completed. Patients were grouped into two categories; Group 1 receiving either no tube feeding or emergent nasogastric (e-NG) or percutaneous gastrostomy (e-PEG) tube and Group 2 which received prophylactic PEG (p-PEG) tube. Hospitalisation rates while on treatment and the three months after treatment were compared via Chi-Square test. Baseline characteristics were compared between groups by either t-tests or chi-square tests. Survival was determined by Kaplan-Meier Method and Log-Rank tests.

**Results:** Overall, 203 patients treated between 2006 and 2016 were included with median follow-up of 22 months. Incidence was predominantly male at 82%. Median age at diagnosis was 62 years with most common sites treated being oropharynx (72%; 31% of these being base of tongue) followed by larynx (15%) and nasopharynx (8%). Seventy-two percent of all patients received primary chemoradiation therapy with most common fractionation regimen being 70 Gy in 35 daily fractions. Both groups were evenly matched in terms of age (62 years) and male predilection (82% versus 86%). Disease site ( $p = 0.08$ ) for groups 1 and 2 respectively were predominantly oropharynx (75% versus 43%) followed by larynx (14% versus 29%), nasopharynx (7% versus 14%) and hypopharynx (3% versus 14%). Histology ( $p = 0.73$ ) was almost entirely of squamous cell origin (99.5% versus 100%) with p16 positivity identified in 49% and 29% of obtained samples. Social history was marked by a predisposition for higher overall tobacco use ( $p = 0.43$ ) in Group 2 (57% versus 44% former smokers, 24% versus 30% current smokers and 31 years versus 25 years median pack-year history) though greater alcohol use ( $p = 0.16$ ) was seen in group 1 (>10 drinks a week in 30% versus 24%). AJCC Stage ( $p = 0.76$ ) distribution for Groups 1 and 2 were as follows: Stage I 2% versus 0%, Stage II 6% versus 5%, Stage III 25% versus 14%, Stage IVA 63% versus 76% and Stage IVB 5% versus 1%. Enteral nutrition rates for Group 1 was 51% receiving none, 28% receiving e-NG and 21% receiving e-PEG. All patients in Group 2, by definition, received p-PEG. Hospitalization ( $p = 0.62$ ) either during treatment or within three months following treatment totalled 37% versus 43% in Groups 1 and 2. Of the 60 patients in either group who had a PEG tube placed, 53% went on to have a tube dependent lifestyle. Finally, median survival was 63 months for group 1 and 35 months for Group 2 ( $p < 0.001$ ).

**Conclusions:** In definitive CRT treated head and neck cancer, patients with prophylactic PEG enteral nutrition possessed several negative prognostic factors such as higher smoking rates, lower HPV association and more advanced stage disease at time of presentation. These patients also required hospitalization at a higher rate and had poorer median survival. This likely demonstrates current practice patterns for prophylactic enteral feeding but does not provide convincing evidence in favour of prophylactic PEG tube placement.

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### COMPARISON OF A RADIATION SPECIFIC SCORING SYSTEM (CPI) AND ALBI TO PREDICT LIVER CANCER PATIENT OUTCOMES

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**Purpose:** Providing outcome information for liver cancer patients, researchers, and clinicians to identify those suitable for treatment is important. Previously, Child-Pugh (CP) grade was the most accepted system to predict outcome. The ALBI grade, based on the serum albumin and bilirubin only, has become a new standard in surgical and interventional radiology for primary and secondary liver cancer. The advantages it has over the CP grade include objectivity and simplicity by eliminating two relatively unreliable parameters. However, we know that liver patients are more heterogeneous and additional parameters are needed to better explain the statistical variance seen in current prediction models. Furthermore, the ALBI index was developed

from patients not treated by radiation and has not been widely validated for its utility in predicting outcomes after radiation therapy. The purpose of this study is to understand the effectiveness of ALBI in predicting survival outcomes in liver patients undergoing radiation by validation against a model developed on patients eligible for radiation, the Clinical Prognostic Index (CPI). The CPI was developed to identify patients who would not benefit from radiation through multivariate analysis of pre-treatment factors of liver cancer patients including GTV, serum albumin, presence of extrahepatic disease, origin of primary.

**Materials and Methods:** In a prospective database of liver cancer patients treated at a tertiary cancer center between July 2004 and June 2014, 188 patients were treated with radiation therapy. The radiation doses were 15 to 88 Gy and were given in 5 to 30 fractions using a radiobiologically-guided protocol. The concordance index was calculated for mortality at each month between four to 12 months and averaged.

**Results:** There were 116 males and 72 females in the database utilized for this analysis. For both indices, OS was significantly related to the index grade ( $p < 0.01$ ). There was significant association between the two indices as well with higher ALBI grades predisposing a higher CPI grade and vice versa ( $p < 0.01$ ). The median overall survival for both indices decreased as grade increased (21.9, 7.8, 2.1 months for CPI 0, 2, 3; 20.6, 7.4, 1.9 months for ALBI 1, 2, 3;  $p < 0.01$ ). The mean C-index for ALBI was not significantly different compared to the CPI in hepatocellular carcinoma (HCC) patients (0.67 versus 0.69). The mean C-index for ALBI was significantly lower than the CPI for metastases patients (0.61 versus 0.65,  $p = 0.01$ ).

**Conclusions:** This is the first study to investigate the ALBI index in comparison to an index specifically designed to predict survival after radiation therapy in liver cancer patients. ALBI performed as well as the CPI for HCC patients in predicting survival and can be used in the prognosis of these patients undergoing radiation therapy. The improvement of the CPI over ALBI in metastases patients may require further study of the index in this population.

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#### STEREOTACTIC RADIOTHERAPY FOR PANCREATIC CANCER: A RETROSPECTIVE INSTITUTIONAL REVIEW

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**Purpose:** Despite treatment advances, the prognosis of clinically localized or locally advanced pancreas cancer (LAPC) remains poor. Treatment for unresectable LAPC remains varied and includes systemic therapy and radiotherapy (RT). Stereotactic body RT (SBRT), which delivers highly conformal high dose per fraction RT, is an emerging treatment option based on encouraging local control results and minimizing time off systemic therapy.

**Materials and Methods:** This is a single institution retrospective review of patients with pancreatic adenocarcinoma treated with SBRT from 2015-2017. Forty-one patients received pancreatic SBRT delivered in 3 fractions to a dose between 21-36 Gy (median dose, 27 Gy) that was determined by dose limits to organs-at-risk. Co-registration on cone beam CT was performed with either fiducial markers, stent, or surgical clips. Patients were followed every three months with CT scans as clinically indicated. Local progression was defined as two successive increases in the size of the pancreatic tumour on imaging to avoid potentially attributing radiation-induced edema to disease progression. Toxicity was assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0.

**Results:** Of the 41 patients in this cohort, 22 (54%) had unresectable LAPC, three (7%) had borderline resectable disease with SBRT delivered neoadjuvantly (with one proceeding to Whipple resection, one was not surgically resectable due to vascular involvement, and one died with metastatic disease), seven (17%) had resectable disease but declined surgical intervention, three (7%) had medically inoperable disease, five (12%) had metastatic disease, and one (2%) had locally recurrent disease. The median follow-up was 9.9 months (range, 1-40.8 months). By the time of last follow-up, one patient (2%) developed local progression, 15 patients (37%) developed systemic disease, and one patient (2%) developed local and systemic progression. Thirty-nine patients (95%) had no evidence of local progression of disease. Twenty-five patients (61%) died throughout

follow-up. There were nine late gastrointestinal (GI) toxicities in six patients (15%). Two patients had Grade 1 gastrointestinal (GI) bleeds. There were seven Grade 3 GI toxicity events in five patients (12%) including duodenal hemorrhage requiring blood transfusion, duodenal obstruction secondary to stricture without stenting, duodenal stenosis due to extrinsic compression without stenting, fistulisation of mass to duodenum (two patients), portal vein stenosis requiring stenting, and gastric outlet obstruction requiring hospitalization. Median duodenum V30 Gy and V16.5 Gy were 0 cc (range, 0-0.52 cc) and 9.08 cc (range, 0-18.7 cc), respectively.

**Conclusions:** SBRT is an effective treatment for local control of pancreatic cancer. There is a modest risk of severe late GI toxicities and future strategies will be needed to reduce this toxicity. Systemic therapies remain important, given the proportion of patients who develop distant metastases.

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#### RE-IRRADIATION OF PRIMARY ADULT CNS TUMOURS: OUTCOMES AND TOXICITIES

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**Purpose:** The aim of this study was to evaluate the outcomes, toxicities, and cumulative doses to tumours and critical structures following fractionated re-irradiation of primary brain tumours in adults.

**Materials and Methods:** We reviewed our institutional database for adult patients treated between 2007 and 2017, who received external beam re-irradiation of the brain, defined as overlap of the 25% of prescription isodose volumes. Doses were converted to biologically effective dose, expressed as 2 Gy per fraction equivalent dose (EQD2;  $\alpha/\beta = 3$  versus 10). Toxicity was graded according to CTCAE v4. The Kaplan-Meier method was used for survival analyses.

**Results:** We identified 58 patients who underwent re-irradiation. The median interval between courses was 4.5 years for WHO Grade (G)-I/II, 6.4 years for G-III and 1.2 years for G-IV tumours. The primary diagnoses were meningioma ( $n = 20$ ), glioblastoma multiforme ( $n = 11$ ), G-III glioma ( $n = 12$ ), G-I/II glioma ( $n = 9$ ), and others ( $n = 5$ ). The median cumulative prescribed EQD2 ( $\alpha/\beta 10$ Gy) was 106.2 Gy (range 74.8-120 Gy). Radiation necrosis occurred in 10 patients following re-irradiation ranging between G1 ( $n = 4$ ) to G3 ( $n = 4$ ). Two of these patients received Bevacizumab and two had surgical resection. In total, G $\geq 3$  RT-related toxicities were noted in nine patients, while no G-IV/V toxicities were observed. Twelve- and 24-month overall survival (OS) rates after re-irradiation for G-I/II tumours were 77% and 46%, respectively. For G-III/IV, 12-month OS was 48% and 24-month OS was 29%. Median progression-free survival following repeat RT was 10.2 and 6.2 months for G-I/II and G-III/IV tumours, respectively.

**Conclusions:** Re-irradiation for recurrent primary brain tumours was associated with acceptable rates of toxicity. Re-irradiation for recurrent primary brain tumours was associated with acceptable rates of toxicity. We are currently calculating cumulative doses to critical structures (optic chiasm, cranial nerves, cochlea, brainstem, retina, and hippocampus) and plan to correlate those results to radiation-associated toxicities.

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#### IS THE IMPORTANCE OF HEART DOSE OVERSTATED IN THE TREATMENT OF NON-SMALL CELL LUNG CANCER? A SYSTEMATIC REVIEW OF THE LITERATURE

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**Purpose:** Thoracic radiation has been associated with increased cardiac toxicity and mortality in studies of patients with breast cancer and Hodgkin Lymphoma. However, this impact is not well studied in patients with non-small cell lung cancer (NSCLC). Recent studies have suggested a relationship between cardiac dose and mortality, but the strength of the relationship and the optimal dosimetric predictors are unknown. The goal of this study was to conduct a systematic review and meta-analysis to provide an evidence-

based estimate of the relationship between cardiac dose and mortality in patients with NSCLC.

**Materials and Methods:** A systematic review of MEDLINE (PubMed) and Embase databases (inception to January 2018) according to PRISMA guidelines was performed. Studies which evaluated cardiac dosimetric factors in patients with NSCLC and which include outcomes of cardiac events, cardiac mortality and overall survival were identified. After the initial search ( $n = 461$ ), studies were screened by title ( $n = 78$ ), then by abstract ( $n = 33$ ), and then included for full text review ( $n = 22$ ).

**Results:** From 6240 patients across 22 studies, a total of 214 cardiac dosimetric parameters (84 unique parameters) were assessed as possible predictors of cardiac toxicity or death, with a mean of 10 dosimetric factors assessed per study. Predictors assessed included general dosimetric factors (e.g. mean and maximum heart doses), factors based on threshold doses (e.g. heart V5), and factors based on doses to anatomic structures or sub-volumes (e.g. atria, ventricles). The most commonly analyzed parameters were mean heart dose (MHD), heart V5 and V30. Most studies did not make corrections for multiplicity of testing. For the endpoint of overall survival, V5 was found to be significant on multivariable analysis (MVA) in one of 11 studies, V30 significant in two of 12 studies and MHD was not significant in any of eight studies. For the endpoint of cardiac events, V5 was found to be significant on MVA in two of four studies, V30 in one of three studies, and MHD in two of four studies. There was little overlap in the sub-volume parameters included in multivariable models across studies. A meta-analysis of the data could not be performed, as most negative studies did not report effect estimates (e.g. hazard ratios) and could not be meta-analyzed.

**Conclusions:** Heart dose-volume constraints are not consistently associated with overall survival of NSCLC patients. Multiplicity of testing is a major issue and likely inflates the overall rate of type I error in the literature. Future studies should specify predictors a priori, correct for multiplicity of testing, and report effect estimates for non-significant variables.

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#### STEREOTACTIC BODY RADIOTHERAPY FOR METASTATIC COLORECTAL CANCER: COMPREHENSIVE REVIEW FROM A LARGE SINGLE INSTITUTION

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**Purpose:** Surgical resection of colorectal cancer (CRC) metastases is an accepted standard of care option in select patients. Multi-site stereotactic body radiotherapy (SBRT) has emerged as another ablative therapy technique. The purpose of this study was to review the clinical outcomes of SBRT in patients with metastatic CRC from a large academic institution.

**Materials and Methods:** Metastatic CRC patients treated with extracranial SBRT were identified from an institutional database. Treatment indications were: 1) oligometastases, where the goal was to treat all visible tumours ( $\leq 5$ ), 2) oligoprogression, where the goal was to treat only the progressing tumours ( $\leq 5$ ) while other metastases were stable, and 3) local control of dominant tumours, where the goal was to treat tumours in unfavourable locations to prevent or improve symptoms even while other metastases may be progressing. Endpoints calculated using Kaplan-Meier methodology included overall survival (OS), progression-free survival (PFS), and time to starting/changing systemic therapy (SCST). Competing risk analysis was used to calculate cumulative incidence of local failure (LF). Univariate analyses were performed to look for predictive factors.

**Results:** One hundred sixty-five patients were treated. Median age of patients was 69.0 years, with 102 patients (61.8%) being male. SBRT was delivered for oligometastases in 130 patients, oligoprogression in 16 patients, and local control of dominant tumours in 19 patients. For the entire cohort, median OS was 39.4 months, with a three-year OS rate of 56.3%. Median PFS and time to SCST was 9.9 months, and 34.5 months, respectively. In 72 patients who did experience SCST, the median time to the event was 14.5 months. Treatment indication, number of lines previous systemic therapy, pre-treatment CEA, primary tumour in situ or not, and location of metastases were all significant predictors of OS, PFS, and time to SCST (all  $p < 0.05$ ).

Oligometastatic patients had the best outcomes with a median OS of 49.3 months, three-year OS rate of 67.5%, median PFS of 12.4 months, and median time to SCST of 42.3 months. Two hundred sixty-two metastases were irradiated, which included 122 lung tumours, 95 liver tumours, and 25 spine tumours. The cumulative incidence of LF was 26.9% at three years for all tumours, with lung metastases having lowest cumulative incidence of LF of 15.2% at three years. Lung tumours, smaller PTV volume, and higher mean PTV dose were all significant predictors of lower LF (all  $p < 0.05$ ). Nine patients developed Grade 3 toxicities.

**Conclusions:** Oligometastatic CRC patients treated with SBRT have favourable OS which is comparable to those historically treated with metastatectomy. Use of SBRT to treat select metastatic CRC patients may significantly delay the need for SCST. Higher SBRT doses may further optimize local control of CRC metastases.

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#### OUTCOMES OF INTENSITY MODULATED IRRADIATION FOR SINONASAL CANCERS IN THE MODERN ERA

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**Purpose:** To report outcomes, patterns of failure and predictive factors of disease-free survival (DFS) in sinonasal cancers treated with intensity modulated irradiation.

**Materials and Methods:** A retrospective analysis of patients with sinonasal cancers treated with either intensity modulated radiotherapy (IMRT) or intensity modulated proton therapy (IMPT) using conventional fractionation at MD Anderson Cancer Center from 2000 to 2016 was conducted. Patients with prior radiotherapy (RT), melanoma or lymphoma histologies were excluded. Kaplan Meier method was used for estimation of local control (LC), regional control (RC), distant metastasis rate (DM), DFS and overall survival (OS). Cox proportional hazard ratio models were used for univariate and multivariate analysis of potential predictive variables of DFS. Variables associated with DFS in univariate analysis ( $p < 0.05$ ) were entered in a recursive partitioning analysis (RPA) to identify appropriate cut-off points.

**Results:** Three hundred forty-nine patients were included in the analysis, including 331 patients treated with IMRT and 18 with IMPT. Median age was 57-years-old (range, 20-90). The most common primary sites were nasal cavity (41%), maxillary sinus (29%) and ethmoid sinus (15%); the most common histologies included squamous cell carcinoma (35%), adenoid cystic (14%), sinonasal undifferentiated carcinoma (14%) and esthesioneuroblastoma (12%). Sixty-five percent of patients were treated with surgery and adjuvant RT +/- chemotherapy (CT) while 35% were treated with definitive RT +/- CT. Induction CT was given to 46% of patients and 40% were treated with concurrent chemoradiation. Median follow-up was 43 months (range; 1-186). Five-year LC, RC and DM rates were 82%, 92%, and 21%, respectively. DFS at two- and five-year were 68% and 52%, while OS at two- and five-year was 80% and 66%, respectively. On univariate analysis, age ( $p = 0.006$ ), history of tobacco use ( $p = 0.004$ ), T stage ( $p = 0.0001$ ), N stage ( $p = 0.004$ ), RT dose ( $p = 0.04$ ) and use of induction chemotherapy were associated with DFS. Outcomes were similar between the adjuvant RT versus definitive RT groups, as well as across histologies. On multivariate analysis, increasing age (0.04), T stage ( $p < 0.0001$ ) and N stage ( $p = 0.04$ ) were predictive of DFS. RPA identified age  $\geq 43$  years, T4 stage, N stage  $\geq 2$  as significant cut-offs for adverse DFS outcome; in the adjuvant RT group, a dose  $< 64.8$  Gy was associated with adverse DFS outcome.

**Conclusions:** Results from this large cohort of sinonasal cancer support good disease control rates with acceptable survival with intensity modulated irradiation. Comparable outcomes across histologies is likely explained by selective treatment intensification. Age, T stage and N stage are independent correlates of worse DFS.

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#### EARLY TOXICITY AND QUALITY OF LIFE RESULTS OF TUMOUR-TARGETED DOSE ESCALATION FOR LOCALIZED PROSTATE CANCER

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**Purpose:** To report dosimetry and early toxicity-QoL outcomes of tumour-targeted dose-escalation delivered by integrated VMAT (IB-VMAT) or MR-guided HDR brachytherapy (HDR) boost for prostate cancer.

**Materials and Methods:** Patients diagnosed with localized prostate cancer with at least one identifiable lesion (> 5 mm and < 33% total prostate volume) on multiparametric MRI (mpMRI) were enrolled in a prospective phase II study. Participants received EBRT 76 Gy in 38 fractions to the prostate plus an integrated 95 Gy VMAT boost or single fraction 10 Gy MR-guided HDR boost to the GTV. GTV was contoured on mpMRI and deformably registered onto planning CTs. CTV76 was prostate + 5 mm around GTV avoiding penile bulb (PB), urethra (U), rectal wall (RW) and bladder wall (BW). PTV76 was the same for IB-VMAT and HDR (CTV + 5 mm AP/ SI; 3 mm LR). PTV95 was GTV + 5mm AP/ SI and 3mm LR (IB-VMAT). PTV10 was GTV + 2 mm SI and 1mm AP/RL (HDR). HDR dose was estimated by deformable registration and then summed with the external beam dose. Dosimetry was converted to EQD2 assuming  $\alpha/\beta$  3 Gy for comparison. Toxicity and QoL data prospectively collected using CTCAE v.4.0 and EPIC. Fisher's exact test was used to compare toxicity between techniques. General linear mixed model was conducted to assess the changes in EPIC domain scores over time and comparison between both groups using Wilcoxon's test.

**Results:** Forty received IB-VMAT and 40 HDR boost. PTV76 (means) were 93.2cc and 90.2 cc, PTV (GTV) volume was 11.7 cc and 3.2 cc for IB-VMAT and HDR, respectively. OAR and target minimal doses were comparable between the two arms. HDR achieved higher mean and maximal tumour doses ( $p < 0.05$ ). Median follow-up was 24 months (range 6-36). Acute Grade 2 GU toxicity was 40% and 42.5% in VMAT and HDR patients, while GI toxicity was 7.5% and 10% respectively. One IB-VMAT patient had Grade 3 GU acute toxicity (urinary retention). Of 69 patients with >12 months follow up (33 VMAT and 36 HDR), 18.1% (IB-VMAT) and 19.4% (HDR) developed Grade 2 GU toxicity, while Grade 2 GI toxicity rates were 6% (IB-VMAT) and 2.7% (HDR). Late Grade 3 toxicity was observed in two patients (IB-VMAT): one GU (hematuria attributable to a new bladder cancer) and one GI (rectal ulcer in the context of concurrent HIV antiviral therapy). Deterioration in sexual function occurred in 20% IB-VMAT and 12.5% HDR patients. Compared to baseline, urinary and bowel HRQoL domains declined by week 6 of treatment (all  $p < 0.01$ ) and returned to baseline at 6 months ( $p > 0.1$ ). Our population had reduced sexual domain at baseline and this deteriorated over subsequent follow up ( $p < 0.01$ ). No statistically significant difference in toxicity or QoL domains between the groups were found.

**Conclusions:** Intraprostatic tumour dose escalation using IB-VMAT or MR-guided HDR boost achieved comparable OAR dosimetry, early toxicity and QoL outcomes, but higher mean and maximal tumour dose was achieved with the HDR technique. Further follow-up will determine long-term outcomes including disease control.

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#### RETROSPECTIVE MONTE CARLO DOSE-VOLUME ANALYSIS OF A SWEEPING-BEAM TOTAL BODY IRRADIATION TECHNIQUE

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**Purpose:** A parallel-opposed pair (POP) sweeping-beam Cobalt-60 technique has been in place at our clinic for total body irradiation (TBI) for over 23 years. A change to a more sophisticated linac-based technique with VMAT is being considered to improve the patient treatment experience. To reproduce our existing treatment on a new platform, detailed organ dose constraints must be retrieved from our current technique. We employ a novel Monte

Carlo (MC) dosimetry technique to obtain this information.

**Materials and Methods:** A research ethics board approved retrospective study is underway for adult and pediatric patients recently treated with TBI whole body prescriptions of 1200 cGy  $\pm$  10% in 6 fractions. MC phantoms are produced for each patient including the planning CT image volume, the patient-specific lead lung compensators, and a polystyrene flattening filter placed beneath our Cobalt unit treatment head. The MC simulation procedure has been validated by measurements both in water tanks and in phantoms mimicking patient treatment conditions, at extended SSD and with lung foam between blocks of solid water under lead compensators. Two MC phantoms are produced for each patient corresponding to the supine and prone deliveries of each fraction in our TBI technique. The results from the two simulations are summed with a deformable registration tool. The lungs, kidneys, liver, thyroid, and body are contoured and dose-volume statistics are obtained for each.

**Results:** We present the results from the first 16 patients simulated in our study. While the mean body dose for all patients falls within the prescription tolerance (range: 10.91-11.90 Gy), some individual organ doses fall outside this range reflecting the unavoidable challenges of using a POP technique for TBI. There is a linear trend with the smaller patients receiving lower mean body doses and vice versa. The liver and lung doses are typically below the mean body dose for each patient (ranges: liver, 10.73-11.69 Gy; left lung, 10.44-11.62 Gy; right lung, 10.48-11.46 Gy) while the thyroid and kidney doses are typically above (ranges: thyroid, 10.83-12.32 Gy; left kidney, 10.98-12.15 Gy; right kidney, 10.90-12.29 Gy).

**Conclusions:** Retrospective analysis of TBI treatments reveals that all patients received doses within the accepted  $\pm$  10% tolerance. The MC dosimetry pipeline for our procedure is robust and reliable, could feasibly be implemented for clinical quality assurance, and yields organ dose data previously unavailable for a sweeping-beam technique. These data may be implemented as constraints in designing a future VMAT technique, or other TBI protocols calling for non-standard organ doses and may lead to a deeper understanding of toxicities arising from TBI protocols.

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#### ACCOMPANYING PATIENT - AN ORGANIZATIONAL RESOURCE AS A MEANS TO IMPROVE THE EXPERIENCE OF PATIENTS WITH CANCER: A NEEDS ASSESSMENT STUDY

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**Purpose:** A recent report by the Canadian Partnership Against Cancer found that one in four patients were not satisfied with the emotional support they received during oncology care. One way to meet this need is to introduce Accompanying Patients (APs) into current patients' care environments as part of the clinical team. APs are patients who have already experienced an episode of cancer and who are willing and ready to use their experiential knowledge of both the disease and the health system to support patients undergoing treatment. Since the role of APs complements the scientific knowledge and the experience of professionals, we hypothesize that this approach will improve the healthcare in oncology. With that goal in mind, this needs assessment study looks at the implementation of this organizational innovation in our institution.

**Materials and Methods:** Co-built with professionals and APs, this project examines quantitative and qualitative data collected through questionnaires. Two online surveys aiming to better define the patients' and professionals' needs and expectations were built, and 202 patients and 62 professionals have completed the surveys.

**Results:** Ninety-four per cent and 90% of the professionals and patients respectively recognized that patient partnership in oncology and the introduction of APs into clinical settings is critical for healthcare improvement. Patients need primarily to share their experience and to receive more information and emotional support. They also needed more information on the following issues: emotional aspects of the disease, relationship with family, sexuality, return to work, financial impact, and social perception of illness, issues for the most part not fully addressed during the medical consultation. However, two-thirds of the professionals voiced concerns about organizational issues and legal or ethical obligations relating to APs.

**Conclusions:** Although there is a definite openness to patient partnership

in the clinic from professionals and patients alike, the framework, moment and contents of the APs' interventions remain to be defined. In sum, APs in health care services are needed to make healthcare organizations more humane and responsive to patients' needs.

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#### WORKLOAD ESTIMATES USING PAIRED DETECTORS

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**Purpose:** Determination of linac workload by energy is a requirement for the CNSC Annual Compliance Report. We can determine the MU delivered from a mixture of low and high energy photons by using a photon (TLD) and neutron (CR39) pair of badges. Each detector type has a different energy response and the paired detectors allow us to sort out contributions to the collective badge signals from the low- and high-energy beams. Effectively, once calibrated, the pair allows us to solve two equations with two unknowns. **Materials and Methods:** The experiments look at the exposures under carefully controlled set-up conditions. The first phase calibrates the badges by looking at reproducibility and linearity over a range of 500,000 MU exposures for both low- and high-energy photons. The reproducibility experiment shows a 2% spread in response and the linearity experiment is very good with a coefficient of determination  $R^2 = 0.998$ . In fact, the linearity is so good, we found it is possible to calibrate with as little as 5,000 MU and accurately predict MU as high as 500,000.

**Results:** Once calibrated the second phase of the experiments exposed badge pairs to mixed exposures of low- and high-energy photons. The number of MU of each type of beam is known but randomly selected. The integrated signals of each badge were separated into low- and high-energy contributions and then converted into predicted MU from our calibration curves. The predicted and actual MU are compared and analyzed statistically. The predicted MU were within 5% of the actual MU.

**Conclusions:** This experiment is an important first step to the proof-of-concept. This technique offers an alternative to the traditional methods used to determine the MU and is robust because it collects signal regardless if the linac is in clinical mode or service mode.

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#### ADVANCED PROSTATE IMAGING OF RECURRENT CANCER AFTER RADIOTHERAPY (PICS): INTERIM RESULTS OF A PROSPECTIVE, MULTI-CENTRE TRIAL

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**Purpose:** [18F]-DCFPyL is a second generation positron emission tomography (PET) probe targeting PSMA - a trans-membrane protein overexpressed in prostate cancer. PICS seeks to evaluate [18F]-DCFPyL PET/CT in restaging men with biochemical failure (BF) after primary radiation therapy.

**Materials and Methods:** PICS (NCT02793284) is a prospective, single arm study conducted at four cancer centres in Ontario of men with BF (Phoenix definition) after primary radiation for localized (T1/T2, Gleason <8, PSA<20) prostate cancer. Participants undergo conventional imaging (CI: computed tomography (CT) thorax/ abdomen/ pelvis, bone scan, and multiparametric MRI pelvis) followed by [18F]-DCFPyL PET/CT (PET). PET was reported by nuclear medicine physicians at each cancer centre with central review. In cases of disagreement a third read is specified by the protocol. Primary endpoint is the proportion of men with metastatic disease

detected by PET compared to CI. Secondary endpoints include number of lesions outside the prostate detected by PET compared to CI, and changes in patient management plan based on results of PET versus CI.

**Results:** Since opening in January 2017, 50 of a planned 80 patients have been accrued; the first 35 patients are reported here. At enrollment, median age was 75, median PSA 7.1, median PSA doubling time was 11.0 months, and median time from end of definitive radiation treatment to BF was 65.4 months. Stage and grade at the time of definitive radiotherapy was T1 (18/35, 51%) or T2 (17/35, 49%) and Gleason 6 (9/35, 26%), 7(25/35, 71%), or 8 (1/35, 3%). Previous treatment included external beam radiotherapy (24/35, 69%) or brachytherapy (11/35, 31%). Overall, any site of recurrence was identified in 33/35 (94%) men by both CI and PET. Extra-prostatic metastases were detected in 10/35 (29%) patients by CI and in 13/35 (37%) by PET. Isolated intra-prostatic recurrence was identified by CI in 21/35 (60%); PET detected additional, unrecognized extra-prostatic metastases in 4/21 (19%). A change in management plan based on PET versus CI occurred in 17/35 men (49%). Changes included the addition of salvage RT (8/17, 47%), ADT (4/17, 24%), biopsy (3/17, 18%), and HIFU (1/17, 6%).

**Conclusions:** For men with BF after primary RT, [18F]-DCFPyL PET/CT detects additional sites of disease that result in changes in management compared to CI. Identification of extra-prostatic metastases among men where CI identifies isolated intra-prostatic recurrence suggests a role for [18F]-DCFPyL PET/CT in optimizing selection for local salvage treatments. Updated results will be presented.

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#### CANNABIS UTILIZATION RATES IN THE CANCER PATIENT POPULATION

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**Purpose:** A comprehensive assessment of cannabis use among patients with cancer has not previously been reported. This study aimed to characterize patient perspectives on cannabis and its use.

**Materials and Methods:** An anonymous survey regarding cannabis use was offered to patients 18 years and older attending two comprehensive, and two community cancer centres which comprise an entire provincial healthcare jurisdiction in Canada. Ethics ID: HREBA-17011.

**Results:** 3138 surveys were administered and 2040 surveys were returned (65%) of which 1987 were sufficiently complete (response rate: 63%). 812 (41%) of respondents were under age 60. Forty-five percent identified as male and 55% as female. Forty-four percent had completed college or higher education. Overall, 43% reported any lifetime cannabis use. This was independent of age, gender, education level, and cancer histology. Cannabis was acquired through friends (80%), regulated medical dispensaries (10%) and other means (6%). Eighty-one per cent of patients with any use had used dried leaves. Among 356 patients (18% of respondents with sufficiently complete surveys) who reported cannabis use within the six months prior to survey, 36% were new users. Their reasons for utilization included cancer-related pain 46%, nausea 34%, other cancer symptoms 31%, and non-cancer related reasons 56%.

**Conclusions:** This survey demonstrated that cannabis use among patients with cancer was widespread (43%). One in eight respondents identified at least one cancer-related symptom for which they were using cannabis.

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#### RADIATION INDUCED MENINGIOMA IN ADULT SURVIVORS OF CHILDHOOD LEUKEMIA OR PRIMARY BRAIN TUMOUR TREATED WITH CRANIAL RADIOTHERAPY: INCIDENCE AND SCREENING RECOMMENDATIONS

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**Purpose:** Cranial radiotherapy (CRT) was commonly given for childhood leukemia and brain tumours. Survivors are at risk of late effects including radiation-induced meningioma (RIM). In our province, surveillance for

RIM is not standardized. We aimed to determine the incidence, latency, and screening patterns for RIM.

**Materials and Methods:** A retrospective chart review was performed of all patients aged  $\leq 18$  years at the time of radiation (RT), treated with CRT for leukemia or a brain tumour in our province between 1981-2006. Patient, tumour, and treatment characteristics were collected. Actuarial statistics were calculated with Kaplan-Meier Curves. Patients were censored at the date of last normal cranial imaging, or development of a RIM.

**Results:** Three hundred ninety-two patients were identified. The median age (range) at treatment was 9.6 years (0.8-18). The median CRT dose was 28 Gy. The original diagnosis was leukemia in 50%, glioma in 13%, medulloblastoma in 8%, ependymoma in 7%, neuroectodermal tumour in 7%, germ cell tumour in 5%, craniopharyngioma in 4%, and other pathologies in 6%. The median (range) of clinical follow-up (FU) was 13.2 (0-37.5) years. The median (range) of cranial imaging FU was 15.5 (0-21.2) years. There was no documented cranial imaging FU in 144 patients. Forty-eight patients developed a RIM. The median age (range) at RT for patients with RIM was 6.7 years (1.3-18). Only eight of these cases presented with associated symptoms. The earliest RIM in our cohort occurred 10.2 years after CRT. On actuarial analysis, the median (95% CI) time to development of a meningioma was 29.8 (28.9-30.7) years. Incidence (95% CI) of meningioma at 10 years was 0%, 15 years was five (2-9)%, 20 years was 12 (6-18)%, 25 years was 33 (23-43)% and 30 years was 47 (37-68)%. Amongst patients with a RIM, the median dose of CRT was 45 Gy. The lowest dose of RT in a patient who developed RIM was 12 Gy. RT was delivered to the whole brain in 58% and partial brain in 42% of patients with a RIM.

**Conclusions:** After CRT in pediatric patients, there is a significant risk of developing a RIM and there is a steady increase in this risk with ongoing follow-up. We recommend standardization of surveillance for these patients with screening beginning 10 years after completion of CRT.

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#### REPORT EXPLORING THE INFLUENCE OF ABDOMINAL COMPRESSION ON DOSIMETRY OF ADJACENT GASTRO-INTESTINAL CRITICAL STRUCTURES AND TOXICITIES FOR PATIENTS TREATED WITH NON-HEPATIC ABDOMINAL SBRT

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**Purpose:** There is a concern that use of abdominal compression (AC) for respiratory motion management in abdominal SBRT might result in dosimetric inconsistency between predicted and delivered dose for nearby critical structures (CS) especially the gastro-intestinal (GI) CS. The current study aimed at evaluating the impact of AC on the dosimetry of GI-CS and toxicities for patients treated with non-hepatic abdominal SBRT.

**Materials and Methods:** Two sets of CT scans (planning CT scans with AC and pre-treatment diagnostic CT scans without AC) were analyzed for a cohort of patients, treated with AC with prescribed dose to planning target volume (PTV)  $\geq 25$  Gy/5-fractions. Target volumes were delineated on both scans and PTV was expanded by 2 cm (PTV+2) and 4 cm (PTV+4). All GI-CS (duodenum, stomach, small bowel and large bowel) were contoured on both sets of scans. They were fused to create a composite CS (GI-lumen). Rigid registration of AC and non-AC scans was done using Velocity AI (Velocity Medical Systems, GA). The quality of the rigid registration was ascertained by Dice similarity coefficient (DSC).  $DSC \geq 0.85$  was considered acceptable. Rigid registration allowed transfer of GI-CS from non-AC to AC-CT scans, resulting in required dose information for them. We calculated the volume of GI-CS within PTV+2 and PTV+4 and dose-volume parameters including V30, and D0.2cc. Two-sample t-test was used for statistical comparison (AC versus non-AC). Toxicity scores were obtained using prospectively collected clinical data.

**Results:** A total of 12 patients met the DSC criterion. Primary targets included retro-peritoneal nodal mass (n = 6), pancreas (n = 3), adrenal gland mass (n = 3). No difference was seen between the AC versus non-AC with respect to volume of stomach (22.3 cc versus 20.3 cc; p = 0.88), duodenum (17.2 cc versus 5.8 cc; p = 0.1), small bowel (30.9 cc versus 47.5 cc; p = 0.37), large bowel (28.9 cc versus 30.1 cc; p = 0.95) and GI-lumen (120.6 cc versus 107 cc; p = 0.75) within PTV+2. Similarly, there was no difference

in volume of any GI-CS within PTV+4: stomach (61.1 cc versus 69.9 cc; p = 0.77), duodenum (34.2 cc versus 14 cc; p = 0.13), small bowel (83.9 cc versus 129.4 cc; p = 0.26), large bowel (80.3 cc versus 86.1 cc; p = 0.88) and GI-lumen (258.7 cc versus 297.3 cc; p = 0.59) between AC versus non-AC respectively. There was a significant improvement in V30 of GI-lumen with AC (0.11 cc versus 4.9 cc) (p = 0.03). However, no significant difference in the V30 of stomach (0.01 cc versus 0.65 cc; p = 0.33), duodenum (0.05cc versus 0.01 cc; p = 0.41), small bowel (0.04 cc versus 3.3 cc; p = 0.09) or large bowel (0.01 cc versus 0.3 cc; p = 0.33) was noted with AC. There was no difference in D0.2cc of GI-lumen (26.1 Gy versus 30.4 Gy; p = 0.2) or other GI-CS between AC versus non-AC. Three patients had acute Grade-1 anorexia, one patient had acute Grade-2 gastritis. There was no Grade  $\geq 3$  acute or chronic toxicity.

**Conclusions:** Use of AC did not confer any dosimetric inconsistency for GI-CS in our study. There was a significant improvement in V30 of GI-lumen with use of AC. The current cohort, originally treated using AC, completed their treatment course with minimal toxicity.

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#### PRESENTING STAGE AND RISK GROUP IN MEN WHO DIE OF PROSTATE CANCER

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**Purpose:** To describe the stage and risk groups at diagnosis of patients that die of prostate cancer at a population level.

**Materials and Methods:** All men who died of prostate cancer between January 2013 and December 2015 were identified in a provincial cancer registry. Patients were excluded if they had other cancer diagnosis or had diagnosis on death certificate or autopsy. Cases were linked to administrative records stage, Gleason grade and baseline PSA to define stage and risk group categories using a predefined algorithm. This "Administrative Risk Group" in (ARG) was then compared to risk group attained on chart review in a random sample of cases. All cases that had unknown ARG had chart reviews of available medical records to define a "Chart Review Risk Group" (CRRG). Main risk groupings were localized, regional, metastatic, or unknown. Localized was further characterized as low, moderate, or high risk (using Canadian Consensus risk groupings) and localized not-otherwise-specified (NOS). A best combined stage grouping was developed using ARG and CRRG (where ARG was unknown stage).

**Results:** 1256 patients were identified. Initial presenting stage groups were as follows: 57% localized (low 3.6%, intermediate 8.9%, high 39.1%), 3% regional, 32% metastatic, and 7% unknown. Median survival within subgroups was: eight years for localized (low 12 years, intermediate 13.4 years, high 6.6 years), four years for regional, 1.7 years for metastatic, and 11.3 years for unknown. Of those with known stage at diagnosis, 80% presented with either localized high risk, regional or metastatic disease. ARG and CRRG were in agreement for localized versus metastatic presentation in over 90% of random sample cases.

**Conclusions:** The majority of patients that die of prostate cancer present with either high risk localized, regional or metastatic disease. In order to alter the death rate from prostate cancer, interventions need to focus on altering the natural history of these advanced presentations. Whether interventions to prevent, identify or intervene at an earlier stage of the disease would alter mortality is unclear.

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#### EPID RECONSTRUCTION OF THE DELIVERED PATIENT RADIATION DOSE FOR NON-COPLANAR BEAM THERAPY

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**Purpose:** External beam photon therapy techniques, including VMAT, attempt to deliver high doses of radiation to the tumour while limiting doses

to normal tissues and critical organs. To improve on current approaches to achieve this, in recent years many research groups have investigated the opportunity of using non-coplanar beam arrangements by introducing dynamic couch movements into clinical VMAT plans. This approach can reduce irradiation of critical structures and provide better dose conformity to the target. However, the use of a moving treatment couch leads to the necessity of more stringent quality assurance. In particular, an in vivo measurement of the dose actually delivered to the patient, based on transmission EPID images, can be used. Currently, CancerCare Manitoba has implemented such an in vivo patient dose reconstruction system, but it only works with standard coplanar beam geometry.

**Materials and Methods:** The purpose of this research was, therefore, to add new functionality to the previously developed patient 3D dose verification system, allowing it to work with prospective treatment techniques that use non-coplanar beam arrangements. Five non-coplanar trajectories were created in Varian Developer mode, since the clinically used treatment planning system (Eclipse, Varian Medical Systems) does not support dynamic couch yet. Couch coordinates were introduced into existing Matlab program code of the dose reconstruction model, to account for patient/phantom movement during beam delivery. The test trajectories were delivered on an Edge linear accelerator (Varian Medical Systems) with the EPID deployed and acquiring images in “continuous” mode.

**Results:** The experimental 3D dose distributions were then calculated and validated against reference distributions obtained from Eclipse (for static couch non-coplanar arcs) and Varian Virtual Linac (for trajectories using dynamic couch). The chi-comparison test with 3%/3 mm criteria between experimental and predicted dose matrices resulted in at least 97.7% pass rate for all trajectories.

**Conclusions:** This comparison demonstrates that EPID dose reconstruction is a promising method for in vivo patient 3D dose verification that can be used for quality assurance of complex non-coplanar treatments incorporating dynamic couch movements.

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#### LAYING THE GROUNDWORK FOR ACCURATE CHERENKOV EMISSION-BASED ELECTRON BEAM DOSIMETRY

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**Purpose:** Develop and evaluate an uncertainty benchmark for a Cherenkov emission (CE)-based dosimetry formalism through simulations and experiments with electrons.

**Materials and Methods:** The proposed formalism consists of CE detection from water with optics at specified field of view (FOV), primary standards-traceable calibration  $N$ , and equation  $D(Q) = M(Q) N kC(\theta \pm \delta\theta, Q)$ , where  $Q$  is beam quality,  $D$  is central-axis absorbed dose under reference conditions,  $M$  is temperature-corrected reading, and  $kC$  is the CE-to-dose conversion for CE detection polar angles  $\theta \pm \delta\theta$  relative to beam. SPRRZnrc was modified (med2 stopping power changed to med1 CE power) to calculate  $kC$  for twenty 4-22 MeV electron beams from 4 clinical BEAMnrc models,  $10 \times 10$  cm<sup>2</sup> field, 100-cm SSD, and  $\theta \pm \delta\theta$  of  $90^\circ \pm 90^\circ$  ( $4\pi$ ),  $90^\circ \pm 5^\circ$ ,  $42^\circ \pm 5^\circ$ . Relative experimental feasibility was evaluated with 6-20 MeV at  $90^\circ$  and  $FOV \leq 2^\circ$ , using preliminary detector design with spherical optics and geometrical approximations. Beam quality and reference depth specification based on  $R50$ , obtained from 50% CE depth  $C50$ , are proposed and a preliminary uncertainty budget is calculated.

**Results:** For 0.1-50 MeV electrons in a 1- $\mu$ m slab, calculated CE intensity and angle were in agreement with theory to  $\pm 0.03\%$  and  $\pm 0.01^\circ$ . Due to practical considerations,  $42^\circ$  detection was found unsuitable for CE-based dosimetry. For dosimetry near  $d_{ref}$  and  $R50$ ,  $90^\circ$  may be recommended. For surface dosimetry, due to high  $kC(90^\circ \pm 5^\circ)$  depth dependence, alternative configurations may be necessary. Measured relative  $kC$  factors were in agreement with simulation within 1% for depth variations about  $d_{max}$  of the order of 1 cm. At other depths, deviations were in accordance with known detector limitations. Reproducibility was  $\leq 1\%$  for percent-depth  $CE > 50\%$  with reassembly, refocus, recollimation, and  $\pm 1$  cm lens curvature/position changes. Variations in  $\delta\theta$  of  $4^\circ$  resulted in calculated  $kC(90^\circ \pm 5^\circ)$

uncertainties of  $< 6\%$  at surface and  $< 2\%$  elsewhere. Variations of  $0.5^\circ$  in the FOV corresponded to experimental relative  $kC$  uncertainties of  $\leq 1\%$  for percent-depth  $CE > 50\%$  (dominated by reproducibility). Calculated  $R50$  was fit in terms of  $C50$  (in units of cm) as  $R50 = 0.0007484 C50 + 1.0106 C50 + 0.1294$  for  $4\pi$  detection (rmsd = 0.05 mm, maximum deviation = 0.10 mm) and  $R50 = -0.0108 C50 + 1.041 C50 + 0.001$  for  $90^\circ \pm 5^\circ$  detection (rmsd = 0.19 mm, max. dev. = 0.30 mm). Calculated  $kC$  at  $d_{ref}$  was fit in terms of  $R50$  (in units of cm) as  $kC = 0.0077794 R50^{0.13365} + 0.006572 R50^{-0.7050}$ ,  $d_{ref} = 0.6 R50 - 0.1$ , at  $4\pi$  (rmsd = 0.30%, max. dev. = 0.51%) and  $kC = 0.1238 R50^{0.6525} + 1.113 R50^{-4.067}$ ,  $d_{ref} = 0.5 R50 + 0.1$ , at  $90^\circ \pm 5^\circ$  (rmsd = 0.56%, max. dev. = 1.27%). The standard uncertainty calculated from our simulation and relative experimental results was 1.0% at  $4\pi$  and 1.2% at  $90^\circ \pm 5^\circ$  detection.

**Conclusions:** We lay the groundwork for clinical implementation of CE-based electron beam dosimetry and demonstrate potential uncertainty on the order of 1%.

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#### A COMPARATIVE STUDY OF QUALITY OF LIFE IN PATIENTS WITH LOW- AND INTERMEDIATE-RISK PROSTATE CANCER: STEREOTACTIC RADIOTHERAPY VERSUS HIGH DOSE-RATE BRACHYTHERAPY MONOTHERAPY VERSUS HIGH DOSE-RATE BRACHYTHERAPY BOOST

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**Purpose:** Stereotactic ablative radiation therapy (SABR) and high dose-rate brachytherapy (HDR) have been investigated as methods of dose escalation for the treatment of localized prostate cancer (PCa), with excellent reported disease control rates, yet substantially different toxicity profiles. We aim to compare the health-related quality of life (HRQoL) deterioration at 12 months in favourable PCa patients treated with SABR, HDR monotherapy and HDR boost.

**Materials and Methods:** Patients treated as part of seven prospective clinical trials were included in this analysis. All patients had low- or intermediate-risk PCa. Three dose escalation strategies were considered: 1) SABR [35-40Gy/5 fr], 2) HDR monotherapy [19-27Gy/1-2 fr], 3) HDR boost [HDR 15-20 Gy/1-2 fr + external beam radiotherapy (EBRT) 37.5-45 Gy /15-25 fr]. HRQoL was prospectively measured at baseline and 12 months in all trials, using the Expanded Prostate Index Composite (EPIC). A minimally important difference (MID) was defined as a deterioration of HRQoL scores at 12 months compared to baseline  $\geq 0.5$  standard deviation of baseline score. Univariate and multivariable logistic regression using generalized estimating equations were used to compare the proportion of patients having MID between groups. To test the robustness of the results, a set of sensitivity analyses was conducted. Dynamic changes over time were compared using general linear mixed models after assuming individual patient and trial with random effect. A two-tailed  $p$ -value  $\leq 0.05$  was considered statistically significant.

**Results:** Six hundred and forty-eight patients were included; 288, 173 and 187 respectively in the SABR, HDR monotherapy and HDR boost group. Overall, patients treated with SABR were older (mean age:  $69 \pm 7$ ,  $65 \pm 7$  and  $67 \pm 7$ ,  $p < 0.001$ ) with larger prostates [median volume: 37cc, (interquartile range (IQR): 28-51), 35cc, (IQR: 27-41) and 33cc (IQR: 25-40),  $p < 0.001$ ). On univariate and multivariable analyses, SABR and HDR monotherapy compared to HDR boost, were associated with less deterioration in the urinary (38%, 40% versus 55%; OR: 0.543, 95% CI: 0.320-0.922,  $p = 0.024$ ; OR: 0.468, 95% CI: 0.432-0.507,  $p < 0.001$ ) and sexual domains (38%, 42% versus 47%; OR: 762, 95% CI: 0.645-0.900,  $p = 0.001$ ; OR: 0.786, 95% CI: 0.650-0.949,  $p = 0.012$ ). In the bowel domain, the odds of having bowel MID were 65% lower if patients were treated with HDR monotherapy (19% versus 40%; OR: 0.354, 95% CI: 0.278-0.449,  $p < 0.001$ ) compared to HDR boost, however no significant difference was found between SABR and HDR boost (39% versus 40%,  $p = 0.85$ ). The comparison of dynamic changes of normalized EPIC scores between the three groups suggested similar results. These findings were robust to a variety of sensitivity analyses.

**Conclusions:** In the absence of a randomized clinical trial, this analysis suggests that monotherapeutic approaches should be preferred in the

setting of favourable-risk PCa to preserve patients HRQoL. Ultimately, the questions of efficacy, toxicity, and HRQoL will be best answered by a randomized clinical trial.

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### SUBCUTANEOUS SPACER INJECTION TO REDUCE SKIN TOXICITY FOR ACCELERATED PARTIAL BREAST BRACHYTHERAPY

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**Purpose:** Accelerated partial breast irradiation (APBI) is a treatment option for selected early stage breast cancer patients. Some APBI techniques may lead to delayed and permanent skin side effects with the skin being the main risk factor. Biodegradable spacers are proposed in prostate brachytherapy as an effective and safe method to protect the rectum wall. We hypothesize that similarly a spacer injection between the skin and the target volume reduces the skin dose in breast brachytherapy. This work tests two different spacers in mastectomy specimens.

**Materials and Methods:** Ultrasound guided spacer injections, using hyaluronic acid (HA) or iodinated polyethylene glycol (PEG), were performed on fresh mastectomy specimens. Injection success was defined as the creation of a subcutaneous space  $\geq 5$  mm with at least a 20 mm radius. Usability was scored using the System Usability Scale (SUS, 0-100 score). Pre- and post-injection CT-scans were used to generate brachytherapy plans, segmenting a virtual clinical target volume (CTV). To evaluate the plans, the V100 and V200 were calculated. Maximum dose to small skin volumes (D0.2cc) and the existence of skin hotspots (corresponding to isodose  $\geq 90\%$  on 1 cm<sup>2</sup> of the skin surface) were calculated as skin toxicity indicators.

**Results:** We collected 22 mastectomy specimens. Half had an HA injection and the other half a PEG injection. Intervention success was 100% for HA and 90.9% for PEG ( $p = \text{NS}$ ). Hydro-dissection was feasible in 81.8% with HA and 63.6% with PEG. Median SUS score was 97.5 for HA and 82.5 for PEG ( $p < 0.001$ ). Mean D0.2cc was 80.8 Gy without spacer and 53.7 Gy with spacer ( $p < 0.001$ ). Skin hotspots were present in 40.9% of the plans without spacer but none with spacer injection ( $p < 0.001$ ).

**Conclusions:** A spacer injection in the human breast is feasible to create an extra protection layer for the skin. An extra 5 mm space was always achieved, thereby reducing the skin dose significantly in breast brachytherapy.

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### THE IMPACT OF INTRAPROSTATIC CALCIFICATIONS ON BIOCHEMICAL CONTROL AFTER PERMANENT PROSTATE IMPLANT

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**Purpose:** To evaluate the impact of intraprostatic calcifications on long term tumour control in patients treated with Iodine 125 permanent implant for localized prostate cancer.

**Materials and Methods:** Data from 609 prostate cancer patients treated with I-125 seeds were retrospectively reviewed. The presence of intraprostatic calcifications was determined by reviewing the post implant CT images. Doses delivered to the target were determined using the Monte Carlo method taking into account the heterogeneities and the standard TG43 approach as previously described in [1,2]. The biochemical relapses at seven and 10 years were determined according to Phoenix definition. Long-term biochemical relapse-free survival (bRFS) was determined using Kaplan Meier estimates with log rank test. Cox proportional hazard models were used for univariate and multivariate analysis predictor factors of biochemical recurrence. The acute and late GU and GI toxicity were evaluated and compared with Chi-square test (or Fisher exact test).

**Results:** The review of the post implant CT images revealed intraprostatic calcification in 68 (11.1%) out of 609 patients. Mean age was slightly higher in

patients with Calcifications: 64.8 versus 63.1 years ( $p = 0.049$ ) while Median follow-up was not different between groups: 82 (with) versus 83 months (without) ( $p = 0.651$ ). Clinical Stage, PSA, Gleason score, D'Amico risk group and ADT use were comparable between the two groups. The seven-, 10-year bRFS for the entire cohort were 94.1% and 90.6%. The bRFS at seven years was 90.5% (with) versus 94.5% (without) ( $p = 0.198$ ). The corresponding values at 10 years were 78.8% versus 91.8% ( $p = 0.046$ ). On Cox regression model, only prostatic calcifications appeared to be a significant risk factor for biochemical relapse (HR: 2.30; IC95% 1.05-5.00;  $p = 0.037$  and HR: 3.94; IC95% 1.00-15.38;  $p = 0.049$  for univariate and multivariate analysis). There was no difference between the two groups for urinary symptoms (IPSS) as well as acute and late RTOG GU and GI toxicity. No Grade 4 toxicity was observed. There were only two cases of Grade 3 acute GU toxicity in patients without calcifications. As previously published, the presence of calcifications in the prostate were associated with localized cold spots on Monte Carlo post-implant dosimetry that translated into up to 25% lower whole gland V100 and D90 not taken in account with TG43 dosimetry.

**Conclusions:** The presence of calcifications in patients treated with permanent seed implant decreases V100 and D90 on the post-implant Monte Carlo dosimetry. These calcifications are also associated with an increased risk of bRFS in multivariate analysis and a lower 10-year bRFS. Seed implants should be used with caution in patient with intraprostatic calcifications. Model-based dose calculation is important to evaluate the potential cold spots caused by these calcifications.

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### RESULTS OF A PHASE II PROSPECTIVE STUDY ON DOSE ESCALATION TO THE DOMINANT INTRA-PROSTATIC LESIONS (DILS) WITH ULTRASOUND (US)-PLANNED HDR PROSTATE BRACHYTHERAPY

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**Purpose:** Dose escalation for prostate cancer improves biochemical failure-free survival. Dose fractionation in HDR prostate brachytherapy (BT) has been steadily evolving as fraction number is reduced. Current fractionation is based on tolerance for whole gland treatment. We investigated whether 25% dose escalation to the DIL would alter efficacy or tolerance.

**Materials and Methods:** Twenty-six patients with predominantly unilateral intermediate or high risk prostate cancer were recruited to this IRB-approved Phase II trial. Treatment consisted of HDR BT in 2 fractions of 10 Gy and pelvic external beam radiotherapy (EBRT: 46Gy/23 fractions) +/- androgen deprivation (ADT). The first HDR fraction was five days before starting EBRT and the second one week into EBRT. Prior to treatment, multiparametric MRI (1.5T+ endorectal coil) was performed to identify and contour the DIL. The mpMRI was registered with the pre-procedure TRUS to transfer the DIL to the US which intra-operatively can be easily registered to the US image set with the treatment needles. Planned DIL dose escalation was  $> 25\%$  while respecting critical organ and homogeneity constraints. We compare results for this cohort to a previous cohort of 25 patients treated identically but without DIL identification. Toxicity was graded using CTCAE v.3.0. Descriptive and inferential statistics were used.

**Results:** Fifty-one patients were analysed. Median follow-up is 61 months (range: 47-79), age 65 years (50-79), iPSA 9.3 ng/ml (1.3-20.0) and baseline IPSS score 5 (0-21). Ninety-two per cent were intermediate risk, predominantly (92%) Gleason 7. Mean prostate volume was 40cc (SD 11). ADT was used in 29% for a median of six months (2-12). Mean PSA nadir for non-failing patients with no prior ADT was 0.07 (SD 0.07) ng/mL at a mean of 53 months (SD 8) (not yet reached in three patients). Five-year PSA is 0.10 (SD 0.11). Failure occurred in seven patients: one biochemical, one local (salvaged by radical prostatectomy), two regional and three distant. Mean time to return to baseline IPSS was 3.4 months (SD 3.7). Two patients had urethral strictures requiring urethrotomy. Five patients experienced late hematuria. Late rectal toxicity was 10% G1, 4% G2 and 2% G3. Twenty-five

of 26 patients had a DIL (three multiple) on mpMRI. Mean DIL D90 was 132% (SD 10%) of prescription. When comparing the two groups, follow-up was longer in the non-DIL cohort, 65 versus 56 months ( $p < 0.001$ ) with no significant differences in baseline characteristics, toxicity or treatment failure. However, time to PSA nadir was significantly shorter in the DIL dose escalation cohort, 49 versus 56 months ( $p = 0.03$ ), with a nadir of 0.06 versus 0.08 despite shorter follow up.

**Conclusions:** Incorporation of mpMRI into the workflow of US-planned HDR prostate BT is feasible, permitting dose escalation to DILs while respecting the tolerance of adjacent organs-at-risk. Focal dose escalation may shorten the time to nadir, with no additional late toxicity. Longer follow up is necessary to demonstrate ultimate efficacy.

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### ISODOSE SURFACE VOLUMES IN CERVIX CANCER BRACHYTHERAPY: COMPARISON OF STANDARD (POINT A) AND INDIVIDUALIZED IMAGE GUIDED ADAPTIVE (EMBRACE) BRACHYTHERAPY

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**Purpose:** To investigate the isodose surface volumes (ISVs) for 85, 75 and 60 Gy EQD2 for locally advanced cervix cancer patients enrolled in the multi-institutional EMBRACE clinical trial. The hypothesis of this analysis was that individualized Image Guided Adaptive Brachytherapy (IGABT) in conjunction with the use of combined intracavitary/interstitial brachytherapy (IC/IS-BT) leads to improved dose conformity and an overall reduction of the ISVs as compared to standard loading, point A based BT.

**Materials and Methods:** 1201 patients accrued in the EMBRACE study were analysed. EBRT with concomitant chemotherapy was followed by MR based IGABT. Different EBRT/BT fractionation schedules, BT dose rates (HDR/PDR), applicator designs (T&O, T&R, moulds, etc) and implant types (IC or IC/IS) were used. For the ISV calculation of the standard loading systems, 85, 75 and 65Gy EQD2 Point A-prescribed plans were produced in Oncentra treatment planning system for different sized T&R and T&O applicators, including tandem lengths from 4-6 cm, ring diameters of 26, 30 and 34 mm and ovoid inter-channel spacing of 15, 20 and 25 mm. The EMBRACE EQD2 ISVs were calculated for both a/b 10 Gy (tumour) and 3 Gy (late adverse effects) using a predictive model based on Total Reference Air Kerma (TRAK). ISVs and conformity index (CI) were evaluated for IC and IC/IS BT and T&R or T&O applicators.

**Results:** Median HR CTV D90% and volume were 89.9 Gy and 28.4 cm<sup>3</sup>, respectively. The median HR CTV volume treated with IC/IS-BT was 38.0 cm<sup>3</sup> versus 23.6 cm<sup>3</sup> for IC-BT. Median EQD2\_10 V85 Gy, V75 Gy and V60 Gy were 71 cm<sup>3</sup>, 99 cm<sup>3</sup> and 230 cm<sup>3</sup>, respectively, and depended on HR CTV volume. For small (<25 cm<sup>3</sup>), intermediate (25–35 cm<sup>3</sup>) and large (>35 cm<sup>3</sup>) HR CTV volumes, the V85 Gy increased from 57 cm<sup>3</sup>, to 70 cm<sup>3</sup> and 88 cm<sup>3</sup>, respectively. Median V85 Gy was 24% smaller than in standard 85 Gy Point A prescription. Thirty-seven percent of patients were treated with ISVs similar to those of standard loading of 75–85 Gy to Point A. Forty-two percent of patients were treated with V85 Gy smaller than with standard 75 Gy at Point A, proving volume de-escalation with IGABT. Twenty-one percent of patients, of which two thirds had large HR CTV (> 35 cm<sup>3</sup>), were treated with V85 Gy larger than in standard 85 Gy to Point A to ensure adequate target coverage. T&R was more conformal than T&O with CI being 23% and 16% smaller for T&R in the IC and IC/IS groups, respectively. CI was 9% and 17% smaller for IC/IS than for IC in T&R and T&O groups, respectively. For the same treated V85Gy EQD2\_10, the corresponding V85Gy EQD2\_3 were, on average, 30% larger for HDR and 14% for PDR.

**Conclusions:** The MR-IGABT led to improved target coverage/conformity

while the irradiated volumes, on average, were reduced compared to standard plans. The ISVs depended strongly on HR CTV volume proving dose adaptation according to individual response. Dose conformity increased with the use of T&R and with more frequent application of IC/IS implants.

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### MULTI-INSTITUTIONAL STUDY OF SALVAGE IRRADIATION WITH SINGLE-MODALITY INTERSTITIAL BRACHYTHERAPY FOR THE TREATMENT OF RECURRENT GYNECOLOGICAL TUMOURS IN THE PELVIS

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**Purpose:** Recurrent gynecological (GYN) tumours can cause significant morbidities for patients with limited options of salvage therapy. Patients who are not candidates for aggressive salvage surgery are often managed with a palliative approach. This study investigates the strategy of high-dose salvage radiation with single-modality interstitial brachytherapy (SM-ISBT) for the management of recurrent GYN pelvic disease at two specialized interstitial brachytherapy centres.

**Materials and Methods:** Patients with gynecological malignancies who had received SM-ISBT for salvage treatment from September 2008 to January 2017 were included. All patients had recurrent gynecological tumours confined to the pelvis with no distant metastasis. Local and regional control, distant metastasis and long-term toxicities were evaluated.

**Results:** A total of 27 patients with a median follow-up of 20 months (IQR 11–31) after SM-ISBT were included. The primary cancer sites were endometrium (20), cervix (three), vulva (one), vagina (two), rectum (one). All patients had prior pelvic radiation [external-beam radiation (11), brachytherapy (one) or both (15)], and SM-ISBT was delivered as salvage re-irradiation. Median disease-free survival was 20.8 months (IQR 12.1–32.4). SM-ISBT was delivered with a dose of 500 to 700c Gy for 3 to 6 fractions over two to 19 days, with a median EQD2 of 28.4 Gy (range 19–50 Gy). Overlap with previous radiation volume was complete (52%), partial (44.5%), or none (3.5%). Median EQD2 in complete, partial, and no overlap group was 26.8, 32.7 and 35.5 Gy, respectively ( $p = 0.59$ ). After SM-ISBT, complete and partial response were achieved in 17 (63%) and six (22.2%) patients, respectively. Two (7.4%) patient had Grade 3 toxicities (both vaginal stenosis), with no patients experiencing Grade 4 complications. Ten (37%) patients had Grade 1 or 2 toxicities. Seventeen patients (63%) had recurrence, including local, regional and metastatic in 15 (55.5%), seven (6%), and four (14.8%) patients, respectively. At the last follow up, 17 patients (63%) were alive.

**Conclusions:** Salvage radiation with SM-ISBT for recurrent GYN malignancies in the pelvis is feasible and safe and is associated with acceptable rates of toxicities with reasonable local control rates. With limited treatment options available for recurrent GYN tumours in the pelvis, developing strategies to address this morbid local disease is a priority. Prospective multi-institutional studies are warranted to further investigate SM-ISBT as a standard option for salvage GYN treatment.

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### COMPARISON OF LOCAL FAILURE AND RADIONECROSIS ACCORDING TO DOSE PRESCRIPTION FOR SMALL TO MEDIUM SIZED BRAIN METASTASIS TREATED WITH RADIOSURGERY

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**Purpose:** To examine the impact of gamma knife radiosurgery (SRS) marginal prescription dose (PD) (15 Gy versus 16–20 Gy versus > 20 Gy) on local failure (LF) and radionecrosis (RN) for small- to medium-sized ( $\leq 2$  cm) brain metastasis (BM) in a large single-institution series.

**Materials and Methods:** We identified patients from a prospective registry of BM patients treated with SRS between 2006 and 2017. At our institution, we commonly treat lesions adjacent to eloquent structures with a lower PD

to reduce the likelihood of toxicity. We used defined criteria to differentiate LF from RN, including pathology, when available. Cumulative incidences of LF and RN were calculated using Fine and Gray's competing event analysis, with death as a competing event. Patient, tumour, and treatment factors were assessed for their impact on LF and RN.

**Results:** We reviewed 462 patients with 1609 BM  $\leq 2$  cm. Lung (51.1%), melanoma (14.3%) and breast (13.9%) were the most common primary histology. Sixty percent of the patients received pre- or post-SRS (including salvage) whole brain brain radiotherapy. Median overall survival and radiographic follow-up was 19.7 months (95%CI 17.4 to 23.3 months and 13.4 months (IQR 7.9-22.4 months), respectively. 1065 lesions (66%) were treated with PD  $> 20$  Gy, 80 lesions (5%) with 16-20 Gy and 464 lesions (29%) with  $< 15$  Gy. Cumulative LF rates at two years were 15.2% (95%CI 6.2-24.3%) for 15 Gy, 11.9% (95%CI 0-29.5%) for 16-20 Gy, and 6.4% (95%CI 2.2-10.6%) for  $> 20$  Gy ( $p < 0.0001$ ). Cumulative RN rates at two years were 5.5% (95%CI 0-11.6%) for 15 Gy, 6.2% (95%CI 0-17.9%) for 16-20 Gy and 6.4% (95%CI 2.4-10.3%) for  $> 20$  Gy ( $p = 0.2381$ ). Tumour size  $\leq 1$  cm was associated with a significantly lower rate of LF (HR 0.318 (95%CI 0.216-0.468;  $p < 0.0001$ ) and RN (HR 0.194 (95%CI 0.120-0.314;  $p < 0.0001$ ) compared to BM  $> 1$  cm. Cumulative LF and RN rates at two years for lesions  $\leq 1$  cm was 4.7% (95%CI 0.08-8%), and 2.6% (95%CI 0-5.4%), respectively. Cumulative LF and RN rates at two years for lesions  $> 1$  cm was 15.3% (95%CI 8%-22%) and 11.8% (5.1-18.5%), respectively. For lesions  $> 1$  cm, LF occurred in 9.5% versus 5% of tumours treated with 15 Gy and  $> 20$  Gy, respectively ( $p = 0.0003$ ). There was a significantly increased risk of RN for lesions  $> 1$  cm treated with  $> 20$  Gy versus 15 Gy (6.10% versus 3.23%;  $p = 0.0011$ ).

**Conclusions:** Our results suggest that for BM  $> 1$  cm treated with SRS, 15 Gy provides inferior local control compared to  $> 20$  Gy, but is associated with a lower rate of RN. For lesions  $\leq 1$  cm, LF and RN incidences are both  $< 5\%$ .

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#### COMPARISON OF THE CLINICAL BEHAVIOUR OF N3 HPV RELATED AND UNRELATED HEAD AND NECK CANCER IN THE IMRT ERA

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**Purpose:** N3 disease is accepted as having grave prognosis in all forms of head and neck cancer (HNC). We wished to compare clinical presentation, radiological nodal response, and neck outcome after definitive IMRT in N3 HPV-related (HPV+) versus -unrelated (HPV-) HNC.

**Materials and Methods:** We retrospectively reviewed all N3 HNCs undergoing definitive IMRT  $\pm$  chemotherapy from 2005-2015. HPV status was tested by p16 staining for all oropharyngeal cancers (OPC) and cancer of unknown primary (CUP). HPV untested laryngo-hypopharyngeal cancer (LHC) were considered HPV-. Clinical presentation, radiological complete response [CR, e.g. Lymph node (LN)  $\leq 1.0$  cm] at 8-12 weeks following IMRT, and oncologic outcomes were compared between HPV+ versus HPV- cohorts. Multivariable analyses (MVA) identified prognostic factors for regional failure (RF).

**Results:** Of 129 consecutive N3 HNC, HPV status was ascertained in 119 (92%) revealing 66 HPV+ (OPC/CUP: 65, LHC: 1) and 53 HPV- (OPC/CUP: 29, LHC: 24) cases. Compared to HPV-, HPV+ patients were younger (median 58 versus 62 years,  $p = 0.006$ ), had fewer smoking pack-years (median 14.5 versus 40  $p < 0.001$ ), but similar proportions of T3-4 disease (47% versus 39%,  $p = 0.48$ ). HPV+ LNs were more often cystic (41% versus 23%,  $p = 0.049$ ), non-conglomerate (23% versus 8%,  $p = 0.04$ ), and had less skin invasion (30% versus 51%  $p = 0.025$ ) or carotid encasement (21% versus 42%,  $p = 0.02$ ). Rates of retropharyngeal LNs (38% versus 27%,  $p = 0.11$ ), bilateral LNs (45% versus 43%,  $p = 0.85$ ), necrotic LNs (85% versus 89%,  $p = 0.60$ ) and radiological extranodal extension (64% versus 64%,  $p > 0.99$ ) were similar. Concurrent systemic treatment was given in 83% HPV+ versus 57% HPV- ( $p = 0.006$ ). More HPV+ N3 achieved radiological CR (44%

versus 25%,  $p = 0.034$ ). Post-IMRT neck dissection (PRND) was negative in all three CRs (HPV+ 2; HPV- 1) but positive in five of 19 (26%) HPV+ and seven of 13 (58%) HPV- non-CRs ( $p = 0.15$ ). Median follow-up was 4.6 years. RF occurred in 36 (HPV+ 11, HPV- 25). No CR without PRND patients (HPV+: 27, HPV-: 12) had isolated RF. HPV+ patients had higher three-year overall survival (67% versus 28%,  $p < 0.001$ ), local control (97% versus 85%,  $p = 0.021$ ), and regional control (RC) (85% versus 53%,  $p = 0.021$ ) but similar distant control (77% versus 60%,  $p = 0.078$ ). HPV- non-CR patients had lower three-year RC versus CRs (43% versus 85%,  $p = 0.01$ ) and was marginally lower in HPV+ (76% versus 96%,  $p = 0.05$ ). No significant difference in three-year RC was evident in CR patients by HPV status (96% versus 85%,  $p = 0.44$ ). Presence of post-IMRT necrotic LNs (HR 2.8, 95% CI 1.2-6.6,  $p = 0.02$ ) carried a higher RF risk in MVA.

**Conclusions:** This study shows that HPV+ N3 HNC has unique clinical presentation (less dermal involvement and degree of carotid encasement) and outcomes, relative to HPV- HNC patients. CR is achievable in nearly half the HPV+ and a quarter of HPV- cases with IMRT. Although the sample size is small, patients with CR appear to have good RC in both cohorts. This suggests that careful surveillance is a reasonable option for those with CR. Presence of post-IMRT necrotic LN carries a higher RF risk.

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#### CHANGE OF RADIOTHERAPY PRACTICE PATTERN IN LYMPHOMA AT A LARGE ACADEMIC CENTRE

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**Purpose:** To compare the practice pattern of radiotherapy (RT) in lymphoma between 2000 and 2015 at a large academic centre with stable volumes and referral pattern. Decrease utilization of RT has been observed in population studies over the last 20 years, however, little has been reported in the change of practice pattern.

**Materials and Methods:** All patients who received RT in 2000 or 2015 for lymphoma at our centre were reviewed. In patients who received multiple courses of RT in the same year, the first course was indexed. Proportions of groups between the two calendar years were compared by Pearson Chi-square/Fisher exact tests and adjusted for multiple comparisons when indicated. Wilcoxon rank-sum test were used to compare RT doses.

**Results:** Our centre provided RT to 270 lymphoma patients (300 courses) in 2000 and 253 patients (282 courses) in 2015. Shift in lymphoma types that received RT was observed with a decrease in Hodgkin's lymphoma (HL,  $n = 72$  versus 44, 27% versus 17%,  $p = 0.075$ ) and an increase in mantle cell lymphoma (MCL,  $n = 5$  versus 19, 2% versus 8%,  $p = 0.016$ ) while other types remained stable: DLBCL 39% versus 32%; follicular lymphoma (FL) 13% versus 15%; MALT lymphoma 11% versus 12%, primary CNS lymphoma 2% versus 6%, others 7 versus 9% (comparing 2000 versus 2015). RT use as a component in primary management has decreased ( $n = 195$  versus 140, 72% versus 55%,  $p < 0.001$ ). Overall, significant change in the role of RT was observed from 2000 to 2015 ( $p < 0.001$ ) with decreased combine modality therapy received (CMT,  $n = 126$  versus 70, 47% versus 28%,  $p < 0.001$ ); while palliative RT increased ( $n = 52$  versus 103, 19% versus 41%,  $p < 0.001$ ). Conditioning total body irradiation in the setting of stem cell transplant increased due to its use in MCL in 2015 ( $n = 0$  versus 12, 0 versus 5%,  $p = 0.002$ ). For adult HL patients, the absolute number of cases of CMT decreased from 48 to 23 in 2015. The prophylactic upper abdominal RT in Stage I-II HL ( $n = 18$ , 34% in 2000) was not used in 2015 ( $p < 0.001$ ). The RT dose for CMT in HL and DLBCL had decreased from 2000 to 2015 (median 35 Gy versus 30 Gy,  $p < 0.001$ ). For DLBCL, a trend of decrease in CMT ( $n = 60$  versus 32, 58% versus 39%,  $p = 0.057$ ) and an increase in palliation ( $n = 22$  versus 33, 21% versus 40%,  $p = 0.028$ ) were observed. No significant practice pattern change was seen in FL and MALT lymphoma.

**Conclusions:** Significant practice change of RT in lymphoma has been observed over 15-year period at a large academic institution. The shifting RT role toward palliative setting was observed.

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### WHAT'S THE MATTER WITH MATTED NODES? SIGNIFICANCE OF MATTED LYMPH NODES IN HPV-RELATED OROPHARYNGEAL SQUAMOUS CELL CARCINOMA: A MULTI- INSTITUTIONAL POPULATION-BASED COHORT STUDY

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**Purpose:** HPV-related oropharyngeal squamous cell carcinoma (OP SCC) is associated with favourable outcomes compared to non-HPV related OP SCC. Given its poor prognostic significance, the presence of matted lymph nodes has even become an exclusion criteria from some treatment de-escalation trials. However, its prognostic significance should be independently validated and the radiologic criteria for matted nodes needs to be further defined.

**Materials and Methods:** Patients diagnosed with p16+, Stage III-IVb OP SCC, treated with curative intent, diagnosed between January 2007 to April 2013, with available diagnostic CT images were retrospectively reviewed. Pre-treatment images were independently scored by a radiologist according to three radiologic nodal characteristic groups: two or more abutting nodes (group A); one or more lymph nodes (LNs) with surrounding extracapsular spread (ECS) (Group E); nodes with intervening ECS between abutting LNs but not around them (Group I). Overall survival (OS) and local, regional and distant recurrence-free survival (RFS) was calculated based on Kaplan-Meier (KM) method and compared by log-rank test. Multivariate analysis, accounting for age, sex, comorbidity, smoking status, primary treatment modality, subsite and stage, was also performed.

**Results:** Between January 2007 to April 2013, 260 patients with locally advanced p16+ OP SCC were diagnosed and treated with curative intent. Median follow-up was median 4.96 years (range 0.21-5.00 years) and mean age was 57 years ( $\pm$  SD 8). Distribution of radiologic nodal characteristic groups is as follows: A (n = 54), E (n = 46), I (n = 79). Overall survival at five years was 79.6% (A) versus 78.6% (no A), p = 0.87; 65.2% (E) versus 81.8% (no E), p = 0.01; and 81.0% (I) versus 77.9% (no I), p = 0.57. RFS at five years was 81.5% (A) versus 84% (no A), p = 0.66; 72% (E) versus 86% (no E), p = 0.02; and 86.1% (I) versus 82.3% (no I), p = 0.45. By univariate analysis, the presence of E versus no E is significantly associated with OS, RFS, and distant RFS (all p = 0.01); and the presence of I nodes versus no I is significantly associated with local RFS (p = 0.02). By multivariate Cox regression analysis, at five years, E nodes was statistically significantly associated with distant RFS with a hazard ratio (HR) of 5.2 and 95% CI [1.2-22.1] (p = 0.02).

**Conclusions:** In this multi-institutional study, the prognostic significance of three different radiologic nodal characteristic groups in Stage III-IVb, p16+ OP SCC is evaluated, and previously variable definition of matted nodes is further defined. The presence of group E nodes was significantly associated with five-year OS, RFS, and distant RFS by univariate analysis and distant RFS by multivariate analysis. This suggests that ECS is a strong prognostic indicator and should be considered in clinical decision-making, and for inclusion in future AJCC staging systems for p16+ OP SCC.

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### WHOLE GENOME CHARACTERIZATION OF CERVICAL CANCER

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**Purpose:** A number of chromosomal alterations have been identified as important factors in the initiation and progression of cervical cancer. These data, however, are mainly derived from surgical specimens of early stage tumours. The purpose of our study was to analyze the whole genome profile of locally advanced cervical cancers treated with radiotherapy and concurrent Cisplatin (RTCT) and to identify recurrent DNA copy number alterations associated with the malignant phenotype.

**Materials and Methods:** Tumour biopsies of locally advanced cervical cancers were obtained at the time of examination under anesthesia, prior to RTCT. All biopsies were reviewed by a gynecologic pathologist. Macro-dissected tumour samples were co-isolated using the Qiagen All-Prep DNA/RNA/miRNA universal kit. DNA samples were submitted for shallow whole genome sequencing where reads were aligned to the hg19 reference genome with an average sequencing coverage of 0.38x. Copy-number was estimated using QDNaseq and ichorCNA by segmenting the genome into genomic bins of 50kb or 1000kb. Age, histology, grade, stage and lymph node status were recorded. Patients were treated with external radiotherapy (45-50 Gy) and concurrent weekly Cisplatin (40 mg/m<sup>2</sup>), followed by pulsed-dose-rate (PDR) brachytherapy (40 Gy). Median follow up was 8.4 (range: 0.2-16.5) years.

**Results:** One hundred and twenty-one patients were enrolled in the study from October 1999 to March 2012. They were representative of the cervical cancer population treated with RTCT. The median age was 48.5 (range: 26-84) years. FIGO stage was 1B in 31%, IIA-IIB in 40%, and IIIA-IIIB in 29%. The median percent genome altered (PGA) was 13.2% (range: 0-47.5%). Recurrent copy number amplification events were consistent with previously reported data and include: 11q22.1 (YAP1, BIRC2, BIRC3), 3q26.2 (MECOM, TERC), 1q23.3, 8q24.23 (MYC, PVT2), 20q11.21 (BCL2L1), and 9p24.1 (CD274, PDCDILG2). In contrast to previous reports, locus 7p11.2 coding EGFR was not amplified. Recurrent copy number deletions included: 2q37.1, 2q36.3, 11q23.3, 3p12.3, 19p13.3, and 13q14.11. Previously identified deletions at loci 4q35.2 (FAT1) and 10q23.31 (PTEN) were not seen in our cohort. There were no associations between PGA and any of the baseline clinical factors. There was no association between PGA and disease-free survival.

**Conclusions:** In summary, this study improves our understanding of the genomic landscape in locally advanced cervical cancer. While our findings are similar to those reported previously for earlier stage disease, we also identified potentially important differences that warrant further evaluation. Future analyses will explore relationships between specific chromosomal alterations and gene expression profiles as well as their integrated effects on treatment response and survival. The ultimate goal is to identify genomics biomarkers to aid in the subclassification of disease, prediction of prognosis, and selection of patients who may benefit from treatment intensification.

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### OPTIMIZING RECTAL SPACER GEL PLANNING

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**Purpose:** Spacer gels (SG) have been shown to reduce rectal dose during prostate radiation by increasing the prostate-rectum space (PRS). The optimal method of incorporating SG in treatment planning is not known. In this study, the SG and the rectum are combined into a composite rectal structure in the planning of hypofractionated external beam radiation (EBRT) to determine whether enhanced rectal sparing can be achieved over planning with the rectum alone while using two different planning algorithms.

**Materials and Methods:** Thirteen prostate cancer patients treated radically with EBRT had SG (SpaceOAR<sup>®</sup>, Augmentix<sup>®</sup>, Waltham, MA, USA) injected in the PRS and three fiducial markers implanted in the prostate at least a week before a planning CT scan and MRI. Patients also underwent a pre-gel CT scan. For each patient, a total of six treatment plans with a dose fractionation of 60 Gy in 20 were generated by a single planner: two on the pre-gel CT with a standard rectal wall (RW) structure in a standard clinical optimization approach (STD) and a more rectal-sparing driven optimization approach (RDO); and four on the post-gel CT using both optimization approaches (STD, RDO) and including either the RW or a composite rectal wall (CRW) structure (which includes the rectal wall and SG) in the optimization. Dosimetric data was collected and statistical analysis performed to compare the planning approaches.

**Results:** There was no difference in mean CTV V60 Gy, PTV V57 Gy, and bladder wall (V46 Gy and V37 Gy) between plans, regardless of optimization technique, rectal structure definition, or presence of SG. PTV V63Gy was larger in all RDO plans compared to STD plans (0.1-0.2 cc versus 0.0 cc). Using the STD optimization with RW structure resulted in a mean RW -V46 Gy and -V37 Gy of 17.2% and 23.5% when no SG was present versus 14.3%

and 22.0% when SG was present. By using CRW in the STD optimization the mean RW -V46Gy and -V37Gy improved to 11.8% and 19.2% respectively. The RDO approach with RW structure resulted in mean RW -V46Gy and -V37Gy of 14.2% and 21.4% when no SG was present versus 6.3% and 14.2% with SG present. Using CRW in RDO resulted in RW -V46Gy and -V37Gy of 8.4% and 16.2%.

**Conclusions:** Use of SG resulted in a significant reduction in rectal doses irrespective of optimization approach (STD or RDO) or type of rectal structure used (RW or CRW) in optimization. Use of a CRW in STD optimization statistically improved rectal sparing compared to RW but resulted in statistically less rectal dose sparing when used in RDO approach. Compared to STD optimization, RDO approach resulted in a small increase in hot spots within PTV. RDO approach using RW structure should be considered when the primary goal is to minimize rectal dose.

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#### PROSTATE OR BONE? COMPARING THE EFFICACY OF IMAGE GUIDANCE SURROGATES FOR PELVIS AND PROSTATE RADIOTHERAPY USING ACCUMULATED DELIVERED DOSE

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**Purpose:** Efficacy of an image guidance surrogate for pelvis and prostate radiotherapy has previously been reported based on geometric coverage only. Using the dose accumulation process, this study assessed the impact of dosimetry to both the target and normal tissue when either Bony Anatomy (BA) or Prostate (PRO) was used as surrogates for image guidance for pelvis and prostate radiotherapy.

**Materials and Methods:** Nine patients who received treatment to both the Pelvic Lymph Nodes (PLN) and prostate were included. A two-arc VMAT plan was generated to deliver 50-54 Gy to the PTVs (PLN + 5 mm; prostate + 10/7 mm). Daily acquired CBCTs were rigidly registered to the CT using BA and PRO to simulate two different treatment positions. Daily dose was computed on all CBCTs and then accumulated on the planning CT using the output from the CT-CBCT deformable image registration. The Accumulated Delivered Dose (DAcc) of PLN, prostate, bladder and rectum for each surrogate were compared with the planned dose Deviation from the planned dose ( $\Delta$ DAcc-Plan) of >5% was considered significant.

**Results:** A total of 227 CBCTs was used to measure DAcc across nine patients. Mean  $\Delta$ DAcc-Plan for all study endpoints was < 2% when PRO was used. While BA achieved similar result as PRO,  $\Delta$ DAcc-Plan was large for accumulated rectum D50 (mean: 7%; range: -3 - 20%), and was significantly different from PRO ( $p = 0.01$ ). A pairwise comparison indicated PRO achieved a lower rectum DAcc for seven out of nine patients than BA (range of difference for D50: 4 - 14% and D30: 1 - 9%). A PTV margin of 5 mm was considered adequate for PLN when PRO was used, even when the distance between PLN and prostate was >5mm in 37% and 64% of fraction in two patients.

**Conclusions:** The use of either BA or PRO for image guidance could deliver dose to PLN and prostate with minimal deviation from the plan using existing PTV margins. However, deviation for rectum was significant when BA was used. Investigation with a larger sample size and reduced margin is ongoing.

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#### DOES ACCUMULATED DOSE TO PAROTID GLANDS IMPROVE PREDICTION OF PATIENT REPORTED OUTCOMES RELATED TO SALIVARY FUNCTION IN NASOPHARYNGEAL CANCER PATIENTS?

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**Purpose:** To compare delivered dose with planned dose to parotid glands in nasopharyngeal patients using deformable image registration and dose accumulation, and investigate the relationship to patient reported outcomes (PRO) related to salivary function.

**Materials and Methods:** Retrospective dose accumulation using daily cone-beam CT (CBCT) was performed on 50 nasopharynx patients treated with chemoradiotherapy [70 Gy (high-dose) and 56 Gy (low-dose) in 35 fractions] from 2013 to 2015. Of this cohort, 21 patients had baseline (pre-radiation therapy (RT)) and six months post-RT MDASI (MD Anderson Symptom Inventory)-HN scores reported (Scale 1 to 10, with higher score indicating worsening symptoms). For each patient, the change in score for salivary functions from baseline to six months post-RT was analyzed. All patients had right and left parotid contours except one patient that did not have a left parotid contoured. A total of 99 parotid glands were analyzed. Both planned and delivered doses were extracted for the parotids. Individual parotid sparing thresholds were 26 Gy and 30 Gy for mean dose and D50% respectively. Changes in MDASI-HN score for dry mouth and mucus were compared to both planned and delivered parotid doses.

**Results:** The average planned mean dose to the parotid gland was 41.2 Gy  $\pm$  9.9 Gy, increasing to 42.7 Gy  $\pm$  9.9 Gy for delivered dose. Only 3% of parotids met the sparing criteria of < 26 Gy for mean dose ( $n = 99$ ), with only 1% meeting criteria in delivered dose. The average planned D50% was 38.4 Gy  $\pm$  13.3 Gy, increasing to 40.9 Gy  $\pm$  13.3 Gy for delivered dose. The planning goal for D50% was achieved in 31.3% of the parotids, with 19.3% of these receiving a delivered dose > 30 Gy. Of the 21 patients with PRO, the mean increase in MDASI-HN mucus score was 3.15(R:-2 to 8) in cases that were planned to spare and 3.0(R:-3 to 6) in those that were not planned to spare. The separation between the two groups increased if delivered dose was evaluated: patients with spared parotids have a score increase that was lower (2.6(R:-2 to 8)) than patients without parotid sparing (3.5(R: 0 to 7)). Those with planned parotid sparing had an increase of 2.2 (R: 0 to 6) and those without planned parotid sparing had an increase of only 0.8 (R:-3 to 4) in MDASI-HN dry mouth scores. Patients with actually spared parotids had a score increase of 1.8(R:0 to 4) while the patients without actually spared parotids had a score increase of 1.5 (R:0 to 7). The improved separation in groups using the delivered dose was not reflected in the scoring of dry mouth, however revision of the sparing criteria reduced the mean score increase in the spared group.

**Conclusions:** Dose accumulation is a useful tool to estimate delivered dose to the parotids which is higher than planned dose in this cohort. Delivered dose is potentially a better predictor of salivary PROs. This observation could prove useful in management of patients and in designing appropriate adaptive strategies.

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#### SEMI-AUTOMATED VOLUMETRIC MODULATED ARC THERAPY PLANNING FOR POST-OPERATIVE RADIOTHERAPY IN ENDOMETRIAL CANCER: IMPROVEMENTS IN NORMAL TISSUE SPARING AND PLANNING TIME

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**Purpose:** To investigate the potential for improved normal tissue sparing achievable using state-of-the-art personalized treatment planning for post-operative radiotherapy in endometrial cancer. Specifically, we compared a semi-automated 2-arc volumetric modulated arc therapy (VMAT) planning technique with intensity modulated radiation therapy (IMRT) planning. We investigated both plan quality differences using VMAT and planning time savings with our semi-automated planning approach.

**Materials and Methods:** We identified 10 patients, who had been planned with 8-field step-and-shoot IMRT in Pinnacle v9.8, and created a new 2-arc VMAT plan for each patient in RayStation v4.7 using semi-automated scripts we developed. Prescribed dose (Rx) was 45 Gy in 25 fractions with the objective of achieving 98% coverage of the PTV (D98) with 95% of the Rx dose. We created the internal target volume (ITV), by combining the vagina and parametrium contours on a planning CT (full bladder) and T2-weighted MRI (empty bladder). We assessed VMAT performance using the conformity index (CI), low dose (50% Rx) volume outside the PTV, PTV coverage, and organ-at-risk (OAR) sparing using institution-specific dose constraints. We quantified differences in planning time with the semi-automated versus manual approach in a subset of five patients. All differences were assessed using the paired two-tailed Student's t-test.

**Results:** The CI index (mean  $\pm$  STD) for VMAT was significantly lower than IMRT (1.05  $\pm$  0.02 versus 1.36  $\pm$  0.07,  $p < 0.001$ ), and similarly the 50% Rx dose volume was significantly lower for VMAT than IMRT (2386  $\pm$  433 cm<sup>3</sup> versus 4477  $\pm$  626 cm<sup>3</sup>,  $p < 0.001$ ). There was no significant difference in target coverage between techniques. For the OARs, mean D30% for the femurs was significantly lower for VMAT compared to IMRT (18.2 Gy versus 30.1 Gy,  $p < 0.001$ ). Mean small bowel D30% was 8.7 Gy lower using VMAT (21.8 Gy versus 30.5 Gy,  $p < 0.001$ ). Mean rectal wall D35% was 4.2 Gy lower with VMAT (37.9 Gy versus 42.1 Gy,  $p < 0.005$ ), whereas no significant difference was observed for the bladder wall D35%. Use of scripting to automate key steps including generating ITV, contour operations and adding the plan and beams reduced active planning time by 54  $\pm$  1 minutes.

**Conclusions:** Here we demonstrate the dosimetric advantages for a highly conformal 2-arc VMAT approach compared with conventional IMRT for post-operative treatment of endometrial cancer. Use of script-based semi-automation substantially reduce the time needed for simple planning tasks. Implementation of 2-arc VMAT significantly improved normal tissue sparing, particularly for the bowel and femurs without compromising target coverage. In future, we plan to investigate impact of interfraction uncertainties on target coverage and OAR sparing with the more conformal VMAT approach.

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#### ENSURING A REPRODUCIBLE PATIENT POSITION FOR PERMANENT BREAST SEED IMPLANT

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**Purpose:** Permanent breast seed implant (PBSI) is a convenient, single day radiation treatment option for partial breast radiotherapy for early stage breast cancer following lumpectomy. The seroma plus a margin is treated to 90 Gy with Pd-103 seeds. To date, over 60 patients have been treated with PBSI in Kelowna, BC.

**Materials and Methods:** The goal of patient set-up is to establish a position that is suitable for both the planning CT and the implant, and reproducible between these two events. The initial positioning occurs at the CT simulation using a breast board with lateral indexing, isocentric lasers, and tattoos. On the surgical day, a mock set-up is performed using the CT simulator in-room lasers and table shifts to locate the fiducial entry point and transpose the PTV to the skin surface. The patient is then brought to the operating room, anesthetized and her position reproduced on the breast board. The implant is then performed under ultrasound guidance.

**Results:** Reproducing the original CT position in the OR is complicated by a number of factors. Under anesthesia, the muscle relaxation causes the skin breast to sag, affecting the patient's reference skin marks. The ipsilateral arm position may be slightly altered to relieve strain on the brachial plexus, and gel pads are added under pressure points. The radiation therapists are then challenged with reproducing an identical patient position without in room lasers in the OR. We have met these challenges with the use of a portable table laser, careful skin mark-up, and referencing table heights. The radiation oncologist confirms the seroma location and the implant is performed under live ultrasound guidance.

**Conclusions:** Including a radiation therapist in the pre-implant skin markup will allow continuity of patient set-up and positioning. A collaborative team approach is important to overcome the unique challenges with PBSI. Our outcomes are very good despite these challenges and our technique has been successful.

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#### FROM CT-GUIDED TO MR-GUIDED INTRACAVITARY BRACHYTHERAPY FOR CERVICAL CANCER: WHAT DO THE KEY STAKEHOLDERS HAVE TO SAY ABOUT THE TRANSITION?

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**Purpose:** International brachytherapy consortiums are advocating for the incorporation of magnetic resonance imaging (MRI) into the cervical

brachytherapy process as a standard of care. Although some evaluations have been performed to quantify the effect on procedural time, little is known about the views and experiences of key stakeholders during the transition from CT to MR-guided brachytherapy. This qualitative research project explored insights from key stakeholders related to a change in the gynaecological brachytherapy process.

**Materials and Methods:** Semi-structured interviews were designed using Lean Methodology principles and all key members in the gynaecological brachytherapy team were approached for participation: radiation oncologists, medical physicists, radiation therapists, lead MR technologist and the ward nurse manager. Interviews were recorded and transcribed, analysis was performed to identify themes from the data.

**Results:** Ten of twelve (83% participation rate) key members of the team were interviewed. Four themes emerged from the data: challenges to efficiency, staff availability, patient history and disease characteristics and team communication. The stakeholders expressed that the challenges during this transition was procedural inefficiency (sharing of the MRI scanner and increased procedure length due to increased complexity in contouring and planning), staff availability (radiation oncologist and transportation staff). The clinical team identified the value of communicating patient history and disease characteristics ahead of the brachytherapy procedure day, and also using an inclusive mode of communication during the procedure were beneficial.

**Conclusions:** This research provides nuanced insights into process and practice changes that occur when one imaging technology is simply swapped for another, emphasizing how intertwined and complex brachytherapy procedures can be. It emphasizes that not all challenges to efficiency are considered Lean Wastes, and that seemingly simple procedural changes can result in unanticipated differences in staff availability, communication pathways, and knowledge requirements.

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#### EXTRACTING FROM PATIENT EXPERIENCE: ATTITUDE TOWARDS BRACHYTHERAPY IN BRITISH COLUMBIA

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Bodies such as Accreditation Canada and the Canadian Partnership for Quality Radiation Therapy emphasize the importance of engaging patients and the public in decision making around how cancer care is delivered. While the rationale for doing so is self-evident, how to accomplish this in a meaningful manner is less obvious. We present our experiences in engaging specific patient populations in the development of a strategic plan for the provincial delivery of brachytherapy (BRY) services.

**Purpose:** 1) To discuss the process of engaging patients in strategic planning for BRY; 2) To review patients responses to surveys and the alignment of the responses with the final plan.

**Materials and Methods:** As part of a strategic planning exercise, qualitative feedback about the current and future landscape of the BRY program at a large oncology institution were gathered from 200 patients who received brachytherapy for PC or GC. Surveys were performed at two stages: 1) Prior to strategic plan: to gather opinions with respect to planning parameters, 2) After strategic plan: to validate recommendations made in the strategic plan. Surveys included items on access to services, acceptable travel times and distances, availability of services, quality of services provided, inconveniences endured during treatment, the desirability of renovations of infrastructure to meet various standards, and considerations related to balancing treatment access and maintenance of practitioner expertise.

**Results:** The overall response rate was 47% for Survey 1, and 43% for Survey 2. Over 90% either reported mostly or completely satisfied with the services received. Patients with gynecological cancer (GC) reported being more inconvenienced by treatment than patients with prostate cancer (PC). This may be attributed to multiple treatments required for gynecological patients. For the initial consultation, 34% of patients with GC, and < 4% of patients with PC, reported they waited < 2 weeks. Over 75% of patients with GC but < 15% of patients with PC, reported receiving an initial treatment within four weeks. Over 50% of patients with GC travelled < 30 minutes, and 80% travelled < 60 minutes one way for each treatment. Patients with PC reported longer travel times, with only 43% travelling for < 60 minutes.

Patients with longer travel times were more likely to report that longer travel was reasonable. More than 60% of respondents agree on upgrading facilities, but nearly 50% do not believe BRY should be limited to specific facilities. Over 80% reported BRY should be available to all regardless of residence location. Regarding balance between increasing accessing services versus maintaining expertise, > 83% indicated maintaining high expertise was most important.

**Conclusions:** The majority of responding patients were satisfied with the manner in which services are currently provided, and broadly agreed with the recommendations of the final plan, particularly with respect to the balancing of access to services compared to maintenance of core expertise. Engaging a specific patient population in a strategic planning exercise, via the use of pre- and post-surveys, was valuable in informing the overall recommendations of a complex strategic plan.

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### EVALUATING DOSE-ESCALATED TOTAL MARROW IRRADIATION (TMI) FOR RELAPSED MULTIPLE MYELOMA

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**Purpose:** Multiple myeloma (MM) relapsing following an autologous stem cell transplant (ASCT) has a poor prognosis and new treatment approaches are required. We developed a Phase I/II dose-escalation study utilizing total marrow irradiation (TMI) as the sole conditioning regimen for a second ASCT. **Materials and Methods:** Patients with relapsed MM following ASCT, and who had not previously received radiation, were approached to participate. The entire bony skeleton was targeted to receive the prescribed dose while sparing uninvolved adjacent normal tissues/organs using an IMRT technique utilizing helical Tomotherapy<sup>®</sup>. We started at a dose of 1400cGy/7fr bid/3.5 days and are increasing the total dose by 200 cGy until the maximal tolerated dose is reached.

**Results:** Since January 2010, 14 patients have been enrolled and treated; 12 (86%) men and two (14%) women, with a median age of 59.5 (range 37-68) years. Three patients have been treated in each of the following dose level cohorts; 1400cGy/7fr/3.5days, 1600cGy/8fr//4days, 1800cGy/9fr/4.5 days and 2000cGy/10fr/5days. One patient received a dose of 1980cGy/9fr/4.5days and one received 2200cGy/10fr/5days. There was successful engraftment at a median of 12 (range 9-16) days. The median duration of follow up is 32.4 months. The median progression-free survival after TMI-ASCT was 17.2 months compared to 16.2 months after the initial ASCT ( $p = 0.495$ ). The median overall survival was 5.3 years from the time of TMI-ASCT, 9.7 years from the initial ASCT, and 10.2 years from diagnosis. Acute toxicity (measured with the Bearman scale) was manageable (Grade 1-2), and commonly consisted of stomatitis and diarrhea. No treatment-related deaths have occurred and dose limiting toxicity has not been reached. Relapses have occurred among 12 patients post-TMI-ASCT. Late toxicity has generally been mild, and mainly includes xerostomia, fatigue and muscle pain.

**Conclusions:** It is possible to safely deliver a total dose of 2000cGy/10fr/5days to the entire bony skeleton with our TMI technique. Further dose escalation appears feasible and treatment response is encouraging. We are currently in the process of treating to a total dose of 2200cGy/10fr bid/5days.

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### VARIABILITY IN EXPERT DELINEATION OF TARGETS AND ORGANS-AT-RISK IN GLIOMAS FOR CT-MRI AND MRI-ONLY WORKFLOWS

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**Purpose:** Magnetic Resonance Imaging (MRI) has been used for radiotherapy definition of brain anatomical structures since its inception, and the emergence of MR-guided radiotherapy systems have motivated the development of an MRI-only workflow. We report a multi-institutional study of inter-observer variability in the delineation of targets and organs-at-risk (OARs) in glioma for both CT-MRI and MRI-only workflow.

**Materials and Methods:** Ten cases consisting of five glioblastomas (GBM) and five WHO Grade II or III gliomas were chosen for the study with varying tumour location and proximity to white matter pathways. Six experienced neuro-radiation oncologists from five international institutions contoured the gross tumour volume (GTV) and clinical target volume (CTV) in addition to OARs including lenses, globes, optic nerves, optic chiasm, brainstem, and cochlea. CTV expansion was 1.5 cm for GBM and 1.0 cm for Grade II or III gliomas respecting anatomic boundaries and potential routes of spread. Each case was first contoured on MRI only with access to T1 post-gadolinium and T2/FLAIR sequences, and then re-contoured with the additional information provided by a fused CT. STAPLE contours were created from the volumes and inter-observer variability was evaluated using combinatorial pair-wise Dice similarity coefficient (DSC) and the Hausdorff distance (HD).

**Results:** A high level of agreement was observed between the GTV contours in the MRI-only workflow with mean DSC and HD of 0.86 and 13.1 mm, respectively, which did not change appreciably in the CT-MRI workflow ( $p = 0.84$ ,  $p = 0.98$ , respectively). Similarly, for the CTV contours in the MRI-only workflow, the mean DSC and HD were 0.88 and 14.2 mm, respectively, with no statistically significant difference seen when compared to the CT-MRI workflow ( $p = 0.79$ ,  $p = 0.97$ , respectively). In the MRI-only workflow, cochlea contours demonstrated a poor mean DSC of 0.17 – 0.20 and HD of 5.6 – 5.7 mm, which significantly improved with the addition of CT information to 0.59 – 0.62, and 3.2 – 3.9 mm ( $p < 0.0001$ ,  $p < 0.0001$ , respectively). With respect to the optic chiasm, the mean DSC and HD were 0.49 and 11.5 mm, respectively, for both the MRI-only and CT-MRI workflows. Moderate to high level of agreement was observed in all other contoured OARs with a mean DSC range of 0.63 – 0.90 and mean HD range of 1.9 – 8.9 mm.

**Conclusions:** The addition of CT to an MRI-only workflow does not provide additional anatomical information in gliomas to significantly reduce inter-observer contouring variability with the exception of cochlea. Dedicated MRI sequences may be required for consistent delineation of the cochlea when inclusion of the OAR is indicated. A high level of agreement in target and OAR contours was observed and principles in CTV delineation with respect to anatomical barriers and pathways of spread were established, which will serve as a baseline for further guideline development.

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### AN IN VIVO MODEL TO STUDY THE USE OF NANOPARTICLES AS A RADIOSENSITIZER IN RADIATION BEAMS GENERATED FROM A LOW Z TARGET

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**Purpose:** Nanoparticles made of high atomic number (Z) elements have been shown to sensitize cancer cells to radiation beams generated from linacs in vitro and in vivo. This effect occurs due to the emission of low energy photoelectrons and Auger electrons. Gold (GNP) and gadolinium (GdNP) based nanoparticles are biocompatible, and accumulate passively in tumours due to the enhanced permeability and retention effect, and there is growing evidence that localized radiation-induced tumour vascular damage can be used to clinical advantage. The introduction of low Z (sintered diamond) linac target instead of a standard Cu/W target results in a predicted 7.7 fold enhancement in the immediate proximity of the NP. The efficacy of combining the low Z target beam with NPs remains to be verified in vivo. To this end, we employed an established zebrafish xenotransplantation platform to quantify tumour cell proliferation. The zebrafish model offers

the advantages of using a transparent fish to allow in vivo monitoring of grafts, as well as enabling large sample sizes.

**Materials and Methods:** Beam set-up: The samples were irradiated using a standard 6 MV or a custom 2.5 MV/diamond target x-ray beam from a TrueBeam linac. The 2.5 MV/diamond beam was generated by 2.5 MeV electron beam incident upon a sintered diamond target in the carousel. Cell line screen: Panc1 (pancreas), FaDu (hypopharynx), A673 (Ewings), MDA-MB-231 (breast), LNCaP (prostate), A549 (lung) were labeled in vitro with NPs. They were irradiated with 8 Gy using the low Z or conventional target beam. Proliferation was assayed using Alamar Blue. Xenograft assay: Cells were co-labeled in vitro with NPs and a lipophilic fluorescent dye. Labeled cells were injected into the yolk sac of dechorinated casper zebrafish embryos and irradiated one day post-injection (DPI) with 8 Gy. Tumour viability was measured by a standard ex vivo proliferation assay at three DPI.

**Results:** Cells showed differential responses to being irradiated with standard or low-Z target beam in the presence of GNP or GdNP. Among the cell lines tested, FaDu cells were the most sensitive to NP mediated irradiation. The low-Z target beam showed a 19% decrease in cell proliferation compared to the standard beam for the GdNP labeled cells.

**Conclusions:** In a proof of principle experiment, we have shown a differential effect between low-Z target and standard beam irradiation in NP labeled cells. We are in the process of testing the model in a xenograft setting with plans to examine tumour response in adult fish model.

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#### REAL WORLD IMMUNOTHERAPY RESPONSE AND PULMONARY TOXICITY IN PATIENTS TREATED WITH CHEST RADIOTHERAPY

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**Purpose:** Pivotal clinical trials (KEYNOTE-001) have demonstrated improved response and increased pulmonary toxicity in non-small cell lung cancer (NSCLC) patients treated with both radiotherapy (RT) and immunotherapy (IO). The purpose of this study was to document pulmonary toxicity and response rates in patients receiving both RT and IO in routine clinical practice.

**Materials and Methods:** All metastatic NSCLC patients treated with Nivolumab or Pembrolizumab between November 2015 and October 2017 in one Canadian province were identified. Demographic, tumour, treatment, toxicity, and response data were collected. Fisher's Exact Test and Chi Squared Test were used to assess the relationship between treatment characteristics and outcome.

**Results:** Two-hundred seventy-one patients treated with IO were identified. Median follow up was 10 months. One hundred seventy patients (63%) received thoracic RT; 65 received curative intent RT, including four who received stereotactic RT. In total, 207 courses of thoracic RT were delivered; 25 patients received two courses, six received >2 courses. Median RT dose was 30 Gy (range: 4-70 Gy). There was no difference in physician assessed response rates in patients treated with chest RT compared to those not treated with RT (55% versus 45%,  $\chi^2$  test  $p = 0.12$ ). Ten patients (3%) developed pneumonitis while on IO; two Grade 1, four Grade 2, one Grade 3, one Grade 4 and two Grade 5. Both cases of Grade 5 pneumonitis were in patients treated with previous chest RT, including one treated curatively. There was no difference in pneumonitis rates in patients treated with thoracic RT compared to those not treated with RT (4.1% versus 3.0%,  $p = 0.74$ ). Radical intent RT (3.1% versus 3.9%,  $p = 1.0$ ), conformal RT (5.0% versus 2.9%,  $p = 0.50$ ) and VMAT (4.8% versus 3.4%,  $p = 0.70$ ) were not associated with increased toxicity.

**Conclusions:** In keeping with previous clinical trials, pneumonitis was a rare complication in this real world cohort. There was no difference in response rates or pneumonitis rates with IO between those treated with or without thoracic RT.

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#### DEVELOPMENT OF BEST PRACTICES OF PEER REVIEW IN LUNG RADIATION THERAPY

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**Purpose:** Given the increasing complexity in lung radiation therapy (RT), peer review (PR) is an important component in ensuring high quality and consistent RT plans. However there are inconsistencies in the extent, timing, and minimum requirements for PR across centres. We sought to develop guidelines of best practices for PR in curative lung RT through a Pan-Canadian expert consensus process.

**Materials and Methods:** A modified Delphi process was conducted. A literature review was first carried out to define important elements for PR with respect to target delineation, organs-at-risk (OAR), and dosimetric plan quality, which was followed with an initial review by a dedicated steering committee. Candidate PR elements were then stratified by cases pertaining to treatment of locally-advanced (LA) disease with conventional RT, or stereotactic ablative body radiotherapy (SABR) for early-stage disease. A pan-Canadian, multidisciplinary Delphi panel was then assembled, and three Delphi rounds were undertaken (one pre-meeting survey, one face-to-face meeting, and one post-meeting ratification survey) to quantify participants' rankings of the importance of each PR element, as well as the clarity of the wording for each. Finally, all endorsed elements were discussed for final wording by the steering committee.

**Results:** For LA cases, a total of six elements were considered as essential in the PR process. These included i) indications to treat with RT, ii) gross tumour volume (GTV), iii) clinical target volume (CTV), iv) internal target volume (ITV), v) dose/fractionation selection, and vi) normal lung dosimetry (i.e. V20, mean lung dose). Of these six elements, 90-100% of the panel in the final round endorsed these to be important to PR, and 80% felt that the PR should be done by a second radiation oncologist (RO). There were an additional three elements deemed optional for PR in these cases, including OAR contour review, PTV dosimetric coverage and maximum point dose, with review conditional dependent on the clinical scenario. In the cases of SABR, a total of six PR elements were deemed essential. These included i) indications to treat, ii) GTV, iii) CTV/ITV, iv) OAR contours, v) choice of dose/fractionation, and vi) review of composite plan for cases treated with previous RT. On the final round, 90-100% of panel members felt these elements to be important to PR, and unanimously agreed that PR should be done by a second RO. A further four elements were deemed optional based on the clinical scenario, including PTV dosimetric coverage, maximum point dose, OAR dosimetry, and best practices for daily image guidance.

**Conclusions:** A suite of elements for lung radiation PR has been developed and endorsed with high consensus across a multidisciplinary group of national experts in lung RT. These elements should serve as a basis to help streamline and create consistency among PR practices across centres, and to help develop novel PR approaches going forward.

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#### PROGRAMMATIC COMPARISON AND DISSEMINATION OF SINGLE FRACTION RADIOTHERAPY PRESCRIBING PRACTICES FOR BONE METASTASES CAN RESULT IN MEANINGFUL AND LASTING CHANGE IN PRACTICE ON A POPULATION LEVEL

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**Purpose:** There is ample evidence that a single fraction of radiation therapy (SFRT) is as equally efficacious as more costly and potentially morbid multi-fraction regimens. In our large provincial program, we previously demonstrated that a multi-pronged educational and audit intervention increased the use of SFRT in all regional cancer centres the year following.

However, other investigators have demonstrated interventions focused on guideline dissemination were only associated with a transient one year change in prescribing practices, and therefore we sought to determine if our use of SFRT also returned to baseline or persisted.

**Materials and Methods:** Several province-wide interventions were implemented in 2012 to increase the use of SFRT, including an audit of prescribing practices of individual physicians (anonymized) and centre averages (non-anonymized) and subsequent presentation of these results to leaders and oncologists. After individual patient chart review, we subsequently compared the use of SFRT in all patients treated with bone metastases in our provincial program from 2007-2011 (pre-intervention) and 2013-2016 (post-intervention), and performed comparison across all six provincial cancer centres.

**Results:** Prior to the intervention, the rates of SFRT in 2007, 2008, 2009, 2010, and 2011 were 51, 51, 48, 49, and, 48%, while the rates post intervention in 2013, 2014, 2015, and 2016 were 60, 60, 57, and 54% ( $p < 0.001$ ). In the most recent year of this study (2016), four of the six provincial centres prescribed in a relatively narrow range (45, 48, 53, and 54%). However, there was little change in the centre with the lowest use of SFRT (26% to 25%) or in the centre with the highest use of SFRT (73% to 75%).

**Conclusions:** Our audit and education-based intervention resulted in a lasting change in practice, though a trend toward decreasing SFRT was observed. Our provincial rate is similar to a previously published recommended benchmarks rate of 60%, though we continue to see significant variation by centre, suggesting further room for improvement in provincial standardization. With the potential of emerging evidence in support of stereotactic ablative radiotherapy for select populations of patients with bone metastases, future benchmark rates of SFRT use should be readdressed, though our data suggest programmatic comparison and dissemination of SFRT prescribing practices can achieve a population-based SFRT utilization rate of over 50%.

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#### IMPACT OF DOSE-CAPPING WITH CONCURRENT CHEMORADIOTHERAPY IN RECTAL CANCER PATIENTS

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**Purpose:** We retrospectively examined rectal cancer patients treated with concurrent chemoradiotherapy to determine the effect of chemotherapy dose-capping on disease recurrence, toxicity, and survival.

**Materials and Methods:** Five hundred and eighty-four consecutive rectal cancer patients treated with concurrent chemoradiotherapy from 1997 to 2009 were identified. Dose-capped patients were defined as having a body surface area (BSA)  $\geq 2$  square metres and who received  $< 95\%$  full weight-based chemotherapy dose. A subgroup analysis was also conducted among patients with BSA  $\geq 2$  square metres, comparing those who received dose-capping and those who received full weight-based chemotherapy dose without capping. The primary objective of the study was to evaluate the incidence of cancer recurrence in patients treated with dose-capped chemoradiation versus those who were treated without dose-capping. The secondary objectives were to compare the incidence of toxicities requiring a dose reduction or treatment break, the rate of sphincter-preserving surgeries (SPS), and overall (OS) and recurrence-free survival (RFS).

**Results:** The rate of disease recurrence was significantly higher in dose-capped patients (33.3%) compared to those without dose-capping (23.5%,  $p = 0.04$ ). The adjusted odds ratio for dose-capped patients experiencing recurrence was 1.83 compared to uncapped patients (95% CI, 1.07 – 3.11). Among patients with BSA  $\geq 2$  square metres, the rate of disease recurrence in patients treated with full weight-based chemotherapy dose was 22.0%, compared to 33.3% in those treated with dose-capping ( $p = 0.05$ ). Overall, dose-capped patients were less likely to experience significant toxicity requiring dose reduction and/or treatment break when compared to uncapped patients (15.2% and 30.3% respectively,  $p = 0.002$ ). Despite receiving full weight-based chemotherapy dose, patients with BSA  $\geq 2$  square metres in the uncapped cohort did not experience higher rates of treatment-related toxicity compared to uncapped patients with BSA  $< 2$  square metres (23.5% versus 32.9% respectively,  $p = 0.05$ ). No significant differences were seen

between groups in rates of SPS, OS, or RFS.

**Conclusions:** Rectal cancer patients treated with dose-capped chemoradiotherapy were at increased risk of disease recurrence. Patients with increased BSA and dosed (within 5%) by actual weight did not experience excessive toxicity. We recommend that chemotherapy dose-capping based on BSA should not be routinely practiced in rectal cancer patients undergoing chemoradiotherapy.

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#### DEFERRAL OF SURGERY POST-CHEMORADIATION FOR LOCALLY ADVANCED RECTAL CANCER: THE EXPERIENCE OF THE MCGILL UNIVERSITY HEALTH CENTRE

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**Purpose:** In an effort to avoid the morbidity of conventional surgery, consideration of a “wait and see” approach for rectal cancer patients who achieve complete clinical response (cCR) after neoadjuvant chemoradiotherapy is growing. We report the experience of a single Canadian institution on this topic.

**Materials and Methods:** Patients with locally advanced rectal cancer (T3-4 or N1-2, M0) eligible for TME resection were invited to participate in this IRB approved phase II study. They were treated with IMRT to a dose of 45 Gy in 25 fractions to the posterior pelvis, followed by a 9 Gy in 5 fraction boost, combined with concurrent radiosensitizing chemotherapy. Patients subsequently followed a surveillance protocol including MRI pelvis, DRE, biopsy of suspicious lesions and control endoscopic examination every two months. Surveillance continued as long as tumoural regression was observed at each assessment; curative surgery was performed in the event of tumour regrowth or failure to achieve cCR at 12 months.

**Results:** Between September 2015 and March 2017, 17 patients participated in the “wait and see” protocol. Twelve of 17 (71%) achieved cCR. Time to achieve cCR ranged from 1.8 to 5.8 months. Nine of the 12 complete responders have no sign of recurrence at time of analysis (December 2017). Follow up for these 12 patients after achieving cCR ranges from 3.6 to 16.3 months, with five of them showing no evidence of regrowth at more than 12 months. Actuarial local control at 12 months from the date cCR was achieved is 70%. For the three patients that developed tumour regrowth after cCR (mean time to regrowth being 6.1 months), two subsequently underwent LAR and remain disease-free and one patient declined surgery. Except for one patient who died from intercurrent disease, all others (16) remain alive. Actuarial overall survival at 12 months is 92.3%.

**Conclusions:** In our experience, rectal tumours that demonstrate cCR to chemoradiotherapy typically did so by six months post-treatment. Seventy-one percent (12/17) of patients under surveillance achieved cCR. Fifty-three percent (nine of 17) remained clinically free of tumour at the time of analysis, five of these patients now followed for more than 12 months since achieving cCR. These numbers are encouraging and motivate continued exploration of this alternative.

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#### RADIOBIOLOGICALLY-GUIDED RADIOTHERAPY IN LARGE PRIMARY AND METASTATIC HEPATIC LESIONS

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**Purpose:** Radiobiologically-guided radiotherapy (RT) for hepatic lesions is an emerging treatment modality, however most prospective studies have included patients with smaller lesions, often  $\leq 2$  cm. This aim of this study is to report outcomes for patients who underwent radiobiologically-guided RT for large hepatic lesions of hepatocellular carcinoma (HCC) or metastases (MET). Size, as a stratification variable, was evaluated in terms of the toxicity, overall survival (OS) and progression-free survival (PFS).

**Materials and Methods:** This single-institution database study included 107 patients with lesions  $> 2$  cm treated between 2004 to 2012. Patients were stratified based on previously proposed size criteria for management

of hepatic lesions with ablative radiation; we identified 44 patients with medium (>2 to ≤ 5 cm), 47 with large (>5 to ≤ 10 cm) and 16 with huge (>10 cm) lesions. Radiation dose prescriptions varied between 29 to 88 Gy in 5 to 25 fractions using individualized radiobiological guidance. OS was evaluated by the Kaplan-Meier method and log-rank tests. Differences in rates of acute and late grade toxicities among the three size stratifications were evaluated by chi2.

**Results:** Our series included 44 HCC and 63 METs patients. Median diameter of medium, large and huge lesions were 3.5, 7.0 and 12.8 cm, respectively. Child-Pugh (CP) class was A, B and C in 76.6%, 22.4% and 0.9% of patients respectively. OS for cohort was OS for the cohort was 47.6% at 12 months and 30.9% at 24 months. On univariate analysis, factors significant to OS were: large lesions (hazard ratio, HR = 1.8, p = 0.014), huge lesions (HR = 1.9, p = 0.034), CP of B or C (HR = 3.1, p = 0.00), previous chemoembolization (HR = 0.50, p = 0.027) and equivalent dose in 2 Gy fractions as a continuous variable (EQD2) (HR = 0.98, p = 0.001). All factors, aside from huge lesions, remained significant on multivariate analysis. PFS at 12 months was 26.2%. On univariate analysis, significant factors affecting PFS included extrahepatic disease (HR = 1.6, p = 0.032), previous chemoembolization (HR = 0.51, p = 0.029) and large lesion status (HR = 1.6, p = 0.031). These remained significant on multivariate analysis. There were 42 episodes of acute Grade 2 toxicities and 13 episodes of acute Grade 3 toxicities, while there were 25 episodes of late Grade 2 toxicities and 13 episodes of late Grade 3 toxicities. There were no Grade 4 toxicities. Observed toxicities included fatigue (n = 45), abdominal pain (n = 40), rectal bleeding (n = 2) and nausea (n = 6). Between different lesions sizes, rates of Grade 1-3 toxicities were not significantly greater in the acute setting (chi2 = 4.1, p = 0.67) or the late setting (chi2 = 6.5, p = 0.37).

**Conclusions:** Lesion size was a significant variable related to worse OS and PFS, but not rates of toxicity. Individualized radiobiological constraints appear to result in the ability to treat large lesions safely.

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#### A PROSPECTIVE, MULTINATIONAL COMPARISON OF MULTI-PARAMETRIC AND WHOLE BODY MAGNETIC RESONANCE IMAGING (MP-MRI AND WB- MRI) F-18 FLUORO-METHYL-CHOLINE (FCH) AND GA-68 HBED-CC- (PSMA) IN HIGH RISK MEN BEING CONSIDERED FOR SALVAGE RADIATION TREATMENT FOR BIOCHEMICAL FAILURE POST RADICAL PROSTATECTOMY: DETECTION RATES, MANAGEMENT IMPACT AND TREATMENT RESPONSE

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**Purpose:** Men presenting with rising PSA following radical prostatectomy (RP) may be cured by salvage radiotherapy (SRT) directed to the prostatic fossa (PF). However, a significant proportion of men will not benefit from SRT presumably due to spread of cancer outside the PF not detected by conventional imaging. The purpose of this study was to evaluate the predictive value of new methods of imaging with FCH and PSMA PET/CT and MRI in identifying men at high risk of having extra-PF disease who are being considered for SRT for biochemical failure after RP.

**Materials and Methods:** Prospective, multisite, international trial in men post-RP with negative or equivocal conventional imaging, high risk features (PSA > 0.2ng/ml and >GSC 7 or PSA doubling time < 10 months, or PSA > 1.0 ng/ml) and rising PSA being considered for SRT. Ninety-one eligible enrolled men underwent FCH PET/CT, multi-parametric MRI of the pelvis (mpMRI) and WBMRI within two weeks, with additional PSMA PET/CT

in (31/91). All imaging was interpreted by two readers. Treatment plan was documented before and after imaging to assess management impact, and all subsequent treatments, biopsies and serial PSA collected. Imaging results were validated using a composite reference standard. Treatment response was defined as a PSA drop of > 50% after SRT only (no concurrent or adjuvant androgen deprivation).

**Results:** Median PSA at imaging was 0.41±1.2, median Gleason score 8 and median PSA doubling time 5.0 months. By modality, detection rates for any recurrent prostate cancer were (24/89) 27%, (29/91) 32% and (13/31) 43% for mpMRI, FCH PET/CT and PSMA PET/CT respectively (WBMRI reported separately). In men with positive scans, extra-PF disease was identified in (11/24) 41% (mpMRI), (17/29) 58% (FCH) and (nine of 13) 69% (PSMA). Comparing PSMA and FCH imaging, PSMA identified 36 sites of disease (in 13/30 men) compared to 20 sites (in 13/30 men) on FCH (p < 0.005). Imaging findings changed expected management in 46% (42/91) due to FCH, and 23% (21/90) MRI. PSMA provided incremental management change in seven of 31 (23%) over FCH. Treatment response to SRT was higher in men with negative or PF confined FCH PET/CT uptake versus uptake outside the PF (33/45; 72% versus 3/9; 33%, p < 0.03). Likewise, response was higher in negative or PF confined PSMA PET/CT uptake (7/8; 87% versus 1/7; 14%, p < 0.009).

**Conclusions:** A high incidence of extra-PF disease was identified with FCH, PSMA and MRI in high risk men with (negative conventional imaging) rising PSA post-RP being considered for salvage radiotherapy, with a consequent high management impact. Men with negative or uptake confined to the PF had the highest response rates to salvage RT.

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#### COST-UTILITY ANALYSIS OF DIFFERENT RADIATION MODALITIES FOR INTERMEDIATE-RISK PROSTATE CANCER

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**Purpose:** To estimate the cost-utility of different radiation modalities for the treatment of intermediate risk prostate cancer. Those modalities are standard fractionated IMRT, hypofractionated IMRT, combined external beam radiation and high dose rate brachytherapy, high dose rate monotherapy (HDR), low-dose rate monotherapy (LDR) and Stereotactic Body Radiation Therapy (SBRT).

**Materials and Methods:** A Markov model was developed with a base case modelling the lifetime disease trajectory of 60-year-old men diagnosed with intermediate risk prostate cancer following standard fractionated IMRT. The main focus was on acute or chronic gastrointestinal and genitourinary toxicities as well as a biochemical recurrence and survival rates. The cost utility analysis from the perspective of the health system compared alternative modalities' lifetime costs and patient utility to the base case. Input parameters were based on literature search yielding 68 publications. A probabilistic sensitivity analysis was performed, varying all model parameters simultaneously according to their distributions.

**Results:** Preliminary results find that all treatments outperform standard fractionated IMRT in improving patient life expectancy and quality of life. The base case found that SBRT dominated treatments in being most cost-saving and having highest improvements in quality adjusted life years. However, there is a high level of uncertainty around the SBRT parameters. Monte Carlo analysis finds that the five alternative modalities are roughly the same in likelihood of being cost-effective, but have a high likelihood of dominating standard IMRT. Sensitivity analysis finds that the largest source of model uncertainty is in incidence of gastrointestinal and genitourinary toxicity.

**Conclusions:** Chronic gastrointestinal and genitourinary toxicities have a major effect on quality of life for patients, meaning even modest improvements in acute and late toxicity risk had a major impact on a modality's likelihood of being cost-effective. The cost-utility results confirm that lifetime costs and patient outcomes are closely correlated; toxicity incidence and biochemical recurrence incur significant cost to the health system as well as being the primary drivers of patient quality of life. The initial treatment cost remains the single largest cost driver, though this is in part because the patient

population modeled is more advanced in years, shortening the lifetime costs of care. Model uncertainty is largely due to this relying on compiled literature sources.

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#### HYPOFRACTIONATED INTENSITY MODULATED RADIATION THERAPY TO PROSTATE AND PELVIC NODES PLUS ANDROGEN SUPPRESSION IN HIGH RISK PROSTATE CANCER

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**Purpose:** A 20-fraction hypofractionated course of radiotherapy (RT) to the prostate volume only has been shown to be an effective strategy in low- and intermediate-risk prostate cancer patients. We report five-year outcomes for high risk prostate cancer patients treated with androgen suppression (AS) and 20-fraction hypofractionated RT (HypoRT) delivered to the prostate and pelvic nodal areas.

**Materials and Methods:** Patients with localized, high risk prostate cancer (T3/4, or PSA > 20, or Gleason score 8-10) were treated with a HypoRT regimen of 60 Gy in 20 fractions (four weeks) to the prostate volume while the nodal areas received 44 Gy in 20 fractions delivered with IMRT with a simultaneous integrated boost technique. AS started two to three months before HypoRT. After HypoRT, patients were followed every six months with PSA, testosterone and imaging as needed. Toxicity was prospectively assessed and graded according to the CTC/AE V3.

**Results:** We reviewed the first consecutive 105 patients treated between October 2010 and December 2013. Median follow-up was 60 months (14-86). Median age was 72 years. Median AS duration was 18 months. The five-year overall survival was 92% and the five-year biochemical relapse-free survival was 87%. The worst Grade 2 or higher late GI or GU toxicity was seen in 7% and 9%, respectively. Grade 3 late GI or GU toxicity occurred in 2% in either site. There was no Grade 4 or 5 toxicity.

**Conclusions:** HypoRT delivered in 20 fractions to the prostate and pelvic nodes is practical and well tolerated. The preliminary five-year results compare favourably with longer duration EBRT using standard fractionation or combined with brachytherapy boost. HypoRT shortens total treatment duration, is cost-effective, convenient for patients and to the health system. These results support a randomized trial.

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#### CLINICAL EVALUATION OF A MACHINE LEARNING-BASED AUTOMATED TREATMENT PLANNING METHOD FOR PROSTATE RADIOTHERAPY

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**Purpose:** The purpose of this study was to evaluate the clinical applicability of an in-house developed automated planning method for radical prostate volumetric modulated arc therapy (VMAT) planning through direct blinded comparison of the automated plans to clinical plans.

**Materials and Methods:** Our machine learning-based automated planning method requires only the planning image dataset and contours for the target and organs-at-risk (OARs) as inputs. After training, the algorithm estimates the dose-per-voxel for a novel input patient based on the image features and OAR information from the most similar patients in the training database. In the final dose-mimicking step, a complete clinical plan, incorporating machine parameters and beam geometry effects, is produced. 116 consecutive clinically-approved radical prostate VMAT radiotherapy plans were used for algorithm training and testing. Two plans were left out due to incomplete contours. The automated planning framework was trained on 94 of the plans, and 20 independent plans were used for testing and clinical evaluation. Clinical and automatically-generated plans were evaluated by three independent blinded expert reviewers (two genitourinary radiation oncologists and one medical physicist). Reviewers evaluated six plan quality criterion as acceptable or unacceptable: target coverage, OAR sparing, high dose conformity, dose gradient at rectum, lateral dose symmetry, and overall approval. Reviewers were also asked to compare the

two blinded plans head-to-head and chose a preferred plan.

**Results:** Automated plans were successfully generated for all 20 patients; three patients were removed from analysis due to metallic hip implants. In blinded review, both automated and clinical plans were considered clinically acceptable in 49/51 (96%) of the 17 cases across three reviewers. The overall majority score for each of the six scoring criteria was predominantly equivalent between the automated and clinical plans. When the evaluations differed, automated plans had higher approval rates than clinical plans for target coverage (100% versus 90%) and OAR sparing (95% versus 86%), and lower approval rates for high dose conformity (84% versus 88%), dose gradient at the rectum (88% versus 92%), and lateral dose symmetry (82% versus 94%). In the head-to-head comparison, averaged across all three reviewers, automated plans were preferred for 12 patients, the plans were deemed equivalent (no preference) for three patients, and the clinical plans were preferred for two patients.

**Conclusions:** Our machine learning-based automated planning framework has potential to be integrated into the clinic to improve efficiency and consistency in prostate VMAT radiotherapy planning. Incorporation of this approach into our clinical practice, including prospective evaluation, is ongoing.

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#### THE CLINICAL CASE FOR SIMULTANEOUSLY-OPTIMIZED MIXED ELECTRON-PHOTON RADIOTHERAPY ON STANDARD RADIOTHERAPY LINACS: BREAST AND SOFT TISSUE SARCOMA IRRADIATION

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**Purpose:** Mixed beam electron-photon RT (MBRT) will improve normal tissue sparing for any case involving a target with a superficial component, without sacrificing target coverage. We hypothesize that for selected clinical sites, MBRT is superior to modulated photon-only RT. To validate our hypothesis, we performed a treatment planning comparison between standard multi-leaf collimator (MLC) modulated photon beams and MLC modulated, mixed photon/electron beams for chest wall (CW) with intramammary and axilla/supraclavicular nodes, partial breast (PB), and soft tissue sarcoma (STS) irradiation.

**Materials and Methods:** Nine patients (three requiring loco-regional CW RT, three PB RT and three RT for STS) were retrospectively planned with modulated MBRT using an in-house treatment planning system (TPS). A direct aperture optimisation model based on the column generation method was used to iteratively create treatment plans by forming candidate apertures from each of 6 MV photons and 6, 9, 12, 16 and 20 MeV electron modalities. The photon component of MBRT used standard coplanar IMRT/VMAT while the electron component used 3 to 5 coplanar electron incidences at approximately 80 cm SSD. The clinical technique was TOMO/VMAT for CW, non-coplanar 3DCRT/VMAT for PBI and STS. Clinically, all CW cases were planned with bolus, while for the STS cases the bolus was used only when skin was involved. The PTV contour was extended to skin when bolused, otherwise was cropped 5 mm from skin. For MBRT, PTV was cropped 3 mm from skin and no bolus was used. Target dose uniformity was evaluated by the homogeneity index defined as the ratio of near maximum to near minimum dose: HI = D2%/D98%. The MBRT and clinical plans were compared and the difference in relevant dose-volume metrics was reported.

**Results:** The average mean dose to ipsilateral lung, heart, contralateral breast and lung for CW cases decreased with MBRT from 14.3 to 12.4 Gy, 7.0 to 6.3 Gy, 10.5 to 5.0 Gy and 5.4 to 2.4 Gy, respectively. On average, MBRT yielded a 68% and 76% reduction to the V5Gy for the contralateral breast and lung, respectively. For the PBI cases, MBRT achieved a substantial gain in sparing the ipsilateral breast, with V50% reduced by on average, 21%, while maintaining similar mean doses to the ipsilateral lung and heart. The average V20Gy for the strip of normal tissue for STS cases was reduced by 90% with MBRT. For CW, the MBRT achieved similar HI compared to clinical, with an average of 1.12 versus 1.10 for clinical plans. Finally, MBRT improved the HI over clinical from 1.10 to 1.07 for PBI, and 1.11 to 1.04 for STS.

**Conclusions:** The purpose of this study was to demonstrate the clinical case for integrating an already existing modality on clinical accelerators,

e.g. electrons, in a simultaneously optimized methodology. We showed that the combination of electrons with photons, modulated by means of already-existing MLCs, and simultaneous dose optimization can dramatically reduce the dose to the contralateral or further seated organs-at-risk while achieving at least the same target coverage/homogeneity. Additionally, improved skin or subcutaneous tissue coverage is now possible with the mixed beam modality without the use of bolus typical for photon RT.

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#### AUTOMATED TREATMENT PLANNING FOR STEREOTACTIC BRAIN RADIOSURGERY

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**Purpose:** Develop an automated planning technique for stereotactic brain radiosurgery, with the goals of reducing planning time and improving the uniformity of plan quality throughout the clinic.

**Materials and Methods:** A cohort of 33 patients was analyzed retrospectively to generate a predictive model of the dose distribution for single-lesion brain stereotactic radiosurgery treatments. From this cohort, 3D dose falloff gradients were correlated to PTV sizes and fed into the dose prediction model. A Python script was written for our TPS (RayStation) to automate the process of predicting the dose and creating a clinically-acceptable treatment plan. The script automatically: 1) selects a treatment technique amongst 3DC, IMRT or VMAT, 2) predicts OAR DVHs, and 3) optimizes the treatment plan. The script was batch-tested on 23 patients with a single lesion and 13 patients with multiple tumours.

**Results:** Relative to the final dose distribution, the script predicted brain V10 and V12 with a root mean square error of 7% for single lesion and 15% for multiple lesion plans. Compared to the clinically treated plans, the automated plans presented equivalent or superior dose distributions in 95% of the cases. The plans with multiple lesions showed the most improvement with decreased low dose spillage and brain V12 reduced by an average 12%.

**Conclusions:** The automated planning script is able to create a clinically acceptable plan for the majority of the patients tested in approximately 20 minutes. The immediate proximity of optic structures or the brainstem still requires planner intervention to achieve optimal results.

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#### WITHDRAWN

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#### MICROCT IMAGING DOSE FOR A COMMERCIAL IMAGE-GUIDED SMALL ANIMAL IRRADIATOR

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**Purpose:** MicroCT imaging dose in small animal irradiators, especially from serial scans, may be high enough to affect the biological model and tumour growth of the animal. We establish microCT imaging dose to mouse organs for the Small Animal Radiation Research Platform (SARRP), one of two commercial small animal irradiators available, and determine imaging protocols for preventing whole-body and flank-tumour doses from exceeding doses of 10 cGy that may cause deterministic effects.

**Materials and Methods:** A Monte Carlo (MC) model of the SARRP was built in the BEAMnrc code and validated with a series of homogenous and heterogeneous phantom measurements. A microCT scan of a mouse was segmented in OsiriX and used in DOSXYZnrc to determine mouse whole-body, flank-tumour, and organ (cranium, ribs, spine, brain, kidneys, heart, and lungs) microCT imaging doses. Imaging dose to 15-35 g mice for 40-80 kVp tube voltages were examined.

**Results:** For a standard 60 kVp, 0.8 mA, 60 second imaging protocol, dose to an average 20 g mouse was 3.5, 3.4, 10.5, 9.3, 8.1, 3.1, 2.8, 2.7, and 2.7 cGy for the body, tumour, cranium, ribs, spine brain, kidney, heart, and lungs, respectively. Dose decreased by 2-6% for every 5 g increase in mouse weight, with a greater percentage difference seen at lower tube voltages. Tube voltage increases of 40-50, 50-60, 60-70, and 70-80 kVp increased dose by 43, 31,

24, and 19%, respectively. Current-exposure times above 323, 203, 147, 116, and 95 mAs for 40, 50, 60, 70, and 80 kVp tube voltages, respectively, will increase tumour and body doses above 10 cGy. For the standard imaging protocol, three serial scans or a single three-minute scan produced tumour and body doses above 10 cGy.

**Conclusions:** We have established organ imaging dose to 15-35 g mice for 40-80 kVp imaging beams for the SARRP. Maximum current-exposure times for each imaging tube voltage have been determined to prevent whole-body and flank-tumour doses from causing deterministic radiation effects from small animal x-ray imaging.

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#### A REVIEW OF THE CURRENT STATE OF PHYSICS AND DOSIMETRY REPORTING IN RADIATION BIOLOGY RESEARCH

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**Purpose:** In recent years, there has been significant discussion surrounding the inability to reproduce or replicate more than half of studies published in peer-reviewed scientific and medical journals. The biological effects of radiation at the cellular, molecular and physiological level in tumour and normal tissue depend on the source and quality of the radiation delivered. In 2011, a symposium held by NIST and sponsored by the NCI, NIAID, and the NIST outlined recommendations to the radiobiology community defining a list of 12 criteria required for a study to be reproducible and interpretable. Despite those recommendations, the research community has been slow to adopt best-practices in radiation delivery and method reporting in the published literature. The objective of this study was to evaluate the current state of reporting on basic radiation physics and dosimetry aspects of the experimental protocol.

**Materials and Methods:** We evaluated 3542 peer-reviewed articles from 471 journals published in the last 20 years, representing the first large-scale review of physics and dosimetry reporting in radiation biology research. The methods section of each article was evaluated using the recommendations from the NIST symposium in these broad categories: radiation source specification, dose specification, absolute radiation dosimetry calibration, and irradiation geometry. In each instance, a note was made of whether each specific physics experimental detail was reported, as well as the journal impact factor, number of citations, and publication year.

**Results:** While nearly all manuscripts reported the radiation source and dose delivered, fewer than two thirds reported the dose rate or the energy/beam quality of the radiation source, and less than a third reported any details concerning the irradiation geometry. Absolute dosimetry was the worst category, with fewer than 13% of studies reporting any details of the calibration of the experimental irradiator. In general, there was a negative correlation between the reporting of basic physics and dosimetric experimental details, and various metrics of publication quality such as journal impact factor, citations, or citation per year.

**Conclusions:** These data indicate the majority of studies involving radiation currently fail to report the basic experimental details necessary to interpret and replicate the study results. This has serious implications on the reliability of the reported mechanisms underlying tissue response and efficacy of therapeutic interventions.

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#### EFFECT OF REDUCED DOSE OF GADOLINIUM CONTRAST IN TUMOUR VOLUME DELINEATION AIDED BY DCE-MRI FOR SINGLE FRACTION RADIOTHERAPY IN EARLY STAGE BREAST CANCER PATIENTS

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**Purpose:** Dynamic contrast enhanced (DCE) MRI is increasingly used in

radiotherapy for breast cancer for its superior soft tissue contrast and high sensitivity. However, recent studies have reported residual signal intensity in brain and bone associated with gadolinium contrast agents (CA), and measurable quantities in post-mortem studies of patients who received CAs – long after contrast enhanced MRI. While no pathological risks have been identified, it is prudent to reduce exposure of CA as much as possible. One method is to reduce the dose of CA used - but the effect on target volume delineation should be considered. The objective of this study was to determine how reducing the dose of CA affects delineation of the clinical target volume (CTV) in early stage breast cancer treated with neoadjuvant stereotactic body radiation therapy.

**Materials and Methods:** Three-Dimensional fat suppressed fast low angle shot (spatial/time resolution of 1.0x2.1x1.2mm/18s) images were acquired on a 3T-PET/MRI system (Siemens Biograph mMR) as part of the SIGNAL trial (Guidolin et al., 2015), which included one pre- and 28 post-contrast images. Initially, 13 patients received a clinical dose of CA (0.1 mM/kg). However, due to the findings above, the next nine patients received half (0.05 mM/kg). A late post-contrast MR image was manually aligned to the radiation treatment planning simulation CT using Mim v6.8.0 beta (Mim Software, Cleveland, USA). Five experts contoured the gross-tumour-volume (GTV) on the CT with the aid of a post-contrast MR. Analysis was performed on the CTV generated by uniformly expanding the GTV by 0.5 cm. The conformity index (CI) was calculated for each observer pair, as well as the volume per patient for the full and half contrast group. Interobserver variability was assessed using the intraclass correlation coefficient (ICC) for the volume measurements for each group and groups compared. To determine systematic differences between the groups, a t-test was used to compare the CI (averaged across observer pairs) and volume measurements (averaged across observers).

**Results:** A high degree of reliability was found in the volumes contoured for both the full (ICC = 0.969) and half groups (ICC = 0.972) with no significant differences. There were no significant differences in the CI or volume measurements between groups. However, there was a trend towards smaller volumes in the half dose group (mean [range] for full and half = 7.19 [2.52-17.76] cc and 5.89 [2.62-16.62] cc, respectively).

**Conclusions:** We found that there were no significant changes in terms of the interobserver variability, the contoured volume, or the degree of overlap between observers. Therefore, reducing the dose of gadolinium in DCE-MRI may be an effective strategy in reducing risk to patients as the use of DCE-MRI becomes the standard for radiotherapy planning in the future.

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### DEFINING BACKGROUND IN RECTAL CANCER FDG-PET SCANS BY DECOMPOSING DIFFERENTIAL UPTAKE VOLUME HISTOGRAMS

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**Purpose:** We present a new methodology to define background for use with FDG-PET/CT data. This technique uses the decomposition of FDG-PET based differential uptake volumes histograms (dUVHs) into analytical functions to calculate patient-specific background values. This method of dUVH analysis was originally developed to extract glycolysis-based sub-volumes within tumours but was constrained by requiring a paired healthy organ to determine background. This work in background definition expands the methodology to rectal cancer and other unpaired sites.

**Materials and Methods:** Our retrospective cohort consists of 20 histopathologically confirmed pT3N0 rectal adenocarcinoma patients. FDG-PET/CT scans were acquired for all patients prior to pre-operative endorectal brachytherapy. The cohort was selected such that after surgery 10 patients had a complete response to brachytherapy (restaged pT0N0) and 10 had a minimal response (remained pT3N0). FDG uptake values (Bq/mL) were sampled after co-registering PET/CT images. Regions of interest (ROIs) were drawn to include tumour and healthy rectal tissue while avoiding gas/feces. A dUVH was then created for each patient, to be decomposed into a minimum number of Gaussian functions.

**Results:** The central uptake of the fitted function with the lowest uptake

was used to normalize each patient's dUVH, creating signal to background ratio (S/B) values. This follows the assumption that this value corresponds to the uptake of healthy rectal tissue. The largest S/B value (S/B) max was found for every patient and the two sub-cohorts were compared. For the patients that completely responded to the brachytherapy (pT0), the average (S/B) max value ( $10.1 \pm 0.8$ ) was determined to be significantly higher than the non-responders (pT3;  $5.6 \pm 0.8$ ) (determined with a two-sample paired t-test with  $p < 0.00001$ ).

**Conclusions:** The results we present indicate that the analysis of dUVHs can be used to aid in the definition of healthy tissue background in PET imaging. This methodology extends dUVH analysis to unpaired organs, previously being limited to sites with a healthy contralateral organ for background definition. Lastly, we showed that (S/B) max values may potentially be viable in the assessment of a tumour's response to radiotherapy – possibly allowing patient-specific treatment plans in the future.

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### THE FEASIBILITY OF REGISTERING INTRA-OPERATIVE CONE-BEAM CT IMAGING TO RADIATION PLANNING CT IMAGES FOR HEAD AND NECK CANCER

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**Purpose:** Post-operative radiation therapy is applied to head and neck patients who present with a positive biopsy following surgical resection of the tumour. Radiation planning for such cases uses the post-operative planning CT image registered to pre-operative imaging in combination with surgical notes to aid in defining the surgical resection margin, referred to as the High Risk Treatment Volume (HTV). Since this margin is difficult to define, HTV margins are ~10mm. Deployment of intra-operative imaging potentially provides a quantitative method of relating the surgical procedure to the radiation planning process. Such information may provide a more accurate description of the resection margin, which could reduce the HV margin or enable an integrated surgery and radiation planning process that could reduce radiation toxicity. This study was performed to determine the feasibility of registering intra-operative CBCT images to planning CT images and assess the registration errors for such a process.

**Materials and Methods:** Five cases were examined in which intra-operative imaging was performed during surgery followed by RT several weeks later. Intra-operative images included pre-resection, post-resection and when possible post-reconstruction cone-beam CT images acquired using the Siemens Zeego. Three registration steps were performed using RayStation (Ver. 6.1). First, pre-operative MRI images were registered to the pre-resection scans to guide the contouring of the tumour on the pre-resection image. Second, pre- and post-resection images were registered together and used to contour the resected tissue volume (RTV). Finally, the post-resection image was registered to the planning CT to map the surgical excision margin to the radiation plan. Target registration points (~6-10 per image) were used to measure the registration error for each of these steps. HTVs were compared to RTVs for each patient. Radiation dose to the HTV and RTV were compared.

**Results:** Rigid registration was sufficient to register the intra-operative images, based primarily on bony landmarks. Rigid and deformable registrations were tested for all steps. Deformable image registration showed only minor improvements in registration accuracy. Target registration error (TRE) was 3-5 mm based. Coverage of the RTV varied significantly and in several cases reflected surgical decisions rather than any inaccuracy in the definition of the HTV.

**Conclusions:** The analysis of a surgically removed region, tumour, and the HTV on the registered image sets allows for the conclusion that it is feasible to register intra-operative CBCT images to planning CT images. However this process is time consuming and must be individualized for each patient. The complexity may be warranted in difficult cases where there is a trade-off between surgical excision accuracy and radiation exposure of normal tissue.

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### PERFORMANCE COMPARISON BETWEEN THREE DIFFERENT IMAGE FUSION METHODS FOR THE REGISTRATION OF LIVER REGION IN PLANNING CT AND POST RADIATION THERAPY PRIMOVIST ENHANCED MRI

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**Purpose:** Information from various imaging modalities can be useful for a post-radiation therapy analysis such as radiation delivery accuracy assessment. Specifically, Primovist™ enhanced MRI has demonstrated radiation dose-related contrast enhancement in the liver region post stereotactic body radiation therapy (SBRT) and hence can be used for verification and accuracy of dose deposition. To ensure maximal volumetric overlap, image registration is performed between the planning CT and Primovist™ MRI. While used traditionally, rigid image registration may not be adequate due to volumetric changes, and different immobilization conditions. The purpose of our study is to assess and compare three types of image registration methods in Velocity AI (Velocity Medical Systems, Atlanta, GA) using anatomical landmarks and Jaccard metric. Anatomical landmarks allow for the quantification of the target registration error (TRE), and Jaccard metric measures the overlap of structures, which allows for the more comprehensive assessment of image registration. The three registration methods evaluated were: rigid registration (RR), deformable image registration (DIR), and Structure-Guided DIR (SG-DIR). Unlike RR and DIR, SG-DIR utilizes structure outlines of the organ(s) of interest for better alignment within the image volume.

**Materials and Methods:** Five patients' planning CT scans along with post-SBRT Primovist™ enhanced MRI scans were obtained for the study. Patients received the total dose of 50 Gy in 5 fractions, and MRI scans were obtained 8-12 weeks after completion of the treatment. A radiation oncologist selected anatomical landmarks in the form of bifurcations and calcifications on corresponding scans. An average of 10 landmarks per patient and 49 landmarks for the entire patient cohort were selected. Liver contours were verified by a radiation oncologist on CT and the MRI. TRE and Jaccard were quantified for the three registration methods. One-way ANOVA was performed to compare TRE means ( $\alpha = 0.05$ ).

**Results:** Average TRE was 7.9mm for RR, 16.8mm for DIR, and 8.2 mm for SG-DIR. RR and SG-DIR means were significantly different from DIR ( $p = 0.01$ ), while there was no significant difference between RR and SG-DIR ( $p = 1.0$ ). Average Jaccard for the five patient group (Mean±SD) was  $0.77 \pm 0.03$ ,  $0.61 \pm 0.17$ , and  $0.86 \pm 0.02$  for RR, DIR, and SG-DIR respectively. TRE assessment of SG-DIR and RR has shown that the two methods perform similarly with respect to one another, however TRE does not necessarily suggest an agreement of structures in the 3D image volume. SG-DIR demonstrates the best volumetric agreement as per Jaccard metric with almost 10% more overlap.

**Conclusions:** Based on the metrics used in this study, we have shown that SG-DIR for registration of planning CT and post-SBRT Primovist™ enhanced MRI is the preferred image registration method.

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### TEXTURE FEATURES FROM EARLY ENHANCEMENT POST-CONTRAST MRI ARE PREDICTIVE OF METASTATIC SARCOMA

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**Purpose:** Pulmonary metastatic disease develops in over 20% of patients with soft tissue sarcoma following primary treatment. One promising approach for predicting metastasis is through texture analysis on post-contrast magnetic resonance imaging (MRI). Conventional post-contrast images are typically acquired over minutes with high spatial resolution and do not capture the short-lived early enhancement – indicative of highly vascularized regions of the tumour – that occurs within the first minute following the tracer injection. This study evaluates whether texture analysis of the early enhancement is a better predictor for lung metastasis than the late enhancement.

**Materials and Methods:** Dynamic T1-weighted MRI series were acquired in 18 patients with soft tissue sarcoma, at 10-second intervals following a tracer

injection. Five of these patients developed lung metastases (median follow up 22 months, range of 10-37 months). Texture analysis was performed on images at early enhancement (approximately 30 seconds post-injection) and late enhancement (approximately 360 seconds post-injection). A gray level co-occurrence matrix was computed for each tumour using 8 gray levels, from which four statistics were derived: Contrast, Correlation, Energy, and Homogeneity. The predictive value of texture features was compared using the receiver operating characteristic (ROC) curve.

**Results:** Energy computed on early enhancement images had the highest area under the ROC curve (AUC) equal to 0.78, with an accuracy of 0.89, specificity of 0.92 and sensitivity of 0.80 at a threshold value of 0.17. In comparison, energy from the late enhancement image had an AUC of 0.71, with an accuracy of 0.78, specificity of 0.77 and sensitivity of 0.80. The AUC was also higher for Contrast and Homogeneity at early enhancement (0.77 and 0.75, respectively) than at late enhancement (both below 0.7).

**Conclusions:** The results suggest that metastatic sarcoma can be predicted by texture analysis on an early post-contrast MRI scan. An accuracy of 0.89 was obtained using a single texture feature on early enhancement data for a cohort of 18 patients. Additional data in a larger cohort of patients will be required to verify the findings.

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### RENAL CT PERFUSION IMAGING DURING HEMODIALYSIS: RELATING KIDNEY BLOOD FLOW TO RESIDUAL RENAL FUNCTION LOSS

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**Purpose:** Normal renal function is adversely affected by diabetes and high blood pressure, leading to chronic kidney disease and eventually end-stage renal disease (ESRD), where most or all native renal function is lost. These patients must undergo renal replacement therapy (RRT), the most common type being hemodialysis (HD), an extracorporeal therapy which mimics normal renal function. Most ESRD patients who start RRT are not entirely anuric. The presence and preservation of some residual renal function (RRF) after RRT initiation is linked to better clinical outcomes and improved HD patient survival. Despite its importance, RRF declines in patients with ESRD after HD initiation, necessitating more aggressive fluid removal in future HD sessions. The pathophysiology of RRF decline in HD patients remains poorly understood and effective RRF preservation strategies have not been identified. It has been shown that circulatory stress during HD is associated with reduced perfusion in other organs. This recurrent sub-clinical ischemic injury over many HD sessions correlates with increased morbidity and mortality in patients. It has been postulated that recurrent HD-induced renal ischemic insults lead to RRF decline. We conducted a study to test how HD affects renal hemodynamics by measuring renal perfusion serially during HD using CT perfusion (CTP) imaging.

**Materials and Methods:** Renal perfusion was measured in 14 HD patients using CTP imaging with a 256-slice CT scanner. Imaging was done at four timepoints (before, one and three hours into, and after HD) without interruption to HD treatment. Each scan was done without breath-hold for two minutes immediately following a bolus injection of iodinated contrast agent. The three-hour measurement point represents peak intradialytic stress as defined from previous studies of HD-induced myocardial injury. Parametric renal perfusion maps were generated from the registered (non-rigid registration) CTP images. Echocardiography was done at baseline and peak stress to detect the development of regional wall motion abnormalities (myocardial stunning) as a reference for ischemic response to HD-induced circulatory stress.

**Results:** Baseline renal perfusion ( $31.8 \pm 20.0$  mL/min/100g) was markedly reduced compared to normal control values and was related to dialysis vintage ( $r = -0.68$ ,  $p < 0.001$ ). HD resulted in the reduction of renal perfusion to 88.4% of baseline at peak stress. Severity of myocardial stunning was associated with the most severe reductions in renal perfusion.

**Conclusions:** Renal perfusion drops acutely during HD and is related to demonstrable perfusion disturbance in another vulnerable vascular bed. Cumulative exposure to circulatory stress may be a key pathophysiological factor in declining RRF. Longitudinal studies are needed to examine whether circulatory stress amelioration during hemodialysis helps preserve RRF.

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### A COMPARISON OF USER EXPERIENCE AND ACCURACY OF SET-UP IN THE USE OF THERMOPLASTIC AND 3D PRINTED BEAM DIRECTIONAL SHELLS FOR EXTERNAL BEAM RADIOTHERAPY

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**Purpose:** The precision of a patient's set-up for the accurate delivery of radiotherapy is paramount. For patients receiving radiotherapy for head and neck cancer it is particularly critical due to the need to prescribe the maximum therapeutic dose to the tumour while sparing normal tissue in very close proximity (Prabhakar et al 2010). Through advances in new technology three-dimensional (3D) printing gives the potential for creating an anatomically precise 3D printed beam directional shell (BDS) directly from a 3D computer model. The aim of this study is to determine the viability of using 3D printed BDSs by directly comparing user experience and set-up accuracy to the currently used thermoplastic BDSs.

**Materials and Methods:** The prototype for the 3D printed BDS was designed, edited and produced by the authors. To examine the prototype seventeen healthy volunteers were recruited and had both types of BDS created. An Anterior and two Lateral surface marks were positioned on each BDS to be used as a baseline for set-up. The baseline marks allowed Vertical, Lateral, Longitudinal and Rotation to be assessed over four sessions. After each session of wearing the BDS, the volunteers immediately completed a State Trait Anxiety Inventory (STAI) Part 1 (Spielberger et al 1983) to evaluate their emotional experience whilst wearing that particular BDS.

**Results:** It was found that there was no significant difference in the external set-up of the 3D printed BDS compared to the thermoplastic BDS for the Vertical and Lateral variables. There was a significant difference in between Sessions for the Longitudinal variable. It was found that the thermoplastic BDSs produced a statistically significant difference for the Rotational variable compared to the 3D printed BDSs. Furthermore, the results from the STAI Part 1 suggested that the 3D printed BDS produced significantly lower scores in anxiety and distress compared to the thermoplastic BDS.

**Conclusions:** The results obtained give encouraging evidence to indicate that 3D printed BDSs could be a viable immobilisation device for patients requiring External Beam Radiotherapy to the head and neck region. Further work is required to bring 3D printed BDSs into clinical use. This would involve dosimetry analysis of different materials and using patients to assess set-up accuracy with kV and cone beam imaging.

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### RADIATION THERAPY STAFFING LEVELS AND WORKLOAD IN CANADA

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**Purpose:** The safe delivery of radiation therapy is dependent in part on the availability of sufficient specialized staff, such as radiation oncologists, physicists and radiation therapists (RTs). General recommendations for staffing levels for RTs have been published, primarily from Australia, Europe, the USA and Ontario, but there are challenges in relating these recommendations to a Canadian, provincial jurisdictional context. As such, there is a paucity of Canadian data on staffing levels of RTs and the models used to establish these levels. This project sought to establish and compare the staffing models used for Canadian RTs, and the staffing levels and workload resulting from these models.

**Materials and Methods:** An electronic survey was sent to all radiation treatment facilities in Canada. This survey requested information on a variety of staffing and practice variables for the 2014/2015 fiscal year.

**Results:** Staffing levels and workload for RTs vary widely across the country. Cancer centres with the highest staffing levels have twice the RTs per linear

accelerator operating hour (linac hour) compared to centres with the lowest staffing levels. In Canada, 89% of radiation treatment facilities are operating below levels of more than 1.0 RTs per linac hour recommended by recent publications from both Australia and Canada. Workload also varies significantly; ranging from 32 courses/RT/year to 75.5 courses/RT/year. Differences in staffing levels or workload could not be accounted for by treatment complexity, number of specialty programs, number of RTs working in specialty non-treatment roles, or size of the treatment centre. While staffing levels were not associated with the use of different staffing models, there was an association between staffing model used and workload. **Conclusions:** With a lack of national staffing standards, there exists a significant degree of variability in staffing levels and workload for RTs in Canada. This variability could not be explained by patterns of practice, roles or responsibilities of RTs at responding centres.

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### INTEGRATING TREATMENT COMPLEXITY INTO RADIATION THERAPY CASE COSTING

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**Purpose:** Accurately estimating radiotherapy costs per case supports the ongoing evaluation of clinical service delivery. Variation exists across the radiation therapy case mix and case costing is not a straightforward process. This initiative aimed to develop a case costing framework to account for various complexities across radiotherapy case types.

**Materials and Methods:** Total direct operational expenses related to radiation medicine service delivery were determined for fiscal year 2016/2017. Expenses were mapped to standard patient activity workload codes. The total expense was then distributed across the number of times the activity was captured in fiscal year 2016/2017. For activities directly performed by staff, the expense was distributed based on activity duration, number of times performed, and number of staff required for the activity. Expert judgement was used to validate durations associated with activity codes. For staffing that supports, but does not directly perform a patient activity, the expense was distributed across the number of times a supported procedure was captured. Non-staffing expenses (e.g. supplies, service contracts) were mapped to patient activity codes. Staffing and non-staffing expenses were tallied to determine the total cost of an individual activity. Cases were categorized based on Radiation Oncology Care Plan, intent, disease site, prescription and technique. Planned activity codes for each case type were determined and summed to calculate total cost.

**Results:** A total of 77 radical and 120 palliative case types were categorized. Significant variations of planned costs per case were observed. For example, within the breast site, a threefold increase in the cost per case was observed when comparing treatment for early stage right-sided breast cancer, to treatment for advanced stage left-sided breast cancer with boost treatment and active breathing coordination.

**Conclusions:** The proposed approach supports the classification of case types and accounts for complexity in radiotherapy case costing. As a future direction, the inclusion of actual time study data, for activity durations in treatment planning and delivery, could be incorporated to further refine case costing calculations.

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### EVALUATION OF RADIOTHERAPY PATIENT DATA COLLECTION IN BREAST CANCER PEER REVIEW ROUNDS

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**Purpose:** Multidisciplinary peer review rounds ensure the quality and safety of individual radiation therapy (RT) treatment plans while providing a tool for continuous quality improvement. At our institution, breast cancer RT peer-review rounds are conducted weekly over one-hour session, with attendance from radiation oncology, therapy, physics staff and trainees. All

newly diagnosed breast cancer patients undergoing adjuvant/neoadjuvant or definitive RT are scheduled for peer-review approximately one week prior to their treatment start date. One challenge in conducting peer review for a large disease site is the ability to systematically review all patients within the limited time constraints. Our objective is to develop a comprehensive patient list with essential patient, tumour, and treatment factors for peer review and to evaluate its feasibility.

**Materials and Methods:** A list of the core patient information necessary to undertake quality peer-review was developed by the site group. Each patient's clinicopathologic parameters were entered into the RT Electronic Medical Record (RT-EMR) by the clinician at the time of RT prescription. Patient information included: age, clinical/pathological stage, surgery type, chemotherapy sequence, tumour size, histology, tumour grade, lympho-vascular invasion, margin status, nodal positivity, ER, PR, and HER2 status, and a comment section. Aside from tumour size, margins, nodal status and comments, all data inputs used dropdown menus, which ensured data consistency and reduced free-text entries. Standard RT prescription selections were templated in accordance with our institutional practice guidelines to facilitate uniformity. All patient parameters extracted from the RT-EMR were transferred to a spreadsheet and evaluated for completeness by a Clinical Specialist Radiation Therapist (CSRT) prior to rounds. For patients with insufficient data for peer-review, missing data were retrieved manually and entered by the CSRT through review of dictated clinic notes. The rate of completion and time required to retrieve missing information were captured following the implementation of the automated data extraction process.

**Results:** RT-EMR data were collected over 40 weeks between April 2015 and April 2016. The average patient data completion during the first month of implementation was 64% (SD10) and increased significantly over time to 86% (SD4) in the final month ( $p < 0.001$ ). The time required to ensure data completion was inversely correlated with the overall data completion rate (Pearson  $r = -0.702$ ;  $p < 0.001$ ). An average of 18 (SD4) patients were reviewed weekly in rounds. The standardization of RT prescription selection and clinicopathologic data streamlined the peer-review process in rounds and significantly decreased preparatory time; mean reduction from 2hr:40 mins (first month) to 1hr:15 mins in the final month ( $p = 0.005$ ).

**Conclusions:** The use of a comprehensive peer review list is feasible and supports peer review of all radical breast RT plans, even in the absence of the attending radiation oncologist. Direct entry of patient information at the time of RT decision-making enhances efficiency and allows prospective data capture, reduction of human resources, and avoidance of manually reviewing transcribed clinical notes.

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#### SEVEN DAY MODEL FOR RADIATION THERAPY (SMRT) - CAPACITY MANAGEMENT AT TRILLIUM HEALTH PARTNERS

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**Background:** Within the Carlo Fidani Regional Cancer Centre, Trillium Health Partner's (THP) Oncology Program operates the only radiation therapy program that services two Local Health Integration Network's and also has the highest population of all the Regional Cancer Programs, with the highest incidence of cancer cases in Ontario.

**Purpose:** Increased volumes necessitated the program to increase operational time to 12 hour days as of June 2017. This capacity challenge was further compounded with the replacement of one of six Linear Accelerators in January 2018.

As part of the evaluation and planning to meet this challenge, THP's Oncology Program assessed several options. These included:

1. Extending current weekdays by 2.5 hours to 14.5 hours,
2. Operating seven days a week,
3. Decanting a portion of referrals to nearby Regional Cancer Centers with under-utilized capacity, and;
4. Remaining at status quo.

**Materials and Methods:** Key evaluation and planning considerations included adherence to the Oncology Programs goals and provincial wait times, patient preference, broad engagement of all Radiation Program staff, professional staff and supporting services, machine maintenance/quality

assurance, and safety/risk.

**Results:** Based on the evaluation and planning process, in October 2017 THP decided to begin delivering radiation therapy seven days a week during machine replacement. From October 2017 to January 2018, THP's Radiation Oncology program developed an implementation plan with the objective of beginning the seven day model at the end of January 2018. Details of the decision-making and planning processes employed from planning through implementation will be presented.

**Conclusions:** Given increasing pressures on radiotherapy infrastructure due to population growth, rising cancer incidence and resource constraints, innovative treatment delivery strategies are needed. The structured approach to plan and implement a seven day radiation treatment model at THP provides one example of such a strategy for other regional oncology programs faced with similar challenges.

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#### INVESTIGATING RADIATION THERAPY INCIDENTS: THE POWER OF A COLLABORATIVE INVESTIGATION

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**Purpose:** The Canadian Patient Safety Institute (CPSI) defines incident analysis as a structured process that aims to identify what happened, how/why it happened, what can be done to reduce the risk of recurrence and make care safer. The investigation of an event is integral to the incident learning process and allows team members to further examine contributing factors and their relationship to the incident. The use of a mock (fictional) radiation therapy (RT) incident was used to explore the impact that a rigorous investigation may have on managing a RT incident.

**Materials and Methods:** Fourteen radiation oncology professionals (radiation oncologists, radiation therapists, medical physicists, residents) participated in a three-hour workshop. Participants were given a brief overview of Incidence Reporting and Learning (IRL) of RT incidences followed by a description of a fictional RT incident. Participants were provided with a detailed timeline of the incident, key professionals involved and how the incident actually affected the RT plan/patient. Following a summary of the incident, participants utilized an electronic polling system to anonymously choose the three top contributing factors to the incident from a possible 15 based on the National System for Incident Reporting, Radiation Therapy (NSIR-RT) taxonomy. Participants were divided into three interprofessional groups to investigate the incident. Five volunteer actors, representing each profession involved in the fictional incident (using a pre-defined script), were available for real time questioning during the teams' mock investigation. Afterwards, participants were asked to re-classify the top three contributing factors to the incident. Responses were collected and analyzed using Mentimeter® voting software. Participant's evaluations of the workshop were completed as well.

**Results:** The top three contributing factors chosen pre-investigation were: communication, documentation inadequate; handoffs inadequate; unfamiliar treatment approach/radiation technique. Post-investigation, policies/procedures non-existent/inadequate; human resources inadequate; and communication, documentation inadequate were chosen by participants. Of the 15 possible contributing factors, five elements saw variation of selection pre/post of  $\geq 10\%$ , only two elements remaining unchanged pre/post. Participants reported high satisfaction with the workshop overall with 67% ( $n = 8$ ) of respondents indicating that their practice will be impacted by the workshop and 33% ( $n = 4$ ) felt that it confirmed their current practice. **Conclusions:** Simulated investigation can have a multipronged impact on participants. It has the potential to alleviate assumptions and bias toward the significance of some factors/actions as well as prejudice towards the relevance of facts/data. In addition, it is evidenced to reaffirm and or potentially change the practice of the individuals involved.

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#### FINAL ANALYSIS OF A PHASE III COMPARISON OF PROPHYLACTIC CRANIAL IRRADIATION VERSUS OBSERVATION IN PATIENTS WITH LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER: 10-YEAR UPDATE OF RTOG 0214

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**Purpose:** To determine if prophylactic cranial irradiation (PCI) improves survival in locally advanced non-small-cell lung cancer (LA-NSCLC).

**Materials and Methods:** Patients with Stage III NSCLC without disease progression after treatment with surgery and/or radiation therapy (RT) with or without chemotherapy were eligible. Participants were stratified by stage (IIIA v IIIB), histology (nonsquamous versus squamous), and therapy (surgery versus none) and were randomly assigned to PCI or observation. PCI was delivered to 30 Gy in 15 fractions. The primary end point of the study was overall survival (OS). Secondary end points were disease-free survival (DFS), neurocognitive function (NCF), and quality of life. Kaplan-Meier and log-rank analyses were used for OS and DFS. The incidence of brain metastasis (BM) was evaluated with the logistic regression model.

**Results:** Among 356 patients entered to this study, 340 are eligible for analysis. The median follow-up time was 2.1 years for all patients, and 9.2 years for living patients. The survival estimates and hazard ratio indicate that there appears to be no improvement in survival with the use of PCI ( $p = 0.12$ , HR = 1.23, 95% CI: 0.95-1.59). Of note, with the current data there is only 45% power to detect the hypothesized difference HR = 1.25 at one-sided significance level of 0.025. The DFS estimates are better in the PCI arm ( $p = 0.03$ , HR = 1.32, 95% CI: 1.03-1.69). Patients in the observation arm were 2.33 times more likely to develop BM than those in the PCI arm ( $p = 0.004$ ). On multivariate analysis PCI was significantly associated with decreased BM and improved DFS, but not OS. However, among the 225 non-surgical patients, use of PCI was associated with higher OS ( $p = 0.026$ , HR = 1.42, 95% CI: 1.04-1.94) and DFS ( $p = 0.014$ ), and lower BM ( $p = 0.003$ ).

**Conclusions:** In this 10-year update final analysis, use of PCI continued to significantly improve DFS and reduce brain metastasis. However, the early accrual closure failed to provide adequate power to detect the hypothesized difference in OS and the survival rates were not significantly different between PCI and observation. Subgroup analyses based on stratification factors suggest that PCI may improve survival among non-surgical patients.

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#### LONG TERM OUTCOMES OF A PHASE II TRIAL OF NEOADJUVANT TEMOZOLOMIDE (TMZ) FOLLOWED BY ACCELERATED HYPOFRACTIONATED RADIOTHERAPY (AHRT) AND CONCOMITANT TMZ FOLLOWED BY ADJUVANT TMZ IN PATIENTS WITH NEWLY DIAGNOSED GLIOBLASTOMA (GBM)

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**Purpose:** Encouraging results were observed on analysis of a phase II of neoadjuvant Temozolomide (TMZ) followed by AHRT and TMZ followed by adjuvant TMZ in patients with newly diagnosed GBM. Here, we report long term outcomes.

**Materials and Methods:** Fifty patients were accrued: age >18 years, histologically-proven GBM, KPS > 60 and adequate hematologic, renal, and hepatic functions. Three to four weeks post-surgery, patients started

neo-adjuvant TMZ for two weeks, then concomitant AHRT and TMZ followed by adjuvant TMZ. Inverse IMRT technique was used to deliver 60 Gy in 20 fractions to PTV60 (GTV+5 mm) and 40 Gy in 20 fractions to PTV40 (GTV+ 15 mm)

**Results:** From March 2009 and July 2013, 50 patients were accrued: median age 60 years. MGMT gene promoter was methylated in 21 patients and unmethylated in 27. Gross total and partial resection were performed in 46 patients, and biopsy in four. With a median follow up of 71 months for patients at risk, median OS is 22 months with PFS of 13.2 months. At three and five years, actuarial OS was 34% and 23%, respectively. Methylated MGMT gene promoter patients have OS of 40.9% at five years. Eleven patients had reoperation, five had radiation-effects with no evidence of recurrence. The actuarial freedom from necrosis is 82.5% at 78 months, and plateaued after 32.9 months. Ten patients are alive: ECOG status of 0 in four, ECOG one in two, ECOG two in three, and ECOG three in one patient. Seven patients are off corticosteroids, while three receive Decadron (0.5 to 4 mg QD).

**Conclusions:** With a longer follow up, the initially observed OS was further confirmed, and compares favourably to OS reported by large clinical trials. The long term toxicity continues to be monitored closely, for this special group of patients with long term survival.

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#### COMPETING CAUSES OF DEATH IN PATIENTS WITH EARLY STAGE SEMINOMA: A POPULATION BASED MORTALITY ANALYSIS COMPARING RADIATION THERAPY VERSUS CHEMOTHERAPY

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**Purpose:** The purpose of this study is to evaluate the causes of death in patients with Stage I or II Seminoma treated in British Columbia (BC), and to compare mortality rates between patients managed with radiation therapy, chemotherapy, or active surveillance.

**Materials and Methods:** Consecutive patients with Stage I or II Seminoma ( $n = 1549$ ) diagnosed in British Columbia between 1984 and 2013 were identified from the BC Cancer Registry and included in this study. Patients were managed with radiation therapy (RT;  $n = 663$ ), chemotherapy (CT;  $n = 259$ ) or active surveillance (AS;  $n = 624$ ). Data was extracted from the registry and verified by individual patient chart review. Cumulative mortality rates were computed using competing risk analysis, and compared using the Fine and Gray model. The 10-year testicular-cancer mortality (TCM), second cancer related mortality (SCM), cardiovascular mortality (CVM), and all-cause mortality (ACM) were calculated from diagnosis date.

**Results:** After a median follow-up of 14 years (RT group: 21.5 years, CT group: 10 years, AS group: eight years), the 15-year overall survival was 91.4%. Only nine patients died due to Seminoma, while six died from treatment-related toxicity, 46 from second cancers, 52 from cardio-pulmonary causes, and 30 from other reasons. The 10-year ACM rate was 5.67% (4.72% RT group versus 8.06% CT group versus 5.75% AS group,  $p = ns$ ), TCM was 0.62% (0.60% RT versus 1.83% CT versus 0.22% AS,  $p = ns$ ), SCM was 1.66% (1.53% RT versus 2.52% CT versus 1.29% AS,  $p = ns$ ), CVM was 1.43% (1.37% RT versus 0.84% CT versus 1.87% AS,  $p = ns$ ), the TRM was 0.45%, and the difference between CT and RT groups was statistically significant (0.15% RT versus 1.55% CT versus 0.32% AS,  $p = 0.014$ ). All six of the treatment-related deaths were due to chemotherapy associated toxicity (some events occurred during salvage therapy, however, groups for analysis were based on initial/primary treatment type).

**Conclusions:** Patients with early stage Seminoma have excellent outcomes and very low cancer related mortality rates (0.62% at 10 year). We report higher treatment related mortality rates with the use of chemotherapy (1.55%), as compared to RT or AS.

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### STEREOTACTIC BODY RADIOTHERAPY FOR THE TREATMENT OF VENTRICULAR TACHYCARDIA REFRACTORY TO CATHETER ABLATION: PRELIMINARY RESULTS

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**Purpose:** Ventricular tachycardia (VT) caused by myocardial scarring is an important cause of mortality and morbidity. Stereotactic body radiotherapy (SBRT) is an emerging tool for the management of VT refractory to antiarrhythmic drugs (AAD) and catheter ablation. Recently, some limited series proved the feasibility, efficacy and good immediate tolerance of SBRT for VT treatment. A SBRT program for non-invasive VT ablation was launched at our institution in 2017 after obtaining the approval of our local ethical committee. We present here the outcomes of the first two treated patients.

**Materials and Methods:** Enrolled patients suffered from recurrent VT or electrical storms (ES) refractory to standard treatments including AAD and catheter ablation. Before the procedure, a detailed electroanatomic mapping (EAM) was performed to localize the VT substrate. Patients had a planning CT-scan in supine position. For each case, the electrophysiologist delineated the VT substrate according to the EAM data. A cardiac MRI was co-registered to the planning CT-scan to help in target volume definition. Irradiation was delivered using robotic SBRT with Cyberknife®. The whole treatment was catheter-free as the distal dipole of the implantable cardioverter defibrillator (ICD) lead was used as fiducial marker for tracking.

**Results:** Since September 2017, two patients with VT arising from extensive scars within the interventricular septum were treated. The first case was ambulatory, while the second had been admitted to the intensive care unit because of an ES with >20 ICD shocks requiring general anesthesia and intubation. For both patients, a total dose of 25 Gy was successfully delivered to the VT substrate. The VT substrate volume and mean dose to the heart were 19 cc and 7 Gy for the first case and 21 cc and 6 Gy for the second. Clinical follow-up and ICD interrogation did not document any VT recurrence, which allowed us to interrupt amiodarone in the first case two months after SBRT and to extubate the second case three days after SBRT. Importantly, no SBRT-related complications occurred.

**Conclusions:** SBRT appears as an efficient and safe tool for the treatment of refractory VT caused by myocardial scarring. SBRT can be delivered totally non-invasively by tracking ICD leads using Cyberknife®.

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### DEEP NEURAL NETWORK FOR MR-TO-CT IMAGE TRANSLATION APPLIED TO HEAD AND NECK PATIENT DATA

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**Purpose:** The study focused on the development and validation of a deep neural network (DNN) for the simulation of CT data sets from MR-only image data in head and neck (H&N) patients.

**Materials and Methods:** The supervised learning environment is based on a generative adversarial network (GAN) consisting of two main sub-nets, e.g. generator and discriminator. The sub-nets are trained together and perform specific tasks. The discriminator acts as the cost function of the optimization process and consists of a convolution PatchGAN classifier. In contrast, the generator synthesizes the output images is based on a U-net architecture. A loss function, defined as an objective that ranks the quality of the resulting images, adapts to the task and data available and is derived during the model's automatic learning process. The discriminator deals with two images at a time, labelled as input and unknown - this can represent either a target image (a positive example) or one that was synthesized by a generator (a negative example). The discriminator then learns to distinguish between real and fake images by using its underlying neural net and referring to the positive and negative examples. The generator network learns to deceive the discriminator by generating real-looking images. The simulated CT (sCT)

net was trained using 22 randomly identified image sets (CT and MR(T1w/T2w)) acquired from patients diagnosed with oropharyngeal squamous cell carcinoma and treated with definitive intensity-modulated radiation therapy (IMRT) +/- concurrent chemotherapy at our institution in 2016. Images were acquired following routine clinical protocols, and all patients immobilized in a mask and positioned head first supine. Co-registration of the MR and CT data, followed by resampling in a common system of reference was performed for all cases to prepare the input data for the net training. The process of validating the sCT data includes anatomical feature matching (sCT-CT registration, expert review) and RT plan dosimetry (gamma maps, target/OARs).

**Results:** The sCT net was preliminarily tested and validated in an anthropomorphic phantom and by using H&N patient data. Several H&N sCT models were generated using T1w, T2w and combined T1w+T2w MR image data. The neural net was optimized to minimize the need for model input's training data, and implicitly to reduce the overall MR acquisition time, without a significant penalty on the quality of resulting sCT images. Once the net was trained, the generation a full H&N sCT was under 1 min. The quality of sCT was bounded by the intrinsic specifics of the input MR data (voxel resolution). Ongoing analysis is quantifying the dosimetric differences between CT and sCT by re-computing clinical CT-based plans on the corresponding sCT data sets. The dosimetric deviations (target, OARs) between CT and sCT are expected to be better than 2%.

**Conclusions:** The study achieved the proof of concept for a dedicated neural net applied to the generation of simulated CTs from MR data in the case of H&N patients. The study is ongoing to fully quantify the dosimetric implications of sCT.

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### MC SIMULATIONS OF MIRCOCCT IMAGING ON THE SMALL ANIMAL RADIATION RESEARCH PLATFORM (SARRP)

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**Purpose:** In this work we have investigated the effect of imaging geometry on spatial resolution and noise for an image-guided small animal irradiation system. Here we present data from our experimentally validated Monte Carlo (MC) model of the small animal radiation research platform (SARRP, Xstrahl, Suwanee, GA). The SARRP model was used to image a small animal QA phantom in the pancake (rotation axis perpendicular to the longitudinal axis of the subject) and standard (rotation axis parallel to the longitudinal axis of the subject) geometry. Experimental and simulated MicroCT images were used to calculate the modulation transfer function (MTF) and noise for both geometries.

**Materials and Methods:** Our SARRP MC model was built using the EGSnrc/BEAMnrc MC code package. The MC model was validated using half-value layer (HVL), ionization chamber and EBT3 Gafchromic film (ISP, Wayne, NJ) measurements of the SARRP system. MicroCT imaging was performed on the QA phantom in both the pancake and standard geometry. Experimental images were acquired on the SARRP system. The simulated images were reconstructed using the FDK reconstruction algorithm in MATLAB (The MathWorks, Natick, MA). Imaging simulations of the MC model were performed with a modified version of DOSXYZnrc to allow for the SARRP system imaging geometry. The MTF of each image was calculated using the resolution section of the QA phantom, which contains various arrays of holes with varying size. The noise was calculated as the standard deviation of a centrally located ROI in a uniform region of the phantom.

**Results:** The validation data agree within 3% between our MC model and experiments. An improvement in spatial resolution in the images of both the experimental and simulated pancake geometry is evident. The MTF of the pancake images is higher for all resolution values for the experimental and simulated cases. Noise is observed to be higher in the pancake geometry for both experimental and simulated images.

**Conclusions:** Experimental and simulated microCT of the small-animal QA phantom in the pancake geometry shows an improvement in spatial resolution over the standard geometry. Our MC model of microCT imaging of the SARRP can be used to evaluate various imaging protocols and to test and optimize future microCT imaging systems.

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### DOSIMETRIC EVALUATION OF PSMA PET-DELINEATED DOMINANT INTRA-PROSTATIC LESION SIMULTANEOUS IN-FIELD BOOSTS

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**Purpose:** Prostate cancer is multifocal however there often exists a single dominant focus in the gland responsible for driving the biology of the disease. Dose escalation to the dominant lesion is a proposed strategy to increase tumour control. We applied radiobiological modeling to evaluate the dosimetric feasibility and benefit of dominant intra-prostatic lesion simultaneous in-field boosts (DIL-SIB) to GTVs defined using a novel molecular PET probe (18F-DCFPyL) directed against prostate specific membrane antigen (PSMA). **Materials and Methods:** As part of a prospective clinical trial, IGPC-2, patients with clinically localized, biopsy-proven PCa underwent preoperative 18F-DCFPyL PET/CT. DIL-SIB plans were generated by importing the PET/CT into the Raystation treatment planning system. GTV-PET for the DIL-SIB was defined by the highest %SUVmax that generated a biologically plausible volume (GTV comprised of contiguous voxels without gaps; range 23%SUVmax to 40%SUVmax). Volumetric arc-based plans incorporating prostate plus DIL-SIB treatment were generated. Tumour control probability (TCP) and Normal Tissue Complication Probability (NTCP) with fractionation schemes and boost doses specified in the FLAME (NCT01168479), PROFIT (NCT00304759), PACE (NCT01584258), and hypoFLAME (NCT02853110) protocols were compared.

**Results:** Comparative DIL-SIB plans for six men were generated from the pre-operative 18F-DCFPyL PET/CT. Median boost GTV volume was 1.015 cm<sup>3</sup> (0.42 – 1.83 cm<sup>3</sup>). Two cases were high-risk by NCCN criteria, four were intermediate risk (all generated plans were to prostate only). In two patients with GTV volumes close to the rectal wall, minor compromise in the SIB-DIL boost dose was necessary to maintain trial specified organ-at-risk dose constraints. Median minimum (D99%) DIL-SIB dose for FLAME (35 fractions), PROFIT (25 fractions), PACE (5 fractions) and hypoFLAME (5 fractions) were 97.3 Gy, 80.8 Gy, 46.5 Gy and 51.5 Gy. TCP within the GTV ranged from 84-88% for the standard plan and 95-96%, for the DIL-SIB plans. Within the rest of the prostate TCP ranged from 89-91% for the standard plans and 90-92% for the DIL-SIB plans. NTCP for the rectum NTCP was similar for the DIL-SIB plans (0.3-2.7%) compared to standard plans (0.7-2.6%). Overall, DIL-SIB plans yielded higher uncomplicated tumour control probability (NTCP: 90-94%) versus standard plans (NTCP: 83-85%). **Conclusions:** PSMA PET provides a novel approach to define GTV volumes for SIB-DIL dose escalation. Work is ongoing to validate PSMA PET-delineated GTV volumes through correlation to co-registered post-prostatectomy digitized histopathology.

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### AN OPEN-SOURCE APPLICATION WITH GRAPHICAL USER INTERFACE FOR RAPID 2-D IN VIVO DOSIMETRY BY PORTAL IMAGING

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**Purpose:** In vivo dosimetry in radiotherapy is desirable to improve patient safety and treatment outcomes. Various in vivo dosimetry methods using electronic portal imaging devices (EPIDs) have been developed, including a 2-D in vivo dosimetry method developed by Peca et al, which was the first to be open-source (Technol. Cancer Res. Treat., 2017). This method uses transit EPID images from a treatment beam and patient CT data to reconstruct a patient dose map onto a plane perpendicular to the beam centred at isocentre. The dose reconstruction is done by using correlation ratios that relate dose to EPID signal, and ray-tracing to compute the path through the patient for each EPID pixel. This method was implemented as open-source MATLAB scripts, but its poor computational efficiency and a lack of versatility and user-interface limited its clinical use. We present an open-source MATLAB application with graphical user-interface for 2-D in vivo dosimetry building on this previous method that will make it clinically

viable. We also present computational efficiency and commissioning results of our application.

**Materials and Methods:** Computational efficiency was improved by optimizing the ray-tracing algorithm and by also parallelizing computation for use on readily available dual-/quad-core workstations. This optimization does not require a graphical processing unit and so the application may be run on any workstation. Our application adds an intuitive point-and-click interface for system commissioning and patient dose verification. Use of the application for different treatment units and EPID configurations (e.g. resolution, position) can be switched with a single click and altered easily, allowing for efficient and accurate clinical or research use. This is an improvement upon the previous method which was run by typing MATLAB commands and accepted only a single EPID configuration, making clinical use difficult and error-prone.

**Results:** Computational efficiency was bench-marked on a quad-core Intel i7-3770 (3.40Ghz) processor for EPID images (512x384 pixels) of fields from a 3-D conformal plan. Dose computations were completed in 30s/field with a single core, and as low as 10s/field with four cores. Commissioning tests with slab and pelvis phantoms showed that our application's results match those of the original method when comparing reconstructed dose maps to those from a treatment planning system.

**Conclusions:** An open-source application for 2-D in vivo dosimetry has been developed that can be easily implemented in any clinic at no cost. The application's ease of use is significantly higher than previous methods, and its computational efficiency is high enough to open the door for real-time or eventually arc therapy dosimetry, while maintaining accurate dose calculations.

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### INVESTIGATION OF THE QUININE SULFATE SPECTRAL PROPERTIES AND ITS EFFECTS ON THE CERENKOV EMISSION DOSIMETRY

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**Purpose:** Cerenkov dosimetry has recently been proposed to perform volumetric dosimetry using only water. While extremely interesting, issues with the directionality of the Cerenkov emission yielded skewed percent depth dose measurements (Glaser et al, Phys. Med. Biol., 2013). The addition of a very common scintillator, quinine sulfate, to water has been used to overcome this problem with the hypothesis that the quinine absorbs all the Cerenkov light. This study intends to assess the spectral characteristics of quinine sulfate. Precisely, it aims to quantify the ability of the fluorophore to convert anisotropic Cerenkov emission to isotropic fluorescent light and evaluate its contribution to the total emitted light.

**Materials and Methods:** Aqueous solutions of quinine sulfate were prepared with distilled water at various concentrations between 0.01 g/L and 1.2 g/L. The solutions were irradiated with photon beams at 6 and 23 MV. The dependence of the signal (light produced) as a function of sample concentration was studied using a CCD camera with a fixed integration time for all irradiations. The CCD measurements were also achieved at 6 MV with two liquid commercial scintillators, Ultima Gold (Perkins and Elmer) and CytoScint (MP Biochemicals), to get a basis of comparison of the quinine sulfate emission intensity. Spectral measurements of the luminescent solution and the blank solution (distilled water only) were achieved to deconvolve the Cerenkov and quinine contribution to the overall emission spectrum.

**Results:** The luminescent intensity of the samples was found to follow a logarithmic trend as a function of the quinine sulfate concentration up to 1.0 g/L. The trend fails approaching the maximum solubility limit (1.2g/L) resulting in a significant reduction of the intensity. The collected signal of the 1.0 g/L sulfate quinine solution at 6 MV represents only 2.1% of the Ultima Gold signal and 2.3% of the CytoScint. Spectral measurements revealed that the fraction of Cerenkov light absorbed by the quinine increases following a similar logarithmic trend. The maximum fraction of absorbed Cerenkov light occurred at 1.0 g/L and was 7% for both energies. The spectral deconvolution of the total emitted light showed that 52.4% (6 MV) and 52.7% (23 MV) of the total signal collected comes from the quinine scintillation signal, the rest being Cerenkov light emission in water that was not absorbed by the fluorophore.

**Conclusions:** Cerenkov light absorption by the quinine fluorophore was

found to be relatively low. While it was not mentioned in recent Cerenkov dosimetry publications, adding quinine sulfate to water increased the total light output significantly compared to the water-only Cerenkov signal. In such a scenario, the scintillation light becomes the dominant contributor to dose. The use of aqueous quinine sulfate solution is effectively volumetric scintillation dosimetry.

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#### MAGIC-TYPE POLYMER GEL FOR THREE DIMENSIONAL DOSE DISTRIBUTION OF GRID THERAPY

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**Purpose:** Spatially fractionated radiation therapy (grid therapy) with megavoltage x-ray beam is a radiation therapy technique for the treatment of the patients with advanced and bulky malignant tumours. In this technique, an open x-ray field is being converted to a set of small radiation fields using an external block. The aim of this study is to evaluate the accuracy of three-dimensional MAGIC gel dosimetry for the small fields of the grid block.

**Materials and Methods:** In this study a grid block with the hole diameter of 1.3 cm and the hole spacing of 1.7 cm was designed and manufactured. The grid was designed to be mounted on the wedge position of a linear accelerator. To measure dose, a MAGIC gel and a pin point ionization chamber were used. A cylindrical gel phantom was irradiated through the grid block using a  $10 \times 10$  cm<sup>2</sup> field of 6 MV X-rays beam. A 3T MRI was used to determine the R2 relaxation rate value of gel. Moreover, the dose distribution of the grid also was calculated by the Monte Carlo simulation. The dosimetric characteristics of the grid block including percentage depth dose, beam profiles and peak-to-valley ratio were compared for the three dosimetry methods at different depths.

**Results:** The result comparison of Monte Carlo simulation, Ionization chamber dose measurement and gel dosimetry along the central axis (PDD) and profiles of  $10 \times 10$  cm<sup>2</sup> field, show a good agreement between three methods. More than 90% of the points were passing the gamma criteria to within 3%/3mm.

**Conclusions:** The results of this study provide that MAGIC gel is a useful tool for 3-dimensional dose visualization and qualitative assessment of small field dosimetry which is present in grid beam dosimetry.

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#### PENUMBRA MEASUREMENTS AND COMPARISON OF IN-HOUSE AND STANDARD CIRCULAR CONES BY GAFCHROMIC FILM, PINPOINT ION CHAMBER AND MCNPX MONTE CARLO SIMULATION

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**Purpose:** Stereotactic radiotherapy (SRT) is being widely used in modern radiotherapy. SRT is one of the cancer treatment techniques in which small target volume receives high doses of ionizing radiation in multi fractions. Therefore, due to lateral electron disequilibrium, achieving accurate dosimetric parameters are difficult. The penumbra is an important feature of a radiation beam to obtain a suitable margin surrounding the target volume, so the precise penumbra in SRT is necessary for treatment planning and It should be as small as possible. It seems that Monte Carlo and Gafchromic films could be suitable tools to calculate and measure dosimetric parameters in such situations. The purpose of this study is to determine the penumbra size as one of the most important dosimetric parameters in SRT fields shaped by two different types of circular cones.

**Materials and Methods:** Different diameters of circular cones were mounted on the head of accelerator to produce 12, 20 and 40 mm field sizes at isocenter. Dosimetric measurements were performed with the EBT3 Gafchromic film, PinPoint ion chamber and then MCNPX Monte Carlo simulation was used to evaluate dosimetric parameters.

**Results:** According to the obtained results, the penumbra is increasing by using larger diameters of circular cones. The obtained measured data by PinPoint ion chamber showed larger penumbra compared to those calculated

by Monte Carlo in all field sizes. The gamma index analysis showed the differences of 2%/2 mm at all points. The results of this study showed that in small field dosimetry with PinPoint ion chamber, EBT3 Gafchromic film and Monte Carlo simulation, source to diaphragm distance has a main role in penumbra sizes.

**Conclusions:** The results of this study showed that the EBT3 Gafchromic film is a suitable detector for small field dosimetry specially for measuring beam profile and PDD.

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#### DEVELOPMENT AND CHARACTERIZATION OF A THREE-POINT PLASTIC SCINTILLATOR DOSIMETER IN HDR BRACHYTHERAPY

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**Purpose:** The concept of using multiple scintillation sensors attached to a single optical chain has been demonstrated by our group but its application limited to measurements within 3 cm from an HDR source. The purpose of this study is to demonstrate the increased performance in term of sensitivity and accuracy resulting in a thorough optimization of the optical chain with application to HDR brachytherapy in mind.

**Materials and Methods:** A three-points multipoint plastic scintillator detector (mPSD) was constructed and characterized for HDR brachytherapy. The detector was composed of three scintillators BCF-60, BCF-12 and BCF-10. Scintillation light is transmitted through a single 1 mm diameter clear optical fibre and read by a compact assembly of photomultiplier tubes (PMTs), which are coupled to dichroic mirrors and filters that are chosen to match the scintillators specific light emission profile. Each component is further numerically optimized to allow for signal deconvolution using a multispectral approach, taking care of Cerenkov stem effect as well as extracting the dose to each element. The PMTs are read simultaneously using NI-DAQ USB-6289 M Series Multifunction (National Instrument) at a rate of 1KHz and is controlled via LabView 15.0 (National Instrument). Dose measurements in terms of distance to the source were carried out according to TG43 (full scatter condition from a large water geometry), which was in turn used for quantifying dose deviations. An <sup>192</sup>Ir source (Flexitron, Elekta - Brachy) was remotely controlled and sent to various positions using a home-made PMMA phantom, which ensures 0.1 mm positional accuracy. The system performance was quantified in term of signal to noise ratio (SNR) and signal to background ratio (SBR). Additionally, the mPSD angular response of each scintillator was experimentally obtained for a fixed source-scintillator distance of 40 mm.

**Results:** Differences between the mPSD measurements and TG-43 are below 5% in the range of 0.5 to 5 cm from the source, with the largest differences observed at larger distances. All scintillators showed a standard deviation no greater than 4% of the mean dose reading. In all the explored measurement conditions, the system was able to properly differentiate the produced scintillation signal from the background one: SNR was found to be above five for all dose rates (6-2000 mGy/s) while the minimum SBR measured was three for a distance of 7 cm (6 mGy/s) from the source. The dosimeter further exhibits no angular dependences.

**Conclusions:** mPSD have numerous clinical potential applications beyond currently available dosimeters and build on its intrinsic energy independence and water equivalence (for energy above 100-120 keV). A three-points mPSD was constructed and optimized for HDR brachytherapy dosimetry and enabled measurements over a wide range of dose rate conditions. The mPSD presented in this study appears a promising candidate for HDR in vivo measurements.

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#### A NOVEL METHODOLOGY FOR RESOLVING THE ELECTRON ENERGY FLUENCE OF A RADIATION BEAM

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**Purpose:** Measuring the energy spectrum of a given radiation beam can serve as an indicator of 'beam quality'. This work presents a novel technique for the resolution of the electron energy fluence of a radiation beam.

**Materials and Methods:** Plastic scintillators are organic materials which emit visible light when interacting with ionizing radiation. By using differently energy-dependent plastic scintillators, the energy spectrum can be resolved. Energy dependence is induced through the addition of high Z dopants; this changes the radiation interaction cross-sections and increases low energy sensitivity. If these differently doped scintillators are used in a measurement; the incoming electron energy fluence spectrum can be resolved if the responses to various monoenergetic beams is known (the response function). In this work, an undoped scintillator, as well as the 1.0, 1.5, and 5.0% Pb-doped plastic scintillators were used; the response function was determined using Monte Carlo Geant4.10.3 simulations.

**Results:** The response of the 5.0% Pb-doped plastic scintillator was found to be 7.19x greater than the undoped scintillator at the lowest energy examined (100 kV x-rays; +/- 0.4%). The light emitted by the scintillator was normalized to dose to water at the scintillator's position. The model of each differently doped scintillator was created in the Monte Carlo simulation; simulations are currently underway to determine the response function for various energy bins in order to resolve the electron energy fluence spectrum of a 6 MV linear accelerator x-ray beam.

**Conclusions:** This work presents a novel methodology for the resolution of the energy spectrum of a given radiation beam using differently doped plastic scintillators and Monte Carlo simulations.

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#### EXPERIMENTAL VALIDATION OF THE MONTE CARLO CALCULATED $K_{\{Q_{\{MSR\}}, Q_{\{0\}}\}^{F_{\{MSR\}}, F_{\{REF\}}}}$ FACTORS FOR THE REFERENCE DOSIMETRY OF LEKSELL GAMMA KNIFE ICON UNIT IN THE CONTEXT OF THE IAEA TRS-483 PROTOCOL

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**Purpose:** Clinically, many centres use the TG-21 protocol to determine absorbed dose rate for the calibration of the Leksell Gamma Knife<sup>R</sup> (LGK) treatment units. The recent TRS-483 protocol contains correction factor data on the calibration of the LGK from only a single source. The goal of this study is to experimentally validate our Monte Carlo calculated  $k_{fmsr}; f_{ref}$   $Q_{msr}; Q_0$  factors for the calibration of the LGK Perfexion/Icon unit in the context of the TRS-483 code of practice.

**Materials and Methods:** Dose rate measurements were performed on a LGK Icon unit using two ionization chambers (Exradin A1SL and PTW 31010) and Keithley 6517A electrometer at Sunnybrook Health Sciences Centre. Three phantoms including LGK Solid water, ABS and Lucy phantoms are used in this study. The measurements in ABS and Lucy phantoms are performed for different orientations of the chambers with respect to the LGK unit. Both chambers had a calibration coefficient traceable to a national standards laboratory. Current measurements are corrected for ion recombination, polarity, environmental conditions and leakage. The dose rate is determined using the absorbed dose to water calibration coefficient ( $ND;w$ ) and is corrected with the calculated  $k_{fmsr}; f_{ref}$   $Q_{msr}; Q_0$  factors. The data for the ABS phantom is also corrected for a 0.97% attenuation effect in the frame. The resulting absorbed dose rate is compared to the dose rate measured using Exradin A1SL in ABS phantom and TG-21 protocol.

**Results:** The smallest calculated  $k_{fmsr}; f_{ref}$   $Q_{msr}; Q_0$  factor is 0.1% for A1SL in Lucy phantom (270 degree rotation) and the largest correction is for PTW-31010 2.4% in the ABS phantom (perpendicular to the symmetry axis of the LGK). The total combined standard uncertainty on the measurement and  $k_{fmsr}; f_{ref}$   $Q_{msr}; Q_0$  factors is estimated to be 0.3%. Applying the Monte Carlo calculated  $k_{fmsr}; f_{ref}$   $Q_{msr}; Q_0$  factors to the measured absorbed dose rates for both chambers and all three phantoms and orientations improved the consistency of the results from 0.73% to 0.47%. The average percent difference between the corrected dose rate using the TRS-483 formalism including the correction factors determined in this work and the measured dose rate using TG-21 is found to be 0.39%.

**Conclusions:** In this study the  $k_{fmsr}; f_{ref}$   $Q_{msr}; Q_0$  values introduced in the

IAEA TRS-483 are calculated for two chambers and three phantoms in LGK Icon Unit and validated through measurement. Considering all phantoms, chambers and orientations, applying the correction to the measured dose rates in LGK Icon unit results in dose rates that are consistent within 0.47%.

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#### ANNUAL LINAC CALIBRATION IMPLEMENTATION WITHIN QATRACK+

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**Purpose:** For the initial and yearly calibration of our linacs, we decided to move away from spreadsheets and binders and to implement a database system keeping track of all the parameters and calibration histories for our five dosimetry systems (three Farmer-type and two NACP-02 ionization chambers) and nine linacs.

**Materials and Methods:** We chose QATrack+, a quality assurance (QA) data management software developed at The Ottawa Hospital Cancer Centre by Randle Taylor et al., because it was already used for the QA programme of our linacs. This software implementation provided the opportunity to review thoroughly and update our reference dosimetry process, from the dosimetry system commissioning to the budgeting of linac calibration uncertainties, according to the TG51 protocol and its addendum.

**Results:** A new reference dosimetry workflow was implemented, which determined the test interconnections among test lists in QATrack+. Test lists were created for the commissioning of each dosimetry system, including its Jaffé plots and the determination of  $C_{int}$  and  $C_{gen}$  for the calculation of Pion as a function of dose per pulse. Other interdependent test lists were created to: 1) import the secondary standard calibration coefficients and correction factors from the NRC Canada; 2) measure the dosimetry systems correction factors as part of annual QA; 3) calibrate tertiary standards on linacs; 4) perform clinical linac calibration for photon and electron beams. Uncertainties and their propagation were included in the tests lists at the last stage of the project in order to assess the global uncertainty on linac calibration.

**Conclusions:** All reference dosimetry processes are now in QATrack+, and any parameter history can easily be followed by the physics group. Uncertainty tracking has allowed us to optimize the overall workflow and aim for both accuracy and precision in linac reference dosimetry.

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#### PERFORMANCE OF 9 ELEKTA X-RAY VOLUME IMAGING (XVI) GENERATORS FOR PLANAR AND VOLUME VIEW ACQUISITIONS

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**Purpose:** While implementing CPQR recommendations, we evaluated the performance of 9 Elekta XVI generators. We investigated the reproducibility of the kVp, HVL, number of frames and exposure for both planar view and volume view (CBCT) acquisitions.

**Materials and Methods:** The tests were performed on version 5.0.2 of the XVI software. To evaluate planar view acquisitions, a RaySafe Xi R/F detector was irradiated at the isocenter using two presets (Head 100 kV and AP Pelvis 120 kV). Irradiations were repeated 10 times for each XVI generator and preset to determine reproducibility. Exposure measurements for volume view acquisitions were done with a CT pencil ion chamber placed at the isocenter in a 16 cm CTDI phantom. Volume views were acquired over 360 degrees with both 100 and 120 kV presets. Again, 10 irradiations were performed for each generator and preset.

**Results:** For planar view acquisitions, the exposure measurements varied by up to 57%, the kVp by 9% and the HVL by 5%. The large variation of exposure has two major causes. On one hand, the number of frames per image ranged from 4 to 7 when it is set to 5 in the preset, corresponding to a variation of 60%. On the other hand, the exposure per frame varied by as much as 25%. For volume views, the maximum difference in exposure was 25% and the number of acquired frames varied as much as 13%. In this case, the acquisition is rotational, so the variability of the number of frames

could be due to variation in gantry speed, as the tube is set to deliver 5.5 frames per second.

**Conclusions:** This study showed exposure variations of over 50% for planar view acquisitions and 25% for volume view acquisitions across 9 different XVI generators. Such large variations would require equally large test tolerances in order to avoid systematic QA failures. To tighten tests tolerances and reduce variability in patient on-board imaging doses, the second phase of this ongoing study will focus on improving the reproducibility of XVI delivery by recalibrating linac gantry speed and the XVI tube filament.

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### THE EFFECT OF THE FLATTENING FILTER ON PHOTONEUTRON PRODUCTION AT 10 MV IN THE VARIAN TRUEBEAM LINAC

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**Purpose:** Neutrons are an unavoidable byproduct of high energy radiation therapy treatments that deliver unwanted dose to patients. Previous studies have shown that there is a significant reduction in photoneutron production around linear accelerators operated without a flattening filter. The purpose of this study was to quantify the differences in photoneutron production of the flattened and unflattened photon beams for a Varian TrueBeam linear accelerator operated at 10 MV.

**Materials and Methods:** Neutron fluence spectra for the flattened and unflattened beams were measured using a Nested Neutron Spectrometer(TM). The flattened and unflattened spectra were compared at three measurement locations in the treatment room using two field sizes; 0.5x0.5 cm<sup>2</sup> (closed jaws) and 20x20 cm<sup>2</sup> (open jaws). The same dose rate and number of monitor units (MUs) were used for both beams. To complement these results, an additional set of measurements was acquired to determine the relative neutron yield of the two beams per source particle (electron striking the bremsstrahlung target). This was achieved by operating the linac at the maximum dose rate for the flattened and unflattened beams (600 MU/min and 2400 MU/min respectively) for the same amount of time, with the dose rate servo turned off.

**Results:** At 100 cm off-axis from isocentre with the jaws closed, the neutron fluence was found to be 34% lower per MU for the unflattened beam compared to the flattened beam. Averaged across all three positions, a reduction in neutron fluence of 37% per MU for the unflattened beam was observed. With the jaws opened, the neutron fluence was 38% lower per MU for the unflattened beam at 100 cm from isocentre. When the linac was operated at the maximum dose rate for each beam for the same amount of time, the neutron fluence was found to be 256% higher for the unflattened beam compared to the flattened beam. Thus, per source particle, the unflattened beam actually has a higher photoneutron yield than the flattened beam.

**Conclusions:** At 10 MV on a Varian TrueBeam linac, there is a reduction in the photoneutron yield of the unflattened beam compared to the flattened beam per MU delivered. Thus, despite the unflattened beam having a higher photoneutron yield per source particle, a reduction in neutron dose received by patients treated with the unflattened 10 MV beam may be expected. This is true provided that approximately the same number of MUs are required to meet treatment planning constraints for both beams.

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### COMPARING THE USE OF PLENOPTIC VERSUS STANDARD CAMERAS IN 3D SCINTILLATION-BASED DOSIMETRY SYSTEMS

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**Purpose:** With the increasing use of high-conformity dynamic radiotherapy techniques, measuring the temporal variation of three-dimensional dose distributions is becoming essential for comprehensive quality assurance. Three-dimensional (3D) scintillation-based dosimetry systems are promising tools for such applications; however, the challenge remains in fully capturing the time-resolved volumetric data emitted from the scintillating volume, without using a dosimetry system that physically impedes on the dynamic

treatment delivery. Interest has been shown in using plenoptic cameras for this reason: compared to a conventional camera, a plenoptic imager has a microlens array in front of its sensor, thus capturing spatial and angular information of incident light. The purpose of this work is to compare the performance when using plenoptic cameras versus standard cameras as distinct points of view for imaging a plastic scintillator volume.

**Materials and Methods:** Plenoptic camera and standard camera points of view (PoV) were simulated at 90° angles with respect to a cubic plastic scintillator volume (100x100x100 mm<sup>3</sup> divided into 50x50x50 voxels). For each imager point of view, projection matrices describing each scintillator voxel-to-detector pixel contribution were computed using paraxial ray tracing. 3D dose distributions were reconstructed using an iterative maximum-likelihood expectation-maximization tomographic algorithm. The normalized root mean square deviation (NRMSD) was used as the metric to compare the 3D reconstructed distributions with the reference synthetic 3D distribution.

**Results:** When using only one imaging PoV, the NRMSD values and extracted dose profiles were similar for 3D reconstructed doses obtained solely using a plenoptic or a standard camera. Also, the interior regions of the reconstructed doses were smoother when using a standard camera. As the number of PoV is increased, the combined plenoptic information used in the tomographic reconstruction algorithm resulted in lower NRMSD values. Namely, in the case of three imaging PoV, NRMSD values were 50% lower when using only plenoptic cameras.

**Conclusions:** 3D scintillation-based dosimetry systems can greatly benefit from using combined plenoptic cameras instead of conventional cameras to capture the volumetric light information emitted from a scintillating volume. This work contributes to characterizing the tomographic value contained in plenoptic images and to guiding the design of a fully self-sufficient 3D dosimetry system for dynamic radiotherapy quality assurance.

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### RESPONSE OF AN ORGANIC PHOTODIODE TO MEGAVOLTAGE PHOTON BEAMS

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**Purpose:** To study the response of an organic photodiode to fields of 6 and 18 MV photon beams and to quantify the dependence of the response on energy, average dose rate, and accumulated dose.

**Materials and Methods:** A heterojunction photodiode was fabricated by spin coating a blend of P3HT and PCBM on a glass substrate. The photodiode was irradiated in an unbiased state, at a depth of 10 cm in solid water, SSD of 90 cm, and field size of 5x5 cm<sup>2</sup>. Doses were delivered in 1 Gy increments, with dose rates between 1.26 - 7.55 cGy/s on a Varian 21iX accelerator. The diode was irradiated with a 6 MV photon beam over the reported range of dose rates. The diode was irradiated at 600 MU/min with an 18 MV beam to evaluate the energy dependence in the MV range. The current of the diode was measured using a source measurement unit (Keithley 2614B). All machine outputs were measured with a calibrated ionization chamber. The sensitivity of the diode was calculated by dividing the total charge collected by the dose delivered for each increment of dose. The total charge collected was determined by integrating the area under the curve of the current as a function of time while the beam was on.

**Results:** The diode demonstrated good noise characteristics (off current of 1.1 ± 0.1 pA). When varying the dose rate of a 6 MV photon beam between 1.26 - 7.55 cGy/s the measured current of the diode was 0.24 - 1.44 nA with an R2 of 1 (e.g. there was no dependence of average dose rate). The initial sensitivity of the device was 0.189 ± 0.001 nC/cGy. That value decreased to 0.094 ± 0.002 nC/cGy after an accumulated dose of 200 Gy had been delivered. The energy dependence was less than 2% between 6 and 18 MV.

**Conclusions:** A prototype organic diode was studied in MV photon fields. It demonstrated excellent linearity with average dose rate, good noise characteristics, and little energy dependence. A reduction in sensitivity with absorbed dose was noted, as is the case with conventional silicon diodes.

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### RADIATION DOSE IN CT PROCEDURES USING SIZE SPECIFIC DOSE ESTIMATION

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**Purpose:** The purpose of the study is to estimate actual patient dose undergoing CT imaging using Size specific doses estimation (SSDE) from phantom measured computer tomography dose index (CTDI) and taking into account of patients' anatomical dimensions to correlate with actual patient dose undergoing CT imaging.

**Materials and Methods:** The study was conducted on Light speed 16, a third generation multi-slice helical CT scanner, M/s General Electric CT scanner is used for imaging and dose measurements study. The dosimetry was performed with DCT-10 ionisation chamber having active length 100 mm and active volume of 4.9 cm<sup>3</sup> using dosimax plus A dosimeter, IBA dosimetry, GmbH, Germany. Measurement of CTDI was performed on CT phantoms (polymethyl methacrylate, PMMA (density = 1.19 ± 0.01 g/cm<sup>3</sup>), using body phantom (32 cm diameter), head phantom (16 cm diameter) and 10 cm diameter phantom to simulate paediatric configuration, each having length of 15 cm. To calculate the effective diameter of the patient, AP and Lateral dimensions of the patient were measured from CT images assuming that the patient has a circular cross section. Patient anterior posterior (AP) separation and lateral separation were measured on transverse CT images at every three cm interval and average thickness in AP and lateral direction was taken for the study. Water equivalent effective diameter of patient was taken to be  $\sqrt{(AP \text{ separation} * \text{Lat. separation})}$  as recommended in AAPM report 204. The patient-specific SSDE is calculated by measuring patient effective diameter and applying corresponding conversion factor to CTDI value.

**Results:** All plotted data points were combined and used in the computer fit assuming logarithmic relationship ( $Y = a * \ln(x) + b$ ) between the normalized dose coefficient and effective diameter. The normalised dose coefficient with respect to 32 cm, 16 cm and 10 cm diameter phantoms will be provided for calculation of SSDE. The SSDE was calculated from measured CTDI values and measured patient anatomical dimension from the CT imaging for forty patients for head, chest, pelvis and abdomen CT examinations.

**Conclusions:** The use of SSDE helps to convert CTDIvol data available in CT console into patient size specific radiation dose value that account for patient anatomical dimensions to correlate with actual patient dose in CT imaging that is not available with CTDI parameter alone. This study also reports considerable underestimation of dose from reporting from CTDIvol, which can be corrected by estimation of SSDE. Therefore, we strongly recommend the use of SSDE for normalizing CTDIvol according to patient size. Thus for clinical purpose it is suggested that the term SSDE to be used to indicate that the patient size was taken into account and to estimate the patient dose in CT.

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### 4D-VMAT DOSE CALCULATION USING TREATMENT SPECIFIC RESPIRATORY MOTIONS

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**Purpose:** The interplay between tumour motion and modulated treatment delivery such as VMAT could lead to discrepancies between planned and delivered doses. In this work, we experimentally validate a method to calculate the VMAT dose distribution in 4D (4D-VMAT), accounting for tumour motion using respiratory motion recorded during each treatment delivery. Our method opens the possibility of fraction-specific dose calculations.

**Materials and Methods:** The 4D-VMAT dose calculation method relies on the time sampling of machine parameters and respiratory amplitude-phase,

recorded during each treatment in the Trajectory Log File (TLF) and Motion Waveform (MW) file, respectively. These files are automatically recorded by a TrueBeam™ linac with a motion management system. The recorded phase information is used to sort the TLF into 10 discrete respiratory phases from which 10 "phased" VMAT plans are created and imported into Eclipse™. To validate this process a QUASAR™ respiratory motion phantom and realistic respiratory motions from the QUASAR™ database were used. Six 4DCT scans of the phantom were acquired with different respiratory motions and a helical (static) CT scan of the phantom. Typical respiratory motion with amplitudes up to 15 mm and periods between 3 to 5 seconds as well as highly irregular respiratory motions were tested to verify the accuracy with a variety of signals. For each 4DCT scan, the IGTV was contoured on the MIP, the PTV created by isotropically expanding the IGTV by 5 mm, and 10 VMAT plans were created on the averaged CT. The 10 plans were delivered three times with different respiratory motions (total 30). To validate the 4D-VMAT calculation, the recorded amplitude was used to simulate tumour motion through the following process: each phased plan was reassigned to the static CT dataset with an isocenter shift corresponding to the median tumour amplitude for that respiratory phase. Plans were re-calculated and summed in the treatment planning system (TPS). For each delivery, Gafchromic™ EBT3 film, placed within the phantom and served as the reference for comparison. FilmQA™ Pro was used for quantitative gamma analysis (3%, 3mm).

**Results:** There was a significant difference in the gamma passing rates for 4D-VMAT (M = 89.4%, SD = 8.5%) compared to the TPS (M = 71.6%, SD = 16.4%) (p < 0.001). These results indicate that 4D-VMAT dose distributions have better agreement with the measured dose distributions, under conditions where interplay affects the delivered dose. 4D-VMAT can be applied to any treatment fraction and has better consistency, evidenced by the smaller standard deviation of the gamma passing rates.

**Conclusions:** The results of validation study indicate our method reproduces the delivered dose more accurately during any fraction, compared to the treatment planning system under conditions where interplay affects the delivered dose.

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### DOSE PERTURBATION OF ESOPHAGEAL STENTS IN VOLUMETRIC MODULATED ARC THERAPY

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**Purpose:** Esophageal stents are commonly used to palliate dysphagia in patients with esophageal cancer. There is some concern however about the safety of combining stents with radiotherapy (RT) due to the risk of stent migration and potential impact of the stent on dosimetric parameters that could lead to overdosing the esophagus, which may increase the risk of complications such as perforation or fistula, or underdosing the tumour. While dose perturbations caused by stents with static photon beams are documented, perturbations arising from volumetric modulated arc therapy (VMAT) have not been reported. The aim of this study was to investigate the RT dose perturbations caused by esophageal stents in patients undergoing VMAT for esophageal cancer.

**Materials and Methods:** A silicone-coated, Nitinol wire-braided esophageal stent (WallFlex Fully Covered; Boston Scientific, Marlborough, MA) was examined in this study. The stent had an outer diameter of 18 mm and length of 150 mm. The stent was centred in a water phantom with dimensions of 20 cm × 15 cm × 10 cm. Computed tomography images of the phantom were obtained using a 2.5-mm slice thickness of and 0.5-mm axial resolution. A cylindrical planning target volume (PTV) with a diameter of 4 cm and length 5 cm length was placed in the centre of the phantom surrounding the stent. A 6-MV VMAT plan with 4 Gy prescribed to the PTV was generated with Eclipse treatment planning software (Varian Medical Systems Inc., Palo Alto, CA) using the Anisotropic Analytical Algorithm (AAA) (version 11.0.31) for dose calculations. Gafchromic EBT3 films were placed abutting the stent and the phantom was irradiated with the VMAT plan. Dose distributions measured with film and calculated with AAA were compared using Film QA Pro (version 5.0; Ashland Inc., Bridgewater, NJ).

**Results:** The VMAT plan delivered to the film had a mean dose of 101.5%

Gy (range, 94.9-104.4%) of the prescribed dose to the PTV. The mean ( $\pm$  standard deviation) percentage difference of the dose measured on film versus the dose calculated by the treatment planning software was  $-1.0\% \pm 1.4\%$  at a distance of 2.5 mm from the stent,  $-1.5\% \pm 1.7\%$  at a distance of 5 mm from the stent,  $-1.5\% \pm 2.1\%$  at a distance of 7.5 mm from the stent, and  $-2.1\% \pm 1.7\%$  at a distance 10 mm from the stent.

**Conclusions:** The measured dose distribution at distances greater than 2.5 mm from the stent agrees with the dose calculated by the treatment planning system. Monte Carlo simulations are warranted to investigate dose perturbations at distances less than 2.5 mm from the stent.

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#### INVESTIGATING THE FEASIBILITY OF EPID-BASED FOUR-DIMENSIONAL IN VIVO DOSE VERIFICATION FOR REAL TIME TUMOUR TRACKING

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**Purpose:** The increased use of complex techniques for moving targets irradiation, such as gating and real-time tracking, requires additional quality assurance to mitigate these increased patient risks. To address this need, we are developing an in vivo method of dose delivery verification for real-time aperture tracking techniques, using EPID-based, on-treatment patient dose reconstruction.

**Materials and Methods:** We have modified a previously verified in-house, model-based algorithm to compute full 4D patient dose using 4D volumetric CT (4DCT) datasets that can be combined, through image registration methods, to accumulate dose delivered during real-time tracking. The feasibility of this technique has been investigated using a MLC-tracked, 3D conformal plan delivered to a dynamic thorax phantom (CIRS Inc., Norfolk, VA).

The phantom was scanned, generating a 10-phase 4DCT dataset with a 2 cm diameter tumour insert moving with 1cm amplitude sinusoidal motion in the superior-inferior direction. GTVs were generated for each phase, along with MLC apertures shaped to the target, for a static gantry. These MLC shapes were combined into a single dynamic MLC field tracking the tumour motion. The plan was delivered to the phantom on a 2300ix linear accelerator (Varian Medical Systems) operated in 6 MV mode equipped with an aS1000 EPID. The tumour motion and Linac delivery were synchronized using a RPM system (Varian Medical Systems) in gating mode with a custom breathing trace designed to initiate the dynamic beam start when the moving tumour was in the required phase. A special data-acquisition computer with a dedicated framegrabber and software (iTools Capture, Varian Medical Systems) was connected to the EPID to capture all individual EPID frames before, during and after the beam on treatment. The individual EPID frames were sorted into the corresponding closest phase of the 10-phase 4DCT, and the dose to the tumour was reconstructed for each phase.

Dose accuracy was assessed for the full dynamic plan (all 10 phases) and a single-phase plan (0% phase), which essentially represented a static field test (verifying baseline accuracy). The full 3D dose distributions for Eclipse plans were compared to the EPID dose reconstructions using the chi comparison metric with 3% dose and 3 mm distance-to-agreement metrics.

**Results and Conclusions:** The chi comparison between the Eclipse plan and the EPID dose reconstruction for a single phase resulted in 100% agreement, as expected. For the full dynamic delivery (i.e. all 10 phases tracked in a single delivery), a total of 931 EPID frames were collected, with a time resolution of 0.17 ms. While further work is required to assess the accuracy of this approach, the EPID-based in vivo dose reconstruction model shows promise as a tool that can be used to verify real-time MLC-tracked radiotherapy treatments.

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#### EFFECT OF THIN X-RAY FILTER DESIGN IN MODERN IMAGE-GUIDED SMALL ANIMAL IRRADIATORS ON X-RAY DOSIMETRY AND RADIATION BIOLOGICAL EFFECTIVENESS

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**Purpose:** Recent advances have led to the development and a rapid rise in the utilization of image-guided small-animal irradiators in preclinical and basic radiation biology studies. Two models are commercially available: the SARRP from Xstrahl (Xstrahl Inc., Suwanee, GA, USA) and the SmART from Precision X-ray (PXi, North Brantford, CT, USA). While these irradiators are capable of much more precise delivery of radiation compared to traditional cabinet-style biological irradiators, their design is different from that used in previous radiation biology research. Traditional cabinet-style irradiators are typically operated at 300-320 kVp, using a thoraeus filter comprising a thick component of Tin ( $Z = 50$ ), which filters the lower-energy components of the beam spectrum. In contrast, the SARRP and the SmART use energies of 220/225 kVp, and filter thicknesses of 0.15 /0.30 mm Cu, respectively. This produces comparatively very lightly filtrated beams whose photon spectra are predominantly weighted towards low-energy photons compared to those of traditional cabinet irradiators. In this study, we perform Monte Carlo calculations of absolute dose rate, relative percent depth dose, and radiation biological effectiveness (RBE) of these beams to assess their sensitivity with slight changes in the thickness of their filters.

**Materials and Methods:** We modelled an Xstrahl SARRP using validated Monte Carlo packages. A modified version of PENELOPE that tallies double strand breaks was used for micro-dosimetric simulations of the RBE, which was calculated for 0.15 and 0.30 mm Cu filters, as these correspond to the Xstrahl SARRP and the PXi SmART, respectively, as well as Co-60 for reference. To compare with a typical biological irradiator, the RBE was also calculated for a PXi X-Rad 320 unit using a 320 kVp beam filtered using 0.75 mm Sn+ 0.25 mm Cu + 1.0 mm Al. We used EGSnrc to model the x-ray source for macro-dosimetric simulations of the absolute dose rate. We investigated the effect of varying the thickness of the copper filter in the path of the beam from 0.1-0.3 mm Cu, producing various spectra of varying beam qualities (0.45 mm Cu to 0.90 mm Cu half-value layer) using SpekCalc. These spectra were used to calculate percent depth dose profiles and absolute dose in water.

**Results:** The calculated value for RBE was 2.3 % higher for the SARRP and SmART compared to the X-rad 320 cabinet irradiator, and 7% higher compared to a reference Co-60 beam. Absolute dose and percent-depth dose at 2 cm depth was found to vary at the rate of  $-1.8\%/0.01$  mm Cu and  $+0.4\%/0.01$  mm Cu of filter thickness, respectively.

**Conclusions:** We investigated the influence of thin-filter design on absolute dose, percent-depth dose, and RBE of image-guided small animal irradiators. Compared to the majority of radiation biological studies conducted using heavily filtrated cabinet irradiators, the much thinner filters of image-guided small animal irradiators introduce small changes in the RBE. Furthermore, the beam quality and absolute dose are highly dependent on precise machining of the filter, where a change in 1/100th mm can make a measureable change to the dosimetric properties of the beam. This implies that there may be higher differences in dose and dose rates between different units than in conventional cabinet-style irradiators. These results emphasize the need for careful unit-specific commissioning of image-guided small animal irradiators, particularly when the treatment filter may be damaged or replaced.

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#### COMMISSIONING A SOLID TANK PROTOTYPE FAN-BEAM OPTICAL CT SCANNER FOR 3D RADIATION DOSIMETRY

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**Purpose:** The objective of this work is to design a new prototype fan-beam optical computed tomography (OCT) scanner for three-dimensional radiation dosimetry. Primary distinctions are a solid acrylic "tank" and the inclusion of iterative reconstruction techniques (IR) into the scanning methods. This

scanner attempts to address artifacts related to color and index matching baths that are often found with OCT for gel dosimeters. As a result of the solid tank design there is lensing that the fan-beam experiences while passing through a gel dosimeter, this lensing makes filtered back projection (FBP) less suitable than IR for image reconstruction.

**Materials and Methods:** The two distinct features of this scanner are the use of a solid tank as an alternative to refractive index (RI) matching baths, and the inclusion of IR rather than FBP for image reconstruction. A polished acrylic block functions as a solid tank that is used to reduce the effects of material RI mismatch. Five arrays of 64 photodiode detectors (0.8 mm x 0.7 mm) were run in series to collect optical projection data. The detectors sat flush against the acrylic. A gel is rotating inside a hole in the acrylic block and each projection is taken at 0.5 degree steps for 360 degrees before and after irradiation. The scanner properties were evaluated by imaging radiochromic silicon gel dosimeters. The prototype scanner commissioning involved determining the spatial resolution, low/high contrast resolution, image geometry, and image noise with respect to laser intensity.

**Results:** Spatial resolution was measured using modulation transfer function found from the edge spread function of a cylindrical attenuating object. Low contrast resolution was measured by irradiating a silicon gel in a pattern replicating conventional CT phantoms with a gradient of dose. Image geometry was measured by placing opaque objects of known geometry inside of a gel and comparing the ratio of their pixel distances to their ratio geometric distances. The leading issue with the solid tank design is light pollution. Due to the lack of a collimator on the photodiode detectors there is a much high susceptibility to ambient light pollution or excess laser light pollution. The low critical angle at an air-acrylic interface keeps excess laser rays inside of the block further increasing scatter contribution.

**Conclusions:** This work provides an alternative to traditional matching bath methods of addressing color and index matching for OCT of gel dosimeters. The inclusion of iterative reconstruction provides an alternative to filtered back projection. The system is capable of scanning 0.8 mm slices of cylindrical volumes in under three minutes.

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#### RESOLVING THE FAT GLYCEROL RESONANCE (4.2 PPM) FROM THE WATER SIGNAL IN MAGNETIC RESONANCE SPECTROSCOPY AT 3 T

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**Purpose:** Proton magnetic resonance spectroscopy (MRS) studies of a number of diseases, including cancer, have demonstrated the relevance of fat levels and its composition. The glycerol proton MRS signal of the triglyceride backbone (4.0 – 4.5 ppm) has shown to be useful for measuring fat levels; however, its signal is obscured by water signal (about 4.7 ppm) when employing standard short echo time (TE) Point RESolved Spectroscopy (PRESS) and Stimulated Echo Acquisition Mode (STEAM) in-vivo MRS techniques. The purpose of this work is to find long TE PRESS and STEAM values that enable the glycerol signal to be resolved from that of water at 3 T. Echo times are determined such that water signal has decayed due its T2 relaxation while sufficient glycerol signal is retained despite J-coupling evolution losses. To our knowledge, the response of the fat glycerol signal (about 4.2 ppm) to in-vivo MRS sequences has not been previously investigated.

**Materials and Methods:** Experiments were performed with a whole body 3T Philips MRI scanner on nine oils and on tibial bone marrow in vivo. A transmit/receive coil was employed for phantom experiments while a surface coil was used for reception in vivo. PRESS (TE = 40 to 300 ms in steps of 20 ms) and STEAM (TE = 20 to 300 ms in steps of 20 ms, mixing time = 20 ms) spectra of the oils were acquired with the following parameters: voxel size = 20 x 20 x 20 mm<sup>3</sup>, repetition time = 3 s, number of points = 2048 and sampling frequency = 2000 Hz. Glycerol peak areas in the 4 – 4.5 ppm spectral range were calculated and plotted as a function of TE for both PRESS and STEAM. Spectra were acquired with short TE and with the selected long TE values from tibial bone marrow of four healthy volunteers from an 8 x 8 x 8 mm<sup>3</sup> voxel.

**Results:** The response of the glycerol protons to PRESS and STEAM indicate that for long TE values (TE greater than or equal to 100 ms), J-coupling losses are at a minimum with STEAM when TE = 100 ms and with PRESS

when TE = 180 ms. Tibial bone marrow spectra demonstrate the efficacy of the timings in suppressing water signal while retaining that from the triglyceride glycerol protons.

**Conclusions:** We have shown that a PRESS sequence with TE = 180 ms and a STEAM sequence with TE = 100 ms (mixing time = 20 ms) can be employed to suppress water signal while yielding sufficient triglyceride glycerol signal in tibial bone marrow in vivo at 3T.

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#### ADDRESSING DATA VARIABILITY FROM DIFFERENT INSTITUTIONS FOR ROBUST RADIOMIC MODEL BUILDING

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**Purpose:** The distribution of a radiomic feature can vary between two institutions due to, for example, different image acquisition parameters, imaging systems, and contouring (e.g. tumour delineation) variations between clinicians. We aimed to develop effective statistical methods to successfully apply a radiomics-based predictive model to an external dataset. Monte Carlo (MC) models were used to demonstrate the effect of feature distribution variations on the predictive ability of the feature. Two common feature normalization methods, re-scaling and standardization, were evaluated in terms of their efficacy when applied to datasets containing statistical outliers. Standardization was chosen as the preferred approach, since re-scaling was more sensitive to outliers, and potentially reduced the discrimination power of a feature. It was also demonstrated why a dataset needs to be balanced between positive and negative outcomes before standardization is applied to it.

**Materials and Methods:** The clinical effectiveness of the statistical methods was shown using magnetic resonance images of primary uterine adenocarcinoma. Feature selection was done using 94 samples (Institution X), and feature testing was done using 63 samples (Institution Y). The outcomes studied were lymphovascular space invasion and cancer staging. Logistic regression was used to obtain the prediction accuracy of a feature.

**Results:** When comparing the prediction accuracy, F-score, and Matthews Correlation Coefficient of promising radiomic features in the testing set with and without standardization, there was an improvement due to standardization in most cases for both the studied outcomes. Furthermore, upon applying standardization, the ratio of sensitivity to specificity was close to unity in the testing set, comparable to the ratio in the training set. Without standardization, this ratio deviated significantly from unity in the testing set.

**Conclusions:** An elegant statistical approach of feature standardization using balanced datasets was shown to improve the predictive ability of radiomic features when applied to an independent testing set.

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#### SEMI-AUTOMATED CREATION OF A VARIABLE DENSITY PHANTOM

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**Purpose:** A 3D-printed PET phantom was created previously to mimic the variable tracer uptake seen in lung tumour volumes. This previous work used a hollow inner volume to simulate the high uptake region within the tumour, and a surrounding porous volume comprised of 50% plastic to simulate the low uptake volume. A method has now been developed to create 3D-printed porous volumes computationally rather than the previously-used Computer-Aided Design (CAD) method. The computational method permits the creation of imaging phantoms with interior features that can be used in MRI and PET imaging quality assurance tests or research.

**Materials and Methods:** Software was developed in MATLAB, and consists of two main functions: one creates a background grid with user-defined spacing, and the second creates the variations in density by controlling the dimensions of solid cuboids centred on the grid intersection points. The software outputs files in the Stereolithography (STL) format ready

for 3D printing. The resulting phantom has an open structure enabling water to fill the open spaces. Three simple phantoms were created: a cube containing a sphere with lower plastic density than its surrounding volume, a cube containing a sphere with greater plastic density than its surrounding volume, and a cube featuring a density gradient along one direction. The three phantoms were enclosed in a custom watertight plastic box for testing.

**Results:** Scans of the phantoms were acquired. Internal phantom features are easily identifiable in the images, and are compared to a CT scan of the plastic phantom alone (without water).

**Conclusions:** This approach shows promise in the creation of novel imaging phantoms for MR and PET.

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#### OPTIMIZING AN IN VIVO 1H MAGNETIC RESONANCE SPECTROSCOPY TECHNIQUE FOR THE DETECTION OF 13C4-GLUTAMATE AT 9.4 T TO ENABLE TRICARBOXYLIC ACID CYCLE MEASUREMENTS

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**Purpose:** To optimize the commonly employed Magnetic Resonance Spectroscopy (MRS) Point RESolved Spectroscopy (PRESS) pulse sequence to resolve the  $\approx 2.51$  ppm 13C4 proton (1H) peak of glutamate (Glu) from the  $\approx 2.45$  ppm 1H peak of glutamine (Gln) and the  $\approx 2.49$  ppm 1H peak of N-acetylaspartate (NAA) at 9.4 T. The technique will enable measures of the tricarboxylic acid cycle (relevant to the study of cancer) to be obtained in animal models during the infusion of 13C-labelled glucose.

**Materials and Methods:** The spectral response of 13C4-Glu, Gln, and NAA protons to varying echo times (TE1 and TE2) of a PRESS sequence were investigated numerically. An objective function was created by dividing the peak area of 13C4-Glu by the sum of the peak areas of 13C4-Glu, Gln, and NAA. A contour plot of the function output was created, with TE1 and TE2 varying in steps of 2 ms. The (TE1, TE2) combination with a total TE (TE1 + TE2) of <125 ms that yielded an objective function value >0.5 and that maximized 13C4-Glu 1H peak area while reducing peak areas of Gln and NAA to <40% and <10%, respectively, was considered optimal. The timing set was verified on phantom solutions.

**Results:** The optimal (TE1, TE2) combination was determined to be (26 ms, 98 ms), which yielded an objective function value of 0.51 and simulated peak areas of 52%, 37%, and -7% for 13C4-Glu, Gln, and NAA, respectively, relative to their corresponding (2 ms, 2 ms) values. For phantom solutions, the optimal (TE1, TE2) combination gave peak areas of 61%, 26%, and -17% for 13C4-Glu, Gln, and NAA, respectively, relative to their corresponding short-TE values obtained with (12 ms, 9 ms).

**Conclusions:** A PRESS (TE1, TE2) combination of (26 ms, 98 ms) is suitable for resolving the  $\approx 2.51$  ppm 13C4-Glu proton peak from Gln and NAA at 9.4 T.

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#### A SCANNING METHOD FOR X-RAY FLAT-PANEL CALIBRATION

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**Purpose:** In flat-panel x-ray imagers, the gain and offset of the detector vary from element to element, giving a different response for the same x-ray exposure. The offsets are corrected using dark-field images acquired with no x-ray exposure. In the usual approach, gain calibration is achieved by acquiring a flood-field image using a single x-ray exposure over the full detector area. In some situations, the beam is considerably smaller than the detector, such as when using a fan-beam source at a synchrotron. Furthermore, x-ray tubes do not produce uniform fields, one contributing factor being the anode heel effect. The non-uniformities are incorporated in the gain map and can be corrected as long as the detector remains in exactly the same geometric configuration relative to the source. Such intrinsic incorporation of non-uniformities means that the calibration will be inaccurate if scatter from the phantom constitutes the desired signal, as is the case in x-ray scatter imaging or crystallography. In this work, a scanning technique was employed to generate a true relative gain map using a beam smaller than the detector.

**Materials and Methods:** The monoenergetic fan beam at the Insertion Device beamline of the Biomedical Imaging and Therapy facility at the Canadian Light Source synchrotron was used to calibrate a Hamamatsu C9252DK-14 flat-panel detector. The beam covered 5% of the detector area. Offset correction was performed using dark-field images. First, a map of the fan beam relative intensity was generated by scanning the beam with respect to one specific detector element. Second, the beam was swept over the detector area and the response of each detector element was recorded for three different exposure levels, set by placing different thicknesses of PMMA attenuator in the beam. Only the relative exposures are needed and they were determined using an ion chamber. Based on which part of the beam exposed an element, the output was normalized to the mean beam intensity. All exposures were in the linear response range of the elements and the true relative gain of each element is the slope of the linear fit to the output-versus-relative-exposure data.

**Results:** The offset and gain corrections were successfully applied to the C9252DK-14 detector acquisitions of scatter fields for x-ray scatter imaging. The standard deviation of the relative gain distribution was 4.0% of its mean. The mean  $R^2$  value of the linear fits was 0.998.

**Conclusions:** Flat-panel calibration can be performed without a flood field. The beam scanning technique yields a true relative gain map, which is needed if scatter constitutes the signal or if the detector moves relative to the source.

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#### MRI IMAGING PRE-PROCESSING PIPELINE FOR RADIOMIC STUDIES OF THE BRAIN

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**Purpose:** MRI brain images differ significantly from images acquired using other modalities, like CT scans. The DICOM format is not widely used in brain imaging research, where specialized file types such as the Nifti format (.nii) are favored. With its roots set in radio-oncology, most radiomic analysis tools are designed to work with DICOM images and having regions of interest (ROIs) delineated using the DICOMRT format. The purpose of this work is to create a pre-processing pipeline for Nifti images taking advantage of the available analysis tools for brain imaging such as the FMRIB Software Library (FSL) and to use the resulting segmentation in the DICOM format as input for a radiomics analysis.

**Materials and Methods:** Samples from the Alzheimer's Disease Neuroimaging Initiative (ADNI 1) cohort study are used as input. First, the FSL library is used for standard brain MRI pre-processing such as skull-stripping, RF-field inhomogeneity correction and segmentation into white matter (WM), grey matter (GM) and cerebrospinal fluid (CSF). The skull-stripped images are converted to DICOM format by filling a template and associating a unique identifier (UID) to all images. Then, the resulting segmented images are fed to a C++ ITK program converting the volumetric segmentation to contours. Finally, a published script (Gorthi, S., Insight Journal, 2009) is used to transform the ITK contours to the RTStruct format matching the metadata of the skull-stripped DICOM image. The RTStruct and the DICOM image are used as input for radiomic features extraction.

**Results:** This method can pre-process ADNI MRI Nifti images into the desired segmentation mask (GM, WM, CSF), which is then converted into a RTStruct. Nifti images are converted to DICOM with unique metadata matching its associated RTStruct for radiomic features extraction. The pre-processing pipeline is automated using scripts and take less than five minutes to process a given image, which is negligible compared to the radiomics analysis taking more than an hour.

**Conclusions:** An automatic pre-processing pipeline enables the use of MRI ADNI Nifti brain images with DICOM-based radiomic feature extraction tools designed for oncology without significant time overhead.

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#### SEGMENTATION OF APPLICATORS IN THREE-DIMENSIONAL ULTRASOUND FOR MINIMALLY INVASIVE LIVER THERAPIES

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**Purpose:** Liver cancer incidence in Canada has the second highest average annual percent change since 1992 (Canadian Cancer Statistics 2017). Transplantation and resection have resulted in five-year survival rates of about 40%, but these open surgical procedures are often followed by complications and long patient recovery times. Minimally invasive techniques, such as radiofrequency ablation, offer an alternate cure for early-stage liver cancer patients as they can address open surgery concerns. Yet, insufficient local tumour ablation remains an issue that leads to higher cancer recurrence. The standard of care for these techniques uses CT images for ablation applicator planning with intraoperative guidance provided from 2D ultrasound (US). Limitations with this approach have been associated with 2D US, which can lead to variability in applicator targeting accuracy and poor ablation coverage. Since there is a need to increase targeting accuracy, intraoperative 3D US imaging is being investigated for utility in the current workflow with the addition of a semi-automated segmentation algorithm to improve localization of applicators.

**Materials and Methods:** A manually placed seed point initializes the algorithm and is centered around a generated search space of line segments. The most probable trajectory is selected from this space using a signal-to-background intensity threshold of 1.5. The line segment is extended and a more sensitive intensity threshold (Otsu's method) is employed along the trajectory to determine the tip location. 3D US images were acquired of 10 applicators inserted into an agar phantom to test the segmentation algorithm, followed by a triple-user study on 17 clinical 3D US images from liver ablation procedures. The applicators in the agar phantom images were segmented using three different manual seed points to assess variability in the algorithm. Tip and trajectory errors were assessed independently and computed as the difference from manually segmented segmentations. Since 3-5 cm diameter tumours are typically treated, segmentations were considered a success if the tip error was <10 mm or trajectory error was <6°.

**Results:** The mean trajectory error during phantom trials was  $1.8 \pm 1.1^\circ$  (100% success) with a mean tip error of  $3.0 \pm 2.2$  mm (87% success). For the clinical images, the trajectory identification rates for the novice, intermediate, and expert US users were 94%, 76%, and 94% with corresponding tip identification rates of 76%, 76%, and 88%, respectively. Trajectory errors were  $2.4 \pm 1.8^\circ$ ,  $2.3 \pm 1.1^\circ$ , and  $2.0 \pm 1.2^\circ$  for the novice, intermediate, and expert users, respectively, with tip errors of  $3.6 \pm 2.4$  mm,  $2.9 \pm 1.6$  mm, and  $1.9 \pm 1.2$  mm.

**Conclusions:** Applicator segmentations offer accurate results on phantom and clinical 3D US images, allowing improved workflow during liver ablation procedures. Future work will focus on increasing robustness when used on clinical images and investigation of curved applicator segmentations.

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#### UNPACKING CT RADIOMICS BIOMARKERS IN TUMOURS USING DYNAMIC PET IMAGING

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**Purpose:** The full promise of extracting features from CT images that correlate with patient outcome ("radiomics") will only be realized when patients are stratified for targeted therapies based on these features, with a resulting improvement in outcomes. This requires understanding which physiological properties of tumours are responsible for observed CT gray-level textures and statistics. In this study, co-registered CT and dynamic PET images in pancreatic tumours were used to correlate physiology and CT gray levels, making use of the fact that the kinetics of freely diffusible PET tracers are related to physiological tissue properties such as perfusion and extravascular tracer diffusivity.

**Materials and Methods:** Dynamic PET time-activity curves were analyzed in 34 patients with pancreatic ductal adenocarcinoma injected with the hypoxia-sensitive tracer 18F-fluoroazomycin arabinoside. A pharmacokinetic model was developed that correlated the short-time voxel-scale tracer distribution volume with lipid and mucous content. Using known photon attenuation coefficients for these tissues, this model was used to predict the CT number in the co-registered CT images, providing a way to test the model.

**Results:** Strong correlations were found between the predicted and measured CT number values in CT voxels (down-sampled to the PET resolution)

in pancreatic tumours (average Pearson r value over all tumours = 0.89), indicating that lipid and mucous deposits are primarily responsible for CT gray-level variations in pancreatic tumours.

**Conclusions:** A novel model for PET tracer kinetics can predict CT gray-level features and attribute them to clinically relevant tissue physiology: for pancreatic tumours, the presence of mucous and lipids. This gives a physiological underpinning to known CT radiomics biomarkers for pancreatic tumours in terms of the spatial architecture of such tissues. Current work seeks to extend this model to non-small cell lung tumours, a major subject of radiomics studies.

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#### NON-INVASIVE IMAGING OF TUMOUR HYPOXIA USING EF5 AND PET-CT IN HEAD AND NECK CANCER: A PILOT STUDY

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**Purpose:** Tumour hypoxia is an important factor in treatment failure following radiation therapy for locally advanced head and neck squamous cell carcinoma (HNSCC). This pilot study was performed to evaluate the feasibility of using [18F]EF5 for clinical PET imaging of tumour hypoxia in HNSCC planned for radical radiotherapy.

**Materials and Methods:** Fourteen patients with Stage III/IV HNSCC undergoing radical radiotherapy were enrolled between 2012 and 2016. Patients were imaged before and two weeks into radiation treatment with EF5-PET. All patients had an FDG-PET CT prior to treatment. On the FDG-PET CT, standardized uptake values (SUV) were calculated using a region of interest drawn around the target area images for suspicious primary and nodal disease separately where  $SUV = (\text{peak activity/mL in region of interest}) / (\text{injected activity/g of body weight})$ . These lesions were evaluated for corresponding EF5 uptake on the EF5-PET. After injection of 185 to 370 MBq of [18F]EF5, PET data was obtained in three-dimensional mode. EF5 uptake was evaluated by the tumour-to-muscle activity ratio (TMR) and a ratio of >1.5 was considered EF5 positive. Paired t-test was used to determine whether there is a significant difference between the TMR before and during treatment, based on the 2 EF5-PET scans.

**Results:** Median follow-up was 26 months. All patients except one had two EF5-PET and one FDG-PET CT scan. One patient declined the second EF5-PET scan. No adverse pharmacological reactions were observed after administration of [18F]EF5. Thirteen patients had oropharyngeal cancer (all except one was p16+) and one had nasopharynx cancer. All patients were treated with 70Gy and 12 received concurrent chemotherapy. Thirty-eight lesions were identified on pre-treatment FDG-PET CT imaging. EF5 was positive in 22 lesions (eight primary and 14 nodal sites) before treatment. Six lesions (three primary and three nodal) remained EF5 positive during radiation, although four had borderline TMR ranging between 1.5-1.62. Mean TMR difference pre and during treatment was 0.30 for primary (p = 0.003) and 0.53 for nodal disease (p = 0.001). One patient with p16- oropharynx cancer had EF5+ persistence during treatment and subsequently had local recurrence. Two patients with p16+ oropharynx cancer died of metastatic relapse, one of which was EF5+ pre-treatment which did not persist during treatment.

**Conclusions:** PET imaging with [18F]EF5 was feasible, and adequate image quality was achieved. The single p16- oropharynx cancer patient who had no resolution of tumour hypoxia in lymph node and primary disease had loco-regional recurrence requiring salvage therapy. In this study, EF5+ persistence was not predictive recurrence in p16+ oropharynx cancer, however, larger scale studies to further assess the impact of EF5-PET detected hypoxia prior and during radiation treatment is warranted to evaluate its ability to predict treatment outcomes.

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#### PERSONALIZATION OF CANCER DRUGS CLEARED BY KIDNEYS USING OPTICAL TRANCUTANEOUS PULSE DYE DENSITOMETRY

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**Purpose:** Kidney is the main excretory organ for many cancer drugs like Carboplatin. Renal insufficiencies can lead to drug toxicity due to increased drug concentration in the blood. Therefore, it is imperative to measure kidney function for optimizing drug dosage while minimizing toxicity and complications. Existing methods of measuring kidney function is to determine its clearance rate of a substance filtered from blood as it passes through the glomeruli or glomerular filtration rate (GFR). GFR measurement requires collecting either blood or urine from a couple to 24 hours. In addition, determining the concentration or amount of the glomerular filtered substance in the collected samples can be time consuming leading to delay in reporting the measurement. The goal is to develop a point-of-care GFR measurement method without blood sampling or urine collection, can be performed at physicians' offices within 30 minutes without any delay in the measurement results.

**Materials and Methods:** Light transmission from NIR-TPDD at two wavelengths through an extremity is measured. One wavelength is tuned to the absorption maximum of the NIR dye Cy7.5-inulin, a GFR agent (synthesized by our collaborator Dr. Len Luyt). The other wavelength is in the red region of the visible spectrum where the absorption by Cy7.5-inulin is minimal. With every heartbeat, blood vessels in the extremity pulsate changing their thickness and hence attenuation of light. The recorded intensity of the transmitted light, thus, exhibit peaks and troughs. The ratio of the ratio of the peak and trough transmitted light at the two wavelengths can then be used to calculate the arterial Cy7.5-inulin concentration. The ratio of the ratio (RoR) method ignores scattering of light, we have extended TPDD theory to include scattering based on the theoretical model of Schuster.

**Results:** Using data acquired with our in-house developed TPDD, the measured Cy7.5-inulin concentration curves based on the RoR method with and without scatter were almost the same. Furthermore, these curves were comparable to that measured by the commercially available Nihon Kohden (NK) TPDD.

**Conclusions:** NK-TPDD cannot be used for measuring clearance of Cy7.5-inulin because it is optimized for measuring ICG which is excreted by the liver with a much faster clearance time. As such, the measurement time of the NK unit is limited to 15 minutes while the plasma half-life of Cy7.5-inulin is at least 60 minutes which necessitates a much longer acquisition time than 15 minutes. Our in-house developed TPDD will overcome this limitation to allow point of care monitoring of kidney function with the optical dye Cy7.5-inulin which will lead to accurate dosing of renal excreted cancer drugs for better therapeutic efficacy without excessive drug-related toxicities.

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#### A METHOD OF KINETIC MODELING WITH TUNEABLE LEVEL-OF-DETAIL SUITABLE FOR SPARSE SAMPLING

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**Purpose:** Perfusion modeling is a computationally demanding procedure which can take up to several cpu-days depending on the imaging protocol and desired precision. Computational efforts required for kinetic modeling, the computational method underpinning perfusion imaging, is increasing due to increasing image resolutions, greater reliance on imaging for clinical diagnoses, and fast acquisition modes which create thousands of image slices within a single series. In this article we present a novel technique for tracer kinetic modeling that handles non-uniform and sparse temporal sampling, and also provides a level-of-detail mechanism permitting dynamic accuracy and runtime trade-offs. Use of this method could enable dynamic allocation of computational resources, and reduce computational workload when reduced precision is sufficient.

**Materials and Methods:** An algorithm making use of Chebyshev polynomials and Levenberg-Marquardt least-squares optimization was developed. Forty-three image volumes comprising clinical Dynamic Contrast-Enhanced Computed Tomography data from a prospective study investigating hepatocellular carcinoma were analyzed. Images were collected with sparse temporal sampling. A comparable, optimized method based on linear

interpolation and analytical integration was also implemented and compared on the basis of runtime and residual sum of squares (RSS).

**Results:** 800-cpu days of modeling was performed. Voxels were modeled on average in 1.06s for the (non-Chebyshev) linear interpolation approach. Runtime was reduced for the Chebyshev polynomial implementation at any level-of-detail considered (spanning 0.4-2.0x the number of measurements). Runtime was approximately linear in level-of-detail, ranging from 0.41s/voxel to 0.59s/voxel over the level-of-detail range. The Chebyshev approach median RSS spanned 104-108% that of the linear interpolation approach. **Conclusions:** Kinetic modeling using the proposed technique can reduce runtime without substantially impacting model parameter estimation. The technique is also intrinsically efficient; in the liver perfusion clinical data set employed, runtime was reduced 59% with a corresponding RSS reduction of only 8%.

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#### WITHDRAWN

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#### A PROCEDURE FOR GENERATING ISOVOLUMETRIC ORGAN COMPARTMENTS FOR ORGANS-AT-RISK USING PLANNING CONTOURS

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**Purpose:** Intra-organ radiation dose sensitivity is becoming increasingly relevant in clinical radiotherapy. One method for sensitivity assessment involves partitioning clinical organ-at-risk regions of interest and comparing their relative contribution to patient outcomes. We show that an intuitive method for dividing organ contours, compound (sub-)segmentation, can unintentionally lead to sub-segments with inconsistent volumes, which will bias relative importance assessment. An improved technique, nested segmentation, is introduced and compared.

**Materials and Methods:** Clinical radiotherapy planning parotid contours from 510 patients were segmented. Counts of radiotherapy dose matrix voxels interior to sub-segments were used to determine equivalency of sub-segment volumes. The distribution of voxel counts within sub-segments were compared using Kolmogorov-Smirnov tests and characterized by their dispersion. Analytical solutions for 2D/3D analogues were derived and sub-segment area/volume were compared directly.

**Results:** Both parotid and 2D/3D region of interest analogue segmentation confirmed compound segmentation intrinsically produces sub-segments with volumes that depend on the region of interest shape and selection location. Significant volume differences were observed when sub-segmenting parotid contours into 18ths, and vanishingly small sub-segments were observed when sub-segmenting into 96ths. Central sub-segments were considerably smaller than sub-segments on the periphery. Nested segmentation did not exhibit these shortcomings and produced sub-segments with equivalent volumes when dose grid and contour collinearity was addressed, even when dividing the parotid into 96ths. Nested segmentation was always faster or equivalent in runtime compared to compound segmentation.

**Conclusions:** Nested segmentation is more suited than compound segmentation for analyses requiring equal weighting of sub-segments, and could reduce bias that would confound sub-organ sensitivity assessment.

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#### A RADIOTHERAPY TREATMENT PLANNING TECHNIQUE FOR SECOND COURSES THAT INCORPORATES COMPLETE ORGAN-AT-RISK DOSE HISTORY

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**Purpose:** For incidences of second cancers, historical dose delivered to organs-at-risk must be considered when assessing lifetime toxicity risks.

Commercial treatment planning systems permit inclusion of a base plan to incorporate such historical dose, but do not provide the ability to alter the dose distribution. Historical dose delivered to the diseased tissues is irrelevant, so base plan dose in the vicinity of the second cancer must be ignored with ad-hoc practices such as Boolean contours or phony optimization criteria. We describe a new technique, dose cropping, that permits modified base plans to be used for planning second radiotherapy courses. Dose to diseased tissues now occupied by tumours is excised while organ-at-risk dose history is fully retained.

**Materials and Methods:** Clinical second radiotherapy courses developed with Varian Eclipse were replanned for nine head and neck cancer patients. Clinical courses and replans were compared on the basis of plan conformity, dose heterogeneity, maximum spinal cord and brainstem point-dose, and Lyman-Kutcher-Burman tissue control probability to ensure that replans did not compromise tumour control. All plans adhered to current clinical planning constraints and guidelines. Organs-at-risk did not interfere with diseased tissues in any plan. An open source, cross-platform web application supporting interactive dose cropping was built using the DICOM Automaton framework for the purposes of this study.

**Results:** Replanned courses employing dose cropping were statistically indistinguishable from clinical second courses in terms of plan conformity, dose heterogeneity, and tissue control probability ( $p > 0.31$  in all cases). Replans had reduced organ-at-risk lifetime maximum point-doses in every case (median reductions: -5.2 Gy for spinal cord, -4.4 Gy for brainstem).

**Conclusions:** Dosimetric history cropping is a valuable technique for second cancer radiotherapy planning. It can lead to reduced lifetime organ-at-risk dose without compromising plan conformity, dose heterogeneity, or tissue control probability. Dose cropping is widely applicable and can be incorporated into planning procedures whenever a base plan can be employed.

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#### A NOVEL METHOD OF CALIBRATION FOR IMPROVING ACCURACY AND SENSITIVITY IN DUAL ENERGY COMPUTED TOMOGRAPHY PERFUSION

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**Purpose:** To combine dual energy computed tomography's (DECT) material differentiation, iodine parameterization, and CT perfusion to develop a Dual Energy Perfusion CT technique to overcome the current limitations of CT perfusion and improve the accuracy of imaging-derived pharmacokinetic parameters. Computed tomography perfusion assesses temporal changes in attenuation in tissues following the administration of an iodinated contrast agent. Iodine signal enhancement in tissues, expressed with respect to relative electron density ( $\rho_e$ ), is relatively small due to the inherent low sensitivity of single energy CT in differentiating between iodine and other materials. DECT has the ability to better differentiate between materials with similar  $\rho_e$  values, but different effective atomic numbers ( $Z_{eff}$ ) by acquiring data in high and low energies and decomposing the X-ray attenuation information into  $\rho_e$  and  $Z_{eff}$ . Furthermore, parameterizing the response of the DECT specifically to iodine through stoichiometric calibration can improve the sensitivity of the DECT to iodine, thus improving detectability.

**Materials and Methods:** Dual energy scans of phantoms containing clinically relevant concentrations of the iodinated contrast agent were acquired with a 64-row dual source CT scanner (Siemens Somatom Definition Flash). Values of  $\rho_e$  and  $Z_{eff}$  were calculated in each voxel by modeling the X-ray spectra using SpekCalc software. Response of the DECT scanner to iodine was parameterized using stoichiometric calibration, taking into account both the CT numbers and chemical composition of known contrast materials. The calibrated response was used to create a map of  $Z_{eff}$  for iodine concentrations.

**Results:** The preliminary results indicated that the combination of  $Z_{eff}$  and stoichiometric calibration resulted in a 55% reduction in average error in estimation of iodine across the clinically relevant range of concentrations in phantoms, compared to  $\rho_e$ . Stoichiometric calibration improved the average error in  $Z_{eff}$ -based estimation of iodine concentrations by 10% when compared to the uncalibrated  $Z_{eff}$ .

**Conclusions:** Using DECT and CT number calibration with respect to  $Z_{eff}$ , as opposed to  $\rho_e$ , together with stoichiometric parameterization of the DECT leads to improved accuracy in estimating iodine concentrations. These

results will be applied to DECT perfusion to redefine contrast perfusion enhancement curves with respect to  $Z_{eff}$ . Furthermore, these results will be validated in a head and neck cancer clinical trial to assess their efficacy in improving quantitative analysis of perfusion parametric maps.

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#### USE OF HIGH RESOLUTION ACOUSTIC MICROSCOPY FOR SKIN CANCER DIAGNOSIS: CORRELATION WITH HISTOLOGY

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**Purpose:** Skin cancer is a heterogeneous group with a widely varying prognosis. Histopathologic evaluation using optical microscopy is the current gold standard for skin cancer assays and its application is dependent on a pathologist's training and experience. However, subjectivity still exists in the histopathological interpretation of skin cancer; discordance of melanoma biopsy samples may reach 11% [1]. Given the fact that cutaneous melanoma shows distinct elastic properties compared to benign lesions, it is worthwhile to study if the skin elasticity can be the determinative factor for identifying and classifying skin cancer. Acoustic microscopy shows excellent potential as an efficient diagnostic tool for skin cancer. It allows acquiring images with the contrast based on tissue stiffness without any need for fixing or staining.

**Materials and Methods:** The ultrasonic microscope equipped with a high-frequency transducer allows measuring elastic parameters of the tissue achieving a resolution comparable with the optical microscopy. The technique enables acquiring images with the contrast based on tissue stiffness without any need for fixing or staining. The software evaluates the time difference of the reflections from the tissue and the reference substrate and estimates sound speed and attenuation distribution within the histologic sample. Sound speed can be interpreted into elastic parameters such as bulk modulus.

**Results:** The ultrasonic images of histological slides of infiltrating melanoma, squamous cell carcinoma (SCC), and basal cell carcinoma (BCC) show a good correlation with traditional H&E optical images. Details of skin architecture are distinctly identifiable. We observed statistically significant changes in both sound speed and attenuation in the reticular dermis for melanoma while acoustic properties of the epidermis remain unchanged. SCC demonstrated the substantial rise in both parameters due to abnormal keratin accumulation. BCC affects both epidermal and reticular dermis by changing sound speed and attenuation values. Combination of these parameters along with cell morphology can contribute to the diagnostic decision.

**Conclusions:** A new quantitative imaging tool has been proposed to measure tissue's elasticity in skin squamous cell carcinoma, basal cell carcinoma, and melanoma lesions. The use of the proposed methodology as an adjunctive aide that reduces histological errors would be of great value.

1. Patrawala S. et al., J Am Acad Dermatol. 2016 Jan;74(1):75-80

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#### 3D CHARACTERIZATION OF HUMAN SKIN WITH ACOUSTIC IMPEDANCE MICROSCOPE FOR MELANOMA DETECTION: ESTIMATION OF SKIN LAYERS THICKNESSES

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**Purpose:** High-frequency skin ultrasound is a relatively new diagnostic technique that has been shown potential to be a non-invasive tool in different areas of dermatology. Successful in vivo ultrasonic detection of melanoma depends substantially on the precise focusing the ultrasonic beam at the epidermal/dermal junction. The present work aimed to analyze the ability of acoustic impedance microscope to identify skin layers and estimate how skin thickness varies with ethnic origin and age.

**Materials and Methods:** A new technique of 3D imaging of the skin in terms of acoustic impedance (AI) has been employed. With an ultrasonic

beam focused on the epidermal/dermal junction, it enables non-invasive visualization of outermost structures of the skin. Precise sound field analysis was performed to compensate the incidence errors. Acoustic impedance can be further interpreted into elastic parameter such as bulk modulus. Female and male subjects were distributed into three ethnic groups: Middle Eastern, Caucasians, and Asian. The skin on the cheek and ventral forearm were evaluated using AI microscope with a frequency of 80 MHz.

**Results and Conclusions:** Based on the acoustic impedance evaluation, the thickness of epidermis and papillary dermis in the skin is lower on the cheek compared with the ventral forearm, suggesting that long-focused beam with lower frequency would be preferable for forearm observation. Results confirmed decreasing in thickness of the papillary dermis with age, as has been reported. In spite of limited number of specimens, it looks that east Asians are thinner in skin structure compared with other ethnic groups. From the technical point of view, the acoustic impedance profile is considered to be suitable to evaluate skin morphology based on the elastic modality of the skin. Pathological observations showed that the melanoma in an early stage is mostly found at the epidermal/dermal junction and propagates to the papillary layer. The significant difference in sound speed has been observed earlier for melanoma and carcinoma lesions, suggesting the difference in acoustic impedance as well for these types of cancer. As this new non-invasive technique can distinctly discriminate the skin layers, we believe that this approach has a significant potential for detecting melanoma at early stages.

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#### IMPROVING IMAGE GUIDANCE FOR LIVER SBRT USING GADOXETATE DISODIUM

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**Purpose:** To provide a proof of concept that the liver specific contrast agent, Gadoxetate Disodium (Bayer Healthcare, Primovist), can be used to enhance cone-beam computed tomography (CBCT) images to improve image guided SBRT of the liver.

**Materials and Methods:** Gadoxetate Disodium has a recommended administration dose of 0.025 mmol per kilogram of body weight as an MRI specific contrast agent. We prepared solutions with concentrations ranging from 0.025 to 0.2 mmol/ml from the stock solution of 0.25 mmol/ml. A cylindrical phantom was constructed from tissue equivalent plastic (PMMA) which holds five inserts, each filled with 60 mL of diluted contrast material. The phantom was then filled with water and imaged on a CT simulator, and TrueBeam kV imaging system using different tube current and voltage settings. Image quality was analyzed using the average contrast-to-noise ratio (CNR) over the volume of each solution-filled insert with respect to the water background. The on-board kV system was also modeled using the EGSnrc Monte Carlo code, for the purpose of investigating spectra outside of the clinically available range. This is important for testing dual-energy CBCT, to find the spectral separation that best illustrates the K-edge of gadolinium.

**Results:** CNR analysis illustrated that the Gadoxetate Disodium contrast agent improved visibility for concentrations greater than 0.05 mmol/ml. Images were deemed visible when the average CNR value was greater 1 for clinically available x-ray spectra ranging from 80 – 140 kVp, which occurred for concentrations larger than 0.05 mmol/ml. This was observed for all tube voltages and currents that were tested on both helical and CBCT.

**Conclusions:** The results from this experiment demonstrate a promising solution for improving image guidance for liver SBRT as an alternative for the invasive standard of implanting fiducial markers into the liver.

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#### ANALYTICAL MODELING FOR THE SINGLY-RAYLEIGH-SCATTERED FLUENCE IN CBCT APPLICATION

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**Purpose:** Cone Beam Computed Tomography (CBCT), a volumetric anatomical imaging technique, has been widely applied for patient set-up procedures during the radiation treatment. However, the use of a wide conical beam for image acquisition enhances the detection of scattered photons as compared to conventional CT where narrow fan-beams are used, which significantly degrades the image quality. Several approaches have been proposed to reduce the effects of scattered photons in CBCT imaging. For example, increasing the air gap underneath the patient or adding an anti-scatter grid, demonstrates significant reduction of scattered photons. Another approach is to subtract an estimated scatter x-ray signal from the total measured transmission signal, to obtain the primary photon fluence. For diagnostic energy photons (80-120 kV range), Rayleigh and Compton scatter are the two main photon interaction types that will generate scattered photons entering the detector. Rayleigh scatter becomes more significant as x-ray energy decreases below 100 keV (e.g. Rayleigh scatter dominates Compton scatter below 90 KeV).

**Materials and Methods:** Our group investigated a mathematical model to estimate the first order Rayleigh scattered signal into a flat-panel CBCT detector. Our model is based on first-principles analytical scattering theory in radiation transport. A unique feature of the approach is that atomic composition along radiological path-length calculations is tracked and used in the model. This is important for accurate analytical calculations of Rayleigh scattered photons incident on the imaging panel for heterogeneous cases.

**Results:** To validate the approach, the calculated first-order Rayleigh scattered signal was compared with an EGSnrc-based validation tool for three simple geometric phantoms and using a 100 KeV monoenergetic, square x-ray beam, over a 40x40 cm<sup>2</sup> imaging plane. Over all phantoms tested here, the mean percentage differences between the analytical and EGSnrc predictions for the Rayleigh scattered photons were less than 1.2% and STDM less than 0.5%.

**Conclusions:** Based on a first-principles analytical technique, and taking into account patient heterogeneity, this approach can accurately predict singly Rayleigh-scattered fluence entering a 2D imaging panel. In the future, we will combine our developed analytical methods for estimating Compton and Rayleigh scattering in imaging detectors, and examine more complex phantom geometries and patient CT data.

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#### SIGNAL ENHANCEMENT VOLUME INCREASE IN DCE-MRI AFTER SINGLE FRACTION SBRT OF EARLY STAGE BREAST CANCER

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**Purpose:** The SIGNAL trial is a clinical trial assessing the utility of high dose radiotherapy in early stage breast cancer patients [Guidolin et al 2015]. This provides a unique opportunity to use imaging to potentially assess tumour response to high doses of radiotherapy which may allow us to adapt our treatment to the patient's needs. DCE-MRI, which provides functional information related to angiogenesis, perfusion and extra cellular volume, has been shown to be useful in this context. In this study, we investigated changes seen in DCE-MRI imaging following high dose radiotherapy.

**Materials and Methods:** Three-Dimensional fat suppressed fast low angle shot (spatial/time resolution of 1.0x2.1x1.2mm/18s) images were acquired on a 3T-PET/MRI system (Siemens Biograph mMR), which included one pre- and 28 post-contrast images in five patients before and seven days after a single radiation dose of 21 Gy. Motion was corrected using deformable registration [Mouawad et al. ISMRM 2017]. A rectangular box (volume of interest – VOI) encompassing the tumour was drawn for each patient, using

the same sized box in the post-radiotherapy data. The signal enhancement (SE - ratio of post to pre-contrast image intensity) at three minutes was calculated voxel wise. The SE VOI signal was progressively thresholded from a value of one (post-contrast signal = pre-contrast signal) to five (post-contrast signal is 5x greater than pre-contrast) in increments of 0.05 and the volume of voxels was calculated at each SE threshold to generate SE threshold versus volume curves. Pre and post radiotherapy images were compared by calculating the fractional change in the area under the volume-SE threshold curve (AUC). In addition, the maximum SE threshold that contained 5% of the volume of voxels at SE = 1 was calculated in the pre- and post-radiotherapy data.

**Results:** For every patient at all SE thresholds there was a greater volume of tissue that was enhancing post-radiotherapy. On average, there was a mean ( $\pm$  standard deviation) increase in the AUC of  $2.8 \pm 1.70$ , with all patient ratios greater than one. In all five patients, there was an increase in the maximum SE threshold. The mean ( $\pm$  standard deviation) maximum SE threshold increased from  $1.94 \pm 0.25$  to  $2.3 \pm 0.36$  indicating an overall greater signal enhancement.

**Conclusions:** Following high dose radiotherapy, there is a large increase in the volume of voxels that enhance, and an increase in the maximum SE threshold. This may be due to tumour cell death/permeability increase in the vessels [Janssen et al 2010] or an acute inflammatory effect, as a large increase in tumour volume is unlikely. Further work will look to correlate the spatial distributions of radiotherapy dose and SE increase, as well as acquire simultaneous FDG-PET/MRI to correlate perfusion with metabolic/inflammation markers.

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#### IMPLEMENTATION OF A PIXEL-BASED WEIGHTING FACTOR DUAL-ENERGY X-RAY IMAGING SYSTEM

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**Purpose:** Develop a novel pixel-based weighting factor dual energy (DE) algorithm for effective bone suppression throughout the image and overcome the limitation of the conventional DE algorithm with constant weighting factor, which is restricted to regions with uniform patient thickness.

**Materials and Methods:** A step phantom was constructed consisting of slabs of solid water and bone materials. Thicknesses of bone ranged [0-6] cm in one direction, and solid water [5-30] cm in the other direction. Projection images at 60 and 140 kVp were acquired using Brainlab's ExacTrac system. Optimum weighting factors were found in the range [0-1.6], where bone and soft-tissue contrast-to-noise ratio reached zero. Bone and soft-tissue digitally reconstructed radiographs (DRRs) of a Rando phantom were created using computed tomography images and ray tracing techniques. A weighting factor image for the Rando phantom was calculated using the DRRs and pre-calculated weighting factors from the step phantom. A novel DE image was generated and compared to the conventional DE image which uses a constant weighting factor throughout the image. Signal-to-noise ratios (SNR) were calculated for regions with different soft-tissue and bone thicknesses in the step phantom for both DE techniques.

**Results:** Weighting factor values for the step phantom varied from 0.6 to 1.5, depending on region thickness. Thinner regions had smaller weighting factors for bone cancellation, and thicker regions larger. The novel DE image of the Rando phantom cancelled both ribs and spine, whereas in the conventional DE image only one could be cancelled at a time. The novel DE algorithm had improved SNR over the conventional DE technique for most regions.

**Conclusions:** A novel pixel-based weighting factor DE algorithm was developed which can create improved DE images with enhanced bone cancellation and improved SNR.

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#### A SOFTWARE TOOL TO CONVERT GE PET SINOGRAM RAW DATA INTO STIR INTERFILE FORMAT

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**Purpose:** Data generated by GE PET-CT scanners are being utilized widely both for clinical and research. Often research teams need to access raw PET data or sinograms for various reasons. For instance, raw PET data may be reconstructed by utilizing third-party open source programs such as Software for Tomographic Image Reconstruction (STIR). Currently, GE raw PET data are stored in a GE specific proprietary format which is referred to as raw data file (RDF). Presently, the only mechanism to access the RDF is to use GE PET Toolbox package which offers a wide variety of routines in Matlab (MathWorks, Natick, MA) for handling GE PET-CT data. This includes both reading the raw PET data and image reconstruction algorithms. While the GE PET toolbox offers substantially more than merely accessing raw PET data, this toolbox may not be suitable for a wide distribution if the research teams are only interested in reading the GE raw PET data but prefer using their own reconstruction algorithms or third-party programs such as STIR.

**Materials and Methods:** The goal of this research project is to develop a Matlab software tool to convert the GE raw PET 3D acquisition data files into a format accessible to various research groups. Interfile format is chosen as this format is widely used in Nuclear Medicine community, especially for research purposes.

Sample phantom raw PET data from a GE Discovery STE PET-CT scanner was used. RDF data from PET console extracted as per GE Data Access Utilities Manual and transferred to an external computer. The 3D acquisition mode generates a 4D data set (radial offset, view angle, slice, and tilt angle). However, the RDF format saves it 3D in the memory by stacking the tilt angles. The axial distance coordinate contains information about the slices as well as segments defined by tilt angles. The RDF format combines sinograms axially for segment zero (with a span of 3), while other segments has a span of one. In order to convert to a STIR sinogram compatible format, first all of the segments are converted to a span of 1. The sinograms are then combined to a user defined span >1 to expediate the STIR reconstruction. Finally, finally sinograms were saved as a STIR compatible interfile

**Results and Conclusions:** A software tool in Matlab was developed to read GE PET sinogram data sets and convert them to a STIR compatible interfile format.

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#### THE NEED FOR STANDARDIZATION IN THE MEASUREMENT OF INTRAVOXEL INCOHERENT MOTION PHYSIOLOGICAL PARAMETERS

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**Purpose:** Intravoxel incoherent motion (IVIM) measures diffusion and perfusion but is not standardized. Methods are often used without validation. We compared four methods to compute IVIM parameters in the brain using simulated and human data.

**Materials and Methods:** The IVIM signal equation is  $S(b)/S_0 = f \exp(-b \cdot D_p) + (1-f) \exp(-bD)$  [1] where  $S(b)$  is signal intensity at given gradient strength ( $b$ ),  $S_0$  is signal intensity at  $b=0$ ,  $f$  is perfusion fraction,  $D$  is diffusion coefficient, and  $D_p$  is perfusion coefficient. IVIM acquisitions were performed using standard techniques in a 3T Magnetom Trio MRI. Four methods which use nonlinear fitting were compared: "3-parameter fit" - fit three parameters simultaneously from Eq.1; "2-parameter fit" - measure  $D$  from a low perfusion region, then fit  $f$  and  $D_p$ ; "1-parameter fit" - measure  $f$  and  $D$  from a low perfusion region, then fit  $D_p$  from Eq.1; "ln fit" - weighted logarithm fit of  $f$  and  $D$  from a low perfusion region followed by measuring  $D_p$ . The first three methods have been reported in the literature while the ln fit has not. Fits were performed on simulated data and a human patient with a high-grade glioma. Simulated data included a highly-perfused tissue (tumour) and low-perfused tissue (white matter, WM) computed from literature IVIM parameters. Gaussian noise was added to the simulated data to provide more realism. Quality of fit performance for simulated data was based on accuracy of parameters compared to zero-noise data, as well as the relative change of  $f$  and  $D_p$  in the presence of increasing noise. Human data were analyzed based on fit error and variance of  $f$  and  $D_p$  values between the four fit methods.

**Results:** Noise in simulated data degraded fit performance and increased

parameter variance for  $f$  and  $D_p$ . In both WM and tumour, the 1-parameter fit had the lowest error. Noise affected  $f$  and  $D_p$  measurements in WM more so than in tumour. Moreover,  $D$  remained relatively unaffected by the fit type. In WM,  $f$  was best determined using the 1-parameter fit while  $D_p$  was best found using the 2-parameter fit. In tumour,  $f$  and  $D_p$  were both best determined by the 3-parameter fit. In the patient, the 2-parameter fit had the smallest error in tumour while the 3-parameter fit had the smallest error in WM. In tumour, none of the proposed fit methods could produce a physiologically reasonable  $f$  or  $D_p$  value. In WM, the 1-parameter, 2-parameter, and 3-parameter fit produced similar values for  $f$  and  $D_p$  while the 3-parameter fit produced values outside the range of the other three fits.

**Conclusions:** There is a need for standardized approach to IVIM. We looked at four methods to analyze IVIM data and found inconclusive results. While the 1-parameter fit seemed most appropriate for simulated data, it was not ideal for the human patient. This indicates that careful consideration must be taken when choosing the method to compute IVIM parameters.

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### PRE-CLINICAL VALIDATION OF OPEN SOURCE TOOLS TO CALCULATE AND TRACK MR DISTORTION USING BOTH SMALL AND LARGE FIELD OF VIEW PHANTOMS

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**Purpose:** MR simulation for linac-based SRS is desirable due to its superior soft tissue contrast over CT. However, inherent spatial distortions in MRI have been found to exceed 5 mm. Thus, measuring this distortion is necessary for treatment planning with MRI. Availability of open source algorithms may allow centres to independently test and compare results from vendor provided software during the commissioning of an MRI QA program. In this work we present a robust open source algorithm, which automatically calculates MR distortion for phantoms with varying geometries. The results of this work validates a beta commercial solution when compared to golden grid-point data.

**Materials and Methods:** Using the 603A and 604 phantoms from CIRS Inc., we collected distortion uncorrected and corrected MRI images. Our primary algorithm, which runs as a plugin within 3D Slicer, quickly isolates phantom grid-point intersections (using similar methods outlined by Stanescu et al). A second sub-routine compares the detected MR gridpoints to the user-defined set of golden data (e.g. CAD points). These were written in Python using ITK/VTK based masking, Gaussian filtering, and thresholding techniques.

**Results:** Distortion correction significantly reduced the maximum distortion from 3 mm to under 1 mm. For the 604 phantom, our software calculated 96.3% of the grid-points accurately and found a maximum and average distortion of 1.92 mm and  $0.83 \pm 0.3$  mm. The calculation time for the open source algorithm over the 604 phantom was < 2 minutes, and < 1 minute for the 603A phantom. Initial comparisons between our open source calculated results to CIRS Inc. beta online software yielded similar results (mean difference ~8% over all grid points).

**Conclusions:** The proposed open source MRI distortion software provides a fast and robust method to validate commercial software prior to clinical use.

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### AN IMPROVED TREATMENT PLANNING AND QUALITY ASSURANCE PROCESS FOR EYE PLAQUE BRACHYTHERAPY

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**Purpose:** Episcleral plaque therapy (EPT) is an established treatment technique in the management of ocular melanomas that involves surgical implantation of an eye plaque (between 10-22 mm in diameter) loaded with radioactive sources on the scleral surface over the tumour base. Rather than ordering seeds for every patient, our program re-uses stocks of 125I sources for multiple patients by ordering ~50 seeds every two months with Air Kerma Strength (AKS) of ~9U. Five groups of seeds are retained for planning with AKS ranging from 0.6 – 9U, for a maximum 3-5 plaques per

week. This seed stock enables assembly of plaques with dose distributions that match standard COMS plaques while facilitating a variety of notched and asymmetrically loaded plaques needed for melanomas proximal to the optic nerve. Since program inception, treatment planning was performed using in-house software that could not account for new seed types. Quality assurance of the plaque used a pinhole camera and autoradiography system to image the plaque to verify that loading matches the plan. A second measurement using a calibrated survey meter measurement is used to verify absolute total AKS. While effective, this procedure is costly in terms of required time and materials used. Both planning and QA steps require updating and improvements.

**Materials and Methods:** Treatment planning is performed in Pinnacle using scripts that let the planner choose plaque size and notching. Scripts load in seed positions for each plaque, and five source groups corresponding to the available stock seeds that can be placed into each seed position. Contours are loaded that display the model eye (inner and outer sclera) and the plaque itself. Plaque QA is performed using a modification of our previous pinhole apparatus by replacing x-ray film exposure with an optical camera and scintillating film system. The captured image is processed to remove background and to correct the intensity of seeds on the periphery of the plaque. Total optical counts are measured to provide an estimate of the total plaque AKS.

**Results:** Treatment planning of eye plaques using Pinnacle, in conjunction with our stock inventory of seeds, has been established as standard practice at our centre. Planned plaques can vary from standard uniformly loaded COMS plaques to asymmetrically loaded deep notched plaques. Using the optical camera system for assessment of the seed loadings has decreased the QA time from 25 minutes/plaque to 5 minutes/plaque. Total AKS of each plaque can be measured using the optical camera with an accuracy of 3%.

**Conclusions:** Treatment planning is now performed on a Health Canada approved software that accommodates any plaque loading. The optical image of the plaque provides both required QA metrics that can be compared to the eye plaque plan: absolute total AKS and the relative seed arrangement in the plaque.

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### OPTICAL SURFACE MAPPING FOR EVALUATING THE DOSIMETRIC IMPACT OF WEIGHT LOSS IN HEAD AND NECK PATIENTS

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**Purpose:** Treatment related weight loss is a common occurrence in radical head and neck EBRT patients. Unfortunately, standard CBCT field-of-views used for head and neck IGRT are often insufficient both laterally and in the superior/inferior direction for generating the superficial tissue information required to assess any tissue loss. Although some linacs allow for offline stitching of multiple CBCTs, which could be done in conjunction with wider (non-head) CBCT acquisitions, this approach can add to the treatment appointment time while introducing additional patient imaging dose. The current work aims to determine the utility in using a commercial optical surface mapping system for assessing the dosimetric impact of weight loss in head and neck patients.

**Materials and Methods:** Optical surface maps were generated by an Optical Surface Monitoring System™ (OSMS) installed as part of a TrueBeam Edge™ linac system (Varian Medical Systems). A single surface map was acquired from a small number of radical head and neck patients between fractions 20 and 25 of treatment. The surface was captured between patient alignment and before application of the immobilization shell. Custom Python software tools utilizing Visualization Toolkit (VTK) and pydicom libraries were created for the surface map processing. Raw surface information extracted from the OSMS system was used to generate a 3D patient surface mesh, which was subsequently converted to a set of 2D polylines and written to a custom RTSTRUCT DICOM. The RTSTRUCT was imported into the Varian Eclipse treatment planning system for comparison with contemporaneous CBCT information, and was also referenced against the CT simulation volume to create a tissue loss structure and assess the dosimetric effects of any external contour changes.

**Results and Conclusions:** The surface map processing software has been

successfully demonstrated on a set of pilot data, and collection of head and neck patient surface data is ongoing.

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### A MULTI-DISCIPLINARY APPROACH TO RT DOCUMENTATION

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**Purpose:** Proper documentation of institutional guidelines and procedures is critical to providing safe, high quality radiation therapy for cancer patients. Notwithstanding, in the current era of rising patient numbers and increasing treatment complexity, cancer centres can easily find their resources strained with the result that documentation can be the first casualty. We report on our institutional experience revamping our entire documentation process, from how documents are developed and reviewed, to how they are accessed and maintained.

**Materials and Methods:** In 2015 a small group of motivated staff members from both Physics and Therapy identified the need for an improved documentation process. Management was engaged throughout, both to ensure that the goals and scope of the project continued to align with the broader cancer program goals, as well as to provide the necessary resources for the project to succeed. IT support was provided to build and maintain an online documentation system. Staff time was allocated for a core Process Group to meet weekly as well as for the larger staff population to create the document content. Funding for this project was entirely indirect, provided through staff time.

**Results:** Initial tasks of the Process Group included the creation of Terms of Reference for the project and User Requirements for the online documentation system. A standard document template was developed to provide a consistent format and layout, as well as to drive the process of authoring, reviewing and publishing guidelines and procedures. Six months after the first meeting, the online documentation system was launched, and program-wide training was provided.

It was critical to the project's ongoing success that the Process Group engaged the entire multidisciplinary team in the Radiation Therapy Program, including radiation oncologists, therapists, physicists, dosimetrists, nurses, administrative staff and electronic technicians. These specialists had the knowledge for content, while the Process Group ensured collaboration, rigour, consistency, and overall quality.

**Conclusions:** This project succeeded in an atmosphere that allowed motivated front-line staff to innovate in order to address a need. The core group of initiators were instrumental in creating a structured environment in which content experts were engaged to create documentation. While this project has developed a much-needed process for rigorous documentation at our centre, it has also had unintended effects. We have seen trust and rapport being built between professional groups with an increase in collaboration and mutual understanding.

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### EXPLORING INCIDENT REPORTS FOR RADIATION ONCOLOGY USING NLP TOOLS

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**Purpose:** Incident Learning Systems (ILS) have been shown to improve and standardize the quality of care in participating institutions. Incidents reported to ILS contain information that should inform clinical practice and thus prevent incident recurrence. In this project, we aimed to use natural language processing (NLP) techniques to explore the content of radiation oncology incident reports from the Cedars Cancer Centre of the McGill University Health Centre (MUHC) and compare them to those recorded in the National System for Incident Reporting–Radiation Treatment (NSIR-RT). Our overarching goal was to determine if it is possible to better classify incidents reported in the “other” categories.

**Materials and Methods:** We used two different datasets, the first from

MUHC and the second from NSIR-RT. In both cases, we only used the textual description of the report. We explored some features that characterize reports such as the distribution of words and the lexical richness. We also applied topic modelling to both datasets in an attempt to identify trending topics and the incident reports that belong to each topic. In order to improve the separation of topics, we implemented a strategy for feature selection based on linguistic information analysis.

**Results:** Topic modeling grouped reports that share semantic similarity. We explored these groups using the Primary Problem Type that is used to classify every report according to the NSIR-RT taxonomy. Within each group, the number of incident reports that were classified for each Primary Problem Type were compared. It was found that in most groups one problem type dominated, indicating the potential for automatic classification.

**Conclusions:** We found that NLP techniques, in particular topic modelling, has potential to automatically classify incident reports in radiation oncology. We could suggest that incidents from the same group that were classified using “Other” could instead be classified as most likely belonging to the most frequent (predominant) problem type of the group.

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### LARGE VARIABILITY IN PHYSICS TREATMENT PLAN REVIEW PRACTICE: RESULTS FROM TWO SURVEYS

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**Purpose:** To compare the scope and results of two recent surveys on treatment plan review practices by medical physicists. One review was conducted by the Chart Checking Practices Group of the CancerCare Ontario (CCO) Medical Physics Community of Practice in 2015, and the other by the AAPM Task Group 275 on Strategies for Effective Physics Plan and Chart Review in Radiation Therapy in 2016. The goal of both surveys was to provide a baseline of current practices using a large and diverse population of medical physicists.

The scope of the two surveys was different. The Ontario survey focused only on pre-treatment plan review processes for external photon beam radiotherapy (EBRT) treatments, while the TG-275 survey included other modalities and other QA stages. The Ontario survey asked each medical physics department to complete the survey in a group setting, while the TG-275 survey was completed by individuals. The response rate of the Ontario survey was 100% (15/15 radiotherapy centers), corresponding to about 140 practicing physicists, while the response rate for the TG-275 survey was 1526 respondents, representing a 33% response rate. A comparison of the results of the two surveys will provide some context for interpreting both surveys.

**Materials and Methods:** A total of 33 pre-treatment plan review items from each survey were identified that were common to both. The included items cover all relevant treatment plan aspects such as quality of the contours, treatment plan parameters, patient set-up and treatment imaging. As part of the Ontario survey each medical physics department was asked to self-report the variability in practice within their centre for each review item. These answers were converted into an estimate of the likelihood of that item being checked. This estimate was compared to the reported checking frequency of the corresponding TG-275 review item.

**Results and Conclusions:** Overall, only a moderate correlation was found between physics checking score and TG-275 response rate ( $R^2 = 0.35$ ). Presence or absence of bolus was the item mostly checked by both surveys (92% for TG-275, 100% for Ontario). Items with generally low checking probability show large disagreements between the surveys. For example, the imaging schedule for on-board image guidance was much more likely to be checked by the TG275 respondents than the Ontario physicists (67% versus 32%). Conversely, the HU to electron density conversion table was more likely to be checked by the Ontario physicists (46% versus 77%). The moderate correlation confirms the general variability in chart checking practices. It is not clear whether this variability is due to differences in technology, infrastructure, funding or working conditions. It is likely that

the variation is exacerbated by the lack of official guidelines. Overall, the results indicate that there are opportunities for educating physicists on best chart-checking practices.

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#### PEER REVIEW AT THE MCGILL UNIVERSITY HEALTH CENTRE

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**Purpose:** The Canadian Partnership for Quality Radiotherapy quality assurance (QA) guidelines recommend that radiation oncologists (RO) peer-review (PR) all curative-intent treatment plans, optimally before a patient has received their first fraction. At our institution, the PR process that had been in place for >30 years has been evolving since the introduction of the electronic medical record (EMR) to better align with these standards and to improve patient care quality and safety. In 2017, the program's leadership developed a strategic plan to increase site-group PR and formalize the review process. The purpose of this study was to determine the program's adherence to guidelines and to establish a baseline for future quality improvement initiatives using the tasking feature in Varian ARIA to automate collection of highly accurate and reproducible data.

**Materials and Methods:** QA task completion data were prospectively collected from Varian ARIA from July 2017 to December 2017 from all patients treated within the program. PR was conducted in various settings; weekly department-wide treatment plan PR, selected site- or technique-specific weekly detailed contour and dosimetry PR (breast, CNS, head and neck, lower GI, GU/gyne, SBRT/lung sites), and one-to-one physician contour PR. Participation of at least two ROs was required to constitute PR. Radiation therapists, dosimetrists, and medical physicists were also present at weekly rounds. Following PR, a task specifying the activity is completed. If modifications to contours or planning are recommended, a task suggesting the change is sent to the primary RO. All PR activities are documented in the ARIA chart with a PR note.

**Results:** Eight hundred and eight patients were treated with curative-intent during the specified timeframe. One-hundred per cent of curative intent treatment plans underwent any form of PR. 27.6% of cases were reviewed in 1:1 physician contour PR, and 38.12% of cases were reviewed in a weekly site-specific PR. By site, detailed review occurred in a range of 7.4% (for hematologic malignancies) to 100% (for ENT malignancies). 29.3% of cases were reviewed prior to initiation of treatment, and 55.9% were reviewed prior to 25% of the course delivered. Changes of contours or plan parameters were suggested in 2.7% of cases reviewed, with the highest rates in skin (20%), lower GI (8.3%), and loco-regional breast plans (4.7%). Site-specific weekly meeting and 1:1 PR increased from 38.6% from July-September to 52.2% from October-December.

**Conclusions:** PR activities at our institution are increasing with better use of the EMR with focus on 1:1 contour review and site/technique-specific weekly contour and dosimetry review. Using the tasking feature in ARIA is a novel and accurate method to automate tracking of QA activity frequency and timing for reporting and demonstrating progress.

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#### A RASPBERRY PI AND SCINTILLATOR-BASED IMAGING SYSTEM FOR DETERMINATION OF RESPIRATORY GATING TEMPORAL ACCURACY

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**Purpose:** For gating systems the AAPM report number TG142 recommends a temporal accuracy of 100 msec. The aim of this research is to create and evaluate an inexpensive, easy to use system for RPM quality assurance. For this work we employ a Raspberry Pi2 (Pi2). The Pi2 is a small (5x9cm2) computer employing a 900 MHz quad-core ARM Cortex-A7 CPU with 1GB RAM capable of supporting an 8-megapixel camera module (PiNoIR). The configuration is powerful enough to run the Open Source Computer Vision (OpenCV) library.

**Materials and Methods:** The system is composed of three parts: a Pi2 with a PiNoIR camera, a Varian Real-time Position Management (RPM) gating

dynamic phantom with an optical encoder pattern mounted on its rotating front plate and an anthracene/polyvinyltoluene scintillator surrounded by a pattern (used for identification). The scintillator is positioned in the field and the dynamic phantom and pi2 are arranged such that the phantom and scintillator are both in the camera's field of view with adequate focus. Once set-up, the Pi2 takes an initial image and OpenCV is used to identify the location of both the scintillator and the optical encoder. The Pi2 then monitors the camera image and once it detects an initial beam on, a video recording is started at 60 fps. From the video the Beam On state is detected from changes in scintillator appearance and the RPM rotational position is determined using the optical encoder pattern. From these measurements the gate response time is determined. Measurement error is assumed to be one frame period in addition to an angular error determined through multiple RPM phantom set-ups.

**Results:** The average beam on time was 121 ms (range: 101-133 ms) from gate entry for eight breath cycles and 82 ms (9-10 2ms) for gate exit. We estimate the error in the gate entry and exit angle to be 2° or 26.6 ms and a timing uncertainty of one frame or 15.6ms. When these are added in quadrature the total uncertainty is 31 ms.

**Conclusions:** The respiratory gating system operates to the TG142 specification within the uncertainty of our measurement. In addition, the measurement technique/equipment is adequate, as well as being simple and fast enough for routine QA of the gating system. However, there is room for improvement. A more robust phantom and a higher frame rate would reduce the uncertainty. The Pi2 is capable of recording the video at a much higher frame rate, however, other limitations of the Pi2 makes this a non-trivial modification.

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#### SAFETY IMPACT OF EXCEEDING LINAC VAULT DESIGN WORKLOAD LIMITS

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**Purpose:** To determine whether exceeding the design workload limits potentially results in safety significant increases to occupational and public exposure to radiation around linac vaults in radiotherapy centres.

**Materials and Methods:** Licensees must provide data on accelerator workloads to the CNSC as part of their annual compliance reports (ACR). Over recent years, CNSC staff reviewing these reports have observed a trend towards increased annual workloads, to the extent that in some cases, it has exceeded the design workload limit for the vault. In such cases, it is necessary to evaluate whether or not this increase could result in a significant increase in exposure to facility staff or the public. Annual workloads exceeding design workload limits assumptions were reviewed. When the ACR contained workloads for the different photon beam energies of the linac, the annual workload was calculated by simply summing them. The resulting occupational and public exposure to radiation around the vaults were evaluated using the vault design submitted by the licensee at the commissioning phase, following NCRP Report No. 151 dose estimation formalism and using conservative assumptions.

**Results:** Historically, design workload limits were typically established using the linac's highest photon beam energy. Where intensity-modulated radiotherapy (IMRT) was considered, it was generally assumed to be performed at the highest beam energy, which may include consideration of the impact of using the linac flattening filter free (FFF) mode if available. Furthermore, design workload limits were normally established on the basis of ALARA limiting occupational doses to less than 1 mSv per year and public doses to less than 50 µSv per year. The review found that observed increases in workload are generally at lower beam energies, usually in conjunction with IMRT techniques, FFF mode, or a combination of both. Therefore, marginal increase of the workload over the design workload limit usually had a negligible impact on occupational and public exposure to radiation around linac vaults in radiotherapy centers. There are circumstances where increases in dose could occur, and this must be carefully evaluated.

**Conclusions:** When building a new vault or installing a new linac in an existing vault, it has been common practice in the past to establish the design basis workload using extremely conservative assumptions, to ensure the long term viability of the facility as treatment techniques evolve. However, the recent trend to more complex treatment modalities at lower energies

makes validating the adequacy of the shielding design more complicated. Licensees must carefully review the impact of the radiotherapy techniques (e.g. IMRT) and the operating modes (FFF or FF) used, and establish or review their design workload limits and demonstrate that they are still ALARA before these limits are exceeded.

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#### ITERATIVE DESIGN AND CONSTRUCTION OF AN IN-HOUSE IMMOBILIZATION DEVICE FOR VMAT CRANIAL SPINAL IRRADIATION

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**Purpose:** An interactive, multidisciplinary approach was used to design and build a patient immobilization device for supine VMAT craniospinal irradiation (CSI). The goal was to create a device that improves upon the commercially available full body vacuum bags that are more susceptible to deformations compared to smaller vacuum bags. The device aims to improve reproducibility and accessibility to the patient without adding excessive complexity or high costs. The design was specifically aimed to increase accessibility to the spine for set-up manipulation; increase patient comfort, and therefore decrease probability of intrafraction motion; and, to provide a neutral spine position in the cervical spine area to allow for more homogenous VMAT dose distributions between brain and spine. Another device requirement was adaptability for both pediatric and adult patients with indexing for set-up reproducibility.

**Materials and Methods:** A multidisciplinary group of physicists, therapists, radiation oncologists, and dosimetrists first identified a list of required features for the CSI device. Our in-house mechanical design staff took these ideas and developed prototype components constructed using cheaper, readily-available materials. The design then went through several iterations of review by the group and subsequent modifications until all requirements were satisfied. In its final design, the immobilization device was constructed using 3D printed components made of a carbon fibre-like material, as well as some soft plastic parts, and a carbon fibre base. Measurements were made to characterize radiological properties of treatment beam geometries and energies through the device.

**Results:** An immobilization device is composed of 3D-printed, modular components, for lumbar spine support and hip support. Spine and hips supports are fully adjustable wedges that can comfortably accommodate any size and shape of patient. The device also includes plastic "backpack straps" which ensure shoulders are in a reproducible position for simulation and treatment. The components are indexed to a carbon fiber base which is, in turn, is indexed relative to the thermoplastic mask. All the materials used can be cleaned to infection protection and control standards. Surface dose and attenuation measurements showed no significant perturbation in dose distribution with the use of this device.

**Conclusions:** The device presented here allows for increased patient comfort, superior spine neutrality, and accessibility to the patient for fine set-up adjustments compared to our previous clinical standard. The design required many iterations with input from the multidisciplinary clinical staff, resulting in a final design that is relatively simple and very effective.

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#### CT-BASED ASSESSMENT OF LIVER POSITION STABILITY AND REPRODUCIBILITY WHEN USING ACTIVE BREATHING COORDINATOR

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**Purpose:** Stereotactic body radiation therapy (SBRT) for liver metastases delivers ablative dose of radiation to the target in a small number of fractions. Treatment plans are highly conformal around the target lesion, while maintaining steep dose gradients towards the surrounding normal tissue.

This level of conformality necessitates a very precise treatment delivery technique. However, the accuracy of dose delivery can be compromised by respiratory motion. To mitigate this, our institution implemented an active breathing coordinator (ABC) protocol to eliminate breathing motion during simulation and treatment. The success of the ABC-based treatment relies on the stability and reproducibility of the liver position when patient's breathing is interrupted by the device. Therefore, assessing liver position consistency before initiating ABC-based treatment process is crucial. This work describes our CT based assessment process and preliminary data.

**Materials and Methods:** Liver position consistency is assessed in exhale with a minimum breath hold of 15 s. The patient performs five successive breath holds. Five axial scans (collimation 16x0.75 mm) centred on the superior aspect of the diaphragm are acquired for each breath hold (25 axial scans in total). The axial scans are evenly spaced timewise from the start to the end of the breath hold. The coordinate of the slice containing the superior aspect of the diaphragm serves as a benchmark to assess the liver position in the cranio-caudal direction for each scan. After the axial scan assessment, two helical scans of the patient encompassing the entire liver are acquired with patient locked in the exhale state to allow for evaluation of stability of the liver in terms of rotations and deformations. The whole screening process adds about 20 min to the simulation.

**Results:** Twenty-two patients have been assessed (111 breath holds in total) with breath hold duration ranging from 15-30 s. The position of the superior aspect of the diaphragm showed minor variation during a single breath hold in the majority of the breath holds for all of the patients; the average variation for all the patients was 1.9 mm (SD = 1.5 mm) and the maximum observed drift was 9 mm. A deviation in excess of 5 mm was observed in four patients. In terms of reproducibility, the difference in the position of the diaphragm in cranio-caudal direction across all the breath holds per patient ranged from 2.2 to 13.4 mm (median 5.3 mm). Four patients failed assessment. One patient passed assessment but proved to be unstable on the first day of treatment and one patient had treatment cancelled due to progression of the disease. Sixteen patients successfully completed ABC-based treatment.

**Conclusions:** For most patients, the uncertainty of the liver position is on the order of +/-3 mm from its average position and can be accounted for within standard PTV margins. However, there is a subset of patients for whom ABC does not provide for stable and reproducible liver position. Variation as large as 13.4 mm has been observed necessitating a process to screen patients early in the ABC based treatment process. The CT based liver position assessment described here has proven successful in this regard and has become standard part of the treatment planning process for ABC-based liver SBRT in our clinic.

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#### VALIDATION OF PLANNING CT TO CONE-BEAM CT DEFORMABLE IMAGE REGISTRATION-BASED CONTOUR PROPAGATION FOR ACCELERATED PARTIAL BREAST IRRADIATION

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**Purpose:** The purpose of this work was to validate a commercial deformable image registration (DIR) software as a tool to deform planning CTs and their associated seroma contours onto patient set-up verification cone-beam CTs (CBCTs). Reliable DIR would enable efficient dose-of-the-day calculations for accelerated partial breast irradiation (APBI) patients, which may be used to verify and optimize set-up margins.

**Materials and Methods:** The performance of DIR-based contour propagation from planning CT to CBCT was evaluated by comparing deformed seroma contours to manual physician contouring. Ten patients who underwent external beam APBI (27 Gy delivered in five consecutive daily treatments), with seroma clarity scores  $\geq 3$  according to the British Columbia Cancer Agency Seroma Clarity Scale, were retrospectively selected. DIR (Velocity 3.2.0, Varian Medical Systems, CA) was used to deform the planning CT and seroma contour to match the patient anatomy depicted by the CBCT acquired on the first day of treatment. This process produces a deformed seroma contour on a synthetic CT. For each patient, three radiation oncologists

independently contoured the seroma on the synthetic CT, attempting to replicate the peer-reviewed seroma contour previously drawn on the planning CT. Two measures of contour variability are reported: Dice similarity coefficient (DSC) and centre of mass (COM) shift. Physician-physician concordance was compared to DIR-physician concordance for statistical significance using the two-tailed Mann-Whitney U-Test ( $n = 30$ ,  $\alpha = 0.05$ ).

**Results:** The cohort median (range) physician-physician DSC and COM shift were 0.87 (0.67 – 0.94) and 1.09 mm (0.20 – 4.13 mm), respectively. The cohort median (range) DIR-physician DSC and COM shift were 0.87 (0.68 – 0.94) and 0.90 mm (0.14 – 4.41 mm), respectively. The distributions of physician-physician and DIR-physician concordance, as measured by the DSC ( $p = 0.28$ ) and COM shift ( $p = 0.36$ ), were not found to be statistically different.

**Conclusions:** The DIR-physician concordance is not statistically different from the inter-observer concordance for seromas with clarity scores  $\geq 3$ . This DIR workflow, used to propagate planning CT seroma contours onto CBCTs, is appropriate for this cohort of APBI-eligible patients.

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#### DOSIMETRIC VERIFICATION OF A 7 MM SET-UP MARGIN FOR ACCELERATED PARTIAL BREAST IRRADIATION USING DAILY CONE-BEAM COMPUTED TOMOGRAPHY FOR IMAGE GUIDANCE

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**Purpose:** To use deformable image registration (DIR) to directly account for anatomic changes and set-up errors in external beam accelerated partial breast irradiation (EB-APBI) patients, enabling reconstruction of the delivered dose and dosimetric validation of a 7 mm planning target volume (PTV) margin.

**Materials and Methods:** Fifteen early-stage breast cancer patients treated with EB-APBI (27 Gy in five consecutive daily treatments) underwent a CBCT prior to each treatment for set-up verification. DIR (Velocity 3.2.0, Varian Medical Systems, CA) was used to deform the planning CT and associated contours to match the anatomy depicted by CBCTs acquired on the first and last days of treatment. This process produces two synthetic CTs with deformed contours for each patient. A clinical target volume (CTV) was produced on each synthetic CT by uniformly expanding the deformed seroma contour by 10 mm, and cropping to the chest wall muscle and 5 mm inside the body contour. Planned treatment delivery parameters were applied to the synthetic CTs and their deformed structure sets. The dose delivered to each patient was estimated by averaging the dose distributions calculated on the first and last treatment synthetic CTs. All patients were originally planned such that 98% of the DEV (dose evaluation volume; PTV cropped to the chest wall muscle and 5 mm below the skin surface) received at least 95% of the prescription dose. Delivered CTV coverage was evaluated using the V90%, D98%, and D2%.

**Results:** All 15 patients were planned such that the CTV V90% = 100% and delivered values were all within 0.1%. The percent differences between planned and delivered CTV D2% on a patient-to-patient basis were <1.5%, suggesting delivered dose hotspots consistent with the treatment plans. The cohort median (range) planned and delivered CTV D98% were 96.2% (95.3 – 98.4%) and 95.4% (93.6 – 99.3%), respectively. The largest percent difference between planned and delivered CTV D98% on a patient-to-patient basis was 1.8%. Overall, 13 of 15 patients received CTV D98%  $\geq 95\%$  and the remaining two patients received D98% of 93.6% and 94.9%. The dose delivered to ipsilateral and contralateral breast, ipsilateral lung, and heart were within the planning dose constraints and dose limits recommended in the external beam arm of RTOG 0413.

**Conclusions:** The results of this study illustrate strong agreement between planned and delivered dose distributions for 15 EB-APBI patients. Despite the presence of residual patient set-up errors, the 7 mm PTV margin provides adequate CTV coverage for this patient cohort. This allows us to infer that PTV planning assumptions for the study could be considered to be within safe limits, but analysis of a larger patient population will be required to comprehensively assess whether the PTV margin for CBCT-guided EB-APBI can be further reduced.

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#### REDUCTION OF ELECTRON BACKSCATTER FROM INTRA-ORAL LEAD SHIELDS USING ALUMINUM BAKING SHEETS - A PRACTICAL SOLUTION

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**Purpose:** Intra-oral lead shields are routinely used to reduce radiation exposure to the gums during the treatment of skin cancer of the lip. Unfortunately, electron backscatter created by the lead shields can result in hotspots of up to 160% of the prescribed dose on the inner lip. Aluminum has been previously shown to attenuate electron backscatter at beam energies of 6 MeV and 12 MeV. This study investigates the effectiveness of using aluminum baking sheets to attenuate electron backscatter produced by lead. Due to their flexibility and ease of access, aluminum baking sheets are a practical alternative to using a single thick sheet of aluminum. In collaboration with the Dental Oncology Department, this study proposes a prototype for intra-oral shields made of aluminum and lead, encased by acrylic.

**Materials and Methods:** Electron beams of 6 and 9 MeV were delivered using a Siemens Primus linear accelerator. The dose transmitted through various combinations of lead and aluminum were measured using a PTW Markus Ion Chamber, and again separately, using thermoluminescent dosimeters (TLDs). Four TLDs were used for each measurement; the average reading was calculated. Electron backscatter was measured in an analogous fashion. To simulate treatment conditions, water-equivalent materials were used to create a buildup and a base. All measurements were taken at the depth of maximum dose. To facilitate this, a 1 cm-thick buildup was used for 6 MeV beams and a 2 cm-thick buildup was used for 9 MeV beams. A standard source to surface distance of 100 cm was used for all measurements. Transmission and electron backscatter factor (EBF) were calculated from the raw data. Both are calculated as the ratio of the dose measured when shielding is present to the dose measured when shielding is absent. Measurements for transmission are taken downstream of the shielding, while measurements for EBF are taken upstream.

**Results:** The addition of 2.3 mm worth of aluminum baking sheets to 2 mm of lead reduced the EBF from 158% to 116% for 6 MeV beams. A similar reduction was seen for 9 MeV beams. Generally, increasing the thickness of aluminum decreases the EBF. This relationship was observed at both beam energies. Encasing the aluminum and lead sheets in 1 mm of acrylic further reduced the EBF to 109% at both beam energies. Transmission through the aluminum and lead encased in acrylic was 0.4% and 1.1% for 6 MeV and 9 MeV beams, respectively. Lastly, based on various transmission and electron backscatter measurements, baking sheet aluminum was determined to be equivalent to standard aluminum at equal thicknesses.

**Conclusions:** Aluminum, both in the form of aluminum baking sheets and standard aluminum, effectively attenuates electron backscatter produced by lead, thus reducing hotspots on the inner lip. A 6.3 mm-thick intra-oral shield, made of 2.3 mm aluminum and 2 mm lead encased in 1 mm acrylic, virtually eliminates transmission to the gums and hotspots on the inner lip.

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#### IMPLEMENTATION OF SNC IC PROFILER FOR ANNUAL QA OF 6 MV AND 6 MV FFF BEAMS ON A TRUEBEAM LINAC

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**Purpose:** Beam profile tests such as reproducibility and consistency are part of annual linac quality assurance (QA). The tests typically require the use of a large scanning water tank, with significant time and effort needed for set-up, measurement, and tear-down. To overcome this, the feasibility of using the Sun Nuclear (SNC) Ion Chamber Profiler (IC Profiler) as a substitute to a bulky water tank is examined. The IC Profiler, marketed as “The Waterless Water Tank”, can measure X and Y profiles of fields up to 32x32cm, with ion chamber spacing of 5mm. The validity of the IC profiler is first established by performing beam profile reproducibility and consistency tests against commissioning data acquired using a BluePhantom water tank with diode and ion chamber detectors. Upon validation, a baseline for the IC profiler is established and long term reproducibility test is conducted.

**Materials and Methods:** To validate the accuracy of the IC profiler, beam

profiles were acquired for both 6MV and 6MV flattening filter free (FFF) beams on a Varian TrueBeam unit, using eight field sizes (5x5, 7x7, 10x10, 15x15, 20x20, 30x30, 5x20, 20x5cm<sup>2</sup>) and three depths (1.5, 5, 10 cm). All measurements were done at 100cm SAD, with 10 cm of solid water placed underneath the IC profiler as backscatter. These profiles were compared to commissioning profiles measured with the BluePhantom water tank. For the reproducibility, flatness and symmetry change from baseline are used as CPQR does not specify which metrics to be used. Moreover, for beam profile consistency, the metric that compares the off axis ratio between baseline and testing measurement is used as recommended by TG-142. With the IC Profiler accuracy validated, long term reproducibility is planned to be evaluated by obtaining weekly profiles under the same measurement conditions.

**Results:** For 6 MV beam, flatness changes from baseline were 0.55+/-0.50%, 0.37+/-0.26%, and 0.32+/-0.18%, for depth of 1.5, 5, and 10cm, respectively. Symmetry changes from baseline were 0.30+/-0.46%, 0.19+/-0.14%, and 0.11+/-0.07%. Beam profile consistency yielded 0.62+/-0.48%, 0.43+/-0.15%, and 0.35+/-0.09%. For 6 MV FFF beam, flatness, symmetry changes from baseline and beam profile consistency at depth of 10cm yielded 0.32+/-0.25%, 0.12+/-0.08%, and 0.60+/-0.15%, respectively. Since the TG-142 recommended tolerance for flatness and symmetry changes is 1%, and CPQR recommends the 2% of photon beam profile reproducibility, the results all fall within tolerances.

**Conclusions:** From the preliminary results, the differences between the measurement from IC profiler and that from a water tank are well under the tolerance as recommended by TG-142 and CPQR guidelines. Therefore, the IC profiler may be employed as a clinically feasible substitute of conventional water tank to check beam profile consistency and reproducibility during annual QA.

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#### IMAGE COUNTING AND THE INCREASED USE OF IGRT FOR PATIENT SET-UP

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**Purpose:** To provide a demonstration of compliance with IGRT protocols at a large university hospital.

**Materials and Methods:** An independent report was generated using the existing Aria database that counts images taken per patient and categorizes them by image type (kV set-up, MV set-up, MV port, CBCT, etc.) while also reporting the number of discarded images that were not used for set-up. Reports can be run for any treatment group using a number of user defined search parameters.

**Results:** Initial use of the reports revealed that the number of images taken can far exceeds the number prescribed. For example, breast patients were found for whom more than 200 images were taken in a course of 25 fractions. In addition, individual treatment sessions with more than 20 images were found. In addition to the unexpected frequency, some general observations were that there were significantly more images taken for breast DIBH patients than free breathing patients and frequent off-protocol use of kV set-up images in other sites. The results of the image counting report was also cross correlated with the results of the incident learning system to see if disposed images or session where IGRT was challenging were reported as incidents. Reports of imaging incidents of all kinds were rare and in most cases where we observed "excessive" imaging for a particular patient or session, there is no incident report.

**Conclusions:** The imaging report has resulted in a re-evaluation of imaging practices at our institution. The practice of off-protocol use of imaging by therapists for set-up efficiency, lack of IGRT-related incident reporting, and misalignment of the imaging frequency and clinical goals is being evaluated.

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#### WITHDRAWN

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#### IMPACT OF JAW TRACKING ON BEAM DELIVERY TIME

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**Purpose:** A current breast treatment trial is intended to provide hypofractionated treatment to a localized region of the breast, with the goal of improving cosmesis and reducing course treatment length. Intensity modulated radiation therapy (IMRT) is used solely for trial plans with the intention of minimizing dose to normal tissues, more so than standard breast treatments. Although it is not currently in the trial protocol, a potential further step to reducing dose to normal tissues is to use deep inspiration breath hold to spare the heart in left-sided breast patients. A complicating factor is the use of jaw tracking in IMRT, which can increase the actual beam delivery time, by using beam holds in cases where a jaw needs to move significantly.

**Materials and Methods:** Matlab is used to assess dynamic MLC / IMRT fields from Eclipse plans to determine the number of jaw motions that require beam holds. Additional time to deliver the beam can be determined from the amount of jaw motion observed.

**Results:** Initial results indicate that jaw tracking can add several seconds (1.3-7.6s on a test plan) as the jaws move 12-46 times per field. Further analysis is forthcoming and may include the effect of collimator rotation.

**Conclusions:** A relatively simple assessment of a dynamic MLC plan can determine the actual beam delivery time for each field, which may not be accurately reflected in Eclipse or on the treatment unit, due to current limitations in calculation. The impact of jaw tracking should be considered during patient assessment for deep inspiration breath hold, with the option to disable jaw tracking if the actual beam delivery time is increased substantially.

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#### THE IMPACT OF HYDROGEL SPACER ON PROSTATE INTRA-FRACTION MOTION BASED ON PRE- AND POST-CBCTS

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**Purpose:** The goal of this study was to quantify intra-fraction motion in prostate patients with a PEG hydrogel spacer (SpaceOAR<sup>®</sup>, Augmentix<sup>®</sup>, Waltham, MA, USA) using daily pre- and post- CBCTs and more specifically ascertain if SpaceOAR<sup>®</sup> reduces the systematic intra-fraction posterior shift.

**Materials and Methods:** Thirteen patients with histologically proven prostate cancer in 2017 were selected for this study. At least a week before the planning CT scan, patients were implanted with three fiducial markers (FMs) via transrectal ultrasound guidance and received a 10ml injection of a PEG hydrogel spacer between the Denonvilliers' fascia and the rectum. A 5 to 7 field IMRT plan was generated after patients underwent a planning CT scan with a full bladder and empty rectum. To help visualize the hydrogel spacer, a MRI scan was acquired with same bladder and rectum preparation and registered with the planning CT. For treatment, patients were aligned to skin marks and orthogonal kV pair matching of FM was executed with 3D couch translations. After matching and couch motions, pre- and post-treatment CBCTs were acquired. Intra-fraction motion was quantified for the SpaceOAR<sup>®</sup> group by calculating the difference in the FMs centroid location from the pre- and post-CBCTs, and compared to a cohort of 13 prostate patients without spacers treated with IMRT in 2017. Intra-fraction motion for 13 patients without spacers was estimated by measuring the difference in FM 3D positions from post-treatment orthogonal kV images relative to the pre-treatment FM matched positions.

**Results:** For the cohort of patients included in this study, dose-fractionation ranged from 60 Gy in 20 fractions to 79 Gy in 39 fractions. Thus far, 228 pre-treatment and post-treatment CBCTs and 243 kV pairs have been analyzed. The mean intra-fraction motion was -0.2 ± 1.4 mm (AP), -0.2 ± 1.3 mm (SI), -0.1 ± 0.9 mm (LR) and 1.7 ± 1.3 mm (3D vector) for the SpaceOAR<sup>®</sup> group and 0.8 ± 1.9 mm (AP), -0.1 ± 1.7 mm (SI), -0.2 ± 1.0 mm (LR) and 2.3 ± 1.6 mm (3D vector) for the group without spacers. Posterior, inferior and left motions are defined as positive while anterior, superior and right motions are defined as negative. Observed differences in the AP and 3D vector mean motion and standard deviation were statistically different (p < 0.001) based on a two-sample Student t-test for the mean and a Fisher's exact test for the standard deviation.

**Conclusions:** Fiducial marker intra-fraction AP motion for patients with PEG hydrogel was approximately 1.0 mm less than those patients without

the gel, suggesting that the hydrogel may help reduce the intra-fraction posterior drift often observed in IMRT treatment of prostate patient. A more comprehensive analysis including more data will be undertaken to rule out other possible contributing factors.

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#### USE OF 3D PRINTING TECHNOLOGY FOR RIGID BOLUS PRODUCTION USING OPTICAL OR CT SCAN BASED IMAGING DATA: A CASE SERIES

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**Purpose:** The use of 3D printing in rigid bolus fabrication with CT imaging has been adopted by few institutions globally whereas use of optical scan images instead of CT imaging is fairly new technique adopted at our institution. We present a single institution case series looking at the clinical implementation of this technology in delivering radiation treatment.

**Materials and Methods:** Over a one-year period, 10 patients considered suboptimal for traditional bolus were identified based on contour and tumour location. Bolus fabrication was based on CT data in seven patients and optical scanning was utilized in three patients with superficial tumours. Six patients were treated with megavoltage photons and four with electrons. Dose and fractionation schedules varied based on pathological and patient characteristics. Multidisciplinary discussion to determine bolus extent and thickness took place. All printed boluses underwent Quality assurance procedures.

**Results:** Mean age of patients was 68.4. 50% of patients had a diagnosis of Basal Cell Carcinoma, two had plasmacytoma, one had squamous cell carcinoma of skin, one had myeloid sarcoma of scalp and one had follicular lymphoma of the lacrimal gland. Seventy per cent of patients were treated with radical intent, two were treated palliatively and one patient was treated in the adjuvant setting. 3D printed boluses were successfully utilized with the exception of 1 nasal plasmacytoma whose dosimetrics were met without the aid of a bolus. 3D-Printing took 6-12 hours and varied based on the complexity of contours, size and thickness of the bolus.

**Conclusions:** 3D printing technology using imaging data from CT scan or Optical scan for printing boluses is an innovative method and superior to tradition bolus in certain circumstances. This technique has been adopted as standard of care at our institution. No clinically significant issues were reported by physicians, physicists or radiation therapists when using this technique.

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#### CONCURRENT CRANIOSPINAL IRRADIATION (CSI) WITH TEMOZOLOMIDE (TMZ) IN PRIMARY DIFFUSE LEPTOMENINGEAL GLIOMATOSIS (PDLG): A CASE REPORT AND REVIEW OF THE LITERATURE

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**Purpose:** PDLG is a rare condition involving widespread infiltration of the meninges by malignant cells of glial origin. Currently there is no standardized management approach and there are no reports of concurrent chemotherapy and CSI within the literature.

**Materials and Methods:** A 21-year-old gentleman with high-grade poorly differentiated glial neoplasm with leptomeningeal spread. He was treated with concurrent TMZ and CSI delivered with rapid arc technique, demonstrating a prolonged clinical and radiologic response.

**Results:** MRI Brain demonstrated diffuse leptomeningeal enhancement with edema of the optic nerve, inferior descent of the cerebellar tonsils and atypical, circumferential enhancement of the right supraclinoid internal carotid artery. Histopathological diagnosis was consistent with a high grade, poorly differentiated neoplasm with leptomeningeal spread of glial origin. He received CSI delivered with rapid arc technique and daily TMZ (50mg/m<sup>2</sup>). A total of 36 gray in 20 fractions were delivered to the brain, cribriform plate and thecal sac with an expansion of 7 mm for the planned treatment volume (PTV). As the posterior fossa and lumbosacral spine appeared to harbor the bulk of disease radiologically they received a boost of 18 gray in

10 fractions with a 5mm expansion for PTV. The patient was then treated with adjuvant TMZ (200mg/m<sup>2</sup>) for a total of 12 planned cycles. He has so far had a marked clinical and radiographic response.

**Conclusions:** We report on a rare histological entity of primary diffuse leptomeningeal gliomatosis with high grade features that has demonstrated a remarkable and prolonged response to concurrent chemo radiotherapy delivered with modern conformal radiation techniques. To our knowledge this has been the first case where concurrent TMZ and CSI has been reported in the literature.

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#### A NOVEL TECHNIQUE OF DELIVERING BREAST RADIOTHERAPY USING VISUALLY MONITORED DEEP INSPIRATION BREATH HOLD FOR PATIENTS WITH HEARING IMPAIRMENT

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**Background:** Deep inspiration breath hold (DIBH) can be used to reduce radiation dose to the heart and lungs in patients treated for breast cancer with radiation therapy. A radiotherapy standard in our department, for patients who would benefit from DIBH, is a validated, reproducible, visually monitored deep inspiration breath hold (VM-DIBH) technique that utilizes couch top to lateral skin marks, in-room lasers, and cameras. Audio coaching is done by the radiation therapist through an intercom system that enables communication with the patient, to manually gate the radiation beam during breath hold. Coaching and communication are essential requirements of a successful visual breath hold technique.

**Purpose:** To describe a novel, low cost solution that enables communication with hearing impaired patients to successfully use a VM-DIBH technique.

**Materials and Methods:** The simple use of a light switch is controlled by the radiation therapist and indicates to the patient to take a deep breath in and hold to acquire the CT scan and during radiation delivery on the treatment unit. A visual signal indicator with two lights is temporarily mounted to the head of the linear accelerator gantry, in a position that is seen by the patient from all treatment angles, as well as seen by the radiation therapist at the treatment console on the in-room camera system. The light indicator cable is connected from the treatment room through a conduit to a two-stage hand switch at the treatment console. The radiation therapist controls the light signals to communicate breath hold actions to the patient.

**Results:** Two patients with breast cancer have been successfully treated with our VM-DIBH technique utilizing a visual signal system to coach for manual beam gating during DIBH. On board imaging was done as part of our standard imaging protocol and no unexpected issues were identified.

**Conclusions:** A simple, yet impressive, visual light indicator is a successful tool that can be used to coach hearing impaired patients for a VM-DIBH technique as a method of radiation dose reduction to organs at risk. This technique can be potentially used for all patients with hearing impairment being considered for DIBH.

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#### TECHNICAL CONSIDERATIONS IN STEREOTACTIC ABLATIVE BODY RADIOTHERAPY FOR LOCALIZED NEUROENDOCRINE CANCER OF THE LUNG

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**Purpose:** Limited-stage small cell lung cancer without nodal involvement is typically treated by lobectomy with lymph node dissection. While a growing body of literature has emerged on clinical outcomes of stereotactic ablative body radiotherapy (SABR) as an alternative for high-risk surgical patients in this scenario, description of the technical considerations is lacking. We present the use of, and identify unique challenges associated with, treating Stage 1 small cell, large cell and neuroendocrine cancer of the lung using SABR. **Materials and Methods:** Institutional experience along with a review of the relevant literature allowed for compilation of technical considerations associated with treating small cell, large cell and neuroendocrine cancers of the lung with SABR.

**Results:** Inter-fraction tumour motion of Stage I non-small cell lung cancer (NSCLC) treated with SABR has been reported in the range of 0.3-4.5 mm with tumour volume reduction as high as 10% during treatment. Following four of the planned eight 7.5 Gy fractions, a case of localized high-grade neuroendocrine carcinoma of the lung had displaced 12 mm with nearly a 2/3 volume reduction. This is in keeping with the known radiosensitivity of neuroendocrine tumours; however, warrants discussion of the unique aspects of image guidance and dose fractionation for these and other radiosensitive lung targets.

With significant volume reduction during treatment, tumour localization on image guidance can be difficult. Similar challenges have been reported in subcentimeter NSCLC, where tumour localization requires inference based on surrounding soft tissue landmarks on approximately 10% of cone-beam CT images. When tumour motion occurs in addition to volume changes, this may not be possible, and adapting the radiation plan should be considered. Alternatively, fiducial markers can facilitate tumour tracking; however, this requires an additional pre-treatment procedure that can be associated with risks such as pneumothorax or marker migration.

Regarding the most appropriate lung SABR dose, single fraction radiosurgery has been evaluated in the context of two recent Phase II trials for Stage I NSCLC. To our knowledge, this strategy has not been evaluated within localized small cell, neuroendocrine or large cell lung cancers, but warrants investigation as it avoids the potential challenges of inter-fraction changes in tumour volume and position.

**Conclusions:** SABR for lung tumours such as small cell, neuroendocrine and large cell carcinoma can involve technical challenges owing to their highly radio-responsive nature. Further outcome-based data and research on technical considerations are warranted given the expected increased incidence of these in the era of CT-based screening and surveillance strategies.

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#### AUTOMATED SEGMENTATION OF THE INTERNAL TARGET VOLUME ON UNGATED CBCT IMAGES IN LUNG SBRT

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**Purpose:** The internal target volume (ITV) for lung stereotactic body radiotherapy (SBRT) is often manually segmented on 4DCT data. On treatment, a slow CBCT image acquisition is performed spanning several breathing cycles. This blurry CBCT is rigidly registered with the 4DCT and patient orientation is corrected via treatment couch translations and rotations. This work validates a deformable image registration method for propagating a planning ITV directly onto a treatment image.

**Materials and Methods:** Our intensity-based registration algorithm aligns the untagged reconstruction from the planning 4DCT and corresponding ITV with the CBCT. This approach was tested on images of an anthropomorphic phantom with a 3 cm diameter target undergoing superior/inferior breathing motion (QUASAR, Modus Medical). 4DCT images of the phantom were acquired with a typical motion waveform and all combinations of 1, 2, 3 cm peak-to-peak motion amplitude and 14, 18 breaths per minute (BPM). CBCT images were obtained with the phantom under all combinations of 0.5, 1, 2, 2.5, 3 cm peak-to-peak amplitude and 14, 18 BPM. The CBCT scans were repeated with the phantom motion simulating target drift. The 4DCT data were used to generate six planning ITVs; each was then positioned on the 20 CBCT images using our method.

**Results:** ITVs placed on CBCT were compared with positions expected given the known target motion trajectory. Overall, the mean error decreased significantly ( $p < 0.001$ ) from  $1.3 \pm 0.2$  mm following affine alignment to  $0.9 \pm 0.1$  mm following deformable registration. Sub-mm error was achieved despite large variances in breathing amplitude, rate, and waveform between planning and treatment.

**Conclusions:** Our method yields acceptable results in a lung SBRT setting although testing with patient images necessary. Availability of ITVs on treatment may be useful in online image guidance decisions or offline computation of treatment accuracy across many patients and fractions.

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#### EVALUATION OF IMRT TREATMENT OF THORAX ESOPHAGEAL CARCINOMA IN ELEKTA AND VARIAN LINAC

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**Purpose:** To evaluation the characteristics of static intensity modulated radiotherapy plans designed on Elekta Synergy and Varian Unique2229 Linac in different esophageal cancer (EC), exploring the characteristic of the two vendors Linac, thus can be better service for clinical.

**Materials and Methods:** The Oncentra4.1 TPS was adopted to design both Varian and Elekta IMRT plans for thirty patients, including 10 cases located in upper, middle and the lower thorax, respectively, who were diagnosed with thoracic EC. The prescription dose to the PTV is 60 Gy in 30 fractions. All treatment plans of the 30 cases were evaluated using the dose volume histogram parameters of PTV and the organs at risk, such as lungs, spinal cord and heart and additional Monitor units (MU), treatment time, and Gamma index comparisons were performed.

**Results:** All plans resulted in abundant dose coverage of PTV for EC of different locations, MUs and gamma index were similar between the two Linac plans. The doses to PTV, HI and OAR in Elekta plans were not statistically different in comparison with Varian plans, with the following exceptions: in upper and lower thoracic EC the PTV's CI, were better in Elekta plans than in Varian plans, while in middle thorax EC Varian plans PTV's D2, D50, PTV-average were better than Elekta plans. Treatment time were significantly decreased in Varian plans as against Elekta plans in the cervical and the middle thorax EC by 14.7% and 20.8%, respectively, while in the lower thoracic EC treatment time were no striking difference.

**Conclusions:** For the the middle thorax EC Varian plans is better than Elekta plans, not only in treatment time but also in the PTV dose, while for the lower thorax EC Elekta plans is the first choice for better CI, for the upper EC usually Elekta plans can increase the CI, while Varian plans can reduce treatment time, can be selected according to the actual situation of the patient treatment.

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#### EVALUATION OF INTENSITY MODULATED RADIATION THERAPY PLANNING FOR CERVICAL CANCER BASED ON AUTO-PLANNING

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**Purpose:** To determine whether Auto-Planning-based intensity modulated radiation therapy (A-IMRT) planning can improve planning efficiency without compromising plan quality compared with current manual trial-and-error-based intensity modulated radiation therapy (M-IMRT) planning for patients with cervical cancer.

**Materials and Methods:** Ten postoperative patients with Stage III cervical cancer were enrolled as subjects. The Pinnacle 9.10 planning system was used to design M-IMRT and A-IMRT plans. Plans were evaluated based on the ability to meet the dose volume histogram. The homogeneity index (HI), conformity index (CI), Dmean values of target volume, the dose of organs at risk, treatment monitor units (MUs) and total planning time were compared. The differences were analyzed by paired t-test model.

**Results:** The results showing that there were no significant differences between A-IMRT plans and the M-IMRT plans in HI or CI (0.060 versus 0.061,  $p = 0.875$ ; 0.915 versus 0.930,  $p = 0.104$ ). Compared with the M-IMRT plans, the A-IMRT plans were superior considering decreasing bladder V40 ( $40 \pm 2.5\%$  versus  $38.6 \pm 2.1\%$ ,  $p = 0.047$ ), bowel V30 ( $38.6 \pm 4.5\%$  versus  $35.6 \pm 5.5\%$ ,  $p = 0.007$ ), and the V30, Dmean, and D50% of the left and right femoral heads and lowdose irradiation volume were slightly reduced. The A-IMRT plans had significantly longer total planning time but significantly shorter manual planning time than the M-IMRT plans (45.2 versus 32.7 min,  $p = 0.000$ ; 4.5 versus 16.5 min,  $p = 0.000$ ) and there were no significant differences in other statistical indexes.

**Conclusions:** Patients with cervical cancer planning with A-IMRT can get equivalent or superior plan quality compared to M-IMRT plans with substantially shorter manual planning time and improved planning efficiency.

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### INFLUENCE OF DEFORMABLE IMAGE REGISTRATION SOFTWARE IMPLEMENTATION ON ADAPTIVE RADIATION THERAPY REPLAN DECISIONS

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**Purpose:** Deformable image registration (DIR) is commonly used in the adaptive radiation therapy (ART) setting to lessen the resources required for calculating inter-fractional dose values. Primarily, it is used to generate contoured synthetic CTs (CT's deformed over the field of view of a CBCT image) or to propagate contours from planning CT to re-CT, automating the laborious task of manual contouring. This study explores the implications of DIR use on clinical ART replan decision-making.

**Materials and Methods:** Fifteen CTs and 105 CBCTs from a retrospective cohort of 15 head and neck cancer patients were created according to vendor recommendations in SmartAdapt® demons- and Velocity™ b-spline-based DIR software (Varian Medical Systems, Palo Alto, CA), yielding 210 synthetic CTs. The original treatment plan was reapplied in each case and dose was re-calculated. A treatment fraction was indicated as requiring a replan if structure-specific dose violations for CTVs and organs-at-risk (OAR) exceeded 5%.

**Results:** Dichotomous replan recommendations occurred for target structures (low- and high-dose CTVs) in 13 of 105 analyzed fractions. For OAR, replan/no replan indications disagreed in 33/105 cases. Overall, when combining target and OAR violations, discrepancies in replan indications occurred in 35/105 fractions. 21.9% of fractions were flagged as requiring a replan by SmartAdapt (primarily for OAR), and 11.4% for Velocity (primarily for target volumes). Six of 15 patients were indicated for replan by SmartAdapt and not Velocity, or vice versa, when considering patient-specific analyzed fractions. Discrepancies appear to arise from a larger allowable deformation extent in SmartAdapt with consequent improved fidelity in reproducing the CBCT external contour. Larger morphological effects estimated by SmartAdapt corresponded to increases in CTV coverage and parotid gland dose. DIR output in Velocity, however, was less prone to artifact and appeared more anatomically realistic; SmartAdapt Synthetic CTs often required additional corrections.

**Conclusions:** Due to Velocity's underestimation of large morphological changes, it is possible that Velocity-based ART workflows may miss outliers, for example, those patients with >2 cm shrinkage of tumour volumes. To compensate for loss of protocol sensitivity, thresholds for replan/no replan decision making may require adjustment. Supplementary metrics, such as on-unit measurements, may aid in identifying outliers and balancing protocol sensitivity and workload. It is essential to verify the fidelity of DIR output for site- and modality-specific use as well as for the extent of anatomical changes expected; modifications to vendor-recommended workflows may be necessary. The effect of variable DIR use among centres should be considered when designing inter-centre ART replan-candidate identification protocols.

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### DOSIMETRIC STUDY ON PATIENT TRANSFER BETWEEN VARIAN CLINAC iX AND TRUEBEAM LINACS

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**Purpose:** Varian Clinac iX and TrueBeam have different head designs and MLC control systems. TrueBeam's primary collimators are thicker and it contains an anti-backscatter filter. Truebeam MLC leaf positioning is more accurate than the Clinac iX which influences dosimetric leaf gap (DLG) and leaf transmission. The objective of this study was to characterize the dosimetric differences in treatment planning and delivery between these two machines in order to assess the potential impact of patient transfer in a center with limited resources.

**Materials and Methods:** Ten pelvis 6MV VMAT plans with large field size, 10 prostate 6MV VMAT plans with regular field size and nine field-in-field breast plans with mixed 6MV and 16MV were planned (Varian Eclipse Version 11) and measured on an iX unit and a TrueBeam unit. Truebeam and iX beam models were based on Varian reference data along with in-house optimized DLG and transmission values. A cylindrical solid water

phantom with multiple ion-chamber insert positions was used to measure the absolute dose in target regions. Measurements were compared against the TPS calculations for two models.

**Results:** The average measured dose differences between the iX and Truebeam models for prostate, pelvis and breast plans were 0.2%, 1%, and 2.3% respectively. The average calculated dose differences between the two machines were 1.4%, 1.8%, and 1.1%, respectively. The TrueBeam dose was lower than the iX dose for all calculated and measured plans due to its anti-backscatter filter and lower DLG and leaf transmission. The maximum differences between the calculated dose for one machine and the delivered dose on the other machine were 1.2%, 1.6%, and 1.9%, respectively.

**Conclusions:** Systemic dosimetric differences were observed between the TrueBeam and iX units for both treatment planning and delivery. These differences were found to be small and of limited clinical significance, suggesting that patient transfer is justifiable at our centre.

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### SYNTHESIS OF GOLD NANOPARTICLES FUNCTIONALIZED WITH PLANT EXTRACT FOR TREATMENT OF PROSTATE CANCER

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**Purpose:** The overall goal of the project is to use biocompatible gold nanoparticles functionalized with curcumin, an extract from the turmeric root, for targeted radiotherapy treatment of prostate cancer. The idea is to utilize the properties of the functionalized gold nanoparticles for multimodal treatment achieved via the chemopreventive properties of curcumin, the radiosensitization of the cancer cells through modification of the cell cycle, and the potential enhancement of dose from external radiation; they also provide an additional benefit of enhancing tumour imaging. In this study, we focus on the effects of synthesis parameters on the particle size distribution and surface charge of curcumin functionalized gold nanoparticles (cur-AuNPs).

**Materials and Methods:** Cur-AuNPs were synthesized through reduction of gold(III) chloride trihydrate (Aldrich) using curcumin (Alexis Biochemicals). In a typical experiment, 200 µL of 100 mM HAuCl<sub>4</sub>·3H<sub>2</sub>O stock solution was added dropwise to 0.5, 1 or 2 mM curcumin solution (prepared in 1, 3, or 5 mM sodium hydroxide solution), and held in an ultrasonic water bath at 44 C. The formation of the cur-AuNPs was first confirmed with the appearance of a ruby red colour. To remove any unreacted ions, the sample was immediately transferred into 3.5 kDa dialysis tubing (Thermo Fisher) and dialyzed repeatedly for ≥20 h. The particle-size distribution and zeta potential of the dialyzed cur-AuNPs were measured using a Malvern Zetasizer Nano-ZS (Malvern Instruments Ltd.).

**Results:** The average diameters (intensity-peak values from Zetasizer measurements) of cur-AuNPs obtained by varying molarities of sodium hydroxide (NaOH) and curcumin were: (i) 91.9±1.6 nm (1 mM NaOH), (ii) 28±1.2 nm (3 mM NaOH), (iii) 22.5±0.5 (5 mM NaOH) with 0.5 mM curcumin; (i) 106±1.7 nm (1 mM NaOH), (ii) 26.2±0.3 nm (3 mM NaOH), (iii) 21.4±0.45 nm (5 mM NaOH) with 1 mM curcumin; (i) 96.3±4 nm (1 mM NaOH), (ii) 47±1.3 nm and 3±0.3 nm (3 mM NaOH), (iii) 22.6±0.5 (5 mM NaOH) with 2 mM curcumin. The zeta potential measurements showed an average surface charge of -29 mV for all samples.

**Conclusions:** All measurements, except cur-AuNPs prepared in 2 mM curcumin and 3 mM NaOH, showed a single intensity peak indicating mono-dispersion. For all 3 molarities of curcumin solutions (0.5, 1 and 2 mM), the mean particle size decreased with increase in the molarity of NaOH solution (from 1 to 5 mM). The relatively high surface charge (-29 mV) of the cur-AuNPs indicate good dispersion of the nanoparticles.

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### QUANTIFICATION AND MONITORING OF MAGNETIC FIELD INDUCED EFFECTS ON A LINEAR ACCELERATOR IN AN MR-GUIDED RT ENVIRONMENT

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**Purpose:** To comprehensively quantify through experimental measurements, numerical simulations and long-term monitoring the magnetic field induced effects on the performance of a therapy linac which was set-up in an MR-guided radiotherapy environment.

**Materials and Methods:** An MR-guided RT facility was developed at our institution which relies on an MR-on-rail scanner optimized for imaging in the proximity of a linear accelerator. The MR/linac dual-purpose room (imaging/therapy) was designed to be utilized in three operation modes: a) linac-only for conventional RT – linac/patient table set-up is standard, b) MR-only for imaging studies with patient in the treatment position, c) MR-guided RT when MR data of the day is used in conjunction with CBCT to perform MR matching with a reference MR and compute couch shifts. While the linac is not meant to operate in unison with the MR, it was repeatedly exposed to MR magnetic fringe fields which can potentially induce remanent effects (transient, permanent). These may be caused by magnetization of key linac sub-components or in the surrounding ferromagnetic environment. The magnetic field in the entire vault was mapped using Hall probes and confirmed via FEM numerical simulations which included the MR, linac structure and table. A boundary value problem was defined and solved to predict the fringe field profile across the linac where direct measurements were not available. The linac electron beam optics was particularly evaluated to assess for field interference. Extensive beam measurements using a 2D matrix of ion chambers were performed for multiple scenarios: a) minimum time required to apply and immediately remove the fringe field, b) anticipated mean scan time for MR guidance (minutes), c) long exposures (days). All data was analyzed with regard to the baseline acquired before the MR was ramped up to field. Data from two other linacs (same make) was also pooled as a reference guide. The metrics used for quantifying the beam performance were output, radial/transverse flatness and symmetry. The measurements were performed as a function of full bi-directional gantry rotations (15° increments). Beam log files (angle/position stirring currents) were also acquired and directly compared to the ion chamber data. Beam steering servos were also turned on/off for a detailed diagnosis. Measurements were performed routinely for over two years.

**Results:** The simulated magnetic field mapping inside the entire RT space was found to be in good agreement with the experimental results within a tolerance of 1 G. At the electron beam optics the fields were less than 15 G. The stirring coils can compensate for the induced fields due to magnetization of various linac gantry parts. The beam flatness and symmetry are maintained within specifications by applying steering currents lower than the maximum allowed. No issues were observed during one year or clinical operation of the linac.

**Conclusions:** The study showed that the linac can be safely and optimally used for RT applications - conventional and under MR-guidance.

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#### EVALUATION OF TUNGSTEN INTERNAL EYE SHIELDS IN KILOVOLTAGE X-RAY BEAMS AND MEGAVOLTAGE ELECTRON BEAMS

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**Purpose:** Kilovoltage (kV) X-ray and megavoltage (MeV) electron beams are often used to treat skin cancer near the eye. An internal eye shield is usually placed underneath the eyelid to protect the cornea, lens and retina. The shield is made of dense metal so that adequate protection can be achieved with reasonable thickness (4 mm or less) to fit inside the eye with minimal discomfort. In the past decade or so, tungsten has replaced lead due to its higher density (19.25 versus 11.34 g/cm<sup>3</sup>), lower atomic number (74 versus 82) and lower toxicity. The purpose of this study is to investigate transmission and backscatter of tungsten eye shields in kV X-ray and MeV electron beams. Clinically, it is desirable to achieve transmission of less than 5% and backscatter of less than 110% (e.g. up to 10% enhancement

of radiation dose).

**Materials and Methods:** Two sets of tungsten internal eye shields purchased from Radiation Products Design, Inc. (5218 Barthel Industrial Drive, Albertville, MN 55301) have been evaluated. Each set consists of three shields with diameters of 17.4, 19.1, and 20.8 mm (small, medium and large, respectively). One set has a thickness of 2 mm while the other 3 mm. Both sets come with a 1 mm aluminum cap to reduce backscatter, which could otherwise produce excessive dose to the inner side of the eyelid. A Gulmay D3300 orthovoltage X-ray unit was used to deliver 100, 120, and 250kVp X-ray beams; while a Varian TrueBeam medical linear accelerator was used to produce 6, 9, and 12MeV electron beams. Thermoluminescent dosimeters (TLDs) were used to measure backscatter and a Markus ion chamber was used to measure transmission. Radiation field sizes ranged from 3 cm diameter to 6x8cm<sup>2</sup>.

**Results:** Backscatter of tungsten eye shields in kV X-ray beams with a 3 cm diameter cone were all below 110%, with or without the 1 mm aluminum cap. Though there was a slight reduction of backscatter when the aluminum cap was used for 250kVp (from 105% to 102%), this effect was less obvious for 120 and 200kVp. For all kV X-ray beams, transmission increased steeply with radiation field size (about 3%, 6%, and 13% for 3, 4, and 6x8cm cones, respectively). For MeV electron beams, 2mm tungsten shield were adequate for 6 and 9MeV while 3mm was required for 12MeV to achieve transmission <5%.

**Conclusions:** For kV X-ray beams, backscatter of less than 110% can be achieved without the use of the 1mm aluminum cap, though the aluminum cap reduces backscatter slightly for 250kVp. Transmission of kV X-ray beams through tungsten eye shields increases steeply with radiation field size, therefore caution must be taken when tungsten shields are used with cones 4cm diameter or larger. For MeV electron beams, while 3mm tungsten eye shields are more effective at reducing transmission, this is only significant at 12MeV, making 2 mm shields an effective option at 6 and 9MeV if patient comfort is an issue.

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#### USE OF 10 MV FFF TO REDUCE THYROID DOSE IN PEDIATRIC WHOLE LUNG IRRADIATION

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**Purpose:** Whole lung irradiation (WLI), used to treat lung metastases in certain pediatric patients exposes the thyroid to peripheral doses that can contribute to late effects such as hypothyroidism and secondary thyroid cancers. This feasibility study aims to assess and compare peripheral thyroid doses after WLI delivered by 6 MV VMAT, the current standard of care, and 10MV flattening filter free (FFF) VMAT, a beam mode that has been shown in literature to reduce peripheral doses.

**Materials and Methods:** Whole lung irradiation was planned on four CT data sets using 6MV-flattened and 10 MV FFF VMAT. Thyroid mean and max doses were assessed using Monte Carlo calculations. The Monte Carlo calculations were corrected for head leakage and scatter (not accounted for in simulation) using a measurement-based model.

**Results:** Both 6 MV VMAT and 10 MV FFF VMAT achieved dosimetrically equivalent plans in the in-field region. However, 10 MV FFF VMAT plans resulted in an average reduction of 9.8% (p = 0.04) in mean thyroid dose compared to 6MV VMAT. The absolute mean thyroid dose reduction ranged between 0.1 - 0.5 Gy.

**Conclusions:** 10 MV VMAT FFF beams present a dosimetric advantage compared to 6 MV VMAT with respect to peripheral dose to the thyroid after whole lung irradiation. Developing a 10 MV FFF VMAT protocol is achievable and aligns with ALARA principles.

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#### IMPROVED DELIVERY ACCURACY AND REDUCED TREATMENT TIME USING DCAT WITH FFF COMPARED TO VMAT FOR LUNG SBRT PATIENTS

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**Purpose:** The accuracy of Volumetric Modulated Arc Therapy (VMAT) for lung stereotactic body radiation therapy (SBRT) is a concern due to small segment sizes, especially for targets exhibiting significant breathing motion. Here we investigate the potential for Dynamic Conformal Arc Therapy (DCAT) with segment shape optimization (SSO) and variable dose rate available in Monaco 5.11 to give larger segments and reduced delivery time. We also test to what degree the use of flattening filter free (FFF) mode can reduce treatment times.

**Materials and Methods:** Six VMAT SBRT lung patients planned for treatment on Elekta linacs with Agility MLC are replanned using DCAT with SSO and variable dose rate using conventional and FFF beams. Comparisons of plan quality, MU/cGy, average segment size, treatment times and ArcCheck pass rates are carried out to evaluate the advantage of using DCAT and DCAT with FFF mode compared to VMAT.

**Results:** Target coverage, high dose conformality and normal tissue doses are equivalent for the DCAT, DCAT with FFF mode and VMAT plans. Although the low dose conformality using DCAT is worse compared to VMAT, it is within an acceptable range. The average MU/cGy is 2.0, 2.2 and 4.0 MU/cGy for the DCAT, DCAT with FFF mode and VMAT plans respectively. The average total beam on time is 5.4, 2.8 and 8.8 minutes for the DCAT, DCAT with FFF mode and VMAT plans respectively. The average segment area is larger for DCAT compared to VMAT plans and the average ArcCheck pass rates at 3%/3mm are higher for DCAT compared to VMAT indicating the potential for improved delivery accuracy.

**Conclusions:** This study demonstrates that DCAT with SSO and variable dose rate can produce equivalent plan quality with reduced treatment time, fewer MU/cGy and potentially greater accuracy compared with VMAT and that implementing FFF mode can further reduce treatment times.

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#### A NEW TECHNIQUE FOR DELIVERING ABLATIVE DOSE TO PANCREATIC CANCER: A PROOF OF CONCEPT

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**Purpose:** Pancreatic stereotactic body radiotherapy (SBRT) is an accepted treatment option for unresectable or borderline resectable locally advanced pancreatic cancer (LAPC). Emerging data suggests biologically equivalent dose (BED, a/b10Gy) of  $^3$ 100 Gy may have improved clinical outcomes. Unfortunately, routinely the SBRT dose has to be lowered to accommodate organs adjacent to the gross tumour or risk overdosing those organs. In this abstract we provide a proof of concept that an ablative dose can be delivered to the target volume, while maintaining normal organs within acceptable dose limits.

**Materials and Methods:** We randomly selected one patient who had undergone our institutional standard SBRT with 33 Gy in 3 fractions (BED a/b10Gy = 69.3Gy) for LAPC (old plan). All of the contours including gross tumour volume (GTV), internal target volume (ITV) and planning target volume (PTV) were transferred to generate a new plan to deliver 50 Gy in 5 fractions (BED a/b10Gy = 100Gy) using the novel approach (new plan). A planning organ at risk volume (PRV) of 5 mm was added to the hollow visceral organs (duodenum, stomach, small and large bowel) close to the tumour. Three PTV volumes were defined, PTV\_35, PTV\_50 and PTV\_65. PTV\_35 was the PTV used in old plan. PTV\_50 was created by trimming PTV\_35 away from the PRVs. PTV\_65 was created by contracting PTV\_50 by 7 mm. A new plan to deliver 50 Gy in 5 fractions to PTV\_50 with simultaneous boost to 65 Gy to PTV\_65 was generated, while the rest of the PTV\_35 was prescribed 35 Gy in 5 fractions. Following criteria were used to develop new plan: PTV\_65 (volume receiving 95% of prescribed dose, V95%)  $\geq$  99%; PTV\_50 (V95%)  $\geq$  95%; PTV\_35 (V95%)  $\geq$  99%; Duodenum Dmax  $\leq$  38 Gy; Small bowel Dmax  $\leq$  38Gy; Stomach Dmax  $\leq$  38Gy; Duodenal PRV V45Gy < 0.5 cc; SB PRV V45Gy < 0.5 cc; Stomach PRV V45Gy < 0.5 cc.

**Results:** A new VMAT plan was successfully developed using the above outlined dose constraints delivering significantly higher BED to a large portion of the original PTV volume, PTV\_65 (V61.75 Gy) = 100%, PTV\_50 (V47.50Gy) = 97%, PTV\_35 (V33.25 Gy) = 100%. Simultaneously, with the new planning technique, the Dmax to the duodenum, bowel and stomach for

late toxicity (a/b3Gy) had meaningful reductions: 34.1 Gy (BED = 163Gy), 23.0 Gy (BED = 82 Gy) and 11.8 Gy (BED = 27 Gy) with old plan versus 38.0 Gy (BED = 134Gy), 21.8 (BED = 53Gy) and 10.2 Gy (BED = 17 Gy) with new plan, respectively.

**Conclusions:** Delivering ablative dose to the LAPC, while respecting OAR dose constraints, is feasible using carefully developed plans with our technique utilizing SBRT methodology. Further, preclinical work and clinical validation is required to develop robust planning protocols.

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#### STOCHASTIC FRONTIER ANALYSIS TO IMPROVE ORGANS-AT-RISK SPARING IN VMAT-TREATED PROSTATE CANCER

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**Purpose:** Radiation therapy treatment planning for advanced techniques often consists in a compromise between delivering the prescribed dose to the target and sparing organs-at-risk (OARs). In order to tackle the problematic, we use Stochastic Frontier Analysis (SFA) as a new knowledge-based planning paradigm to predict achievable OAR sparing in terms of the specific patient morphology.

**Materials and Methods:** In this retrospective study, geometric and dosimetric information was extracted for over 400 patients treated with VMAT for prostate cancer with three prescribed dose levels (36-37.5 Gy, 44-46 Gy and 60-78 Gy). Thirteen different dosimetric indices (e.g. Dmax, VxGy) were inquired for the bladder and the rectum for a total of 38. Relationships between patient morphology and dosimetric indices were defined by using SFA where the distribution of the treatment plans is supposed asymmetric with respect to an optimal frontier. A maximum likelihood technique is used to determine the distribution and the frontier parameters. All possible combinations (127) of seven geometric parameters were tested such as overlap volume and Hausdorff distance extracted from python routine within the 3D Slicer platform.

**Results:** Stochastic frontiers (SF) were obtained for 29 out of 38 dosimetric parameters for the rectum and the bladder. SF give a better mean dosimetric diminution than a least square regression. For example, for the bladder V60Gy, 90% of the plans lie above the optimum frontier and hence could be improved. Its mean dosimetric diminution possible is 8.8% (5.2%). SF were also obtained for the dosimetric indices not used as planning guidelines.

**Conclusions:** Using SFA with a large cohort of patients we obtained several optimal dosimetric indices for a broad range of morphology. These indices can be used for patient-specific sparing of OARs for prostate cancer. We wish to develop a tool able to guide the planning of radiation therapy technique toward an achievable optimum dose configuration.

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#### INVERSE PLANNING AND OPTIMIZATION FOR VMAT MARKER-BASED LUNG TUMOUR TRACKING

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**Purpose:** To investigate the optimization of marker-based VMAT for lung tumour tracking.

**Materials and Methods:** Lung tumour 3-dimensional motion was simulated and obtained via a dynamic thorax phantom. 4DCT data was used to create a VMAT lung SBRT plan with two partial arcs on Varian Eclipse TPS (v11.0.31) and treatment delivered on EDGE Linac. The prescription dose for PTV was 48 Gy over four fractions. The VMAT plan was exported to an inverse planning and optimization platform, MonArc. MonArc utilizes the same progressive resolution optimization (PRO) framework as found on earlier versions of Eclipse TPS. The 4DCT dataset was re-sampled to the gantry angle rotation to obtain a respiratory-correlated plan whereby breathing phases are correlated to control points in the arc, before commencing optimization. Three fiducial markers were implanted in and around the tumour for tracking purposes. We modified MonArc to include fiducial-based constraints (Hard and Soft). Hard constraint imposes visualization for all markers (avoiding blockage

by the MLC apertures), while Soft constraint (discourages MLC blockage) for some markers in the beam's eye-view. Thence, dose distributions from plans with fiducial-based constraints were then compared to VMAT with no fiducial constraints, to analyze the discrepancies. Plans were re-imported into Eclipse and doses calculated with AcurosXB (v13.6.23)

**Results:** The mean dose to the PTV was 107%, 113% and 115% for VMAT plans with no, hard and soft constraints, respectively. Conformity index was 1.23, 1.54 and 1.66. For organs-at-risk, mean dose to the spinal cord was 8%, 19%, and 23%, respectively.

**Conclusions:** In this study, we demonstrated that the dose distributions obtained from imposing fiducial-marker constraints degrade the plan quality, although less significant degradation occurs with hard constraints, as opposed to discouraging MLC blockage in apertures. We hypothesize that this modified optimization can be used for real-time markerless tracking whereby implantation can be avoided.

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### PLANNING PELVIC INGUINAL LYMPH NODE RADIATION THERAPY WITH TOTAL HIP REPLACEMENT

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**Purpose:** A 72-year-old presented with a fungating right inguinal lymph node recurrence of penile squamous cell carcinoma post-penectomy. He received 4600cGy to regional lymph nodes and a 2000cGy boost to GTV in 33 fractions. A total right metallic hip replacement presented challenges in treatment planning relating to entry and exit dose as a large portion of the planning target volume (PTV), as defined on CT, wrapped around the prosthesis on the right, left, and anterior sides.

**Materials and Methods:** Initially, pelvic treatment was planned using VMAT, avoiding delivery through the right anterior region due to the prosthesis. VMAT was determined not to be suitable due to PTV on the distal side of the prosthesis at the majority of beam angles, introducing significant uncertainty in the optimization and dose calculation processes resulting from HU saturation of the CT scan. A fixed beam sliding window IMRT technique was planned to achieve target coverage with zero dose to the PTV from exit radiation through the prosthesis. Fields were defined such that at each angle no portion of the PTV was distal to the prosthesis. Anterior and left anterior oblique field sizes were defined to encompass the entire PTV. Left posterior and right anterior fields were divided into components to cover smaller portions of the PTV. Each region of the PTV was targeted by a minimum of three fields. In total 10 fields were used, six with carriage shift split fields. The fluence was optimized to achieve a hotter plan in order to bring the high dose (>100% of the prescription) within the PTV while monitoring the dose distribution around the bladder, rectum, small bowel, and left femur, bladder.

**Results:** The VMAT plan resulted in acceptable target coverage with PTV V95% = 97.6%, V110% < 1%, and 112% hot spot within the PTV. OAR constraints were generally met with bladder V45 Gy = 18% and rectum V45 Gy = 9%, but small bowel V45 Gy = 35 cc, and left femoral head V30 Gy = 44% exceeded target values. However, beam travelling through the prosthesis to the PTV occurred in the majority of field angles and thus resulted in a high degree of uncertainty in the plan. The IMRT plan had a higher degree of conformity of the dose distribution to the PTV compared to the VMAT plan, and had improved target coverage with PTV V95% = 98.7%. The IMRT plan was generally hotter with V110% = 9% and hot spot of 119%, all within the boost PTV. OAR doses compared favourably with the VMAT plan, with decreased dose to the bladder (V45 Gy = 17%), rectum (V45 Gy = 6%) and small bowel (V45 Gy = 29 cc), but significantly increased dose to the left femoral head (V30 Gy = 60%).

**Conclusions:** A large pelvic target that wrapped around a hip prosthesis was successfully planned using fixed IMRT fields. IMRT was better than standard VMAT planning in terms of dosimetric outcomes, while eliminating the dosimetric uncertainties from the CT HU saturation by designing a beam arrangement to completely avoid PTV distal to the prosthesis.

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### IMRT STRATEGIES FOR DEFINITIVE TREATMENT OF INTACT CERVICAL CANCER: A LITERATURE REVIEW

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**Purpose:** Consensus regarding the implementation and use of intensity modulated radiotherapy (IMRT) for definitive treatment of cervical cancer is limited. Therefore, many regional cancer centers have been reluctant to transition to IMRT due to concerns regarding quality implementation and the potential for geographic miss. The objective of this study was to conduct a literature review to summarize and categorize evidence related to IMRT for intact cervical cancer.

**Materials and Methods:** The CancerCare Ontario GYN Community of Practice was established to drive quality initiatives to ensure gynecological patients in Ontario receive the highest quality of care. Standardized implementation of IMRT for intact cervical cancer has been identified as a high-priority strategic initiative. Therefore, a working group was established with representation by radiation oncology, medical physics, and therapy. A comprehensive literature review was performed to assess evidence related to the implementation of IMRT for intact cervix cancer in anticipation of creating a guidance document.

**Results:** The literature review identified 35 peer-reviewed manuscripts and one clinical trial protocol from 2006-2017. Emergent key themes were: Contouring, Target Motion, PTV margins, Planning Objectives, Image-Guidance, and Re-Plan Strategies. There was one MR-based consensus guideline for CTVs and a CT-based step-by-step pictorial atlas for CTVs/OARs. Inter-fraction CTV motion was well described; however, substantial variation existed in the magnitude of displacement. Therefore, there was no consensus regarding ITV and/or PTV margins; suggested isotropic total margins ranged from 15-37 mm with several studies advocating for non-uniform margins. Three studies reported an image-guidance method based solely on rigid registration of bony anatomy and one study described a complex multidisciplinary evaluation of bladder filling, marker positions, and uterus location within the PTV, for plan-of-the-day adaptive treatment. Furthermore, no published studies outline paradigms for when to re-scan and/or re-plan.

**Conclusions:** There is published guidance for the use of IMRT for intact cervical cancer related to contouring, target motion and planning objectives. Heterogeneity exists regarding recommendations for PTV margins. There is a paucity of evidence regarding image-guidance, dose summation, and adaptive treatment or re-plan strategies. Studies emphasize that implementation and use of IMRT for intact cervix cancer should be site-dependent and based on the level of local expertise. These results will inform the development of a guidance document for implementation and use of IMRT for intact cervical cancer to facilitate harmonization of practice and high-quality implementation within Ontario. These results can be leveraged for use on a national level; however, it is likely that cancer centres will need to also develop institutional policies based on level of expertise.

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### ARMS UP OR ARMS DOWN FOR RADIOTHERAPY IN STAGE III NSCLC? A DOSIMETRIC COMPARISON

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**Purpose:** Stage III lung cancer patients receiving curative intent radiotherapy are often treated using volumetric modulated arc therapy (VMAT) with their arms above their head. As this is a highly co-morbid population, there are often challenges with discomfort, breathing reproducibility, and cooperation maintaining the arms-up position over 6 weeks of treatment. The objectives of this study were: 1) to evaluate the dosimetric impact of changing arm position during treatment, and 2) to compare plan quality for optimization

in the arms-up versus arms-down positions.

**Materials and Methods:** Patients previously treated for Stage III NSCLC lung cancer (n = 10) with 60 Gy in 30 fractions using VMAT were identified. To simulate arms-down treatment, a PET/CT (acquired in the arms-down position) was rigidly registered to the planning CT (acquired in the arms-up position), based on bony anatomy. The arms were contoured and the density set as 1 g/cm<sup>3</sup>. The clinically delivered plan was recalculated on new anatomy that included either the contralateral arm, ipsilateral arm, or both arms down. Plans were also re-optimized for the both arms-down position. Dose-volume parameters (PTV D95, D98, and Dmax; Spinal cord Dmax; Esophagus Dmax and Dmean; Heart Dmean, V5, V25; Lung Dmean V5, V10, V20) were compared for each scenario.

**Results:** The mean (range) IGTV and PTV volumes were 170.5 cc (12.8-383.1) and 696.7 cc (483.8-1150.8), respectively. Moving from the arms-up position to both arms-down for the entire treatment course resulted in an average 3.7% (1.7-6.2) reduction in PTV D95. In all cases, this caused 95% of the PTV to be covered by less than 95% of the prescription dose; the mean PTV D95 was 55.9 Gy (54.8-56.7). The mean D2cc to the arms were 23.1 Gy (11.0-30.0 Gy) and 4.0 Gy (1.2-8.5 Gy) for the ipsilateral and contralateral, respectively. The dosimetric consequences of ipsilateral arm only were similar to both arms down, whereas contralateral arm only had less than 1% effect on PTV D95. When plans were re-optimized to account for the both arms-down position, PTV D95 coverage was recovered with acceptable doses to all organs-at-risk. The arm doses were also decreased; the mean D2cc were 5.5 Gy (4.9-8.2) and 2.3 Gy (1.1-4.9) for the ipsilateral and contralateral, respectively. There was a statistically significant difference in heart V25 and mean heart dose even after adjusting for multiplicity testing (p < 0.001). Still, the magnitude of the difference was small at 4.1% (1.4-8.4) for V25 and 1.7 Gy (0.7-3.8) for mean heart dose and both plans met dose constraints.

**Conclusions:** This planning study suggests that it is feasible to plan and treat locally advanced lung cancer patients in the arms-down position using VMAT with only a modest dosimetric impact. It may also be reasonable to change arm position without re-planning in the final half of treatment, provided the IGRT match remains consistent.

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#### DOSIMETRIC EVALUATION OF DYNAMIC CONFORMAL ARC THERAPY

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**Purpose:** In dynamic conformal arc therapy (DCAT), the photon beam aperture conforms to the target shape during an arc delivery. A recent commercial implementation of DCAT allows for two additional degrees of freedom: variable dose rate and segment shape optimization. The purpose of this study is to evaluate the plan quality of this modern implementation of DCAT against 3DCRT and VMAT for relevant disease sites.

**Materials and Methods:** Three disease sites were identified as most relevant for potential use of modern DCAT: 1) spine metastases, for three times faster optimization with a Monte Carlo dose calculation engine, enabling rapid-access palliative conformal treatments; 2) lung SBRT, for reduced interplay effect; and 3) small brain tumours, to resemble stereotactic cones. The patients included in this study were 25 palliative spine metastases (all spine sections, 1 to 9 vertebrae), 12 lung SBRT (7 to 51 cc target size), and 12 brain tumours (2 to 20 cc target size). For each patient, 3DCRT (spine only), VMAT and DCAT plans were created and evaluated for clinical acceptance by an experienced treatment planner. Each plan was scaled such that 95% of the target volume received the prescription dose, Rx.

**Results:** The results for 3DCRT, DCAT and VMAT for spine metastases were, respectively, as follows. Target D2% (100% of Rx = no hotspots): 112% ± 4%, 107% ± 2% and 105% ± 1%. Target Conformity Index (CI = 1.00 for perfect conformity): 0.33 ± 0.07, 0.75 ± 0.06 and 0.83 ± 0.04. Target Homogeneity Index (HI = 0.00 for perfectly homogenous coverage): 0.13 ± 0.09, 0.08 ± 0.02 and 0.06 ± 0.01. Gradient Index (GI = 1.0 for perfect fall-off outside the target): 2.4 ± 1.5, 3.9 ± 0.6 and 4.0 ± 0.4. For organs-at-risk (OARs), compared to the other two techniques, the cord maximum dose was 2%

lower for VMAT, healthy lungs V5Gy was 15% more lung volume for DCAT, bowel mean dose was 35% higher relative to Rx for 3DCRT, and kidneys mean dose was slightly worse for DCAT (for the same partial arcs as VMAT). For lung SBRT and brain, the target D2%, CI, GI and OAR doses (such as healthy lungs V20 Gy and optic structures maximum dose) were virtually identical for DCAT and VMAT. The exception is for brain tumours directly abutting OARs, in which case VMAT outperforms DCAT in dose carving.

**Conclusions:** For large dense target such as those in palliative spine metastases, DCAT performs midway between the clinically acceptable 3DCRT and VMAT plans, with substantially lower entrance dose compared to 3DCRT and substantially faster optimization time than VMAT. For lung SBRT and brain cases, DCAT plans were very comparable to VMAT, but VMAT outperforms DCAT for complex brain cases. DCAT can be a useful conformal arc delivery technique if VMAT is not available. It can also complement VMAT with minimal overhead to implement.

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#### KNOWLEDGE-BASED PLANNING SCRIPT FOR IMRT LUNG TREATMENT

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**Purpose:** A knowledge-based planning script for lung IMRT (kb-IMRT) was developed. The script adapts the initial optimization values based on patient anatomy and plan complexity in order to improve target coverage and organ-at-risk (OAR) sparing for all cases.

**Materials and Methods:** In our standard lung IMRT technique (s-IMRT), the same set of initial optimization values for target coverage and OAR was used as a starting point for all cases. In the kb-IMRT technique, the initial optimization values are adjusted depending on the anatomy of the patient and the complexity of the case. To do so, the clinical DVH values from the 32 cases already planned with the s-IMRT technique were plotted against various metrics and a lung complexity index (LCI) was determined. When running the script, the LCI is automatically calculated and the initial optimization values for the lungs V5, V10, V20 and mean dose are calculated from the quadratic fit of those plots. Following a similar process, complexity indexes were determined for the heart and the oesophagus allowing us to set the initial optimization values for the heart D46 and mean dose and the oesophagus D40, D50, mean and maximum dose.

**Results:** The resulting kb-IMRT plans were compared with the s-IMRT plans. Coverage of the PTV was improved or stayed at an acceptable clinical value while OAR sparing was significantly better for most cases. On average, V20, V10, V5 and Dmean values for the lungs decreased respectively by 2.1%, 3.9%, 3.2% and 0.5 Gy. Mean doses for the heart and the oesophagus decreased by 0.2 Gy and 1.6 Gy respectively.

**Conclusions:** Our s-IMRT technique was modified in order to obtain better coverage of the PTV and improved sparing of the OARs. The kb-IMRT technique was applied to 32 patients previously treated with the s-IMRT technique. The retrospective study showed that the kb-IMRT technique could be used to treat all lung cases with significant dosimetric improvements.

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#### FISRT YEAR PRACTICE OF PROFIT HYPOFRACTIONATED PROSTATE RADIATION AS STANDARD CARE: PLANNING DOSIMETRY

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**Purpose:** In 2016 the PROFIT trial (NCT003056759) concluded that the hypofractionated prostate radiotherapy (6000cGy/20) is not inferior to the conventional treatment (7800cGy/39) for intermediate-risk patients who could meet the PROFIT criteria and planning dose constraints. In 2017, PROFIT treatment became the standard care at our centre. Herein we share our first year experience in planning dosimetry.

**Materials and Methods:** All intermediate-risk prostate patients treated with single phase external beam in 2017 were included. Treatment planning

system (TPS) Varian Eclipse version11 was used to generate VMAT plans for all patients. Target and OARs delineation followed the PROFIT trial planning guideline. Dose Volume Histogram (DVH) points were extracted by an in-house script. Contours' volume and their overlaps were measured using standard TPS tools.

**Results:** There were 105 patients in total. Sixty-six of 105 patients met the PROFIT dose constraints and were treated with 6000cGy/20. Thirty-five of 105 patients did not meet and were switched to the conventional treatment. Four of 105 patients received 7800cGy as requested by ROs though meeting PROFIT criteria and dose. Among the 35 dosimetrically ineligible patients, 30 patients had rectal wall D30 exceeding the dose limit of 4710cGy with more than 23% of rectal wall inside PTV. Only five patients had bladder wall dose over the limits. These PROFIT ineligible patients have larger prostate CTV volume than the eligible patients, 83.0cc  $\pm$  31.4cc versus 72.6cc  $\pm$  32.8cc. The rectum volumes for these two groups are not much different, 68.2cc  $\pm$  18.2cc versus 70.9cc  $\pm$  20.1cc. In DVH, the rectal wall D30 ranges from 2898cGy to 4710cGy for the PROFIT patients while from 6002cGy to 7235cGy for the ineligible patients.

**Conclusions:** Our first year clinical experience shows that about one-third of intermediate-risk prostate patients could not benefit from PROFIT treatment due to their anatomy. The main factor for exclusion in our practice is more than 23% rectal wall overlapping with PTV.

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#### TARGET VOLUME VARIATION WITH DIFFERENTIAL BLADDER FILLING IN NEOADJUVANT RADIOTHERAPY FOR RECTAL CANCER PATIENTS

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**Purpose:** In the era of modulated treatment for rectal cancer, a more conformal treatment plan can be achieved, thereby reducing dose to organs at risk. However, such conformality can also result in inadequate coverage of target volumes due to organ motion and geometric uncertainty. This study aims to assess whether extremes of bladder filling significantly changes the clinical target volume (CTV) in the setting of neoadjuvant radiation treatment for rectal cancer.

**Materials and Methods:** Planning CT scans were obtained on six patients, three female and three male, with bladder full and bladder empty in the supine position. CTV contours were delineated on both scans. Bladder volumes and rectal volumes were also delineated along with other organs at risk including small bowel, large bowel, and femoral heads. The effect of organ filling on CTV was analyzed. Further target volume and organ-at-risk dosimetry is pending.

**Results:** Between the bladder full and bladder empty planning CT scans, the average change in bladder volume was 247 cm<sup>3</sup>. There was minimal change in rectal volume with an average of 7.5 cm<sup>3</sup>. The average change in CTV was 24 cm<sup>3</sup>. Majority of the variation occurred anteriorly with an average maximal linear difference of 2.87 cm. These differences consistently occurred in the superior portion of the mesorectum at the level of small bowel where variability in small bowel loops resulted in variability in deformation of the CTV. Comparatively in the inferior portion of the mesorectum at the level of the bladder, the average maximal linear difference was much smaller.

**Conclusions:** Differential bladder filling appears to significantly change the CTV in the setting of neoadjuvant radiotherapy for rectal cancer treatment. These changes are predominantly attributed to variability in small bowel loops rather than direct deformation from bladder filling.

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#### DEVELOPMENT AND ASSESSMENT OF A NOVEL AUTOMATIC METHOD OF CBCT DENSITY ASSIGNMENT FOR HEAD AND NECK PATIENTS WITH DENTAL ARTIFACTS

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**Purpose:** Dose calculation on daily cone-beam computed tomography (CBCT) images, which enables dose accumulation, requires bulk density

assignment on the RayStation platform. This density assignment in head and neck (HN) is prone to inter- and intra-user variability and inaccurate in the presence of dental artifacts. This work aims to develop and assess a novel automated approach for density assignment on CBCT for these cases.

**Materials and Methods:** We selected five HN patients with dental artifacts for development and assessment of the automatic algorithm. We first isolated the effect of bulk density assignment on dose calculation using the planning CT alone. The Hounsfield units (HU) were mapped to six density levels using three different step functions (two user defined, and one defined mathematically). Dosimetric parameters were compared for targets and organs at risk (OAR) for clinical and bulk density dose calculations. An algorithm was developed to segment the CBCT into regions of interest (ROI) for each material type. Rigid registration is performed between CT and CBCT focusing on dental implant, followed by the creation of an adaptive, variable-resolution grid. CT artifacts have been corrected using density override in the treatment planning process. When applicable, that density is used instead of original CT density to define baseline tissue volumes. These volumes become constraints when the algorithm assigns density to the CBCT. For each grid element on the CBCT, a histogram is generated, and constrained clustering partitions the intensity range into clusters representing each material. Once the CBCT histogram is partitioned, ROIs are created for each material with corresponding density assignments. Algorithm accuracy was evaluated in the region with artifacts, by comparing the location and volume of bone generated by the automated method and the manual method to the planning CT using the DICE index.

**Results:** Between continuous (A) and binned (B) density mapping on CT, the average (SD) difference (A-B) was less than 20 cGy (prescription of 7000 cGy) for all dosimetric parameters evaluated (targets and OAR). This illustrated minimal impact of bulk density assignment on the dose calculation for HN which confirmed the validity of using bulk density assignment in the automated algorithm for CBCT. The automatic algorithm improves the average (SD) DICE index of voxels classified as bone within the oral cavity between CT and CBCT to 0.72 (0.08) compared to 0.63 (0.08) for manual density assignments. Additionally, in initial evaluation, a reduction up to 10 cc in misclassified tissue was achieved.

**Conclusions:** The impact of bulk density assignment itself on the calculated dose distribution in HN is small based on this initial evaluation. An automatic algorithm has been developed for CBCT images with improved accuracy in density assignment in the region of artifacts. Automation also helps to reduce user variability associated with manual assignments.

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#### SIMULTANEOUS TRAJECTORY AND VOLUMETRIC MODULATED ARC THERAPY OPTIMIZATION

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**Purpose:** Trajectory-based volumetric modulated arc therapy (tr-VMAT) treatment plans involve dynamic rotation of the couch and gantry during treatment delivery. Previous studies involving trajectory-based radiation therapy have followed a two-step approach, in which a VMAT optimization is performed following the specification of a couch-gantry trajectory. In this work, an algorithm is outlined and tested that simultaneously constructs a trajectory during VMAT optimization.

**Materials and Methods:** Trajectory endpoints are initially defined at (gantry angle, couch angle) = (-180°, -90°) and (180°, 90°). Candidate control points are identified for each endpoint through an incremental step in the gantry rotation angle, the couch rotation angle, or both. The column generation approach is used to construct apertures for each candidate control point, and add the best aperture to the treatment plan according to its associated price. This process is followed iteratively until the trajectory endpoints are connected. Following the finalization of a trajectory for a given step size, each pair of successive control points are redefined as endpoints, and are connected using a decreased step size following the above procedure. This allows for adequate initial sampling of the solution space for large step sizes while maintaining finer control point resolution and finer adjustments to the trajectory at later iterations. The simultaneous trajectory-VMAT optimization was tested on a sinus meningioma patient case.

**Results:** To validate the use of the column generation approach for iterative

trajectory construction, 4000 unique random trajectories that connected the endpoints were generated with a conventional VMAT optimization performed on that trajectory. The objective function value, representing the adherence to the treatment planning constraints, for each of the random trajectory VMAT plans was greater than the objective function value for the simultaneous tr-VMAT optimization, demonstrating the performance of the column generation approach. The objective function value was separated from the mean objective function value of the random trajectories by  $1.7\sigma$ . The benefit of systematically increasing step size resolution was also validated through comparison to a simultaneous tr-VMAT optimization performed only at the final step size resolution (objective function values: 1.11 and 10.3 for the increasing step size and final step size only, respectively).

**Conclusions:** The described algorithm defined a simultaneous tr-VMAT treatment plan that outperformed conventional VMAT treatment plans on randomly defined trajectories. Increasing the control point resolution systematically throughout the optimization yielded improved adherence to the treatment planning constraints. Future work will include validation of simultaneous trajectory optimization against two-step approaches, and comparison to clinical VMAT treatment plans for patients presented with cranial targets.

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#### CONSEQUENCES OF REMOVING UPPER DOSE CONSTRAINT FOR PLANNING TARGET VOLUME IN PROSTATE VOLUMETRIC MODULATED ARC THERAPY PLANNING

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**Purpose:** This work systematically and quantitatively investigates the consequences of allowing target dose heterogeneity by comparing prostate Volumetric Modulated Arc Therapy (VMAT) plans with and without an upper dose constraint (UDC) for the planning target volume (PTV) in the inverse planning process.

**Materials and Methods:** Seventeen early-to-intermediate stage prostate patients who were treated using VMAT with a prescription of 78Gy in 39 fractions were selected and anonymized in this study. All the patients were re-planned in the treatment planning system (Eclipse version 13.6, Varian Medical System, Palo Alto, CA) using the progressive resolution optimizer (PRO). For plans from the same patient, the same optimization objectives were used except for the presence or absence of the PTV UDC and no intervention was made during the optimization process. Prostate VMAT plans with and without the PTV UDC were compared in terms of organs-at-risk sparing, clinical target volume (CTV) and PTV coverage and hotspots as well as plan complexity. Two-tail paired Student's t-tests were performed in MATLAB (2016a, The MathWorks, Inc, Natick, Massachusetts, USA) for plan comparisons and  $p \leq 0.05$  was considered statistically significant.

**Results:** By removing the PTV UDC, systematic improvement in the rectum dose volume histograms (DVHs) was shown (e.g. average improvement for V50 Gy, V60 Gy, V65 Gy, V70 Gy and V75 Gy was 9.1%, 4.0%, 2.4%, 1.4% and 0.6%, respectively,  $p < 0.01$ ), leading to an average decrease in normal tissue complication probability of 1.3% ( $p < 0.01$ ). Of six plans unable to meet rectal constraints with the PTV UDC applied, five met them and the last was substantially improved when the PTV UDC was removed. At the same time, coverage was still ensured (changes in CTV and PTV D99 were less than 0.6% on average). Unconstrained, the median CTV and PTV D1cc reached 144.6% compared to 103.7% and 104.9%, constrained respectively. This resulted in an average increase of 3.2% ( $p < 0.01$ ) tumour control probability. An extra 283 monitor units were required on average to deliver the plans without the PTV UDC although the calculated treatment time didn't change.

**Conclusions:** Removing the PTV UDC led to a systematic improvement in the rectal dose and tumour control probability without compromising coverage and with a predictable increase in dose heterogeneity in these 17 patients. This work suggests removing the PTV UDC is a viable option in planning prostate VMAT treatments and may be particularly useful for cases struggling to meet rectum dose constraints.

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#### VALIDATION OF TWO ANATOMICAL PREDICTORS OF HEART DOSE IN LEFT-SIDED BREAST CANCER PATIENTS TREATED WITH ADJUVANT RADIOTHERAPY

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**Purpose:** Breath-hold radiotherapy (BH-RT) is a treatment strategy capable of reducing heart dose in left-sided breast cancer patients. Nevertheless, this technique is time and resource intensive and some patients may not benefit dosimetrically from this treatment strategy. As such, to quickly and reliably identify those patients that do not need BH-RT, simple metrics based on patient thoracic anatomy have been introduced in previous studies. This study aims to validate the performance of these previously developed metrics (4th Arch and ContactHeart) in regard to predict heart dose in left-sided breast cancer patients receiving adjuvant radiotherapy.

**Materials and Methods:** Twenty-three breast cancer patients were retrospectively studied in this external validation. All patients were treated with breast conserving surgery and adjuvant radiotherapy using standard tangents technique with no heart shielding. Organs-at-risk were contoured in accordance to guidelines and a clinically-acceptable plan was obtained using the free-breathing CT. Heart (mean heart dose (MHD), heart V25 Gy) dosimetry was captured and compared against distance metrics under investigation (4th Arch and ContactHeart). Previous defined optimal cut-points, 7 mm and 73 mm, were used for 4th Arch and ContactHeart, respectively. Pearson correlation coefficients evaluated the association between distance metrics and dosimetric endpoints. Univariable linear regression analysis was performed to identify significant predictors of heart dose. Stata 13.0 was used for statistical analysis and a  $p$ -value  $< 0.05$  was considered statistically significant.

**Results:** The mean MHD and heart V25 Gy were 1.8 Gy and 5.9 cm<sup>3</sup>, respectively. With standard tangents, constraints for MHD ( $< 1.7$  Gy and V25 Gy  $< 10$  cm<sup>3</sup>) were unattainable in 48% and 17% of patients, respectively. 4th Arch and ContactHeart sensitivity, specificity and accuracy in regard to MHD  $< 1.7$  Gy were: 80%/82%, 36%/42% and 57%/61%, respectively. 4th Arch and ContactHeart sensitivity, specificity and accuracy in regard to V25 Gy  $< 10$  cm<sup>3</sup> were: 100%/100%, 35%/37% and 48%/48%, respectively. Pearson correlation coefficient was approximately 0.5 (range 0.48-0.51) for both metrics across all heart dosimetry endpoints. 4th Arch was found to be a significant predictor for MHD and V25Gy, while ContactHeart did not reach significance for heart V25 Gy.

**Conclusions:** Both metrics presented a slight drop in specificity and accuracy in comparison to the training cohorts. Nevertheless, sensitivity rates remained elevated, indicating their capability in discriminating patients with elevated heart doses and with potential benefit from BH-RT. The small rate of false negative suggests that both metrics are likely safe for clinical use.

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#### TOTAL MARROW IRRADIATION USING HELICAL TOMOTHERAPY FOR MULTIPLE MYELOMA: A CASE STUDY OF A TALL PATIENT

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**Purpose:** Our technique in a Phase I/II dose escalation study of IG-IMRT using helical tomotherapy (HT) for total marrow irradiation (TMI) of multiple myeloma involves planning on two CT head first scans of the patient. Here we outline the technical and physical challenges of a tall patient.

**Materials and Methods:** TMI patients require upper and lower body CT scans due to imitations of the CT scanner (Phillips BigBore) and the HT planning software. Proper junction calculation requires at least a 20 cm overlap between the two scans. In this case the patient's height and anatomy made scanning the lower body headfirst impractical and unsafe, due to sag and limited couch extension, therefore the lower body was scanned feet first. These images were then rotated by 180° by reversing the slice order and mirroring left to right to allow an image fusion, linking the two scan

sets, the hemi-body PTVs and OARs defined on both CT sets. Treatment plans were calculated using 5.0 cm beams for both scans. Each hemi-body was treated in its scan position.

**Results:** Dose from two plans was summed using the above rotation and fusion offset in ImageJ, providing the total dose distribution in the junction region. Junction planning requires a few iterations to remove cold spots and minimize hot spots. Prior to patient's treatment, DQAs were planned, delivered and analysed in several regions, using the above procedure in the junction with its own phantom offset. At the junction, the DQA phantom was registered to both anatomy and lasers on both scan sets. The DQA results show good agreement, verifying the clinical feasibility of our image fusion and junction planning method.

**Conclusions:** Our method of overcoming technical limitations of scanning and planning, the treatment of tall patients is technically feasible.

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### CHANGING FACE OF PALLIATIVE PRACTICES IN RADIATION THERAPY FOR SIMPLE BONE METASTASIS IN A SINGLE INSTITUTION

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**Purpose:** Radiation therapy (RT) has been used for palliation of painful bone metastasis for many decades with 50-80% of patients having partial pain relief and 25% of patients achieving complete response. Many trials have studied various dose fractionation schedules in palliative radiation therapy for bone metastasis. We now know that single fraction treatment provides equivalent pain relief compared to a multiple fraction regimen. This study investigated local practice patterns at our institution at Cancer Care Manitoba (CCMB) in the use of palliative RT among patients with bone metastasis.

**Materials and Methods:** Cancer patients who underwent palliative radiotherapy for bony metastasis after assessment by a radiation oncologist from 2013 to 2017 were identified at our mid-size cancer centre. In 2017, we introduced peer reviewed pre-defined borders for simple bone sites to increase efficiency in the system and expedite patients receiving same day radiation. **Results:** Despite the introduction of sophisticated radiation techniques such as SBRT, many patients are still being treated using conventional palliative radiation with a focus on improving pain control and quality of life. At CCMB implementation of a simple "Standard" directive with pre-defined borders for the common bone metastatic sites resulted in faster RT planning times but did not move patients onto treatment any faster. With a median of two hours for "General" plans and one hour for "Standard" plans, we likely saved one hour of planning time for each of the 80 pre-defined border plans completed in 2017. In addition, the prescription of single fraction RT more than doubled with a utilization of 42% in 2017 versus 20% in 2013.

**Conclusions:** When palliative RT is used in patients with metastatic bone lesions not suitable for SBRT, simple innovative techniques such as pre-defined standard borders can be introduced to increase efficiency and reduce planning time. Continued education is required to make single fractionation prescription more common in patients with simple bony metastasis.

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### TREATMENT OF STAGE II LYMPH-NODE NEGATIVE ENDOMETRIAL CARCINOMA WITH ADJUVANT VAGINAL BRACHYTHERAPY ALONE

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**Purpose:** Trends in the literature as well as previous data from our centre suggest that adjuvant vaginal vault high dose rate brachytherapy alone may be sufficient in a subset of Stage II endometrial cancer patients to achieve local recurrence control. This study looked at recurrence rates with post-operative treatment with vaginal vault brachytherapy (VB) versus external beam radiotherapy (EBRT) in women with Stage II endometrioid endometrial carcinoma with no lymph-node involvement and negative cytology.

**Materials and Methods:** This study was a retrospective chart review at a single institution between 1995 and 2015. There were 59 patients treated

with adjuvant VB and only five patients were treated with EBRT+VB. Six patients received no adjuvant treatment and two patients received VB and chemotherapy consisting of six cycles of Carboplatin/Paclitaxel. Median follow up was 44.03 months (mean 41.44).

**Results:** There were eight recurrences in the adjuvant VB group. Of these, seven patients recurred in the vaginal vault and one recurred with a pelvic mass. There were no recurrences in the five patients that received adjuvant EBRT and VB but this was a small group. There were two recurrences in the patients who were treated with surgery alone and one patient had distant recurrence in lung after adjuvant treatment of vaginal brachytherapy and chemotherapy.

**Conclusions:** Vaginal vault brachytherapy alone as adjuvant treatment for node-negative stage II endometrial cancer results in good local control but pelvic EBRT or a higher brachytherapy dose may be needed to decrease recurrence rates.

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### AN AUTOMATIC SKIN-FLASH METHOD FOR BREAST IMRT AND THE PERTINENCE OF ADDITIONAL MANUAL MLC RETRACTIONS

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**Purpose:** Breast IMRT requires that the planner extend dose fluence in the air beyond areas where the PTV is at the surface of the body in order to account for possible target movement caused by breathing or swelling. We have devised an optimization-integrated method to automatically withdraw MLCs away from the skin and serve as a simple skin-flash tool for tangent fields. Although mostly successful, this approach is imperfect in that the planner still needs to manually and individually withdraw a small number of non-retracted MLCs post-optimization. In this study we: 1) describe our method; and 2) look at the impact of the additional manual retraction of MLCs on the initial dose distribution resulting from the automatic method.

**Materials and Methods:** Pinnacle plans (50Gy/25Fx) for five breast patients were optimized with an extended PTV obtained through a series of expansions and contractions that yield a non-uniform contour (Flash) which defines a fluence-exposed area outside the body contour. It is designed to compensate for tangent field fluence while leaving unchanged that of perpendicular fields since beam contours of the latter are not impacted by potential in-treatment changes to the body. Each plan was optimized by adding a Minimum Dose objective on the Flash contour with an arbitrary value of 1 and a weight of 0. The result is a plan with a majority of PTV and skin-adjacent MLCs retracted beyond the Flash contour. The planner then manually retracts the few remaining PTV and skin-adjacent MLCs on a copy of the plan and computes the dose to compare both plans. After a < 1% MU tuning to obtain identical V47.5 Gy target coverage for both plans, swelling is simulated with successive water-equivalent 0.5 cm tranches of tissue-mimicking expansions from the skin/PTV and within the Flash contour. Dose distribution is recomputed with each additional layer, maximum dose and percent of volume receiving 47.5 Gy, 50 Gy, and 52.5 Gy of prescription dose (V47.5 Gy, V50 Gy, V52.5 Gy) are calculated for the expanded PTV. The portion of segments and associated MU values impacted by the supplementary manual MLC retractions with respect to the automatically flashed plan is also computed.

**Results:** Even before MU adjustment, no statistically significant difference is seen on the original target coverage (without swelling) for the above mentioned DVH metrics, but a maximum point dose increase of up to 2% is noted within the PTV. Predictably, maximum dose and all DVH differences increase proportionally to swelling and DVH dose values for manually retracted plans with respect to automatic ones. For example, with a 0.5 cm PTV expansion outside the body, manually retracting remaining MLCs can increase V47.5 Gy by up to 9%, whereas the increase is 28% for a larger expansion of 2.5 cm. With V50Gy, the differences are 28% and 65%, for 0.5 cm and 2.5 cm expansions, respectively. Moreover, between 15% and 20% of segments have at least 2 MLCs that were retracted manually in order to obtain the ideal Flash contour conformation of all retracted MLCs. Finally, a similar portion of MUs is impacted by manual flashing.

**Conclusions:** Although our automatic MLC flashing method is able to correctly retract a majority of skin/PTV-adjacent MLCs and significantly reduce planning time, a manual touch-up in anticipation of anatomical

changes of the target is still necessary for enhanced coverage. This strategy can be applied to other anatomical sites that have superficial tumours such as sarcomas.

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#### DEVELOPING A WORKFLOW FOR COMMISSIONING AND QUALITY ASSURANCE OF THE PINNACLE TREATMENT PLANNING-ADAPTIVE PLANNING MODULE

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**Purpose:** This study provides a workflow for commissioning and quality assurance (QA) of the Pinnacle treatment planning system (TPS) Dynamic Planning (DP) module. This module is designed to facilitate treatment adaptation and re-planning by enabling propagation and contours deformation between two datasets and the transfer of plan parameters from one dataset to the next.

**Materials and Methods:** Plan adaptation is initiated by copying the previous plan to the rescan-CT. The Pinnacle-DP module registers the previous-CT and rescan-CT, propagates points, contours and plan to the rescan-CT and re-computes the plan on the rescan-CT. If a re-plan is needed, the dose-accumulation feature creates a composite plan by summing the original and re-plan doses. A custom script was used to verify dose accumulation and a custom research system (RS) was used to verify the propagation and deformation of contours. Rescan-CTs from two treatment sites (six CT-scans per site) were synthesized by applying transformations (transfT) of known magnitude to the previous-CT images and corresponding contours. The DP module was then used to propagate and deform the previous-CT deformed contours to the synthesized rescan-CT contours by applying a transformation-transf-Pinnacle. Similarly, in the RS system, a transformation-transf-RS was used to deform the previous-CT deformed contours to the synthesized rescan-CT contours. All contours were converted into meshes. The results were quantified as the mean distance between the nodes of similar meshes deformed by transf-Pinnacle versus transf-RS. This distance can approach zero for systems with equivalent deformation performance. The distance was averaged for ten different deformable registrations of different magnitudes to emulate various anatomical changes in a patient during a radiotherapy treatment.

**Results:** Dose volume histograms (DVHs) for composite plans created by dose accumulation and custom scripts are numerically identical for plans with identical dose grids. When dose grids of different size but similar resolution were used, only negligible differences (< 1%) to the composite DVHs were observed. The mean distance between mesh nodes ranged from 1.5+/-1.4 (trachea) to 4.1+/-0.9 (lung) mm for thorax contours and 1.7+/-0.6 (eye) to 4.7+/-2.9 (canal) mm for head and neck contours.

**Conclusions:** A workflow for testing the Pinnacle-DP module was developed. While dose accumulation has been validated, the results of deformable contour registration must be used with care. This can be applied to test similar algorithms implemented in other TPSs.

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#### EVALUATION OF MIXED ENERGY PARTIAL ARCS FOR VOLUMETRIC MODULATED ARC THERAPY FOR PROSTATE CANCER

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**Purpose:** To investigate the dosimetric outcome of mixed energy (6-MV, 15-MV) partial arcs (MEPAs) on prostate cancer VMAT plans.

**Materials and Methods:** This study included 25 prostate only cancer patients, with a dose prescription of 79.2 Gy over 44 fractions to the Planning Target Volume (PTV). PTV was defined by adding 5 mm margins to the CTV. The organs-at-risk (OARs) included bladder, rectum, left and right femur. For each case, three VMAT plans were generated using Eclipse™ treatment planning software. Two separate single-energy single-arc plans involving a 6MVsingle-arc (6MV-SA), and a 15MV-SA, respectively, were generated.

A third MEPAs plan involving a composite of 6-MV anterior and posterior partial-arcs and a 15-MV lateral partial-arcs weighted 1:2 was created. The optimization parameters and priority factors for each structure were kept constant for all three plans for all cases. Mean doses of each structure, total monitor-units (MUs), homogeneity index (HI) and conformity number (CN) were analyzed. Dose calculations were performed using the AAA algorithm. Dosimetric parameters were used to compare MEPAs plan with single-energy single-arc, 6MV-SA and 15MV-SA, plans.

**Results:** Mean dose to the PTV, bladder and CN for MEPAs were 81.21 ± 0.43 Gy, 13.58 ± 6.08 Gy and 0.825 ± 0.04, respectively, which were equivalent to 6MV-SA (p > 0.05) and 15MV-SA (p > 0.05). Target homogeneity for MEPAs was lower compared to 6MV-SA (p < 0.05) and 15MV-SA (p < 0.05). Mean dose to rectum and MUs per fraction was significantly lower for MEPAs (23.03 ± 3.60 Gy; 435 ± 104) compared to either 6MV-SA or 15MV-SA (p < 0.05). MEPAs increased mean dose to left (14.90 ± 3.13 Gy) and right (15.28 ± 2.94 Gy) femur by 3 Gy compared to 6MV-SA (p < 0.05) and 15MV-SA (p < 0.05).

**Conclusions:** In comparison with 6MV-SA and 15MV-SA, MEPAs demonstrated possibility of reducing dose to OARs, especially rectum, while maintaining the dose conformity to the PTV.

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#### INTEGRATION OF RADIOBIOLOGICAL MODELLING AND SUMMARY INDICES IN COMPARATIVE PLAN EVALUATION: A STUDY COMPARING VMAT AND 3D-CRT IN PATIENTS WITH LOCALLY ADVANCED NSCLC USING INDIGENOUS SOFTWARE

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**Purpose:** It is often challenging to compare techniques like VMAT and 3D-CRT due to lack of comprehensive clinical and dosimetric data. Our study compared 3D-CRT and VMAT for patients with locally advanced non-small cell carcinoma (LA-NSCLC) based on dosimetric and radiobiological metrics using home-grown customized algorithm for calculation and integration of radiobiological metrics and summary indices.

**Materials and Methods:** The study included 25 patients of LA-NSCLC treated with 3D-CRT at our centre between 2010-2014. The planner generated VMAT plans using clones of the original planning CT with regions of interest (ROI) volumes, which did not include the original 3D plans. Both 3D-CRT and VMAT plans were generated using the same dose-volume (DV) constraints. The DVH parameters for planning target volume (PTV) and relevant organs-at-risk (OAR) were reviewed. The radiobiological calculation engine was written in the "R" programming language; the user interface was developed with the "shiny" "R" web library. DVH data was imported into the calculation engine and tumour control probability (TCP), normal tissue complication probabilities (NTCP) of spinal cord, heart (NTCP-perfusion defect, NTCP-pericarditis), lungs and esophagus, composite indices including cardio-pulmonary toxicity index/CPTI (defined as the sum of NTCP-perfusion defect and NTCP-lung), morbidity index/MI (weighted sum of NTCP of all relevant OARs), uncomplicated-TCP/UTCP (the probability of tumour control while having no probability of complications with equal weightage to TCP and individual NTCP), therapeutic Gain/TG (the probability of tumour control when weighted sum of NTCP values of relevant OARs is zero assigning higher priority to TCP) were calculated. Two sample t-test was used for statistical comparison and p < 0.05 was considered significant.

**Results:** Dosimetric comparison revealed no significant difference between VMAT and 3D-CRT in terms of D99% (57.51 Gy versus 57.54 Gy, p = 0.87) and V98% (91.9% versus 94.4%, p = 0.17) of PTV. V50 of esophagus (16.4% versus 25.8%, p = 0.01) and the V45 of spinal cord (0.01% versus 4.8%, p = 0.005) were improved with VMAT. However, VMAT had significantly higher V10 (50.2% versus 41.1%, p = 0.009) and marginally higher V5 (p = 0.07) of lung-GTV. TCP was better with 3D-CRT (12.6% versus 11.7%, p < 0.001), while VMAT demonstrated superior NTCP-esophagus (7.4% versus 4.5%, p = 0.02), NTCP-spinal cord (0.001% versus 0.009%, p = 0.001) and NTCP-perfusion defect (44.6% versus 56.4%; p = 0.01). There was no difference in NTCP-lung (7.6% versus 6.3%; p = 0.22) and NTCP-pericarditis (0.15% versus 0.01%; p = 0.13) between VMAT & 3D-CRT respectively. VMAT

showed substantial improvement in MI (11% versus 14.3%;  $p = 0.01$ ), CPTI (47.6% versus 59.4%;  $p = 0.03$ ), TG (10.8 versus 10.4;  $p = 0.03$ ) and trend towards superior UTCP ( $p = 0.05$ ).

**Conclusions:** The study highlights the utility of the radiobiological algorithm and summary indices in comparative plan evaluation and demonstrates some benefits of VMAT over 3D-CRT in LA-NSCLC.

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#### PSA BOUNCE AFTER STEREOTACTIC BODY RADIOTHERAPY FOR PROSTATE CANCER: POOLED ANALYSIS FROM FOUR SBRT TRIALS EVALUATING DIFFERENT TIME-DOSE-FRACTION SCHEDULES

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**Purpose:** Prostate serum antigen (PSA) bounce can mimic biochemical failure after stereotactic body radiotherapy (SBRT) for prostate cancer (P-Ca). We carried out a pooled analysis of four SBRT trials for low and intermediate P-Ca to evaluate the incidence of PSA bounce and its correlation with different time-dose-fraction schedules.

**Materials and Methods:** The study included four treatment groups (TG): 35 Gy/5 fractions (F) once per week (QW) ( $n = 84$ ); 40 Gy/5F QW ( $n = 105$ ), 40 Gy/5F every other day (EOD) ( $n = 77$ ); and 26 Gy/2F QW ( $n = 30$ ). Bounce was defined as an increase in PSA to nadir+0.2ng/mL or nadir+2 ng/mL followed by a decrease back to nadir. Kruskal-Wallis test and Fisher exact test were used for continuous and categorical variables.  $P$ -value  $< 0.05$  was considered statistically significant. Univariable and multivariable logistic regression were used to evaluate the influence of patient and treatment factors on bounce incidence.

**Results:** Two hundred eighty-seven patients were included with a median follow-up of 4.9 years (IQR: 3.7-8.7 years). Overall two- and five-year cumulative incidences of PSA bounce by nadir+2 ng/mL were 6.3% and 8%, respectively. Overall cumulative incidences of bounce by nadir+0.2 ng/mL were 22.5% and 31% at two and five years respectively. Results are reported by TG for 35 Gy/5F QW, 40 Gy/5F QW, 40 Gy/5F EOD, and 26 Gy/2F QW, respectively. The two-year cumulative incidences of bounce by nadir+0.2 ng/mL were 28.9%, 21%, 19.6% and 16.7% ( $p = 0.12$ ) and by nadir+2 ng/mL were 7.2%, 8%, 2.7% and 6.7% ( $p = 0.32$ ). Median times from start of radiotherapy to first bounce were not significantly different by nadir+0.2 ng/mL (18.2, 17.7, 17, and 11.5 months;  $p = 0.16$ ) or nadir+2 ng/mL (18.2, 15.7, 10, and 14 months;  $p = 0.09$ ). The duration of bounce was significantly different by nadir+0.2 ng/mL (18.2, 15, 12.8, and 11.9 months;  $p = 0.005$ ) but not nadir+2 ng/mL (16.5, 20.4, 13.7, and 14.6 months;  $p = 0.69$ ). Multivariable analysis revealed that for nadir+0.2 ng/mL bounce, patients with older age (OR 0.95; 95% CI 0.91-0.98) and cT2 tumours (OR 0.43; 95% CI 0.21-0.84) had a lower probability of bounce while for nadir+2 ng/mL bounce, patients with higher baseline PSA were less likely to have bounce (OR 0.49; 95% CI 0.26-0.97).

**Conclusions:** The cumulative incidence of PSA bounce does not differ between the four prostate SBRT schedules used in this pooled analysis. However, one in 13 patients experiences a PSA bounce of nadir+2 ng/mL by five years and may be misdiagnosed as biochemical failures if not followed closely. The duration of PSA bounce does vary significantly when a low threshold of nadir+0.2 ng/mL is used. There is a higher incidence of PSA bounce associated with younger age, cT1 stage, and lower baseline PSA depending on the bounce threshold.

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#### NOVEL RADIATION-ACTIVATED PHOTODYNAMIC (RADIOPDT) NANOPARTICLES FOR TREATING PROSTATE CANCER

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**Introduction:** Current challenges in prostate radiotherapy (RT) involves balancing the benefits of dose escalation to tumours while minimizing dose and toxicity to organs-at-risk, such as the rectum, bladder, and urethra. Photodynamic therapy (PDT) uses photosensitizers (PS) that, when exposed to light, generate reactive singlet oxygen species to cause significant tumour cytotoxicity. Despite the significant clinical benefits shown in Phase III clinical trials for prostate PDT, its use is limited in treating deep-seated tumours due to minimal tissue penetrance of the activating light. By exploiting the greater depth penetration of x-rays, radiation-activated PDT (radioPDT) can augment radiotherapy's efficacy for deep-seated tumours. This is done with scintillating nanoparticles (NSC) to convert x-rays to light for PDT. Prostate tumours can be hypoxic, and hypoxia's effect on radioPDT is unknown. This is important since both RT and PDT are oxygen-dependent.

**Purpose:** We are now reporting the potential of our novel radioPDT nanoparticle (NP) in hypoxic conditions by evaluating singlet oxygen yield, cancer cell death, and in vivo toxicity. We also investigate our NP's potential as a diagnostic agent.

**Materials and Methods:** We developed a novel radioPDT NP by encapsulating NSCs (lanthanum fluoride) and PS (protoporphyrin) into nanospheres (PEG-PLGA). Therapeutic potential was evaluated via singlet oxygen yield and an in vitro cell viability assay in normoxic (20% O<sub>2</sub>) and hypoxic ( $\leq 1\%$  O<sub>2</sub>) conditions under radiation and light PDT. Diagnostic properties were evaluated via CT and MRI, as well as by X-ray imaging of in vivo distribution characteristics using a chorioallantoic membrane (CAM) chick embryo model. An acute radioPDT NP toxicity study in C57/BL mice was performed by escalating NP concentrations; behavioral and weight changes over 48 hours were monitored, and post-mortem vital organ histopathology was done.

**Results:** In vitro assays show virtually no toxicity in prostate cancer and fibroblast cell lines when NPs were not activated, however cancer cell killing was increased by up to 50% ( $p < 0.001$ ) over RT alone, when activated. Imaging showed appreciable signal yield with CT enhancement of 39.6 HU/ La ppm and a MRI T1 relaxivity constant of  $1.12 \times 10^{-7}$  ms/ La ppm. CAM studies showed preferential tumour-targeting. Mice studies showed no significant weight, behavioral, or histopathologic changes in doses up to 1000mg/kg.

**Conclusions:** radioPDT is a novel method of enhancing RT efficacy and minimizing toxicity. Preliminary in vitro data shows radioPDT significantly augments RT, even in hypoxia, via singlet oxygen production, with minimal in vivo toxicity observed. Future in vivo studies exploring diagnostic and therapeutic potential are planned.

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#### OCULAR BRACHYTHERAPY FOR INTRA-OCULAR MELANOMA: EXPERIENCE AND OUTCOMES IN THE PROVINCE OF ALBERTA

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**Introduction:** Uveal melanoma is the most common cause of intra-ocular malignancy, and accounts for about 5% of melanoma diagnoses. It has a 12-year overall survival approaching 60%, and disease-specific mortality ranging from 17% to 21%. Treatment historically was only through surgical enucleation, which conferred morbidity from vision loss, pain, cosmetic and social stigma. A multicentre randomized control trial by the Collaborative Ocular Melanoma Study (COMS) has found no difference in survival between enucleation versus organ preserving ocular brachytherapy for up to 12 years follow-up. This has become the preferred option to spare most of the morbidities of enucleation.

**Purpose:** We perform a first look of Alberta's experience and outcomes with its ocular brachytherapy program since its inception in 2011.

**Materials and Methods:** One hundred seventy-four patients from Alberta

and the western Canada catchment area with intra-ocular melanoma and no evidence of distant metastasis were treated between 2011 and 2017, and followed from time of diagnosis. All patients had ocular ultrasound and CT staging as minimum investigations. Treatment was done with temporary ocular brachytherapy at the Cross Cancer Institute with I-125 high dose seeds (4.14 mCi average activity) mounted in COMS plaque or Eye Physics-brand (Los Alamitos, CA, USA) plaque. Dose calculations were performed using Plaque Simulator (Los Alamitos, CA, USA) treatment planning software, correcting for plaque heterogeneities. All implants and explants were done as day procedures, with general anesthesia for implant and sedation for explants. Implant time ranged from four days to seven days. All cases were prescribed 70 Gy to a prescription point located 0.5 mm beyond the tumour apex. Plaque size, location, and seed loading pattern were chosen to ensure 100% coverage of a margin 2 mm beyond the tumour base, and to minimize OAR doses (fovea, nerve) as much as possible. Analysis was carried out using Cox regression stratified for survival by Gene Expression Profiling (GEP) class and the tumour's Largest Base Diameter (LBD), measuring time from treatment to development of metastasis.

**Results:** Median follow-up to for our cohort was 2.9 years. Median dose achieved was 70.4 Gy. There were 20 cases of disease failure by way of metastatic disease, with no local failures and no post-brachy enucleations. Median time to failure was not reached for GEP class 1a and 1b versus 4.1 years for class 2 ( $p = 0.001$ ). Median time to failure for patients with LBD <12mm was not reached versus 6.8 years for LBD  $\geq 12$  mm ( $p < 0.001$ ). Most metastases were to the liver with some patients salvaged with metastatectomy or SBRT. **Conclusions:** Ocular brachytherapy for uveal melanoma provides excellent local control with disease-free survival that is comparable to surgical enucleation. In the Alberta setting, it continues to be a logistically feasible and effective organ-sparing approach to treating intra-ocular malignancy.

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#### ON THE GEOMETRICAL AND DOSIMETRIC ACCURACY OF SMALL ANIMAL IRRADIATIONS PERFORMED WITH A CONVENTIONAL MEDICAL LINAC

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**Purpose:** Preclinical studies are needed to validate the increasing number of cell and drug therapies being developed. For wound healing studies of irradiated tissues, local and precise irradiation must be performed on small animals in a manner that mimics modern radiation treatments. Dedicated platforms have been developed and shown to be capable of high precision. However, such platforms are expensive and may not be justified for sporadic usage or may be unavailable to generate preliminary data. On the other hand, conventional medical linear accelerators (linacs) are relatively common and could be used for these purposes. Thus, the goal of this work is to assess the geometrical and dosimetric precision of performing mice irradiation on a conventional linac.

**Materials and Methods:** Twenty mice were irradiated as part of an IRB-approved study on skin toxicity. A dedicated positioning system was conceived and a treatment plan was made using a commercial treatment planning system to deliver 45 Gy to a region of 1 cm<sup>2</sup>. Radiochromic film measurements were done in a phantom for initial validation. Animals were first anesthetized then positioned using skin markings by certified radiation therapists. Cone beam computed tomography (CBCT) images were acquired post irradiation to assess the quality of the positioning. Radiation induced skin damage was scored 21 days post-irradiation.

**Results:** Excellent geometrical positioning was observed. The treated isocenter was, on average, within 1.1 mm of the planned isocenter with 1.0 mm standard deviation (SD). In 75% of cases the planned isocenter was within 1.4 mm of the treated isocenter with a maximum deviation seen of 3.2 mm. Surface location for each beam was precise to 0.99 mm (0.64 mm SD) despite up to 20% difference in mice weight. Because the plan was designed to produce a uniform dose over a 1 cm<sup>2</sup> region, these shifts in isocenter should not cause dose variations larger than 1.5%. This was confirmed with in vivo measurements on eight mice. Of these eight measurements, only one showed a statistically significant deviation from the planned dose (7%). After

review, it was found that an important air gap was introduced by error for that specific irradiation. This illustrates the usefulness of in vivo monitoring.

**Conclusions:** This work shows that high geometrical and dosimetric accuracy can be achieved with a conventional linac when used for the irradiation of localized regions on small animals. This is important for preclinical studies where uncertainties related to the radiation dose delivery must be kept to a minimum in order to draw meaningful conclusions.

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#### MOLECULAR TARGETING TO EXPAND THE THERAPEUTIC RATIO IN WOMEN WITH CURABLE CERVICAL CANCER

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**Purpose:** Approximately 30-40% of cervical cancer patients treated with radio(chemo)therapy (RTCT) develop recurrence that can be difficult to treat. New approaches for overcoming treatment failures are needed. The CXCL12/CXCR4 chemokine pathway promotes tumour growth and metastasis in various tumour sites and we have observed the pathway is upregulated in RT treated cervical cancers. Plerixafor, an inhibitor of this pathway, is approved clinically and our initial studies showed the addition of Plerixafor to RTCT enhanced primary tumour response. The current studies examined: 1) different ways of sequencing RTCT and Plerixafor to maximize efficacy; 2) biomarkers of response to RTCT and Plerixafor; and 3) effects of Plerixafor with RTCT on intestinal toxicity, an important dose-limiting consequence of treatment in these patients.

**Materials and Methods:** Orthotopic cervix xenografts were treated with RT (30 Gy; 2 Gy/day) and weekly Cisplatin (4mg/kg) with or without Plerixafor (5mg/kg/day). Plerixafor was administered concurrently with RTCT (three weeks), adjuvantly after RTCT (three weeks) or continuously (six weeks). Biomarker response was evaluated at the end of the concurrent and adjuvant treatments. Tumour growth delay was assessed at later times. Tumour control was assessed after 50 Gy (2Gy/day-5 weeks) with Cisplatin and Plerixafor. Late intestinal toxicity was assessed by histologic examination of the colorectal junction 90 days after treatment.

**Results:** Plerixafor, whether administered concurrently or adjuvantly, prolonged tumour growth delay following RTCT (30 Gy). Adjuvant Plerixafor was associated with longer growth delay. Tumour cure was achieved at a higher RT dose of 50 Gy with RTCT+Plerixafor. RTCT alone increased CXCL12/CXCR4 signalling, PD-L1 (immune checkpoint marker) expression and the tumour accumulation of myeloid cells. The addition of Plerixafor during or after RTCT abrogated these effects. This suggests: 1) RTCT upregulation of the CXCL12/CXCR4 pathway leads to recruitment of immune populations into the tumour that confer treatment resistance and 2) RTCT-induced increases in PD-L1 expression may promote an immunosuppressed tumour microenvironment that impairs treatment response. Plerixafor reduced RT-related intestinal injury, suggesting a protective effect that may relate to modifications of immune cell infiltrates involved with the mobilization of mesenchymal stem cells from the marrow. Further investigation is needed to assess mechanisms underlying these radio-protective effects.

**Conclusions:** Adding Plerixafor to RTCT blunts RTCT-induced upregulation of the CXCL12/CXCR4 pathway and reduces the increase in tumour-associated myeloid cells. These benefits may apply to other tumours where RT plays a curative role. Plerixafor protects normal tissue from RT injury. Few if any drugs have been identified previously that both improve the effectiveness of RT and prevent side effects. The combination of RT and Plerixafor warrants testing in clinical trials to validate these findings.

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#### A NEW COMBINATION OF PRO-APOPTOTIC AGENTS AND RADIOTHERAPY FOR TREATMENT OF SOFT TISSUE SARCOMAS

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**Purpose:** Pre-operative radiotherapy improves local control but often

fail to importantly reduce the tumour size. The aim of this project was to synergistically improve radiation treatment and cancer cell death in soft tissue sarcomas (STS) via addition of pro-apoptotic drugs.

**Materials and Methods:** STS cell lines established from primary human sarcomas were treated with various combinations of irradiation and pro-apoptotic drugs (Venetoclax and Navitoclax) targeting anti-apoptotic BCL-2 family members. The characterization of STS cell responses after irradiation (2 to 10 Gy) was performed by flow cytometry (cell cycle and apoptosis), V-PLEX immunoassays (secretome), and long-term survival (proliferation and colony formation). Cell responses were also evaluated in a 3D culture model.

**Results:** We confirmed that irradiation alone was sufficient to reduce the ability of primary STS cells to form colonies. Irradiated cells demonstrated very low level of cell death but displayed a proliferation arrest that explains reduced colony formation. Alternatively, the addition of pro-apoptotic drugs after radiation induced rapid apoptosis in all irradiated cell lines, with little effect on non-irradiated controls, leading to significant reductions in colony formation via increased cell death. Importantly, combo treatments of irradiation and pro-apoptotic drugs in 3D culture models yielded a diminution in spheroids size as opposed to spheroids treated with irradiation alone.

**Conclusions:** The cytostatic phenotype observed after the irradiation of STS cell lines could reflect the lack of important tumour size reduction following pre-operative radiotherapy. Radiotherapy-induced cytostasis in STS can be overcome through the administration of a pro-apoptotic BCL2/BCLxL inhibitor during the time window between RT and surgery. Important reduction in tumour size will diminish the volume of STS surgery and its associated morbidities.

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#### QUALITY OF LIFE: A PROSPECTIVE RANDOMIZED TRIAL OF PALLIATIVE VOLUMETRIC ARC THERAPY (VMAT) VERSUS CONFORMAL RADIATION THERAPY (CRT)

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**Purpose:** VMAT spares normal tissues from high/intermediate radiation (RT) doses but increases the volume of tissues receiving low doses of RT as compared to CRT. We hypothesized that palliative VMAT would induce less acute quality of life (QOL) detriment than CRT.

**Materials and Methods:** This Phase 2 trial randomized patients to palliative RT using VMAT or CRT to one painful site of metastatic disease in the trunk. Eligible patients were able to complete questionnaires (EORTC QLQ C30 and SF-BPI) and were expected to live >3 months. Patients were ineligible if their KPS < 50, they had prior radiation to the same site, there were planned changes in analgesics or cancer therapy within seven days of the RT. Treating physicians could choose 8 Gy in 1 fraction or 20Gy in 5 fractions, a choice used to stratify randomization. The primary endpoint was EORTC QLQ C30 global QOL subscales at one week post-RT (QOL at four weeks was a secondary endpoint). Paired t-test was used to compare the effect of RT to all patients. Wilcoxon signed-rank test (2-tailed) was used to compare changes in QOL. Only clinically important ( $\geq 10$  point) QOL differences are reported.

**Results:** From July 2014-November 2017, 72 patients were accrued. Three patients did not receive RT, 12 did not return one week post-RT. There were 55 and 46 evaluable patients at one and four weeks post-RT, respectively. The most common diagnoses were NSCLC, breast, and prostate cancer. Median overall survival was nine months. Median pain level was 7/10 at baseline and 5/10 at one and four weeks post-RT ( $p < 0.0001$  and  $p = 0.0013$ ). Median time from consultation to RT was six days. Baseline characteristics (KPS, pain, QOL subscales and time to first RT fraction) were balanced between the groups. At one week post-RT, global QOL subscale was not significantly ( $p = 0.46$ ) different between VMAT versus CRT, but VMAT induced significantly ( $p = 0.027$ ) less nausea and vomiting than CRT. At four weeks post-RT, VMAT induced significantly ( $p = 0.048$ ) less global QOL deterioration. At four weeks, patients who received VMAT maintained better role ( $p = 0.022$ ) and social ( $p = 0.018$ ) functions, but reported more diarrhea symptoms ( $p = 0.033$ ) than patients treated with CRT. Patient age, gender,

RT dose, PTV size and target location (abdomino-pelvic versus thoracic) were not associated with global QOL changes at four weeks.

**Conclusions:** Palliative VMAT appears to induce less QOL detriments than CRT at four weeks post-RT. VMAT reduced iatrogenic nausea and vomiting, which was partially offset by an increase in diarrhea.

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#### EXTERNAL BEAM RADIATION-SENSITIVE BIOPOLYMER FOR TARGETED DRUG DELIVERY

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**Purpose:** Despite the important role of chemotherapy in cancer treatment, the benefit of conventional chemotherapy is often limited by low therapeutic indices and dose-limiting toxicities, as well as poor water solubility. To this end, a drug delivery platform which can deliver chemotherapy agents to the desired target specifically without affecting healthy tissue is desirable. Here we report a drug delivery platform created from the external beam radiation therapy-sensitive biopolymer for simultaneous drug delivery and treatment of cancer.

**Materials and Methods:** Commercially available poly-L-glutamic acid (PGA) was modified for radiation sensitivity. PGA's carboxylic acid group of the side chain was substituted with lipophilic and radiation-sensitive chemical structure to form modified PGA (mPGA) and verified by H NMR Spectra. The encapsulation of radiation-sensitive mPGA around gadolinium-based nanoparticle loaded with doxorubicin (Gd-Dox) was verified using TEM (transmission electron microscopy). The radiosensitive property of mPGA coated Gd-Dox nanoparticle (mPGA-Gd-Dox) was tested by subjecting it to photon radiation in single clinical dose in range of 2 Gy to 30 Gy. The physical changes were observed directly with TEM. The degradation product created secondary to radiolysis of mPGA was quantified by measuring the downstream chemical group with UV Spectrophotometer. The amount of doxorubicin release upon irradiation of mPGA-Gd-Dox was also quantified. The survival fraction of the cancer cells treated with the mPGA-Gd-Dox with or without radiation was determined with clonogenic assay.

**Results:** mPGAs with varying degree of modification were created by varying the ratio of the starting reagents and confirmed by H NMR (proton nuclear magnetic resonance) spectra. The reaction that permitted the highest degree of modification without side reaction was used for the rest of this study. The mPGA encapsulation around Gd-Dox was readily observed with TEM as spherical encapsulating layer around Gd-Dox. The radiolysis of mPGA was also readily apparent under TEM as mPGA coating of mPGA-Gd-Dox disintegrated and Gd-Dox was without any visible layer of encapsulation. The radiolysis of mPGA-Gd-Dox occurred in a radiation dose-dependent manner, as the amount of radiation-induced degradation product increased with the increased radiation dose ranging from 2 Gy to 30 Gy, with the highest amount occurring at 30 Gy. Upon irradiation of mPGA-Gd-Dox, doxorubicin was released effectively compared to the non-irradiated control, releasing over twice the amount of doxorubicin with radiation. The effectiveness of doxorubicin release upon radiation treatment correlated with greater inhibition of cancer cell growth, as the survival fractions were 0.21 and 0.71 in irradiated and non-irradiated cells, respectively.

**Conclusions:** Here we report synthesis and analysis of radiation sensitive mPGA that effectively encapsulates doxorubicin loaded nanoparticle. The mPGA coating lyses in radiation dose-dependent manner and releases loaded doxorubicin efficiently upon radiation stimulus. As a proof of concept, we demonstrate effective radiation -responsive cancer cell growth inhibition in vitro.

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#### GENETIC PROFILING OF OLIGODENDROGLIOMAS (IDH MUTATED AND 1P19Q CO-DELETED) TREATED WITH ADJUVANT RADIOTHERAPY OR OBSERVATION INFORMS PROGNOSIS

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**Purpose:** Recent international sequencing efforts have allowed for the molecular taxonomy of low-grade gliomas (LGG) (The Cancer Genome Atlas (TCGA), 2015). Based on clinical and pathological factors, patients with resected oligodendrogliomas are usually treated with adjuvant radiation or observed. We sought to analyze TCGA gene expression and copy number datasets on oligodendrogliomas patients treated with adjuvant radiation or those observed to discover prognostic markers and pathways.

**Materials and Methods:** Our cohort consists of patients with oligodendroglioma in the TCGA dataset (accessed through <http://www.cbioportal.org/>). mRNA expression, copy number, and clinical information was taken from the TCGA "Brain Lower Grade Glioma" provisional dataset. Survival modeling and ANOVA analysis was performed using the R packages "plsRCox" and "survival". Ten-fold bootstrap, cross-validation was performed using the "rms" and "pec" packages.

**Results:** From 530 potential LGG dataset patients, 164 were included in our analysis with oligodendroglioma or oligoastrocytoma, and both IDH mutation and 1p19q codeletion. Out of our cohort of 164 patients, 137 had documentation of treatment, with 65 receiving adjuvant radiation (median dose 5,940 cGy) and 62 observed. In the cohort that received adjuvant radiotherapy, expression of members of the PDGFRA module (GSTA4, CXXC4, KLRC3, DSCAM, OLIG2, SOX4, SOX8) was associated with shorter progression-free survival (HR = 7.8,  $p < 0.02$ , median C-index = 55.3%). This increased risk was not seen in patients who were observed (HR = 0.86,  $p = 0.83$ ). In addition, expression of circadian clock genes (CSNK1E, CRY2, PER1) was also associated with shorter progression-free survival (HR = 4.9,  $p < 0.03$ , median C-index = 68.6%) when treated with radiation versus observation (HR = 0.33,  $p = 0.11$ ). Median progression-free survival in the radiotherapy cohort positive for the circadian gene signature was 64 months versus 97.2 months for those negative for the signature. Within the observation cohort, expression of genes in the polycomb repressive complex-2 (EZH1, EZH2, SUZ12, EED, and RBBP4) was associated with poor progression-free survival (HR=1.65,  $p < 0.008$ , median C-index = 68.5%). This risk was abrogated in the adjuvant radiation cohort (HR = 1.03,  $p = 0.55$ ). Decreased expression of genes targeted and down-regulated by this complex also was associated with shorter progression-free survival (Chi-sq = 7.4,  $p < 0.007$  median C-index = 66.3%).

**Conclusions:** We identified genes in the PDGFRA and circadian signaling pathways that are associated with poor prognosis in patients with IDH mutated and 1p19q codeleted oligodendroglioma treated with adjuvant radiotherapy. These patients would be potential candidates for treatment intensification. We also identified a PRC-2 gene signature for patients who were more likely to progress on observation. This potentially identifies a cohort who would benefit from upfront adjuvant radiotherapy.

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#### INTERNATIONAL MULTI-CENTER VALIDATION OF AN INTERMEDIATE-RISK SUBCLASSIFICATION OF MEN TREATED WITH RADICAL TREATMENT WITHOUT HORMONE THERAPY

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**Purpose:** National Comprehensive Cancer Network guidelines have recently endorsed the Memorial Sloan Kettering (MSK) subclassification of intermediate risk prostate cancer into favourable (FIR) and unfavourable (UIR) subgroups. These subgroups are often used for decision-making regarding the addition of hormone therapy. However, the subclassification was developed in a heterogeneous cohort of men, many of which received androgen deprivation therapy (ADT), and thus the natural history of hormone therapy naïve FIR and UIR men remains unknown. Herein, we perform the first multicentre validation study across all forms of radical therapy in men with intermediate risk prostate cancer who did not receive

combined hormone therapy.

**Materials and Methods:** After receiving institutional review board approval from three academic centres, intermediate risk men treated with radical monotherapy (dose escalated external beam radiotherapy (DE-EBRT), brachytherapy (BT) as monotherapy, or radical prostatectomy (RP)) without the addition of ADT were included. UIR prostate cancer was defined as any intermediate risk patient with a primary Gleason pattern of 4, percentage of positive biopsy cores  $\geq 50\%$ , or multiple intermediate risk factors (cT2b-c, prostate-specific antigen 10-20 ng/mL, or Gleason score 7). Cumulative incidence curves with competing risk analyses were performed for distant metastasis (DM) and prostate cancer-specific mortality (PCSM).

**Results:** A total of 2550 intermediate risk men (1044 FIR and 1506 UIR) were included, of which 1149 had RP, 1143 had DE-EBRT, and 258 had BT. The median follow-up for the RP, DE-EBRT, and BT cohorts were 60.4, 70.6, 107.4, months respectively. The 10-year cumulative incidence of DM for FIR versus UIR were 0.6% (95%CI:0.6-0.6) versus 10.4% (95%CI:6.5-14.3) for RP ( $p < 0.001$ ), 3.4% (95%CI:1.4-5.4) versus 13.2% (95%CI:9.3-17.1) for DE-EBRT ( $p < 0.001$ ), and 4.4% (95%CI:0.5-8.3) versus 12.4% (95%CI:2.6-22.2) for BT ( $p = 0.025$ ). The 10-year rates for PCSM for FIR versus UIR were 0% (95%CI:0-0) versus 3.4% (95%CI:1.4-5.4) for RP ( $p = 0.031$ ), 1.3% (95%CI:0-3.3) versus 5.2% (95%CI:3.2-7.2) for DE-EBRT ( $p = 0.049$ ), and 0.6 (95%CI:0-2.6) versus 3.0% (95%CI:0-6.9) for BT ( $p = 0.028$ ).

**Conclusions:** This multicentre international effort has independently validated the prognostic value of the MSK intermediate risk subgroup classification in men who are hormone therapy naïve across all radical treatment modalities. Our data demonstrates that the current definition of FIR may not be ideal as 3-4% of men still develop distant metastasis at 10 years even with definitive therapy. These results underscore the need for other biomarkers to improve risk stratification, such as the recently reported clinical-genomic risk group classification, and the necessity of studying the differential impact of treatment intensification strategies, such as ADT, among these subgroups.

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#### PLASMA METABOLOMIC PROFILES IN PATIENTS WITH HEPATOCELLULAR CARCINOMA BEFORE AND AFTER SBRT

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**Purpose:** Grade 1 and 2 toxicities such as fatigue and nausea are common following SBRT for hepatocellular carcinoma (HCC). Less commonly, Grade 3 or higher hepatic and non-hepatic toxicities develop following HCC SBRT, and are often associated with irreversible injury, high morbidity and mortality. There is a need to identify biomarkers that can detect radiation-induced liver/luminal gastrointestinal injury early for appropriate medical intervention or radiation dose reduction and to predict tumour response, allowing tailoring of SBRT to improve the therapeutic ratio for individual patients, ideally prior to completion of SBRT. The objective of this study are two-fold: a) to identify the profile of changes in metabolite levels in the plasma of HCC patients at baseline and following the first or second fraction of SBRT, and b) to correlate such changes with clinical liver/luminal gastrointestinal toxicities and radiologic tumour response.

**Materials and Methods:** HCC patients were treated with SBRT to a total dose of 30-54 Gy in 6 fractions. Plasma samples were collected at baseline and after completion of the first or second fraction of SBRT. Targeted and untargeted metabolomic profiling was performed using LC/MS or GC/MS. Metabolites annotation was performed with comparing the mass spectrum and retention time to commercial available libraries. Paired t-test and spearman correlation were used for statistical analyses.

**Results:** Four hundred and eighty-three metabolites were detected, of which 190 were not annotated. Significant differences were seen following SBRT from baseline in 34 annotated metabolites and 39 non-annotated spectral signatures. Methyl linoleate, cysteine, tryptophan and tyrosine were amongst the metabolites that demonstrated the highest fold increases post-SBRT, while succinic acid, campesterol and complex lipids with low degree of unsaturation in their fatty acid chains were amongst those that showed the highest fold decreases following one or two fractions of SBRT compared to baseline.

**Conclusions:** This study demonstrated significant fold changes in groups

of plasma metabolites following one or two SBRT fractions for HCC. Some of the identified plasma metabolites were shown to be associated with liver injury in previous preclinical studies. Correlation analyses are underway to determine if these metabolites are associated with clinical radiation-induced liver/luminal gastrointestinal toxicities and tumour response.

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#### MONITORING RADIATION RESISTANCE AND RESPONSE OF NON-SMALL CELL LUNG CANCER USING RAMAN SPECTROSCOPIC SIGNATURES OF TUMOUR HYPOXIA

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**Purpose:** This study investigates the link between changes to tumour metabolism and tissue reoxygenation following radiation therapy in human non-small cell lung cancer (NSCLC) murine models. The objective of this work is to establish Raman spectroscopy as a non-invasive technique for monitoring tumour resistance and response to radiation by measuring fluctuations in hypoxic state of the tumour.

**Materials and Methods:** Raman spectroscopy (RS) was used to measure glycogen levels within human NSCLC xenografts grown in NOD.CB17-Prkdcscid/J female mice for unirradiated and irradiated (15 Gy) tumours at 2 hours, 1, 3 and 10 days post treatment. Immunofluorescence (IF) was used to indicate levels of DNA damage (phospho-H2AX) and hypoxia (pimonidazole (PIM), carbonic anhydrase IX (CAIX)) in order to establish global correlations between glycogen alterations and hypoxia within the tissue. Local correlation between Raman glycogen signatures and CAIX were studied by carrying out coincident studies using RS and IF on the same tissue section.

**Results:** RS identified radiation-induced decreases in glycogen levels within the tumour at two hours post treatment; however, irradiated tumours harvested at 1, 3 and 10 days following treatment had elevated levels of glycogen. Furthermore, increased glycogen levels were found to be linearly correlated to reduction in tumour area between treatment and time of death ( $R^2=0.86$ ). Immunofluorescence revealed increased CAIX staining, but reduced PIM staining in irradiated tumours harvested at three days post irradiation. Together with a measured correlation between increased glycogen content and CAIX positive staining ( $R^2=0.90$ ), our results show glycogen can track hypoxic state within a tumour. Specifically, glycogen levels, as indicated using RS, can identify recovery from hypoxia within the tumour in response to radiation therapy.

**Conclusions:** This study shows that Raman spectroscopy can be used to gauge tumour resistance through hypoxia levels in the tumour, and tumour response to radiation by measuring hypoxic recovery within the tumour. Furthermore, we show that Raman spectroscopy can be used to monitor these effects as early as two hours and as late as 10 days post-treatment. Applications of RS therefore show promise as a way to effectively track patient resistance and response to radiation therapy, offering a non-destructive and non-invasive technique for personalizing radiation therapy in NSCLC.

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#### EVALUATION OF 18F-EF5 SUITABILITY FOR DETECTION OF HYPOXIA IN LOCALIZED ADENOCARCINOMA OF THE PROSTATE

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**Purpose:** A common feature of therapy resistant and metastatically aggressive solid tumours is the presence of regions with low oxygen content (ie. hypoxia). In prostate cancer, detection of hypoxia has been understudied and problematic. Between immunohistochemistry (IHC) and non-invasive imaging, clinical studies report non-congruent expression of the classic hypoxia reporting proteins hypoxia inducible factor 1 alpha and carbonic

anhydrase IX, while only two published studies have tested positron emission tomography (PET) of radiolabelled 2-nitroimidazoles with prostate cancer. One study using 18F-FMISO reported a wide range of hypoxia, from 0% to 93% fractional hypoxic volumes, while the second study using 18F-FAZA reported no significant radiotracer uptake in any of 14 patients. These two observations fit with the known limitations of 18F-FMISO and 18F-FAZA, being high amounts of noise and low specific uptake respectively. The purpose of this study was to evaluate the suitability of 18F-EF5, a third nitroimidazole with promising results in xenograft models of prostate cancer, for detection of hypoxia in localized adenocarcinoma of the prostate.

**Materials and Methods:** Prostate cancer patients were recruited from British Columbia Cancer Agency for pre-treatment 18F-EF5 PET imaging along with biopsy collection for IHC analysis of glucose transporter 1 (GLUT1) expression as a check for hypoxic status. To account for the anticipated heterogeneity in tumour oxygenation multiple biopsies were taken from each tumour. Those biopsies with more than 50% of the sample tissue containing prostate cancer cells were subject to IHC for GLUT1. GLUT1 expression was scored by a pathologist for staining intensity and frequency. **Results:** This study was halted after eight patients were recruited and no significant 18F-EF5 uptake could be detected in any tumours. However, significant GLUT1 expression was observed in four of eight tumours. Two of the cases stained strongly positive for GLUT1 with high frequency (> 50% tumour positive), while the two other positive cases exhibited weaker staining and reduced frequency (< 50% tumour positive). This is fitting with inter-individual heterogeneity for prostate tumour hypoxia.

**Conclusions:** These data support that 2-nitroimidazoles are not suitable for detection of hypoxia in clinical prostate tumours. Our study replicates the observations made with the report using 18F-FAZA where no radiotracer uptake was detected despite multiple cases of positive IHC staining for hypoxia induced proteins.

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#### INVESTIGATION OF THE PTV MARGIN IN PERMANENT BREAST SEED IMPLANT (PBSI) BRACHY THERAPY: A PILOT STUDY

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**Purpose:** Permanent breast seed implant (PBSI) brachytherapy is a convenient alternative to whole breast radiation therapy in which Pd-103 seeds are implanted into the breast post-lumpectomy. Limited quantitative analysis exists in determining an optimal PTV margin for PBSI. The purpose of this study is to preliminarily assess the adequacy of the clinical margin given associated implant uncertainties.

**Materials and Methods:** Thirteen patients who underwent PBSI and had a same-day post implant CT with post-plan dosimetry were included in this study. Median (range) planning CTV volume was 7.6cc (1.5-17.4cc). Clinically, the PTV margin was planned as an isotropic expansion of the CTV by nominally 10mm, cropped to the chest wall muscle and skin contour. Treatment plans were created with the CTV coverage goal of V100% equal to 100%. The CTV coverage in this study was assessed using the difference in V90% from the plan to the post plan ( $\Delta V90\%$ ). The seed placement accuracy was defined as the change in seed positions between the plan and the same-day post implant CT when registered using CTV centres, averaged over all seeds for a patient. This was assessed in three directions relevant to the implant orientation: chest wall-skin, left-right, shallow-deep, as well as the absolute total.

**Results:** In the chest wall-skin direction, the seed displacements were median 0.2 mm towards the chest wall (range 3.2 mm towards chest wall to 4.8 mm towards the skin). A displacement away from the chest wall was found to be strongly correlated ( $R\text{-squared} = 0.63$ ) to a loss of CTV coverage. When the average seed displacement was towards the chest wall, this loss of coverage was not observed. The cropping of the PTV to the chest wall resulted in an effective PTV margin that was much smaller in the chest wall-skin direction, increasing the impact that seed displacement had on the dosimetry. In the shallow-deep and left-right directions, the PTV is not cropped, thus potentially mitigating the dosimetric impact of seed displacement in these directions. For one patient for whom the PTV was heavily cropped to both the skin and

chest wall, the reduction in dosimetry was associated with the cropping in both directions. No correlation was observed between shallow-deep, left-right, or total displacement and  $\Delta V90\%$ , despite the largest displacements being in the shallow-deep direction.

**Conclusions:** The chest wall-skin displacement is correlated to the post implant CTV dosimetric coverage when the average displacement is away from the chest wall. This study motivates the need to simulate implant uncertainties in a larger patient cohort to derive the required PTV margin to ensure a robust delivery of the prescription dose to the CTV given the associated uncertainties. The current clinical PTV margin in the chest wall-skin direction may be inadequate to account for seed displacement.

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#### T2-WEIGHTED MRI-DERIVED RADIOMIC FEATURE CHANGES IN THE DOMINANT INTRAPROSTATIC LESION FOR PATIENTS TREATED WITH FOCAL SALVAGE HDR PROSTATE BRACHYTHERAPY

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**Purpose:** The objectives of this study are to explore the changes in T2-weighted (T2w) MRI-derived radiomic features of the dominant intraprostatic lesion (DIL) from focal salvage HDR prostate brachytherapy (HDRB) with prior local recurrence after external-beam radiotherapy (XRT), and to correlate with clinical parameters.

**Materials and Methods:** Eligible patients included those with biopsy-confirmed local recurrence that correlated with multi-parametric MRI (mpMRI: T2w, ADC and DCE); > 30 months post-XRT; pre-salvage PSA < 10ng/mL, and previous definitive XRT  $\leq$  78 Gy. Ultrasound-based salvage HDRB with a dose of 27 Gy in 2 fractions separated by one week to a quadrant including the DIL was used. The mpMRI was repeated one year post-HDRB. The DIL was contoured on the pre-HDRB T2w image, the prostate was contoured on the pre- and post-HDRB T2w image, and contralateral normal prostate tissue was autogenerated as control volumes. The pre- and post-HDRB prostate were rigidly registered to identify the post-HDRB DIL which was not readily visible. The images were then processed using open-source radiomics software (Pyradiomics v1.3.0) to extract radiomic features from each volume-of-interest (VOI) on the T2w images. The large feature set was reduced using Principle Component Analysis (PCA) and multivariable ordinary least squares regression to identify features that correlated with measured clinical outcomes.

**Results:** Pre- and post-HDRB mpMRIs were obtained from 14 trial patients. Median follow up was 30 months with a PSA failure-free rate of 71%. A total of 1,132 features were extracted from each VOI. PCA showed that 18 features contributed to 92.9% of the variance observed in the data. The data consisted of first-order (histogram) features, including five from the unfiltered original image, nine from the original image with a Gaussian filter applied, and four from the original image with a wavelet filter applied. Fifteen out of 18 of the DIL post-HDRB features were significantly different compared to pre-HDRB ( $p < 0.05$ ). Sixteen out of 18 of the DIL features were significantly different from the control volumes in the pre-HDRB images ( $p < 0.001$ ). In the comparison of radiomic features to clinical outcomes, the change in unfiltered first-order minimum correlated with PIRADS score ( $R^2 = 0.966$ ,  $p = 0.040$ ), and complete response ( $R^2 = 0.987$ ,  $p = 0.016$ ). The change in wavelet-filtered first-order minimum correlated with tumour size ( $R^2 = 0.987$ ,  $p = 0.034$ ). Baseline Gleason score strongly correlated with change in unfiltered first-order 10 percentile ( $R^2 = 0.996$ ,  $p = 0.032$ ), entropy ( $R^2 = 0.975$ ,  $p = 0.011$ ), and wavelet-filtered image energy ( $R^2 = 0.991$ ,  $p = 0.031$ ).

**Conclusions:** Exploratory analysis reveals several first-order radiomic features in the T2w image DIL that distinguish the DIL from healthy prostate tissue, change significantly after salvage HDRB, and had strong correlations with several clinical factors. Future analyses will include ADC images to find radiomic features that could predict salvage failure.

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#### AUTOMATIC CONTOUR PROPAGATION OF ORGANS-AT-RISK ON SERIAL MRI AND DOSIMETRIC IMPLICATIONS IN GLIOBLASTOMA PATIENTS UNDERGOING CHEMO-RADIATION

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**Purpose:** Changes in brain anatomy during chemo-radiation (CRT) for glioblastoma (GBM) can be visualized with magnetic resonance imaging (MRI). The objective of this study is to investigate the anatomical changes that occur in organs-at-risk (OAR) on serial MRIs during CRT for GBM patients, and to determine the feasibility of automatic OAR contour propagation and its dosimetric implications for the purpose of an adaptive workflow in MR-guided radiotherapy.

**Materials and Methods:** Fourteen GBM patients treated with 60 Gy in 30 fractions of CRT underwent serial multiparametric MRIs on days 0, 10, 20 of treatment (D0, D10, and D20) and one month post-last fraction (P1M). OARs including the brainstem, globes, lenses, optic nerves, and optic chiasm were manually contoured at each time point on the contrast-enhanced T1-weighted MRI and compared to propagated contours generated based on the STAPLE deformable image registration algorithm. The Dice similarity coefficient (DSC) was used to quantify changes in manual versus propagated contours. Dosimetric comparison between the manual and propagated contours with respect to maximum point doses (Dmax) of OARs was performed using the reference D0 treatment plan. Statistical differences were determined using the Wilcoxon signed-rank test.

**Results:** The mean DSC between the manual and propagated OAR contours varied from OAR to OAR (range 0.63 – 0.95) across all time points. The mean DSC  $\pm$  standard deviation (SD) across all patients and time points for the brainstem was 0.95  $\pm$  0.01. For the optic chiasm, the mean DSC  $\pm$  SD was 0.77  $\pm$  0.15. The mean difference in Dmax for each OAR, between the manual contours at each time point compared to the D0 contours, ranged from 5-375 cGy. For the brainstem, the differences were 21  $\pm$  90 ( $p = 0.68$ ), 53  $\pm$  112 ( $p = 0.19$ ), and 99  $\pm$  205 cGy ( $p = 0.01$ ) at D10, D20, and P1M, respectively. For the optic chiasm, the differences were 81  $\pm$  471 ( $p = 0.90$ ), 64  $\pm$  433, ( $p = 0.58$ ) and 138  $\pm$  909 cGy ( $p = 0.26$ ) at D10, D20, and P1M, respectively. The mean difference in Dmax for each OAR, between the manual and propagated contours, ranged from 0.3-704 cGy. For the brainstem, the differences were 25  $\pm$  116 ( $p = 0.59$ ), 33  $\pm$  77 ( $p = 0.27$ ), and 61  $\pm$  137 cGy ( $p = 0.09$ ) at D10, D20, and P1M, respectively. For the optic chiasm, the differences were 59  $\pm$  566 ( $p = 0.67$ ), 512  $\pm$  671, ( $p < 0.01$ ) and 441  $\pm$  915 cGy ( $p = 0.03$ ) at D10, D20, and P1M, respectively.

**Conclusions:** Significant anatomical changes and resultant changes in OAR Dmax occur over the course of CRT for GBM. Automatic contour propagation using deformable image registration in an MR-guided radiotherapy workflow is feasible. The performance of contour propagation varies depending on the OAR and implications in dosimetric differences warrant further investigation.

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#### NEOADJUVANT RADIOTHERAPY AND BRACHYTHERAPY IN ENDOMETRIAL CANCER WITH GROSS CERVICAL INVOLVEMENT: A CHIRENDO RESEARCH GROUP STUDY

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**Purpose:** Historically, radical hysterectomy followed by tailored adjuvant radiation therapy has been offered to some patients with endometrial cancer who have gross cervical involvement, however this approach is known to carry considerable morbidity. Neoadjuvant radiation therapy followed by extrafascial hysterectomy has been proposed as an alternative treatment but has been poorly studied to date. The objective of this study is to evaluate the outcomes associated with this therapeutic strategy.

**Materials and Methods:** A retrospective cohort study of 30 endometrial cancer patients with gross cervical involvement treated between 2006-2016 at a Montreal centre was carried out. Treatment protocol consisted of neoadjuvant pelvic radiation therapy and high-dose rate brachytherapy

followed by extrafascial hysterectomy. Descriptive analyses were performed and Kaplan-Meier curves were used for overall and disease-free survival (DFS) data.

**Results:** Twenty percent were clinical Stage IIIB and 43% had suspicious lymph nodes at diagnosis. Thirteen percent had extended-field radiation therapy and 37% had adjuvant chemotherapy. Ten percent had Grade 3 radiation-related complications; no Grade 4-5 complications were noted. On surgical specimen, 66% and 77% had a complete cervical and nodal response, respectively. Margins were negative in 93% of cases. Twenty-one percent of surgeries were done by minimal invasive technique. Grade 3-4 surgical morbidity was noted in 6.9% of cases. Five recurrences were identified, all with distant failure and one with concomitant local failure. Five-year overall survival and DFS was 96.0% and 86.7%, respectively.

**Conclusions:** Neoadjuvant radiation therapy and brachytherapy followed by extrafascial hysterectomy offers excellent clinical and survival outcomes with low treatment-related morbidity.

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#### NON-UNIFORM LOADING OF EPISCLERAL PLAQUES IN TREATMENT OF UVEAL MELANOMA: A CONFORMAL AND COST-EFFECTIVE APPROACH

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**Purpose:** To assess a dosimetrically-advantageous cost effective program for treatment of Uveal Melanoma using episcleral plaques and a reusable variable-activity inventory of seeds.

**Materials and Methods:** 125-I was chosen in our institution as the preferred isotope seed type for treatment of Uveal Melanoma using episcleral COMS plaque. Since half-life of 125-I is 59.4 days, rather than ordering seeds for every patient, which is the most common practice, we decided to establish a program of re-using stocks of 125-I sources for a number of patients in our treatment capacity based on availability of staff and OR time. In our program, we order 40-50 125-I seeds with Air Kerma Strength (AKS) of ~9U (cGy<sup>2</sup>/h) every two months (6x per year). In order to treat a maximum of three patients per week, we established a stock inventory of 125-I seeds such that we have at least four useful seed groups of different AKS at any time. The resultant four groups of 40 seeds with AKS of 1U-9U, allows us to plan maximum three plaques per week using the standard COMS plaque protocol with a prescribed dose of 85 Gy for tumours up to 10 mm in apical height. The seed inventory also enables treatments using asymmetrically loaded plaques for cases of irregular tumour shapes or those close to the optic nerve. In cases where the tumour has grown between the time of original planning and the insertion date, our seed inventory also allows us to rapidly change the treatment plans to match the latest available clinical information. Besides flexibility in planning, our seed inventory program enables considerable cost saving.

**Results:** During 30 years of episcleral plaque therapy practice for Uveal Melanoma in our institution, over 2,000 patients have been treated. The inventory based program allows for optimizing and conforming of the dose distribution to irregular shape tumours and dose sparing of OARs. This program also has significantly lowered the cost of Uveal Melanoma treatments in our hospital for past 30 years. The cost of 125-I seed for our institution is ~\$200/seed. Ordering 6 x 40 seeds per year costs approximately \$48,000. With an average of 100 patients treated per year, the average cost per patient is approximately \$480. This is considerably lower than ordering individual seeds for each patient which we estimate to be \$3,000/patient (assuming ~15 seeds per treatment).

**Conclusions:** Institutions with patient load of more than two patients per month can benefit from variable-activity inventory based planning for treatment of Uveal Melanoma using 125-I seeds. This program is not limited to COMS plaques and can potentially be used with other available plaques on the market. However, such an approach is not advantageous with low half-life radioactive seeds like 103-Pd and 131-Cs. Further, the use of up to four different AKS-value seed stocks in a given plaque requires advanced treatment planning systems such as Plaque Simulator (IsoAid,

LLC) or Pinnacle (Elekta Inc), and added QA procedures.

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#### RESULTS OF A PHASE I RANDOMIZED-CONTROLLED TRIAL EVALUATING CONVENTIONAL VERSUS MACHINE LEARNING TREATMENT PLANNING FOR PROSTATE LOW-DOSE-RATE BRACHYTHERAPY

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**Purpose:** We report results of the first-ever single-blind, Phase I randomized controlled trial evaluating a machine learning-based workflow for treatment planning in prostate low-dose-rate (LDR) brachytherapy. The purpose of the study was to evaluate the non-inferiority of postoperative dosimetry between machine learning (ML) and brachytherapy dosimetrist (RT) treatment planning approaches, as well as the impact on planning efficiency. **Materials and Methods:** A total accrual of 42 patients was required to demonstrate significance as part of this IRB-approved, single-institution study. From October to January 2017, 37 patients with low- or intermediate-risk prostate cancer were accrued into the study. Patients were block-randomized to receive either a ML (n = 20) or RT generated (n = 17) prostate LDR brachytherapy treatment plan (145 Gy or 144 Gy monotherapy). The radiation oncologist (RO) was blinded to the origin of the plan prior to completing any additional plan modifications. Treatment plan modifications made by the treating RO were evaluated by computing the Dice coefficient of the prostate V150% isodose between the ML and RO (DICE\_ML), and between the RT and RO (DICE\_RT) plans. Additionally, planning time was evaluated for each treatment arm. Post-implant dosimetric outcomes were evaluated at one-month post-implant using centre-specific criteria. A paired t-test was used for all statistical comparisons with p ≤ 0.05 considered significant.

**Results:** As of January 2 2018, 30 patients had completed prostate LDR treatment, two patients no longer met the inclusion criteria and did not receive LDR brachytherapy. Of the patients who had completed LDR treatment 15 had completed 1-month postoperative follow-up at the time of submission. No significant differences were observed in the average postoperative prostate D90, V100, rectum D1cc, or rectum V100 between ML (n = 8) and RT (n = 7) arms. The magnitude of plan modifications done to the RT and ML plans were not statistically different (p = 0.243) with a DICE\_RT = 0.873 ± 0.144 (range = 0.57 - 1.00) and DICE\_ML = 0.775 ± 0.161 (range = 0.56 - 1.00). Total planning time was significantly different (p = 0.02) between the RT (44.52 ± 57.21 min, range = 7 - 227) and ML (7.25 ± 0.77 min, range = 6.07 - 8.60) plans.

**Conclusions:** Follow-up results for all 42 patients are expected by the date of the conference. An ML planning workflow has the potential to offer significant time savings and operational efficiencies, while producing non-inferior post-operative dosimetry to that of expert treatment planners.

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#### PERIOPERATIVE BRACHYTHERAPY FOR MARGIN CONTROL IN ORAL TONGUE CANCER

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**Purpose:** To assess the feasibility and effectiveness of using peri-operative brachytherapy (BRTx) for positive/narrow margins present post primary surgical resection of oral tongue squamous cell carcinoma (OTSCC).

**Materials and Methods:** This is a prospective single-institution study of patients with OTSCC (T1-3, N0-3, M0) treated with resection of primary tumour ± regional nodal resection and intra-operative insertion of BRTx catheters. BRTx was administered twice daily at 40.8 Gy/12Fr for "Positive" (≤ 2mm) margins, at 34 Gy/10Fr for "Narrow" (2.1-5 mm) margins, and not given for "Clear" (> 5 mm) margins over the course of five to six days, three to five days post-operatively.

**Results:** Out of 55 patients recruited 41 patients (74.6%) were treated with BRTx, as 12 patients had clear margins and two patients had unfavourable

tumour anatomy for catheter insertion. EBRTx was avoided in 64.3% of patients. Overall survival (OS) at three and five years was 75.6% and 59.1% respectively, while disease-specific survival (DSS) was 82.3% and 68.6% at three and five years respectively. Recurrence and survival outcomes were not associated with margin status or the use of or specific dose of BRTx on Cox regression analysis. Acute and late toxicity secondary to BRTx was minimal. **Conclusions:** The use of BRTx after primary OTSCC resection with positive/narrow margins  $\pm$  EBRTx to the neck  $\pm$  CTx achieves outcomes comparable to traditional treatment of surgery followed by re-resection or EBRTx  $\pm$  CTx. Morbidity associated with oral cavity EBRTx or secondary resection and reconstruction is thus avoided. Both acute and late toxicity rates are low and compare favourably with other BRTx OTSCC studies.

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#### IMPLEMENTATION AND VALIDATION OF IPSA ON GPU ARCHITECTURE FOR FAST MULTI-CRITERIA OPTIMIZATION FOR HDR BRACHYTHERAPY

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**Purpose:** Current implementation of Inverse Planning Simulated Annealing (IPSA) algorithm for clinical uses requires the physicists to manually tune the input weights used during the optimization process. This workflow generates a single plan which might not meet all the plan goals set by the physicians. Therefore, manual adjustment of the input weights will depend on the skill of the user and available time as it might require multiple trials to meet the plan goals. The purpose of this work is to present a graphics processing unit (GPU) based implementation of IPSA which can generate multiple plans in parallel for high dose rate (HDR) brachytherapy.

**Materials and Methods:** An HDR prostate brachytherapy geometry was used to compare the performance of CPU and GPU implementations of IPSA (cIPSA and gIPSA, respectively). PyOpenCL 2017.2.2 python library was used to implement the simulated annealing engine on the GPU. The dose points and the dwell positions were generated using our research version of cIPSA and were used in both cIPSA and gIPSA optimizations. For both codes, the same input weights were used for every plan generated. The calculations were done on a NVIDIA Titan X for gIPSA and on an Intel® Xeon® CPU E5-2620 v3 @ 2.40 GHz for cIPSA. The computation efficiency of gIPSA was obtained by timing the simulated annealing loop in both codes for 1e5 iterations and by varying the number of generated plans with gIPSA from 1 to 1e3 plans. The convergence was validated by comparing the cost functions obtained with gIPSA to the cost functions obtained with cIPSA from 1e3 plans each with 1e6 iterations using random initial seeds using the same random number generator in both codes.

**Results:** The mean value of the cost functions obtained with cIPSA was 60208 (range: 60152-60259) against 60208 (range: 60147-60275) with gIPSA based on 1e3 plans and 1e6 iterations for each plan. The computation time of the simulated annealing loop for a single plan (1e5 iterations) was 15 seconds for cIPSA and 91 seconds for gIPSA, with an overhead time of 33 seconds to run the same code by launching empty kernels on the GPU. The number of plans needed to be as efficient as cIPSA with gIPSA is around seven plans for this clinical site. Finally, for 1e3 parallel-generated plans, the computation time per plan was below 0.3 seconds for a total runtime of 222 seconds (below 4 min), which would be clinically acceptable even for this non-optimized code.

**Conclusions:** A GPU version of IPSA was implemented for HDR brachytherapy. The convergence of the mean objective function of gIPSA agrees with cIPSA. The computation time per plan decreases as the number of parallel plan increases while the overall computation time increases slowly below 1e3 plans. By varying the target and organs-at-risk weights around the standard values, multi-criteria optimization is now clinically achievable.

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#### SEXUAL FUNCTION AFTER PROSTATE SEED BRACHYTHERAPY-LONG-TERM SINGLE CENTRE EXPERIENCE

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**Purpose:** Prostate brachytherapy (PB) with radioactive seeds has been shown to have a favourable outcome in preserving erections. In this present study we analyze its long-term effect on erectile function (EF) and other influencing factors.

**Materials and Methods:** We included all patients treated with seed- PB as monotherapy who were prospectively followed and EF evaluated and recorded at our center. All patients had to have recorded pretreatment EF and at least one post-PB evaluation. EF was graded with the Common Terminology Criteria for Adverse Events (CTCAE), Version 4.0: 0 = no dysfunction; 1 = decrease, but no intervention needed; 2 = decrease, intervention indicated; 3 = decrease but erectile intervention not helpful. Only potent patients were included (CTCAE $\leq$ 2). A total of 627 patients were studied. All had an evaluation a median of eight months post-PB, n = 538 at 17 months, n = 440 at 26 months, n = 272 at 44 months and n = 124 at 65 months. Binary logistic regression analysis was used to predict factors associated with preserved EF after PB, defined as having sufficient EF for sexual activity with or without the help of medication (CTCAE $\leq$ 2).

**Results:** Median age was 64 years (IQR 60-68), 12% had diabetes, 44% hypertension, 10% a previous cardiac event. At baseline, 62% had good EF (Grade 0), 26% Grade 1 and 11% Grade 2 dysfunction. In general, of patients potent (Grade 0-2) at baseline from the time of the first evaluation throughout the last evaluation (8-65 months) 11-16% were unable to have intercourse (Grade 3 toxicity). Of the patient who did not need any medical or mechanical help at baseline, only 10-24% latter needed help (Grade 2 dysfunction) and 9-14% became important (Grade 3). Erectile dysfunction plateaued at 26 months. At this point of time, of the evaluated predictive factors for impotence (Grade 3) diabetes, hypertension, age and EF before PB were the most important factors on univariate analysis. On multivariate analysis diabetes (HR 3.9, 95%CI 1.8-8.1, p < 0.001) age >65 years (HR 2.4, 1.2-4.8, p = 0.009) and EF at baseline (HR per point increase 2.43, 1.6-6.4, p < 0.001) remained significant, but not hypertension (p = 0.1).

**Conclusions:** Preservation of EF after PB in potent patients is excellent. Only 14% lose their EF at a maximum of 65 months of follow-up. Known risk-factors for arteriosclerosis as well as age and baseline EF determine whether a patient will be able to remain sexually active after PB.

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#### RISK FACTORS FOR BIOCHEMICAL RECURRENCE AFTER A TISSUE-ABLATIVE PSA

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**Purpose:** A PSA nadir <0.2 ng/mL after any prostate cancer therapy is generally considered as tissue-ablative and at low risk for recurrence. We analyzed risk factors for recurrence after attaining such a low PSA nadir.

**Materials and Methods:** We identified patients from our institutionalized database with either D'Amico low- or intermediate-risk prostate cancer that were treated with either monotherapy low-dose rate prostate brachytherapy (LDR-PB) or monotherapy external-beam radiotherapy (EBRT) given as normofractionation (1.8-2.0 Gy per day) or hypofractionation (3 Gy per day or 5 -7.25 Gy once weekly). We compared patients who attained a nadir <0.2 ng/mL and subsequently developed biochemical failure (bF) to patients who did not experience bF using Chi-square test and Student t-test. Survival analysis was performed using the Kaplan-Meier method (log-rank test).

**Results:** From the 892 patients included for analysis, 560 (63%) achieved a nadir <0.2 ng/mL. The median value of the last PSA in patients without bF was 0.05 ng/mL (interquartile-range 0.02-0.10). A nadir <0.2 ng/mL was achieved in 38% in the normofractionation group, 31% in the hypofractionation group and 77% in the LDR-PB group (p < 0.001). The median follow-up in patients without bF was 78 months (IQR 56-102). Only 23 out of the 560 patients who achieved <0.2ng/mL (4.1%) later developed bF. The seven-year Kaplan-Meier biochemical recurrence-free survival for patients with a PSA

nadir of  $<0.2$  ng/mL was 96%. The PSA nadir was essentially identical ( $p = 0.21$ ) between patients who later developed bF versus patients without bF;  $0.044$  ng/mL ( $0.048$ ) versus  $0.057$  ng/mL ( $0.048$ ), resp. Patients who later experienced bF were more likely to have CAPRA intermediate- or high-risk cancer; (74% versus 40%,  $p < 0.001$ ), were more likely to have a diagnostic PSA  $> 6.0$  ng/mL; (66% versus 43%  $p < 0.001$ ) and had a Gleason score  $\geq 3+4$  (52% versus 34%,  $p = 0.005$ ) compared to Gleason 6. They were also more likely to be older ( $p = 0.003$ ); mean (SD)  $70.3y$  ( $6.4$ ) versus  $66.2y$  ( $6.5$ ) and have a time to PSA nadir that was significantly shorter ( $p = 0.013$ ); mean (SD)  $51.8$  months ( $29.6$ ) versus  $65.2$  ( $25.1$ ). On multivariate analysis adjusted for type of treatment, younger age (HR for 70y:  $3.1$ , 95% CI  $1.3-7.5$ ,  $p = 0.01$ ), time to PSA nadir  $> 48$  months (HR  $0.30$ , 95% CI  $0.13-0.71$ ,  $p = 0.006$ ) and lower CAPRA-score risk-group (HR  $2.81$ , 95% CI  $1.34-5.90$ ,  $p = 0.006$ ) all retained their prognostic significance predicting for lesser risk of bF.

**Conclusions:** Biochemical failure following EBRT or LDR-BT is rare after attaining a PSA nadir  $<0.2$  ng/mL. Biochemical failure is more frequent in patients with more aggressive cancers at diagnosis and in older patients. These patients should benefit from a prolonged follow-up with specialized physicians.

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#### CAN A DOMINANT INTRAPROSTATIC LESION (DIL) BOOST WITH PERMANENT I-125 PROSTATE IMPLANTS, ALTERED OUTCOMES AND IMPROVE BIOCHEMICAL DISEASE-FREE SURVIVAL (BDFS) IN INTERMEDIATE RISK PROSTATE CANCER?

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**Purpose:** To compare bDFS and toxicity outcomes in population of intermediate risk prostate cancer patients treated using I-125 LDR brachytherapy with or without DIL boost based on multiple core biopsy maps.

**Materials and Methods:** Between January 2005 and December 2013, all our intermediate risk (NCCN) prostate cancer patients treated with low dose rate I-125 brachytherapy were reviewed. Exclusion criteria were: prior pelvis irradiation, missing dosimetric data and follow-up  $\leq 4$  years. All patients were given  $144$  Gy to the prostate with a  $3$  mm margin. When data was available, a pathologic DIL distribution (defined by sextant biopsy) was contoured prospectively prior to planning, to be covered by  $150\%$  isodose line. Of the  $165$  patients treated,  $55$  received a DIL boost. Plans were generated using an inverse plan simulated annealing algorithm (IPSA). Patients completed prospectively the International Prostate Symptom Score (IPSS) questionnaire, as well as a sexual and bowel function questionnaire created at our center. Gastro-intestinal toxicities were graded according to Common Terminology Criteria for Adverse Events (CTCAE v4.03). A patient was considered to have erectile dysfunction if he was unable to achieve erection to perform intercourse. BDFS was determined according to the Phoenix consensus definitions.

**Results:** The pre-treatment age, initial PSA level, Gleason score, stage, biopsy invasion ratio, baseline IPSS score and erectile function were similar for both groups. The median follow-up was  $78$  months. More patients in the DIL group were treated with cytoreductive hormone therapy ( $21.8$  versus  $7.3\%$ ,  $p = 0.011$ ). The seven-year biochemical failure-free survival rate estimated was  $89\%$  (95% CI,  $79-94\%$ ) in the control group versus  $96\%$  (95% CI,  $74-99\%$ ) ( $p = 0.188$ ) in the DIL group. There was no difference between groups in urinary, gastro-intestinal or sexual toxicities up to five years follow-up. There was no difference in urinary obstruction with catheterization between control versus DIL groups ( $0.028$  versus  $0.036\%$ ,  $p = 1.00$ ). Only one patient in the DIL group had a Grade 3 (TURP) urinary toxicity and none in the control group. No Grade 3 or 4 gastro-intestinal toxicities were reported.

**Conclusions:** Boost to DIL shows a trend toward improvement of an excellent biochemical control with permanent seed prostate implant for intermediate risk cancer patient. No differences in toxicities were demonstrated. A prospective study with a larger population and a control cytoreductive hormone therapy may be necessary to show a statistically significant difference.

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#### SHOULD BONES BE CONSIDERED AS ORGANS AT RISK FOR INTERMEDIATE ENERGY BRACHYTHERAPY SOURCES?

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**Purpose:** Several radionuclides with high ( $^{60}\text{Co}$ ,  $^{75}\text{Se}$ ) and intermediate ( $^{169}\text{Yb}$ ,  $^{153}\text{Gd}$ ) energies have been investigated as alternatives to  $^{192}\text{Ir}$  for high dose rate (HDR) brachytherapy. The purpose of this study was to evaluate the effect of tissue heterogeneities for  $^{60}\text{Co}$ ,  $^{192}\text{Ir}$ ,  $^{75}\text{Se}$ ,  $^{169}\text{Yb}$  and  $^{153}\text{Gd}$  for prostate and oral tongue brachytherapy.

**Materials and Methods:** Plans were generated for a cohort of prostate ( $n = 10$ ) and oral tongue ( $n = 10$ ) patients. Dose calculations were performed using RapidBrachyMC, a Geant4-based Monte Carlo (MC) dose calculation engine. Treatment plans were simulated using  $^{60}\text{Co}$ ,  $^{192}\text{Ir}$ ,  $^{75}\text{Se}$ ,  $^{169}\text{Yb}$  and  $^{153}\text{Gd}$  as the active core of the microSelectron v2 source. Two MC dose calculation scenarios were presented: 1) dose to water in water (Dw,w); and 2) dose to medium in medium (Dm,m).

**Results:** The impact of tissue heterogeneities on DVH metrics generally increased with decreasing photon energy. For the prostate cases, the average PTV D90 reduction was  $1.1\%$  (range:  $0.3\%-1.2\%$ ),  $1.0\%$  (range:  $0.8\%-1.9\%$ ),  $1.0\%$  (range:  $0.8\%-1.6\%$ ),  $1.4\%$  (range:  $0.8\%-3.2\%$ ) and  $2.1\%$  (range:  $1.0\%-4.1\%$ ) for  $^{60}\text{Co}$ ,  $^{192}\text{Ir}$ ,  $^{75}\text{Se}$ ,  $^{169}\text{Yb}$  and  $^{153}\text{Gd}$ , respectively. For the tongue cases, the average PTV D90 reduction was  $1.1\%$  (range:  $0.4\%-2.0\%$ ),  $1.2\%$  (range:  $0.3\%-1.7\%$ ),  $1.3\%$  (range:  $0.6\%-2.2\%$ ),  $4.1\%$  (range:  $3.0\%-5.1\%$ ) and  $7.0\%$  (range:  $5.4\%-9.2\%$ ), respectively. By accounting for tissue heterogeneities, dose to bones were increased two- to three-fold for  $^{169}\text{Yb}$  and four- to five-fold for  $^{153}\text{Gd}$ . Given similar target coverage, for the prostate cases there was an elevated dose to the pelvic bone, up to  $50\%$  and  $70\%$  of prescribed dose for  $^{169}\text{Yb}$  and  $^{153}\text{Gd}$ , respectively, and femoral heads received up to  $30\%$  and  $50\%$  for  $^{169}\text{Yb}$  and  $^{153}\text{Gd}$ , respectively. For the tongue cases, mandibles received up to  $300\%$  of prescribed dose for  $^{169}\text{Yb}$  and  $500\%$  for  $^{153}\text{Gd}$ .

**Conclusions:** This work shows the importance of accounting for tissue heterogeneities for the evaluation of alternative sources for HDR brachytherapy. TG-43 dosimetry underestimates the dose absorbed in bones and overestimates the dose to soft tissues for radionuclides with energies lower than  $^{192}\text{Ir}$ . Intermediate energy sources may not be ideal in cases where bony structures are close to the tumour.

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#### AUTOMATIC OPTIMIZATION OF TREATMENT DOSIMETRY TO IMPROVE VISUAL OUTCOMES IN EPISCLERAL PLAQUE BRACHYTHERAPY

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**Purpose:** Current software used for planning ocular plaque brachytherapy (BT) treatments is limited to manual forward-planning. Therefore, use of differential seed strengths (Sk) or loading patterns is complicated and time-consuming. The purpose of this project is to explore the opportunity to incorporate these variables in an automated inverse-planning algorithm to provide improved dosimetry.

**Materials and Methods:** Plans were generated using COMS plaques (diameters from  $10$  to  $22$  mm) for treating tumours of various dimensions (base and height). An optimization routine using the Simulated Annealing algorithm (SAA) was generated with Matlab to solve for uniform Sk for all seeds in fully loaded plaques that best achieved the prescription dose (Dp;  $70$  Gy delivered over  $96$  hours) at the tumour apex. This algorithm was modified to determine different Sk for each seed used in the plaque so as to deliver the Dp to the tumour apex while maximizing uniformity of the basal dose (Db) distribution and achieving conformal tumour coverage. Sk values were limited to lie within the clinically available range ( $0.5-11$  U). The differential Sks obtained from the algorithm for each situation were then manually input into Plaque Simulator (PS), the clinical planning system. The dosimetry using SAA and PS was compared using point doses, dose profiles, and dose uniformity. The generated algorithm was tested for several clinical scenarios: variations in tumour dimension, location, and plaque size. This algorithm will be extended to multiple optimization goals, such as minimizing scleral hot spots or avoidance of critical vision structures.

**Results:** Treatments of a 5 mm tall tumour with basal dimensions (including 2 mm margin) equalling COMS plaque diameters of 12, 16, and 22 mm and normalized to deliver 70 Gy Dp with SAA are discussed here. For the 3 plaque sizes, SAA yielded median [min-max] Sk values of 9.94 [0.97-9.94] U, 6.05 [0.77-8.25] U, and 2.85 [1.22-6.21] U, respectively, and average Db of 228.5±35.9 Gy, 169.3±31.9 Gy, and 153.4±6.73 Gy, respectively. This technique of using differential Sk reduced the Db variation on average by 46.2% to using uniform Sk. As a comparison, Sk values generated by SAA and input into PS yielded on average doses to apex 3.0% lower for all the above scenarios. The dose profiles at the base and through the center of the tumour were comparable to the differences seen for point doses. A similar trend was seen for a 3 mm tall tumour. Investigation of changing tumour location on the eye is under progress.

**Conclusions:** An automated dose optimization algorithm is presented, capable of generating ocular plaque BT treatment plans employing non-uniform seed strengths or complex loading patterns. This allows for improved treatments aimed at maximizing dose conformality and critical structure avoidance, with the potential of improving patient visual outcomes.

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#### OCULAR BRACHYTHERAPY TUMOUR APEX AND SCLERAL DOSES DURING CONCURRENT SILICONE OIL VITRECTOMY TREATMENT

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**Purpose:** To determine the dose differences at the tumour apex and along the inner sclera for two patient and three generic cases when performing I-125 COMS plaque brachytherapy for patients having concurrent vitrectomy treatments, in which the vitreous has been replaced with polymethylsiloxane (PDMS) silicone oil.

**Materials and Methods:** Monte Carlo simulations using MCNP6 were performed to compare dosimetry for all eye materials assigned as water, and for the vitreous (excluding the tumour) composed of PDMS oil. Both simulations include the plaque materials (Modulay and Silastic) and interseed attenuation. Generic cases were simulated with a tumour height of 5 mm and basal diameter 4 mm smaller than the plaque diameter, for 12, 16, and 20 mm COMS plaques. Two patient cases were analyzed for which the patients had undergone a PDMS vitrectomy to treat intra-ocular pathologies; not for attenuation/shielding purposes. One patient had a tumour height and basal diameter of 6 mm and 7 mm, respectively, requiring a 16 mm plaque, which caused the line of sight between the outer seeds and the tumour apex to cross nearly equal parts of PDMS oil and tumour before reaching the tumour apex. The other case, treated with a 20 mm plaque, had a wider tumour with a height and maximum basal diameter of 10.5 mm and 18 mm, respectively, such that the line of sight of seeds did not pass through oil to reach the apex.

**Results:** The doses were substantially decreased along the sclera when PDMS oil replaced water in the vitreous chamber, ranging from a decrease of 1% at the tumour-scleral edge, to a maximum of 63% at the opposing sclera. The tumour apex doses were decreased by 3.1-9.4%, the largest decrease being for the 16 mm COMS patient case. The highly attenuating PDMS oil decreases photon backscatter into the tumour at the tumour/PDMS interface, causing a decrease in dose to the tumour while substantially shielding other parts of the eye.

**Conclusions:** Previous studies have focused on the shielding effects of silicone oil for critical structures in the eye, but have not assessed changes in dose within the tumour volume. The present study confirms the shielding effects, and further indicates that tumours could be under-dosed if the presence of the silicone oil is not accounted for. The amount of shielding achieved was also found to depend on both tumour size and distance from the tumour.

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#### TRUEBEAM EDGE VMAT SRS TREATMENT PROCESS OF A PINEAL PARENCHYMAL TUMOUR

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**Purpose:** Pineal parenchymal tumours (PPT) are uncommon in general and rare in the adult population. Currently, the optimal treatment for PPT of intermediate differentiation (PPTID) in older patients is unknown. Radiosurgery has been used as both primary and adjuvant therapy, with single or fractionated doses using Gamma Knife or CyberKnife. A 77-year-old female presented with gait instability and cognitive decline secondary to hydrocephalus from a PPTID. Biopsy confirmed PPTID and negative CSF; she was initially treated with ventriculostomy and external ventricular drain. To limit radiation toxicity to normal brain and considering logistical concerns as well as the patient's age, whole craniospinal and ventricular irradiation were decided against and she was treated with single fraction VMAT-based stereotactic radiosurgery (SRS) with a Varian TrueBeam Edge linear accelerator. This work presents the treatment process for PPT using VMAT-based SRS.

**Materials and Methods:** The patient received contrast enhanced MRI and CT imaging for contouring and treatment planning. Tumour and organ-at-risk, particularly the brainstem, contours were verified using the MRI such that the interface between the brainstem and PPT could be accurately determined, as the PPT was located immediately superior to the brainstem. PPT CTV volume was 2.17 cc, and PTV volume was 3.4 cc (1 mm margin expansion). The treatment plan contained three non-coplanar arcs with couch and collimator angles optimized to avoid the brainstem as much as possible. Patient immobilization was performed with an open-faced mask (CDR Systems) and real time motion management using Varian optical surface monitoring system (OSMS). To ensure proper patient set-up at least one kV CBCT was performed before each arc until maximum required shifts were 0.06 cm or 0.3° using six DoF couch motions.

**Results:** The prescription dose was 18 Gy to the 80% isodose to the PTV boundaries. After VMAT optimization the maximum dose in the PTV was 23.7 Gy, the mean dose was 21.2 Gy, and the conformity index was 1.21. Brainstem V10Gy and V15Gy were 0.45 cc and 0.08 cc, respectively, and the brain V12Gy was 9.4 cc (including PTV volume). Mean couch shifts and rotations following kV CBCT alignments before each arc were 0.02 cm and 0.1°. OSMS monitoring indicated average movement of < 0.2 mm and 0.1° in any direction during treatment. The patient will receive repeat MRI's every 6 months to assess tumour control; outcome results are currently pending.

**Conclusions:** Radiosurgery is a viable treatment option for PPT. A treatment process was developed for PPT receiving single fraction SRS. Treatment planning was optimized to cover the tumour while minimizing dose to the brainstem, and multiple patient monitoring and immobilization systems were used to ensure the accuracy of treatment delivery required for such a tumour.

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#### PRIMARY-SCATTER SEPARATED DOSE COMPARISON OF THE ADVANCED COLLAPSED CONE ENGINE FOR AN I-125 BRACHYTHERAPY SOURCE

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**Purpose:** To determine the accuracy of each dose component (primary, first scattered, and multiple scattered) calculated by the Advanced Collapsed cone Engine (ACE) algorithm for a single I-125 seed in water.

**Materials and Methods:** Primary-scatter separated point dose deposition kernels and TG-43 data was generated for the model 6711 I-125 seed and incorporated into a research version (v4.6) of Oncentra Brachy (OcB) containing the ACE algorithm, which allows the user to separately calculate and display each component of dose. A single model 6711 seed was placed in the centre of a 15x15x15 cm<sup>3</sup> water box, and each dose component was calculated on a 0.5x0.5x0.5 mm<sup>3</sup> grid, using the default number of transport

directions for high accuracy mode. The total irradiation time was set to deliver 5 Gy at 1 cm from the source on the transverse axis based on the TG-43 calculations for a 3 mCi (3.81 U) source. The same dwell time was also used for ACE calculations. The identical source model was created in *egs\_brachy* in the centre of a water box and each component of dose was simulated and scored in a matching 0.5x0.5x0.5 mm<sup>3</sup> grid surrounding the source, using the same source strength and dwell time as for ACE calculations. Local and global (relative to the dose at 1 cm from the source on the transverse axis, to assist in assessing clinical relevance) percent differences were compared for each dose component as determined by ACE and Monte Carlo (MC) within a 6x6x6 cm<sup>3</sup> region around the source.

**Results:** Local dose differences calculated by ACE and MC for the total dose and primary dose components were on average 3.6% and 4.6%, respectively, with better agreement closer to the source (0.6% and 0.9%, respectively, within a central 2x2x2 cm<sup>3</sup> region). The first and multiple scatter components showed larger average differences (11.0% and -14.2%, respectively); however as they were opposing in value, once summed, the total scattered component agreed very well, with an average difference of -0.7%. Global percent differences were in general very low, on average < 2% in any region. In general, regions in which the local percent differences were large had very low global percent differences indicating that relative to the dose at 1 cm from the source, the doses are very low; therefore, these differences may not be clinically relevant.

**Conclusions:** Each dose component calculated by the ACE algorithm was compared to MC simulations using *egs\_brachy*. Larger total dose differences were observed further from the source as is typical for collapsed-cone based calculations. Individual scattered dose components were found to show larger differences which may warrant further investigation, however the total scattered dose agreed well. Larger disagreements were generally found in regions of very low dose and therefore are expected to be of less clinical concern.

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#### LONG-TERM TUMOUR CONTROL IN A PROSPECTIVE SINGLE ARM STUDY OF POST-OPERATIVE ADJUVANT PARTIAL BREAST IRRADIATION UTILIZING HIGH DOSE RATE INTERSTITIAL BRACHYTHERAPY

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**Purpose:** To report long-term tumour control in a prospective single arm study of post-operative adjuvant partial breast irradiation utilizing high dose rate interstitial brachytherapy using CT-planned high-dose-rate (HDR) multi-catheter interstitial brachytherapy.

**Materials and Methods:** Between May 2003 and December 2005, 30 subjects with low-risk breast cancer were treated with adjuvant accelerated partial breast irradiation (APBI) using multi-catheter interstitial HDR brachytherapy. All subjects fulfilled the following criteria: age > 50 years; invasive ductal histology; T < 3cm, pN0; ER positive; LVI negative; and surgical margin > 0.2cm. Pre-implant CT was performed four to eight weeks following breast-conserving surgery. The PTV was the excision cavity + 1.5 cm, excluding chest wall and 0.5 cm from skin. An ideal virtual implant was created based on the Paris System. Post-implant CT planning was performed, delivering 32.4Gy in 9 BID fractions over five days, using an Iridium-192 HDR after-loading system. Long-term recurrence rates have been updated.

**Results:** Mean tumour size was 1.2 cm (range: 0.4-2.1 cm). At mean follow-up of 12 years and one month (minimum = 11 years and 10 months; maximum = 14 years and four months), patient and disease status were as follows: twenty-five patients are alive with no evidence of active disease; one died due to systemic relapse at four years and two months; four died due to unrelated causes. One patient developed nodal relapse and two developed cancer in the ipsilateral treated breast. New primaries developed in the contralateral breast in two patients. In the patient with nodal relapse, this developed at three years and eight months from initial treatment and was salvaged with axillary dissection and adjuvant nodal irradiation. The patient has remained alive with no evidence of disease, 12 years and nine months from initial treatment. In one of the two patients who developed further cancer in the treated ipsilateral breast, this occurred in a diagonally opposed quadrant at two years and four months and was managed with

salvage mastectomy and chest wall and nodal irradiation; she has remained alive, 13 years after initial surgery and APBI. In the second patient, cancer developed in the same quadrant at seven years and seven months; she was managed with mastectomy and remains alive, 13 years and three months after initial surgery and APBI. Neither received adjuvant hormonal therapy. In both cases the cancer was reported as pathologically likely represent a second primary than a recurrence.

**Conclusions:** Adjuvant APBI using HDR brachytherapy as delivered in this study appears to provide good local disease control, comparable to that achieved with whole breast irradiation (WBI). Results from large clinical trials comparing APBI to WBI are awaited to confirm equivalency.

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#### A PERMANENT BREAST SEED IMPLANT PILOT STUDY: MEDIUM-TERM DISEASE CONTROL OUTCOMES

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**Purpose:** To present preliminary results from a prospective pilot study of post-operative adjuvant partial breast irradiation employing Permanent Breast Seed Implant (PBSI).

**Materials and Methods:** Between June 2012 and June 2014, a prospective single arm feasibility study of PBSI, using palladium-103. Women aged > 60 years who have undergone breast conserving surgery with low risk of local recurrence were eligible. Other eligibility criteria included T1 N0, LVI negative, ER/PR positive, HER-2 negative, and maximum seroma equivalent diameter 3 cm. The PBSI procedure of was performed under conscious sedation in outpatient. External markers and a back-pointer bridge guided technique were employed. CT planning was with MIM Symphony. A peripheral weighted planning strategy to provide greater than 98% coverage by the 90Gy prescription dose to a PTV was followed. PTV is defined as the seroma + 1 cm margin, cropped 0.5 cm off skin and at chest wall. Post-implant dosimetry is assessed on evaluative PTV (PTV<sub>eval</sub>) defined by seroma plus 0.5 cm margin.

**Results:** Between June 2012 and June 2014, fourteen consenting patients were accrued and treated using this adjuvant partial breast brachytherapy technique. Median age was 68 year (range = 60-82). Median tumour size (largest dimension) was 1.2 cm (range = 0.4-1.8 cm). Nine patients were commenced on adjuvant hormonal therapy (Tamoxifen and/or Aromatase Inhibitor); one of those discontinued after 10 months due to intolerance. Seroma volume ranged from 0.6 - 20.2cc (median 5.5 cc). The resulting pre-planned PTVs, ranging 29-114 cc (median 61 cc) were covered using an average of 80±22 seeds in 19±5 needles. The average post-procedure results at days zero for the PTV<sub>eval</sub> were: D90 = 88 Gy, V100 = 89%, V150 = 62, V200 = 38%, and skin surface dose to 1.0x1.0cm<sup>2</sup> area was 51%. After a median follow-up of 51 months (range = 40-64), no in-breast, nodal or systemic relapse occurred. Of the total 14 treated patients, one died at 39 months after treatment from metastatic serous endometrial adenocarcinoma. There were no radiation safety concerns with PBSI. This was confirmed by partner badge measurements, which all read well below the 5mSv caregiver limit, and patient radiation survey readings performed on day 0 and day 30. Overall, patients report being extremely satisfied at both questionnaire time points. **Conclusions:** Post-operative adjuvant partial breast irradiation with Permanent Breast Seed Implant as used at this centre has produced good medium-term tumour control. Results from large randomized trials comparing adjuvant whole-breast irradiation to partial breast irradiation are awaited. Longer-term follow-up is also required on the patients in this pilot study to better validate its effectiveness.

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#### MECHANICAL PERTURBATION ENHANCED POWER DOPPLER ULTRASOUND IMAGING FOR IMPROVED INTRA-OPERATIVE LOCALIZATION OF INTERSTITIAL BRACHYTHERAPY NEEDLES

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**Purpose:** Ultrasound (US)-guided high dose rate interstitial brachytherapy for the treatment of localized prostate cancer requires efficient and accurate localization of needle tips in a set of multiple needles. It is imperative for both patient safety and treatment success that needle localization overcomes the intrinsic limitations due to artifacts from nearby needles in the field of view. To improve real-time intra-operative needle tip visualization and digitization, we investigate power Doppler (pD) imaging while applying mechanical perturbations to the needle of interest. We report the results of a preliminary set of experiments utilizing the proposed technique in phantom. **Materials and Methods:** A tissue-mimicking agar gel was made with a cavity for use with a biplanar (US) probe, US system and prostate template (Eckert and Ziegler BEBIG, Berlin, Germany) which was used to guide the interstitial needles (Varian Medical Systems, Ca, U.S.) into the phantom. A series of 2D sagittal static US images were acquired at five different needle insertion depths in both brightness (B) and pD modes, and for each depth, the distance from the end of the needle to the template (the "end length") was measured using a ruler. The latter provided the true relative needle tip displacement for four of the positions relative to a reference fifth position. During pD image acquisition, an electromagnetic motor was used to vibrate a metal mandrin placed within the needle of interest. The experiment was then repeated, inserting an additional proximal needle to intentionally produce shadowing and reverberation artifacts. Relative needle tip displacement was measured directly on the US image for each needle position ( $n = 5$ ) and compared to the change in the needle end length.

**Results:** In the first set of measurements, with no shadowing or reverberation artifacts present, the difference between physically and digitally measured needle tip displacement was  $0.7 \pm 1.4$  and  $0.1 \pm 0.3$  mm for B mode and pD respectively (average  $\pm$  standard deviation). In the second case, when a proximal needle was present in the US image, the difference was  $0.6 \pm 2.1$  and  $-0.3 \pm 0.9$  mm for B mode and pD respectively.

**Conclusions:** In this preliminary phantom study, Doppler-based visualization of a mechanically perturbed needle of interest proved possible with reduced error and variability compared to B mode localization of needle tips, and so may offer additional information to the radiation oncologist and physicist for improved needle digitation accuracy and precision in interstitial prostate brachytherapy. Work is currently underway to further validate this technique in a phantom simulating a representative multi-needle implant, concentrating on optimization of the mechanical perturbation and imaging parameters to facilitate its use in the clinic.

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#### TREATMENT RELATED CERVICAL NECROSIS IN THE SETTING OF IMAGE GUIDED ADAPTIVE BRACHYTHERAPY (IGABT): A CASE SERIES WITH DOSIMETRIC ANALYSIS

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**Purpose:** Cervical necrosis has been reported as a rare complication of radical chemoradiation for cervical cancer, with estimated rates 1-2%. Since the implementation of image guided adaptive brachytherapy (IGABT) at our centre, there have been four diagnosed cases. These cases led to concern that the rates of cervical necrosis were higher a result of changes made to the brachytherapy techniques.

**Materials and Methods:** A single institutional retrospective review of consecutive patients treated with IGABT was conducted to determine the incidence of cervical necrosis. Cervical necrosis was diagnosed by biopsy, and recurrent disease excluded by biopsy, imaging and clinical examination on follow up. To determine if the change in brachytherapy technique could be responsible for the increased toxicity rate, standard radiation plans with a dose prescription to Point A were created using the IGABT images. Dose metrics were compared between the standard plan and IGABT delivered plan.

**Results:** A total of 42 patients completed radical chemoradiation for cervical cancer with IGABT from July 2015- April 2018. Patients were treated with a ring and tandem applicator system. Four patients were identified as having cervical necrosis, representing an incident rate of 9.5%. Average age was 44, all were Stage 2B and two smoked cigarettes. Mean time to presentation was 34 weeks post treatment. Treatment varied from observation to antibiotics and pain medications, with symptoms resolving within 1-2 months.

CTV<sub>HR</sub> volumes at time of brachytherapy for the four patients were 17.5, 23.2, 29.4 and 35.0 cm<sup>3</sup>. There were no discernable differences between the delivered plan and standard Point A plans in terms of the Point A dose, CTV<sub>HR</sub> D90, V100, V150, or V200. There was a trend for a higher D98 dose in the delivered plans compared with standard (94.6 vs 86.9,  $p=0.06$ ) and an increase in the average rectovaginal dose point in the delivered plans (71.9 vs. 61.5,  $p=0.05$ ). The ratio of ring dwell time / total (ring+ tandem) dwell time was higher in the IGABT plans as compared to standard Point A plans (29% vs 19%,  $p=0.008$ ). The CTV<sub>HR</sub> D90 (EQD2<sub>10</sub>) of all four patients exceeded the EMBRACE 2 constraint of 95Gy. Three of the four patients had a recto-vaginal dose that exceeded the EMBRACE 2 limits of 65Gy.

**Conclusions:** This study found that the incidence of radiation induced cervical necrosis in our IGABT cohort to be higher than the values reported in literature from the 2D standard planning era. We hypothesize that this increase in toxicity is a result of the increased vaginal / cervical dose received from loading the ring to cover disease. Improvements to IGABT planning at our centre since this study include adopting the upper limit of CTV<sub>HR</sub> D90 of 95Gy, monitoring the dose delivered by the ring, and restricting the recto-vaginal dose to < 65Gy.

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#### RESPONDING TO THE BREAKDOWN OF THE SOLE RADIOTHERAPY MACHINE IN UGANDA

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**Purpose:** Road to Care (RTC) is a Canadian charity that provides Ugandan patients diagnosed with curable cervical cancer the financial and logistical means to access radiotherapy treatment. Between 2009 and 2016, RTC supported 529 patients to access radiotherapy in Uganda at the Uganda Cancer Institute (UCI). This work was interrupted in March 2016 when the sole cobalt radiotherapy machine in Uganda broke down irreparably.

**Materials and Methods:** The decision was made by RTC to look for alternative treatment pathways. Options for out of country radiation therapy were investigated. A care pathway was created for patients to receive external beam radiotherapy at a significant discount at the Aga Khan University Hospital (AKUHN) in Nairobi, and concurrent chemotherapy was offered compassionately by Jalaram Medical Services in Nairobi, Kenya. RTC leased, furnished and stocked an apartment in Nairobi and hired a driver to shuttle patients to and from their appointments. Patients were given funds by RTC to sustain themselves during their stay in Nairobi. By the time the tenth patient had completed treatments under this arrangement, the AKUHN had signed a memorandum of understanding with UCI to provide external beam radiotherapy to Ugandans free of charge.

**Results:** Patients presenting clinical signs of cervical cancer, but unable to afford diagnostics tests and treatment, continued to be referred to RTC. Patients found to have Stage 1B-2B cervical cancer, age < 60 and willing to travel out of country for treatment were enrolled in our alternative pathway. A total of 32 patients qualified and travelled to AKUHN in Nairobi. Two patients were found to have early stage disease (1A) and were treated surgically. Thirty patients completed radical chemoradiation in Nairobi, with seven receiving brachytherapy at AKUHN and 23 returning to UCI for brachytherapy. The patient cohort had an average age of 48, and the majority had Stage 2 disease (78%). A new cobalt radiotherapy has now been installed UCI in Kampala, Uganda and has been treating patients since January 2018.

**Conclusions:** Establishing a financially supported alternative treatment pathway for Ugandan cervical cancer patients was feasible and allowed for 32 women to receive lifesaving treatment in Nairobi, Kenya. International collaboration and cooperation was key to the success of this alternative care pathway.

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### QUALITY ASSURANCE ASSESSMENT FOR THE TREATMENT OF LOCALLY ADVANCED CERVICAL CANCER USING DELPHI CONSENSUS GUIDELINE QUALITY-OF-CARE INDICATORS: A SINGLE-INSTITUTIONAL EXPERIENCE

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**Purpose:** Cervical cancer is the third most common gynecologic cancer in Canada and is the leading cause of cancer death in women worldwide. With advances and variations in treatment of locally advanced cervical cancer (LACC) patients, best-practice guidelines have been developed using a modified Delphi method (Croke, 2016). The purpose of the study is to evaluate the quality of our institutional brachytherapy program based on these guidelines.

**Materials and Methods:** A quality assurance audit was conducted on all patients with LACC treated with external beam radiotherapy (EBRT) and intracavitary brachytherapy in 2016. Compliance to 40 radiation therapy key quality-of-care indicators (KQIs) was assessed, with 25 identified as top-tier indicators.

**Results:** Twenty-three patients with LACC were identified from our institutional brachytherapy database. A compliance rate of 100% was identified in 13 of 25 top-tier indicators, and 26 of 40 KQIs. Non-compliance (<100%) with top-tier indicators was identified as follows: Interval from radiation oncology referral to consultation  $\leq 10$  working days (96%); interval from "ready to treat" to "start of treatment" is  $\leq 10$  working days (87%); reproductive status is documented in the medical record (91%); prescribed EBRT dose is  $\geq 45$  Gy in 1.8-2 Gy per fraction (96%); total external beam plus brachytherapy treatment time is  $\leq 56$  days (91%); complete blood count, creatinine, and magnesium are assessed before each cycle of chemotherapy (91%); 3D conformal RT is used (not including IMRT) (17%); radiation oncology peer review of the treatment plan occurs before 25% of the total dose is delivered (87%); total EBRT plus brachytherapy (point A or HRCTV EQD2) is  $\geq 80$  Gy (96%); use of a vaginal dilator is discussed with the patient post-treatment and documented in the medical record (39%); use of hormone replacement therapy (HRT) is discussed with the patient post-treatment and documented in the medical record (26%); sexual function is documented in the medical record immediately following treatment and at follow-up (43%).

**Conclusions:** The use of quality-of-care indicators identified several areas for improvement in our delivery of cervical cancer patient care, which mostly pertain to the follow-up discussion and formal documentation of vaginal dilator use, HRT and sexual function. Our institutional practice of routine IMRT/VMAT use for cervical cancer is in opposition to these documented quality indicators, but subject to ongoing investigation. Although not considered a top-tier indicator, the discussion of patients at multidisciplinary tumour board before treatment (9% compliance rate) was identified as an area needing improvement. This quality assurance audit identified strengths and weaknesses of our cervical cancer treatment program and will be used as the basis for ongoing service improvement initiatives.

Reference: Radiation therapy quality-of-care indicators for locally advanced cervical cancer: A consensus guideline (Croke)

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### MONTE CARLO DOSE CALCULATIONS MODELLING EDEMA RESOLUTION IN PERMANENT IMPLANT PROSTATE BRACHYTHERAPY

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**Purpose:** To investigate the dosimetric effects of edema for permanent implant prostate brachytherapy (PIPB) using patient-specific advanced model-based (TG186) and deformable dose calculations.

**Materials and Methods:** Clinical datasets for three PIPB patients are considered with varying amounts of prostatic calcifications. Virtual patient models involving non-water tissues are developed from 30-day post-implant CT images. These models are developed for different edema magnitudes corresponding to different time points after seed implantation. The prostate is expanded isotropically about its centre of mass. Implanted seeds (I-125)

and calcifications, identified from post-implant CT, are relocated in a manner consistent with the movement of prostate tissue. Dose distributions are calculated using *egs\_brachy*, a fast EGSnrc-based Monte Carlo (MC) code for brachytherapy. Detailed source models are overlaid on patient geometry and calculated doses are mapped to the 30-day post-implant geometry to compare with the dose calculated ignoring edema.

**Results:** When comparing full-tissue MC dose calculations with and without edema, the edematic swelling in response to source implantation has considerable effects on dose distributions. For the maximum edema magnitude of 0.38 (fractional increase in prostate volume), D90 is reduced by up to 20 Gy while V100 is reduced by up to 18%. All dose metrics are reduced by approximately 17%, with the exception of D99.9 which showed considerable inter-patient variation. All volume metrics are reduced by expansion. Dose distributions demonstrate reduced coverage at the centre of the prostate due to seed movement. Metrics extracted from the doses mapped to the 30-day post-implant geometry are systematically lower than those extracted from the (unmapped) doses calculated on the expanded prostate geometry.

**Conclusions:** Prostatic edema has a considerable effect on dose distributions for PIPB, and should be considered in advanced model-based (MC) dose calculations; large dose differences are expected in comparison with the current clinical standard of water-based TG43 calculations ignoring prostate edema. Future work will investigate different approaches for edema modelling and resolution over a larger patient population.

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### PROSTATE BRACHYTHERAPY INTRAOPERATIVE DOSIMETRY BASED ON TRANSRECTAL-ULTRASOUND PROSTATE CONTOURS THAT HAVE BEEN DEFORMED TO ACCOUNT FOR PROBE REMOVAL

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**Purpose:** Using prostate brachytherapy implanted seeds as control points in a Finite-Element transformation, prostate deformation due to the ultrasound probe pressure was computed and used to perform intraoperative dosimetry. **Materials and Methods:** A research study was designed and approved by our institutional research ethics board. Seven prostate brachytherapy patients who consented to participate in this study underwent the following supplementary imaging interventions intraoperatively: 1) A TRUS volume study performed midway through the implant, and 2) five fluoroscopic images acquired at the end of the implant at different angles around the patient, once with the ultrasound probe inserted (probe-in) and again when it was retracted (probe-out). The prostate boundary along with the seeds present at mid-implant were segmented on the TRUS images. The locations of all the implanted seeds with the probe in and the probe out were obtained via 3D reconstruction of the fluoroscopic images. Localized seeds on the TRUS and fluoroscopic images were used to register the prostate contours to the seed locations, after which dosimetric analysis was performed. The process of removing the probe effect on the prostate boundary involved several steps. First, the probe-out seed cloud was rigidly registered to the probe-in seed cloud. Then, the residual movement of each implanted seed was calculated and used as an input to a finite element algorithm to infer the deformed prostate contour in the absence of the ultrasound probe.

**Results:** Rigidly registering the probe-in seed cloud to the probe-out seed cloud showed translation of the prostate in the craniocaudal and anteroposterior directions, as well as rotation around the patient's horizontal axis, both of which are expected to be due to probe pressure. In order to assess the dosimetric effect of prostate compression from the ultrasound probe, we performed dosimetric analysis with both the original and deformed prostate contours, which showed a root mean square difference of 0.56% for V100% (Volume of the prostate that received 100% of the prescribed dose) and 1.56 Gy for D90% (Dose received by 90% of the prostate volume). We also compared the deformed prostate dosimetry to the standard post-implant (day 0) CT dosimetry, which yielded 3.43 % and 7.18 Gy root mean square difference in V100% and D90%, respectively.

**Conclusions:** The results of this study have demonstrated that the prostate deformation caused by the presence of the ultrasound probe has minimal

effect on the dosimetry. Also, our intraoperative dosimetry result obtained using a combination of US and fluoroscopic imaging appear to be within reasonable range of post-implant CT results, considering that CT dosimetry suffers from relatively large uncertainties due to interobserver variation in prostate contouring.

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#### BRACHYTHERAPY IN THE MANAGEMENT OF ESOPHAGEAL CANCER: A SINGLE INSTITUTION EXPERIENCE

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**Purpose:** Esophageal brachytherapy has been shown to be effective in palliating dysphagia. This treatment enables delivery of a high dose of radiation therapy (RT) to the tumour whereas dose is limited to nearby organs, which allow its use in salvage after a prior external beam RT. Despite known efficacy and available guidelines, brachytherapy remains underutilized. This study evaluates the practice of brachytherapy, symptomatic response to this treatment, and observed toxicities at a single centre.

**Materials and Methods:** A literature review was carried out to identify and review the articles related to brachytherapy in management of esophageal cancer. A retrospective chart review was conducted after identifying 28 patients who received esophageal brachytherapy at our centre from 2009-2017. A review of medical records provided information about their diagnosis, management and follow-up. Descriptive statistics were utilized along with Kaplan and Meier method for time to event variables. The usual brachytherapy dose was 18 Gy in 3 fractions over one to two weeks and the external beam RT dose used was 50 Gy in 25 fractions over five weeks. Mellow and Pinkas dysphagia scoring system was used to assess swallowing.

**Results:** Most (71.4%) patients were male. Approximately two thirds of patients had an adenocarcinoma located in the lower thoracic esophagus. Majority (68%) received brachytherapy for persistent dysphagia with a palliative intent. Eight (29%) patients received brachytherapy after developing a local failure post curative intent treatment for salvage. One patient received curative intent brachytherapy in combination with EBRT. Majority (56%) of patients had an improvement in swallowing following brachytherapy. The median dysphagia-free survival after intraluminal brachytherapy was 13.6 weeks (CI 5.2-21.9). A proportion of patients did not respond where reasons were multifactorial. The observed complication rate was favourable. Only two (7%) patients developed strictures requiring dilatation and three (10.6%) had bleeding that was controlled. There were no esophageal perforations, development of tracheoesophageal fistulas or mortality associated with brachytherapy. Two patients were lost to follow up. Of the remaining 26 patients, four (15.4%) are alive and 22 (84.6%) have died.

**Conclusions:** Literature review supports the use of this modality. Esophageal brachytherapy was fairly well tolerated with an improvement in swallowing by at least one point for most patients. There were no major adverse events. It remains an effective treatment among cases where options are limited such as a local recurrence after an initial curative intent therapy, as well as for relief of dysphagia in a palliative setting. This review found esophageal brachytherapy as an effective and safe management modality. There is a need of an increase in the use of intraluminal brachytherapy and in exposure of radiation oncology trainees to gain technical expertise in its administration.

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#### DOSE TO THE BLADDER NECK: IMPACT ON URINARY TOXICITY AFTER MRI-GUIDED HDR PROSTATE BRACHYTHERAPY

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**Purpose:** The dose to the bladder neck (BN) has been suggested to be a predictor of urinary toxicity. Magnetic resonance imaging (MRI) is one of the best imaging modalities to delineate the BN. We aim to assess the impact of the dose to the BN on physician and patient-reported urinary

toxicity after MRI-guided high dose-rate brachytherapy (HDR-BT) boost. **Materials and Methods:** Fifty-one patients were treated with a single 15 Gy MRI-guided HDR-BT implant followed by external beam radiotherapy (EBRT) as part of a prospective Phase II clinical trial. MRI-based treatment planning was used. The clinical target volume (CTV) was defined as the prostate and a 2 mm craniocaudal extension was added to generate the planning target volume (PTV). Urethra, bladder, rectum and penile bulb were contoured as organs-at-risk (OARs) and dosimetric parameters collected prospectively. The BN was delineated in retrospect on T2-weighted images by the same radiation oncologist and reviewed by an independent physician. Acute ( $\leq 3$  months) toxicity and health-related quality of life (HRQoL) data were collected prospectively using CTCAE v.4 and the expanded prostate index composite (EPIC) respectively. A minimally important difference (MID) was defined as a deterioration of HRQoL scores at three months compared to baseline  $\geq 0.5$  standard deviation of baseline score. Linear and logistic regression models were used as appropriate to assess the impact of BN dose on urinary toxicity and HRQoL. A two-tailed p-value  $\leq 0.05$  was considered statistically significant.

**Results:** The median BN volume was 0.6 cc [interquartile range (IQR): 0.4-0.7]. The median maximum dose to the BN (BNDmax) and urethra (UDmax) was 20.5 Gy (IQR 17.9- 26.1) and 19.8 Gy (IQR 18.8- 21.0) respectively. The median dose to 0.5cc of the urethra (UD0.5) was 17.3 Gy (IQR:16.6-17.3). On univariate linear regression analysis, BNDmax was not significantly associated with any of the urethral dose parameters. In addition only 5.9% of the total amount of variation in BNDmax was explained by the UDmax ( $R^2 = 0.059$ ,  $p = 0.09$ ). Acute Grade 2+ urinary toxicity was observed in 30% of patients. Among those, two patients had an acute urinary retention. No Grade 4+ toxicity was reported. Furthermore, 44% of patients reported a MID in EPIC urinary domain score at three months. None of the dosimetric parameters including BNDmax was associated with acute Grade 2+ urinary toxicity or MID. However, the two patients with urinary retention had a BND max in the highest quartile; 28.3 and 26.4 Gy ( $>175\%$  of prescription dose). **Conclusions:** While a high BN dose was observed in patients who had an acute urinary retention in our cohort, the predictive value of this parameter is yet to be determined in a larger cohort of patients. Meanwhile, with the increased use of MRI in brachytherapy treatment planning, it is worthwhile delineating the BN and paying appropriate caution to doses delivered to this anatomical structure.

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#### DEVELOPING A QUALITY CONTROL TOOL FOR CLINICAL ULTRASOUND-GUIDED HDR PROSTATE BRACHYTHERAPY BASED ON PATIENT-SPECIFIC GEOMETRIC BY USING STOCHASTIC FRONTIER ANALYSIS

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**Purpose:** To develop an experience-based quality control (QC) tool derived from the stochastic frontier analysis concept and based on patient-specific geometric knowledge to improve the quality of planning for ultrasound (US)-guided HDR brachytherapy (BT) treatment.

**Materials and Methods:** The data set in this study includes 100 clinical HDR prostate BT plans in which US was used as the sole imaging modality using Oncentra Prostate (OcP – Elekta Brachy), a real-time prostate imaging and treatment planning system. All the plans in this study were made using Inverse Planning Simulated Annealing algorithm with a single fraction of 15 Gy. ABS dose parameter recommendations for target and organs at risk were followed. The QC tool is developed by taking advantage of an economical modeling method known as statistical frontier (SF) analysis. Links between dosimetric parameters of interest, namely V100 of prostate, V75 of bladder and rectum, and D10 of urethra, and the patients' geometric parameters (GPs)<sup>TM</sup> (the volume of target, the volumes of organs at risk (OARs) including bladder, rectum and urethra) are explored as well as the Hausdorff distance between the target and OARs. SF models for US-guided HDR BT plans are compared to those developed previously based on computed tomography (CT)-guided HDR BT plans. Furthermore, the GPs associated with catheters, such as the ratio of maximum number of used catheters and the maximum surface of prostate, and the ratio of area

enclosing all the applied catheters and the maximum surface of prostate, were looked at as well. A maximum likelihood method implemented in the statistical computing package R as well as its Generalized Simulated Annealing algorithm, was used to optimized SF models. The likelihood ratio test (LRT) and p-value are used to compare the statistical importance of adding a new GP to various SF models. Additionally, the differences ( $\hat{\mu}$ ) between the optimized plans by OcP and the ones predicted from SF model are studied. Moreover, technical efficiency (TE), which represents the planner ability to generate an optimized plan, is measured.

**Results:** The results demonstrate that the prostate production frontier and the OARs cost frontiers developed previously based on computed tomography (CT)-guided HDR BT plans are not applicable in the case of US-guided HDR BT plans, and hence new frontiers are created. The probability density distributions of  $\hat{\mu}$  are negatively truncated for V100 target and negatively truncated for V75 bladder and D10 urethra. Therefore, improvements of target-covering and of bladder- and urethra-sparing are possible. The lowest TE is obtained for the target covering, since 96% of plans are under the production frontier of the V100-prostate model, and for the bladder and urethra as 89% and 78% of their plans are respectively above the cost frontier of V75 of bladder and D10 of urethra. On the other hand, rectum has the largest TE, indicating its V75 is well-optimized due to a significant attention paid clinically to minimize the dose to that OAR. Moreover, the resulted p-values due introducing the GPs of catheters show that those parameters are statistically significant in our model.

**Conclusions:** Our QC tool provides planners with information on how to achieve a balance between target-coverage and OAR-sparing in a US-guided HDR prostate BT treatment. As a result, a planner is able, prior to the treatment planning, to predict the feasible trade-off between target coverage and OARs sparing, and hence avoid OARs under-sparing or wasting time and effort trying to obtain impossible dose objectives.

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#### CNSC EXPECTATIONS FOR THE SECURITY OF PRESCRIBED EQUIPMENT CONTAINING RADIOACTIVE SOURCES, WITH EMPHASIS TOWARDS THE HIGH DOSE RATE (HDR) BRACHYTHERAPY UNITS

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In May of 2013, the Canadian Nuclear Safety Commission, (CNSC) issued Regulatory Document (REGDOC) 2.12.3, the Security of Nuclear Substances: Sealed Sources. A licence condition requiring compliance with this document, including mandatory implementation dates, was then incorporated into all affected licences in January of 2015. The requirements within REGDOC 2.12.3 came into effect for licensees holding Category 1 and 2 sealed sources in May of that year. For the remaining licensees who possess Category 3 to 5 sources the requirements came into effect on May 31 2018.

Although security criteria already exist in the regulations made under the Nuclear Safety and Control Act (NSCA), this REGDOC provides additional explanations, clarifications and guidance on the CNSC's expectations for the security of radioactive sealed sources. To further assist in clarifying expectations, the CNSC published articles and provided webinars, in order to assist licensees meet expectations prior to May 2018. Now that the deadline has passed, the CNSC continues to provide licensees with ongoing guidance on this topic.

This presentation will provide the rationale behind instituting the detailed requirements within REGDOC 2.12.3. It will further explain what constitutes an effective security system for prescribed equipment containing radioactive sources. Examples of both effective and non-effective security programs will be discussed, with the focus on High Dose Rate (HDR) Brachytherapy units. Finally, it will emphasize the security responsibilities of management and the personnel who utilize radioactive sources.

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#### SURFACE MOULD BRACHYTHERAPY FOR SKIN CANCERS: THE BRITISH COLUMBIA CANCER EXPERIENCE

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**Purpose:** To examine and report on the use of surface mould brachytherapy at our institution for the treatment of skin tumours.

**Materials and Methods:** This was a retrospective review for all patients with skin tumours treated using surface mould brachytherapy, from January 1 2010 to December 31 2017, in British Columbia. We identified 65 lesions (59 patients) that were treated with Ir-192 HDR surface mould brachytherapy. Median age at diagnosis was 83 (range = 45- 97). The majority were basal cell carcinomas (54%, n = 35) and 31% (n = 20) were squamous cell carcinomas. The most common site was the forehead or temple (30%, n = 19), 23% on the nose, 22% were on the scalp, 17% on the cheek or lip, and 6 lesions were miscellaneous located. The most commonly used RT dose was 40 Gy/10; all patients had individualized CT-based planning.

**Results:** The 2 year OS was 63.1%; most deaths were due to unrelated causes. Response was assessed in clinic around two to four months after treatment. Our complete response (CR) rate was 95.4%, and partial response (PR) rate was 4.6% (three patients). There were no stable or progressive lesions. We report a two-year Local Control (LC) rate of 88%, with recurrence at the treated site in four patients. The procedure was well tolerated and there was no Grade 3- 5 toxicity acutely or long-term. There was only one case of Grade 2 radionecrosis (CTCAE v. 4.03). The median depth of 100% isodose line was 0.5 cm, and the median surface dose = 126.5%. The median V90 = 92.3% and median V95 = 84.7%.

**Conclusions:** Surface Mould Brachytherapy for skin tumours is a safe and effective modality, with excellent response rates. It is well-tolerated and a non-invasive option that can also be used as a palliative tool for elderly patients with comorbidities.

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#### THREE-DIMENSIONAL-GUIDED PERINEAL-BASED INTERSTITIAL BRACHYTHERAPY IN PRIMARY VAGINAL CANCER: A SYSTEMATIC REVIEW OF LOCAL CONTROL AND TOXICITIES

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**Purpose:** Systematic review to evaluate local control and toxicities of perineal-based interstitial brachytherapy (P-ISBT) in primary vaginal cancers treated with three-dimensional (3D) image-based planning.

**Materials and Methods:** Systematic review of the literature using the PRISMA guideline was conducted through a search of Medline, EMBASE and Cochrane databases. This search resulted in 20 relevant manuscripts plus one manuscript found outside of the search. Selected studies evaluated the role of P-ISBT in vaginal tumours treated using 3D planning. Six of 21 manuscripts contained sufficient information for LC and toxicity calculations. Data were extracted by at least two investigators.

**Results:** A total of 252 vaginal cancer patients were treated with P-ISBT and planned with 3D image-based planning. Clinical outcomes could be identified for 112 patients and ranging from Stage I to IVA and in majority of cases Stage II-III. Most patients received 45–50.4 Gy EBRT to the pelvis followed by a P-ISBT boost with a range of median EQD2 between 23.8 and 33.8 Gy, with majority of patients receiving 28-30 EQD2 Gy. Total dose to patients were in a narrow range in median EQD2Gy (72.2 - 78.4). Patients were treated with either HDR, LDR, or PDR techniques, and a small number (two) received HDR plus PDR. Overall LC was 85% (95/112) with a median follow-up ranging from 17 to 45 months. Half of the patients (49%) had a median follow-up of at least 35 months. No significant procedure-related complications were reported. Combined late gastrointestinal, genitourinary and vaginal Grade 3 and 4 toxicity was 11.6%.

**Conclusions:** Promising LC rates were found in patients with vaginal cancers treated with perineal ISBT with 3D image-based planning. In this systematic review, tumours were most often Stage II or III and yet a LC rate of 85% was found. P-ISBT with 3D planning seems to be an effective and safe treatment for primary vaginal tumours, though further investigation is required to optimize treatment given institutional variations in technique, planning and treatment protocol.

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### A MONTE-CARLO STUDY OF CELLULAR DOSIMETRY OF RADIOACTIVE GOLD-PALLADIUM NANOPARTICLES BASED ON IN VIVO AND EX VIVO DISTRIBUTIONS

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**Purpose:** Injections of radioactive gold-palladium nanoparticles (RadAuNP,  $^{103}\text{Pd}:\text{Pd}@\text{Au}$  NPs) represent a promising prostate cancer brachytherapy method. The potential of RadAuNPs is strongly dependent on the diffusion of the nanoparticles in tumour tissue, as well as on the microscopic internalization within the cells. Obtaining in vivo distribution of RadAuNP and understanding its relationship with the sub-cellular energy deposition are essential for establishing the corresponding dosimetry models.

**Materials and Methods:** In this work, RadAuNPs were injected in a prostate cancer tumour model. Then, the particles were visualized at time-points (two hours, 24 hours and eight days) by computed tomography imaging (CT, in vivo), transmission electron microscopy (TEM, ex vivo) and optical microscopy (ex vivo). The TEM images were manually contoured for cytoplasmic and nucleus geometries, which then serve the geometric model for Monte Carlo (MC) simulation. Images were also analyzed for distribution of RadAuNPs in and around cells, which then serve the sources model of MC. The Geant4-DNA code was used to simulate all energy deposition events, including Auger electrons. Each NP was modeled as a  $\varnothing 10$  nm  $^{103}\text{Pd}$  core plus 20 nm gold coating. Various RadAuNP concentrations (relative concentration: 1 for full packing, 0.375, 0.125, defined as the number of NPs divided by that of the full packing) were simulated. To compare, scenarios of uniform distributions of RadAuNP in cytoplasm and extra-cell were also simulated.

**Results:** The overall NP concentration was estimated 68.9 mg-Au/g-H<sub>2</sub>O in the local region of injection which determines the separation between NPs in the uniform scenarios. Twenty-four hours after injection, the RadAuNPs ex vivo were observed in the form of disc-like vesicles, which is significantly different from uniform hypothetical models mostly found in literatures. For uniform scenarios, energy deposition distribution (EDD) exhibits a dotted pattern, either in cytoplasm or extra-cells only. For ex vivo distribution, the EDD exhibits a completely different pattern where energies are deposited around the vesicles. The histograms of EDD in the nucleus significantly shift towards high energy by orders of magnitude ( $\sim 10^4$ ). The deposited energies increase with increasing RadAuNP concentration superlinearly, indicating the existence of cross-enhancement and shielding effects.

**Conclusions:** This work investigates the energy deposition of a novel nanotherapeutic agent  $^{103}\text{Pd}:\text{Pd}@\text{Au}$  NPs. The observed existence of NP vesicles indicates NPs cannot be simply assumed uniform in the cell cytoplasm (or in the extracellular matrix). As a result the EDD in cell nucleus varies greatly from previously considered scenarios.

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### RISKS OF SECONDARY CANCER FOR WHOLE BREAST AND PARTIAL BREAST IRRADIATIONS - A PROPOSAL FOR A MEAN LUNG DOSE CONSTRAINT

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**Purpose:** The majority of breast cancers are diagnosed at an early-stage and the standard treatment involves limited surgery followed by adjuvant radiotherapy. Non-breast cancer mortality, including cardiac events and secondary cancers, can overshadow the benefit of radiotherapy. If constraints on the mean heart dose have been defined and measures to avert cardiac morbidity have been widely adopted, not such rules have been proposed to prevent secondary cancers. In addition many new breast radiotherapy techniques have been introduced, including accelerated partial breast irradiation (APBI), which can potentially lead to large variations in the total body exposure. This work evaluates the risks of secondary cancer for various breast irradiation techniques and proposes constraints to minimize those risks.

**Materials and Methods:** Secondary cancers Lifetime Attributable Risks

(LAR) were calculated using a modified BEIR-VII formalism to account for the specific survival of breast cancer patients. Those survivals were extracted from the SEER database using the SEER\*Stat 8.3.4 software. Doses scattered to various organs were measured into a Rando phantom with custom-made breast phantoms. Treatments delivered typical doses of brachytherapy APBI (34 Gy in 10 fractions), external beam APBI (38.5 Gy in 10 fractions) using 3D-conformal, Cyberknife stereotactic (CK), or VMAT, as well as whole breast irradiation (WBI) delivering 42.5 Gy in 16 fractions.

**Results:** Lungs had the highest mean doses, ranging from 58 to 202 cGy depending on the breast radiotherapy technique, such that lung cancers accounted for 75% to 95% of all calculated secondary malignancies. Whole breast radiotherapy and VMAT delivered the highest lung doses compared to other techniques and breast brachytherapy delivered the lowest dose. The occurrence of secondary cancers was delayed with a lag time of five years, continuing to increase up to 15 years. For a typical early stage patient irradiated at 50 and surviving beyond 80, the risk of secondary lung cancer were 1.1% for multicatheter HDR, between 2.2% to 2.5% for 3D-CRT or CK, 3.5% for VMAT APBI, and 3.8% for WBI. From the SEER database, 80% of lung cancer will die of their disease. So, the expected excess mortality is less than 1% for brachytherapy but higher than 3% for WBI. This is not acceptable for early stage breast cancer or DCIS patients.

**Conclusions:** Lung carries the highest risk of secondary cancer for good prognosis breast patients treated with adjuvant radiotherapy. APBI reduces this risk compared to WBI and should be recommended for early-stage breast cancer patients. Practically the mean lung dose should be kept below 1 Gy.

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### COST-EFFECTIVENESS ANALYSIS COMPARISON OF LINAC AND ROBOTIC BASED SBRT FOR EARLY STAGE NON-SMALL CELL LUNG CANCER

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**Purpose:** Though it is increasingly diagnosed at an early stage, with about 20% Stage I disease in The Netherlands and 15% in the USA, lung cancer continues to be the leading cause of cancer death. For those earlier stages aggressive surgical or radio-chemotherapy are justified to improve the overall survival. Lung cancer patients often present severe comorbidities precluding surgery. Such that stereotactic body radiotherapy (SBRT) has emerged as an effective solution, achieving local control rates comparable to lobectomy for small and peripheral tumours. SBRT can be delivered using linear accelerator (linac-SBRT) or using a robotic stereotactic body radiotherapy unit (robotic-SBRT). While the second option reduces the amount of normal tissue treated, possibly reducing side effects and improving quality of life, it is unknown which modality is the most cost effective.

**Materials and Methods:** We performed a comparative cost-effectiveness analysis for inoperable patients with peripheral early stage NSCLC treated either with linac-SBRT or robotic SBRT. Costs for each strategy were calculated using the Lievens et al. activity based costing method (ABC). Quality of Life utilities were extracted either from literature for linac-SBRT, or from the Erasmus prospective cohort for robotic-SBRT. A treatment of three fractions without insertion of a fiducial marker was considered. A Markov modelization was developed using the TreeAge software and transition probabilities were extracted from the literature. Incremental cost-effectiveness ratio (ICER) and strategies were evaluated with a willingness-to-pay (WTP) threshold of €50,000 per QALY.

**Results:** Robotic-SBRT treatments are slightly more expensive than linac-SBRT, €2,186 compared to €1,960. However having better outcomes in terms of QoL, robotic-SBRT had a cost effectiveness ratio (CER) of €2,395 per QALY, compared to €2,685 per QALY for linac-SBRT. The ICER for robotic-SBRT was €1,048 per QALY. At a WTP of €50,000 per QALY, all the simulations favored robotic-SBRT.

**Conclusions:** Although differences in cost effectiveness are small, robotic-SBRT was more cost-effective compared to linac-SBRT for the treatment of inoperable, peripheral early stage NSCLC patients. Since the cost of robotic-SBRT is marginally higher its cost-effectiveness superiority reflects the superior QoL outcomes of the technique.

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### ONE-YEAR COSMESIS AND FIBROSIS FROM ACCEL: ACCELERATED PARTIAL BREAST IRRADIATION (APBI) USING 27 GY IN FIVE DAILY FRACTIONS

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**Purpose:** To report one-year outcomes of a prospective trial of APBI using IMRT to deliver 27 Gy in five daily fractions. The aim of the ACCEL trial is to investigate a prescription dose regimen that can be safely delivered in one week and result in favourable efficacy and cosmesis.

**Materials and Methods:** Women  $\geq 50$  years with lymph node-negative, ER positive, HER-2 negative breast cancer or ductal carcinoma in situ (DCIS),  $\leq 3$  cm diameter, were treated following breast conserving surgery with margins  $\geq 2$  mm. After providing written, informed consent, patients with clinic staff-assessed Good or Excellent baseline cosmesis received 27 Gy in 5 daily fractions to the CT-evident seroma plus 1 cm CTV and 0.7 cm PTV margins. Clinical photographs, EORTC cosmetic score and patient reported outcomes were collected prospectively, prior to RT and at one-year post-RT. A protocol-specified, interim analysis was conducted when 50 patients had completed one-year follow-up. A panel of six physicians used two methods of cosmesis assessment: 1) a consensus overall cosmetic score was provided based on baseline and one-year photographs presented individually, blinded to time point; and 2) comparison of baseline and one-year images side-by-side to directly assess for changes over time. Fibrosis and telangiectasia were prospectively assessed at clinic visits.

**Results:** As of February 12, 2018, 55 patients had baseline and one-year post-RT images available. Median age was 65 years, 54% had left-sided tumours, 84% had invasive ductal carcinoma and 16% had DCIS alone. Of the patients with invasive disease, 55% received endocrine therapy and none received chemotherapy. Consensus photo-panel overall cosmesis at baseline was: Excellent – n = 18 (33%), Good – n = 31 (56%), Fair – n = 6 (11%) and Poor – n = 0. Consensus overall cosmesis at one year was: Excellent – n = 28 (51%), Good – n = 23 (42%), Fair – n = 4 (7%) and Poor – n = 0. Most patients had either an improvement (53%) or no change (40%) in cosmesis at one year. Among 49 patients with Good or Excellent consensus panel cosmesis at baseline, two (4%) were scored as Fair and none as Poor at one year post-RT. Comparing baseline and one year images, side-by-side, most changes were resolution of surgical effects such as scar visibility, bruising or edema. Among six patients with consensus-panel Fair cosmesis at baseline, four improved to Good due to resolution of surgical effects. Thirty-three patients (60%) had no fibrosis and 22 patients (40%) had Grade 1 fibrosis at one year. No patients had any evidence of telangiectasia or Grade 2 or higher fibrosis. There were no recurrences and no patients had ipsilateral mastectomy.

**Conclusions:** APBI using 27 Gy in 5 fractions achieved acceptable one-year cosmesis and no Grade 2 fibrosis. A pre-planned stopping rule of 5% Grade 2+ fibrosis was not observed. The trial will continue to the planned target accrual of 274 patients.

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### THE ROLE OF ADJUVANT RADIO CHEMOTHERAPY FOR GASTRIC CANCER: RESULTS OF A META-ANALYSIS

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**Purpose:** Adjuvant chemotherapy in advanced gastric cancer reduces the risk of distant metastasis and most likely increases the survival rate. Patients who are at high risk for tumour recurrence may benefit from more aggressive procedures like combined radio chemotherapy. Recently, the results of six randomized trials addressing this question have become available.

**Materials and Methods:** In the six trials of interest, in total 1171 patients with locally advanced gastric cancer were randomly assigned to receive either adjuvant chemotherapy or combined adjuvant radio chemotherapy. Published hazard ratios and hazard ratios extracted from available survival curves for local regional control and overall survival were basis of the meta-analysis.

Meta-analysis of the effect sizes on local control and overall survival was performed using a random effects model based on parameter estimates of log hazard ratios in Cox models and their standard errors.

**Results:** Additional radio chemotherapy did not result in a significant improvement of overall survival (n = 1171) (Hazard Ratio: 0.86, 95% confidence limits (CL) 0.72-1.04 p = 0.12) but a tendency towards a better benefit cannot be excluded.

**Conclusions:** Combined radio chemotherapy for advanced gastric cancer did not result in a significant improvement of the overall survival rate but a modest benefit cannot be excluded.

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### PLANNING STUDY: FROM VMAT ON A CONVENTIONAL LINAC TO DYNAMIC-TRACKING IMRT ON VERO - THE IMPACT ON RILD RISK CALCULATIONS FOR HEPATOCELLULAR CARCINOMA OF THE LIVER

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**Purpose:** Our institution has been treating hepatocellular carcinoma (HCC) liver patients with Varian TrueBeam volumetric modulated arc therapy (VMAT) since November 2013 and is now offering a Brainlab VERO-based tracking program as a treatment option for managing respiratory-induced tumour motion. The purpose of this study was to assess the impact of this change of treatment technique on previously calculated risk estimates for radiation-induced liver damage (RILD).

**Materials and Methods:** Ten HCC liver patients previously planned with Varian Eclipse treatment planning software (TPS) for VMAT delivery were anonymized and re-planned with Brainlab iPlan TPS for a static-field IMRT dynamic-tracking technique. Seven out of 10 plans were originally planned/treated with a motion-encompassing ITV (internal target volume) method and the remaining three plans were planned/treated with a gated VMAT technique. The PTV for the TrueBeam VMAT plans was generated by adding 5 mm to the CTV (for gating method) or ITV (for motion-encompassing method). For the dynamic tracking re-plan, PTV contours were created by adding a uniform margin of 8 mm from the original GTV contour. This margin was chosen based on literature recommendations for dynamic-tracking. Each dynamic-tracking IMRT re-plan aimed to dosimetrically match the original VMAT plan in terms of PTV coverage, organ-at-risk (OAR) constraints, as well as a calculated RILD risk level (accept < 5%). The RILD risk level was calculated using known Lyman-Kutcher-Burman NTCP model parameters (n = 0.97, m = 12, TD50 (primary cancer) = 39.8 Gy) and was generated from DVH data exported from iPlan using in-house MATLAB code. Tumour motion was also recorded for all ITV VMAT plans in order to explain RILD differences. Finally PTV volume and RILD were compared for all plans.

**Results:** Tumour motion ranged from 1.0 to 1.5 cm in ITV VMAT plans. PTV dose coverage requirements and OAR constraints were all met using the IMRT dynamic-tracked technique. All PTV contours in the dynamic-tracked plans resulted in reduced volumes compared the treated VMAT volumes with of an average reduction of 43 cm<sup>3</sup> (reductions ranging from 4 to 104 cm<sup>3</sup>). The risk of RILD was reduced in eight out of 10 plans (percentage point reductions ranging from 0.3% to 10.5%) while an increase in RILD percentage point of 0.1% occurred in the remaining two plans. For all three TrueBeam gated VMAT plans, the new dynamic-tracking technique resulted in a reduction in the calculated risk of RILD.

**Conclusions:** All VERO-based IMRT dynamic-tracking plans met our current TrueBeam VMAT technique dosimetric constraints. Implementing a dynamic-tracking technique will reduce PTV volumes and RILD risk factors for patients with respiratory motion as low as 1 cm.

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### VERO TRACKING QA IMPLEMENTATION: FROM GATING TO TRACKING

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**Purpose:** Our institution has been treating liver SABR patients with a Varian Truebeam gated VMAT technique since November 2013. A BrainLab VERO-based conformal beam tracking program was commissioned in September 2017. The purpose of this study is to report on the implementation of a patient-specific tracking QA program and to compare this to our current gating QA program.

**Materials and Methods:** The gating QA program uses Quasar Respiratory Motion Phantom (RMP) (Modus QA), while tracking has been implemented with a newer, cylindrical version of the phantom (CRMP). The procedure for both phantoms utilized inserts for a 0.6cc ion chamber and film synchronized with pre-recorded patient respiratory traces. The gating and tracking QA procedures consist of comparisons between ion chamber doses in motion-managed and static (non-moving chamber positioned at TPS point of measurement) scenarios as well as the planned dose. Dose is calculated in Varian Eclipse for gating and BrainLab iPlan for tracking. Film (Ashland, EBT3) analysis is done by comparing static and motion-managed deliveries via gamma analysis. Differences between QA techniques are reported for 40 gating patients versus three tracking patients.

**Results:** The dose distribution inside the insert of the RMP was often non-uniform across the chamber due to the insert's asymmetric location. The CRMP offered a more robust dose distribution for the chamber insert as well as a larger film insert that is more appropriate for liver-tumour target size. Tracking QA results were found to outperform gating results with static versus motion-managed chamber dose differences of less than 1% and film gamma pass rates greater than 99% for 2%/2mm. The chamber versus planned dose differences were on average 3.1% for gated and < 2% for tracked deliveries. The improved results for tracking QA were likely influenced by the inherent uniformity in dose distributions of conformal beams, which are currently used for tracked treatment delivery. The differences in planned and delivered doses were influenced by the treatment planning system and as such cannot be directly compared. Finally, QA beam delivery time and analysis is comparable between the two methods.

**Conclusions:** Shortcomings identified while performing gating QA effectively guided the implementation of a new tracking QA program. A robust and efficient patient-specific tracking QA program was implemented on the VERO treatment platform. Differences between gating and tracking QA results are seen but the reason for the improvement is confounded by differences such as delivery technique and the phantom used.

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#### AN INSTITUTIONAL RETROSPECTIVE REVIEW OF LOCALLY ADVANCED ESOPHAGEAL CANCER PATIENTS TREATED WITH PERIOPERATIVE CHEMOTHERAPY AND CHEMORADIOTHERAPY FOLLOWED BY SURGERY

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**Purpose:** Introduction of multimodality treatment in locally advanced esophageal cancer (LAEC) has produced promising results but the debate continues about the role of perioperative chemotherapy (PCT) versus chemoradiotherapy (CTRT) before definitive surgery. We present an institutional review of patients with esophageal cancer treated with perioperative chemotherapy and neoadjuvant chemoradiation, to assess clinical outcomes, describe the pattern of disease failure and to identify variables predictive of outcomes in these patients.

**Materials and Methods:** Patients diagnosed with LAEC treated with PCT or CTRT followed by surgery were identified through the provincial registry from 2009-2014. Survivals were compared using proportion hazard regression analysis.

**Results:** Twenty-eight patients were treated with CTRT and 21 patients treated with PCT followed by surgery. Median follow up was 28 months in CRT and 32 months in PCT groups. One hundred percent and 79% of the patients were in lower esophagus / gastroesophageal junction in PCT and CTRT groups. Most patients had adenocarcinoma (96% CT and 68% CTRT). Age, sex, histology, tumour location, Pretreatment PET SUV and tumour size were comparable between both groups. Zero out of 28 and

three out of 21 patients had complete pathological response in CTRT and CT groups respectively. One-year and two-year overall survival (OS) was 79 and 64% versus 81% and 67% for CTRT and PCT groups respectively. (HR: 0.94,  $p = 0.87$ ). One and two year recurrence-free survival was 68% and 57% versus 62% and 38% for CTRT and PCT groups (HR = 1.28  $p = 0.51$ ). When patients with complete response were excluded, one- and two-year recurrence-free survival was 61% and 33% in PCT (HR = 1.43,  $p = 0.34$ ). Body Mass Index (25-30) was associated with less recurrence ( $p = 0.022$ ).

**Conclusions:** There was a trend towards improved recurrence-free survival in patients with CTRT compared to PCT. The observed difference became larger when only patients with partial pathological response were compared. It is intriguing that patients with partial response in CTRT group had a trend for improved recurrence-free survival.

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#### MACHINE LEARNING PREDICTION OF EARLY DISTANT PROGRESSION FOR OLIGOMETASTATIC AND OLIGOPROGRESSIVE COLORECTAL CANCER PATIENTS TREATED WITH STEREOTACTIC BODY RADIOTHERAPY

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**Purpose:** Recent studies show SBRT for oligo-metastases (OM) and oligo-progression (OP) confers good outcomes and low morbidity, but clinicians face significant challenges selecting patients who will benefit from SBRT, due to complex interactions of patient, tumour and treatment factors. This study examines the ability of machine learning (ML) based classifiers to identify patients who develop early distant progression (DP,  $\leq 90$  days since treatment completion) in CRC patients receiving SBRT.

**Materials and Methods:** All CRC patients treated with SBRT to any site at a single institution for OM/OP in 2009- 2016 were retrospectively reviewed. Clinical characteristics included age, gender, pre-SBRT CEA, RAS status, ECOG performance, treatment indication (OM/OP), SBRT location, disease-free interval since last treatment (DFI), number of prior lines of systemic of therapy, prior use of ablative local therapy, PTV volume and mean PTV BED. Univariable and multivariable logistic regression was used to identify predictors of DP.

**Classification methods included:** logistic regression (LR) gradient boosting (GBM), adaptive boosting (ADA), and random forest (RF). Data was divided into training (75%) and testing (25%) cohorts with monte carlo cross-validation with 10 trials. Classifier performance was assessed by receiver operating characteristic curves. Area under the curve (AUC) values were compared using a paired t-test with Bonferroni adjustment.

**Results:** One hundred and forty-seven patients with 226 treated lesions were included; 203 treated for OM and 23 OP. 31 (15.2%) of the treated lesions were followed by DP within 90 days. No patients died or were lost to follow-up prior to the 90 days. In univariable analysis, age, CEA, treatment indication, DFI, number of systemic therapy lines and mean PTV BED were significantly associated with early DP ( $p < 0.05$ ). In multivariable analysis treatment indication, DFI, number of systemic therapy lines, and mean PTV BED and were significant predictors of DP ( $p < 0.05$ ). AUC values for the classifiers were: 0.590 (LR), 0.744 (GBM), 0.767 (ADA), 0.821 (RF). All ML classifiers were significantly better at identifying patients with DP compared to the logistic regression model ( $p < 0.05$ ). There was no statistically significant difference in performance between the various ML classifiers. The top ranked variables by the RF classifier were DFI, PTV mean dose, number of systemic therapy lines, CEA and age. These are consistent with predictors found on univariable and multivariable analysis.

**Conclusions:** Treatment indication, DFI, number of systemic therapy lines, and mean PTV BED are associated with DP. ML classifiers were significantly better at identifying patients with DP compared to the logistic regression model. The ability to predict patients at risk of DP would assist clinicians in identifying patients who may benefit minimally from SBRT for OM/OP disease.

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### PATIENT-REPORTED QUALITY OF LIFE FOLLOWING STEREOTACTIC BODY RADIATION THERAPY FOR PRIMARY KIDNEY CANCER: RESULTS FROM A PROSPECTIVE COHORT STUDY

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**Purpose:** There is growing interest in using stereotactic body radiation therapy (SBRT) for the treatment of primary medically inoperable kidney cancer. Previous retrospective studies have shown excellent disease control with minimal toxicity. However, a paucity of data exists on the effect of SBRT on patient-reported quality of life (QOL) following treatment. Here we describe the first report of QOL post-kidney SBRT.

**Materials and Methods:** Twenty-five consecutive patients were treated with kidney SBRT on a multi-institutional prospective cohort trial (NCT03108703). Patients were treated with 5-fraction SBRT ranging from 30-40 Gy in total dose. Prospective QOL assessment was carried out using the European Organization for Research and Cancer Treatment Quality of Life Core Questionnaire-15 Palliative (EORTC QLQ C-15 PAL), the Functional Assessment of Cancer Therapy-Kidney Symptom Index (FACT-FKSI-19), and the EuroQol-5D (EQ-5D) tools at baseline, one month, and three months post-treatment. All raw scores were converted using validated scoring algorithms and means ( $\pm$ standard deviation) were compared at each time point using paired t-tests.

**Results:** A total of 21 patients completed all questionnaires at baseline (84%), with 17 patients having completed them at one month (68%), and 12 patients at three months (48%). When patients did respond, all questionnaires were fully completed. No difference was observed in global QOL comparing baseline to both one and three months either with the QLQ C-15 PAL ( $74.5 \pm 29.3$  versus  $71.6 \pm 29.1$ ,  $p = 0.46$ ;  $77.8 \pm 21.7$  versus  $72.2 \pm 19.2$ ,  $p = 0.27$  respectively), FACT-NKSI total score ( $59.8 \pm 11.4$  versus  $62.8 \pm 10.7$ ,  $p = 0.13$ ;  $60.5 \pm 14.2$  versus  $60.9 \pm 14.5$ ,  $p = 0.88$ ), and EQ-5D health state index ( $0.80 \pm 0.11$  versus  $0.85 \pm 0.11$ ,  $p = 0.07$ ;  $0.82 \pm 0.13$  versus  $0.79 \pm 0.21$ ,  $p = 0.55$ ). Comparable results were observed with the EQ-5D visual analogue scale over time. Using a minimally clinical importance difference (MCID) threshold of 10 points on the EORTC QLQ scale, there was no significant worsening in individual symptom or functional scores over time; conversely, there were improvements reaching the threshold in both nausea (mean improvement of 9.7) and appetite (mean improvement of 11.1) between baseline and three months, but these did not reach statistical significance ( $p = 0.21$ ,  $0.17$ ). No statistically significant declines were observed across all symptom and functional domains. Using an MCID of 10 for the QLQ C-15 PAL, 4 for the FACT-NKSI, and 0.08 for the EQ-5D index, global QOL was stable or better at three months in 66% (eight out of 12), 66% (eight out of 12) and 75% (nine out of 12) of evaluable patients.

**Conclusions:** Patient reported QOL appears to be well-preserved following kidney SBRT. Owing to the small sample size and poor compliance, further prospective and long-term assessment is required to confirm these findings. Future analyses include correlation of QOL with outcomes, clinical factors, and dosimetry metrics.

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### PROSTATE CANCER UPSTAGING BY PLANNING MRI AND ITS IMPACT ON TREATMENT DECISIONS

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**Purpose:** Planning magnetic resonance imaging (MRI) has shown potential in reducing radiation related toxicities for prostate cancer (PC) via improved prostate delineation. Utilization of MRI may also permit improved tumour detection and more accurate T-stage classification. However, it is unclear how to incorporate MRI detected changes in T-stage in clinical practice. Our purpose was to characterize how planning MRI changed T-stage and subsequent treatment-related decisions.

**Materials and Methods:** 1.5 Tesla MRI planning was established at our

centre in January 2016. All patients undergoing MRI planning for PC until January 2018 were analyzed. All patients were evaluated in consultation with a treatment recommendation prior to planning. NCCN guidelines were used for risk stratification. T1 and T2 images were fused to the planning CT simulation. Radiation planning was according to institutional guidelines. All MRIs were radiologist interpreted prior to completion of radiation planning. Treatment modifications based on MRI results were at the discretion of the treating radiation oncologist.

**Results:** One hundred and thirty-seven patients were included in this retrospective analysis. Seventy-nine patients (58%) had a different T-stage on planning MRI than clinical evaluation, of which 13 (10%) were downstaged and 66 (48%) were upstaged. Twenty-one patients (15%) had an increase in their risk category with 17 of these patients moving from low/intermediate to high/very high risk categories. Sixteen of these 17 patients had discussions regarding modification of treatments with six patients (4%) altering the initial treatment plan based on MRI findings. Six patients had hormone therapy added or prolonged; four patients had pelvic node irradiation; two patients had radiation dose modified.

**Conclusions:** Planning MRI interpretation by qualified radiologists can potentially impact treatment decisions. The application of MRI-based staging can potentially identify patients requiring more aggressive therapy, but may potentially lead to over-treatment of others. MRI results should be discussed with patients for informed decision-making.

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### SMALLER PLANNING TARGET VOLUME IN BLADDER RADIATION THERAPY IS POSSIBLE WHEN USING DAILY CBCT AS METHOD FOR AN IMAGE GUIDED TREATMENT DELIVERY

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**Purpose:** To investigate three PTV margin expansions and to determine the most appropriate volume to be used in bladder preservation therapy when using daily CBCT.

**Materials and Methods:** Ten patients with invasive bladder cancer treated by a hypofractionated course of radiotherapy (50 Gy in 20 fractions) delivered with IMRT. Upon target delineation on planning CT simulation, the CTV was the whole empty bladder and the PTV consisted of a uniform 1.5 cm margin around the bladder (PTV 1.5 cm). Patients underwent daily CBCT imaging prior to each treatment. We retrospectively investigated 2 additional smaller PTV margin expansions, created on every CBCT, to determine the most appropriate volume to be used with CBCT as a daily image guided modality. The first additional volume was a uniform PTV margin of 1cm around (PTV 1 cm). A second volume of an anisotropic PTV margin with 1.5 cm superior/anterior and 1 cm in other directions (PTV1/1.5 cm) was created. We recorded the frequency and measured the volume of bladder falling out of each PTV based on the daily CBCT. In two additional patients, a daily pre- and an immediate post-treatment CBCT were obtained to measure the potential change of bladder filling during the treatment delivery.

**Results:** We considered an arbitrary 5 cm<sup>3</sup> of CTV falling out of the designated PTV a clinically significant volumetric miss. The frequency of such miss when applying the uniform PTV 1cm was 1%. However when applying the uniform PTV 1.5cm and the anisotropic PTV 1/1.5cm margins, it was 0.5% and 0.5%, respectively. The median of the difference in bladder volumes as measured in pre- and post- RT CBCTs was 7.6 cm<sup>3</sup>. The median interval time between CBCT sets was seven minutes.

**Conclusions:** The anisotropic PTV expansion 1.5 cm superior/anteriorly and 1 cm in all other directions around the bladder (CTV) provides a safe PTV approach when daily CBCT imaging is used to localize the treatment of an empty bladder. Only minimal bladder filling occurred during a relatively short time frame of treatment delivery. This would limit the volume of treatment in the organs-at-risk limiting the toxicities in this commonly older and fragile patient population.

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### DOSIMETRIC AND CLINICAL PREDICTORS OF RENAL TOXICITY AFTER STEREOTACTIC BODY RADIOTHERAPY FOR PRIMARY RENAL CELL CARCINOMA

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**Purpose:** Stereotactic body radiotherapy (SBRT) is an emerging treatment option for localized, inoperable renal cell carcinoma (RCC). Though previous reports have shown acceptable toxicity rates, clinical and dosimetric predictors of late renal sequelae have not been well-defined in the literature for SBRT fractionation schedules.

**Materials and Methods:** After institutional research ethics board approval, patients with inoperable RCC who were treated with a 5-fraction SBRT protocol between June 2012 and July 2017 were analyzed. Patient characteristics, dosimetric parameters and serum markers were prospectively collected. Toxicity was defined as GFR deterioration crossing at least one chronic kidney disease (CKD) stage. Absolute change in GFR was also examined. Kaplan-Meier estimates and Cox proportional hazards regression were used to examine toxicity outcomes.

**Results:** Fifty-two patients with a median GFR of 62 mL/min, median Charlson Comorbidity Index (CCI) of 8 and median tumour size of 4.1 cm (range 1.2-14.6 cm) were treated with a median dose of 35 Gy in 5 fractions (range 30-45 Gy). Median follow-up time was 9.4 months. Mean change in GFR at the time of last follow-up was -6.3 mL/min ( $p = 0.02$ ). Fourteen patients (27%) developed a worsening of their CKD stage by the time of last follow-up. Median time to toxicity was 24.8 months based on Kaplan-Meier estimates. Those who experienced progression of CKD stage had a mean pre-treatment GFR of 77.2 mL/min, compared to 57.2 mL/min in those who had stable CKD stage ( $p = 0.02$ ). On univariate analysis, higher rates of deterioration in CKD stage were seen in patients with a CCI of less than 8 ( $HR = 9.01$ ,  $p = 0.004$ ), tumour motion of more than 1 cm ( $HR = 6.0$ ,  $p < 0.001$ ), baseline Stage 1-2 CKD ( $HR = 5.9$ ,  $p = 0.02$ ), and those with more than 250cc of cortex outside of the 17.5 Gy isodose line ( $HR = 4.4$ ,  $p < 0.001$ ). No other dosimetric parameters were associated with increased rates of renal toxicity. No significant effects were seen on multivariate analysis.

**Conclusions:** The change in GFR after SBRT for primary RCC was similar to that observed in other kidney-directed treatment modalities. A recent meta-analysis reported a mean decrease in GFR after thermal ablation and partial nephrectomy of -4.5 mL/min and -6.2 mL/min respectively. Uninvolved renal cortex was the only dosimetric feature related to changes in renal function. Higher hazard of toxicity with increased tumour motion also highlights the importance of motion management in this population. Patients with lower burden of comorbidities at the time SBRT are at higher risk of late renal toxicity.

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### OUTCOMES AND TOXICITY OF STEREOTACTIC RADIOTHERAPY FOR METASTATIC BREAST CANCER - A RETROSPECTIVE COHORT STUDY

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**Purpose:** Technological advances in radiotherapy have allowed for the delivery of ablative doses to sites of disease in most parts of the body. In this trial, we describe the outcomes of a group of breast cancer patients treated to sites of metastatic disease with stereotactic radiotherapy (SBRT). Predictors of treatment outcomes are also investigated in this cohort.

**Materials and Methods:** After institutional research ethics board approval, patients with metastatic breast cancer who received SBRT to metastatic disease from 2011 to 2016 were identified by electronic chart review. Patient demographics, histologic information and clinical data were collected from the electronic patient record and the radiation treatment planning system. Outcomes of interest included local control (LC), overall survival (OS), and progression-free survival (PFS). In addition to Kaplan-Meier estimates,

univariate analysis using the log-rank test was used to assess covariates, which were identified a priori.

**Results:** One hundred and twenty patients between the ages of 25 to 82 (median 54.8 years) with 193 treated lesions were identified. Median follow-up was 9.8 months (range 0.03 to 72.31 months). Patients' molecular subtypes were 63.9% luminal A, 10.9% luminal B, 11.7% basal, 4.2% Her-2 positive and 9.2% triple positive. 70.3% had lymph node positive disease at diagnosis. The majority of treated lesions were in the spine (45%), followed by liver (20%), lung (18%) and non-spine bone (14%). There were no recorded Grade 4 or 5 toxicities, with only 5.3% of patients reporting side effects (most commonly mild pain). One-year LC, PFS and OS was 88%, 45% and 84% respectively. On univariate analysis, PFS varied depending on treatment indication (oligometastasis, oligoprogression or areas of dominant professions) with a median PFS of 24.4 months, 5.6 months and 8.1 months respectively ( $p < 0.001$ ). Similarly, a difference in OS by treatment indication was also seen with one-year survival of 91%, 82% and 57% respectively ( $p < 0.001$ ). Survival was influenced by molecular subtype, with the worst survival seen in patients with triple negative disease ( $p = 0.001$ ).

**Conclusions:** Local control rates remain excellent after SBRT to sites of metastatic disease in this population of breast cancer patients. The most significant risk for these patients remains distant failure, with significantly longer PFS in those being treated for oligometastatic disease in comparison to other indications. Favourable PFS observed in the oligometastases subgroup would support further randomized evaluation of the potential benefit of SBRT in this population, as is currently being performed in other tumour histologies.

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### PATHOLOGICALLY NODE POSITIVE CARCINOMA PROSTATE- PREVALENCE, PATTERN OF CARE AND OUTCOME FROM A POPULATION BASED STUDY

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**Purpose:** To evaluate the prevalence, patterns of care and outcome of pathological node-positive (pN+) prostate cancer (P-Ca) after radical prostatectomy (RP) from a provincial database.

**Materials and Methods:** Patients were identified from our provincial cancer registry and Prostate Cancer Outcomes Unit. From January 1 2005 to December 31 2014, there were a total of 31,096 new diagnoses of P-Ca, of which, 167 patients with pN+ P-Ca were identified. Median age was 64 years (range: 41-79); median baseline PSA 12.5 (range: 2.5-108.4). Overall 44 (26%) were in intermediate risk and 121 (73%) were in high risk group. Surgical failure, defined as post-operative PSA > 0.4, was seen in 42 (25%) patients, 15 (36%) of whom were treated with salvage androgen deprivation therapy (ADT) and radiotherapy (RT), and 24 (57%) managed with ADT alone. Of the 125 patients with post-operative PSA ≤ 0.4; 48 (38%) had ADT alone and 58 (62%) had ADT+RT. Survival was estimated with Kaplan-Meier method and univariate and multivariate analyses were done to identify prognostic factors.

**Results:** After a median follow-up of 54 months, distant metastasis free survival (DMFS) at five-years and 10-years were 77% and 58%. Overall survival (OS) at five and ten years was 89% and 80%, respectively, while P-Ca-specific survival (PCSS) was 94% and 87%, at five and 10 years. For patients with post-operative PSA ≤ 0.4, the use of ADT+RT had favorable impact on DMFS ( $p = 0.006$ ) and OS ( $p = 0.048$ ), compared to ADT alone. Although limited by a small sample size (42 patients), we could not demonstrate a survival benefit of ADT+RT in patients with post-op PSA > 0.4 (surgical failure). On univariate-analysis, post-operative PSA > 0.4 ( $p = 0.002$ ), seminal vesicle involvement ( $p = 0.013$ ), number of positive lymph nodes ≥ 2 ( $p = 0.009$ ), and extra-nodal extension (ENE+) ( $p = 0.032$ ), had a poor prognostic impact on DMFS. Only ENE+ had a negative influence on OS ( $p = 0.05$ ). On multivariate-analysis, post-operative PSA > 0.4 ( $p = 0.02$ ) and ENE+ ( $p = 0.037$ ) retained their prognostic impact on DMFS.

**Conclusions:** For patients with pN+ P-Ca, post-operative PSA, and ENE+ are important prognostic factors. We report a benefit in terms of DMFS and OS benefit for the use of ADT+RT for patients who have had adequate

surgery (post-prostatectomy PSA  $\leq$  0.4). We found no benefit to the addition of RT to ADT for the small subset of patients with post-operative PSA  $>$  0.4.

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#### FREE PSA RATIO AS A PREDICTOR OF ADVERSE OUTCOMES AFTER CURATIVE-INTENT EXTERNAL BEAM RADIATION THERAPY FOR PROSTATE CANCER: A NOVEL APPLICATION OF AN "OLD" BIOMARKER

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**Purpose:** Most serum PSA circulates in complex with protease inhibitors, but 5%-45% does it as enzymatically inactive free PSA (fPSA). PSA produced from prostate cancer (PC) cells appears to escape proteolytic processing, resulting in a greater fraction of complexed PSA (e.g. lower fPSA). Based on this, fPSA ratio is commonly used as an adjunct marker to improve the accuracy of PSA for screening. Within the PSA range 4-10 ng/mL, a fPSA ratio higher than 0.15 correlates with lower risk of harbouring PC. Nonetheless, post treatment fPSA is rarely quantified, and its prognostic value after radical external beam radiotherapy (EBRT) remains unexplored. **Materials and Methods:** Institutional databases were queried to identify intermediate- and high-risk PC patients treated between 1992 and 2012 with EBRT, who had at least one ascertainment of fPSA during follow-up. Patients were stratified according to a fPSA cut-off of 0.15. Multivariable Cox regression models were performed to determine the correlation of post-EBRT fPSA and clinical outcomes.

**Results:** A total of 355 patients were identified. Of these, 262 (73.8%) and 93 (26.2%) had a fPSA ratio  $<$  0.15 and  $\geq$  0.15, respectively. Mean age, pre-treatment total PSA, and clinical T-category were similar in both groups. However, patients with a fPSA ratio  $\geq$  0.15 had a higher biopsy Gleason score (GS), NCCN risk group, and were more often treated with combined EBRT and androgen deprivation therapy (ADT). Mean follow-up time was similar in both groups (109.5 months versus 111.9 months,  $p = 0.725$ ). Biochemical recurrence (BCR) rate were similar in both groups (77.6% versus 80.5%,  $p = 0.58$ ), as expected from the Institutional lab policy of ascertaining fPSA when total PSA is in the 4-10ng/mL range and therefore BCR most likely already established. However, the metastasis and castrate resistant prostate cancer (CRPC) rates were higher in the fPSA  $\geq$  0.15 group (41.3% versus 21.5%,  $p < 0.001$ , and 67.4% versus 37.5%,  $p = 0.002$ , respectively). Multivariable models demonstrated that along with higher GS, a fPSA fraction  $\geq$  0.15 conferred a statistically significantly higher hazard ratio (HR) for metastasis (HR 2.027, 95% CI 1.28-3.21,  $p = 0.003$ ), and CRPC (HR 3.066, 95% CI 1.565-6.004,  $p = 0.01$ ).

**Conclusions:** This study suggests that a fPSA ratio  $\geq$  0.15 in the setting of post curative-intent EBRT denotes a more aggressive disease, reflected in higher rates of metastasis and CRPC. Our findings suggest a reversal in the significance of fPSA ratio in the post treatment state, and a potential novel role for this widely available and low-cost biomarker.

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#### RENAL SABR IN PATIENTS WITH A SOLITARY KIDNEY: AN INDIVIDUAL-PATIENT POOLED ANALYSIS FROM THE INTERNATIONAL RADIOSURGERY ONCOLOGY CONSORTIUM FOR KIDNEY (IROCK)

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**Purpose:** SABR is an emerging ablative modality for primary renal cell carcinoma (RCC). Taking a multi-national approach, we sought to evaluate oncologic and renal function outcomes in patients with RCC in solitary kidneys versus bilateral kidneys.

**Materials and Methods:** Individual patient data from nine institutions across Germany, Australia, USA, Canada and Japan within the IROCK group were pooled retrospectively. Toxicities were recorded using CTCAE v4.03. Demographics and treatment outcomes were compared between those patients with solitary versus bilateral functional kidneys using chi-square test, fisher's exact test, two-sample T-test or Wilcoxon rank sum test as appropriate. K-M estimates and Cox proportional hazards regression were generated for survival outcomes.

**Results:** Eighty-one patients (of 223 total) harboring a solitary kidney underwent renal SABR. Mean age in this cohort was 62.5 years, 69% of patients were male, and 97.5% had good performance status (ECOG 0-1). Pathological confirmation was obtained in 91.4% (all clear cell RCC) with a further 8.6% demonstrating tumour growth on serial imaging. Median [IQR] diameter of solitary kidney tumours was 3.7cm [2.5-4.3], which was smaller ( $p < 0.001$ ) than those in patients with bilateral kidneys (4.3 cm [3.0-5.5]). While both median (range) total dose of 25 Gy (14-70) and number of fractions of 1 (1-10) were significantly lower in the solitary cohort ( $p \leq 0.001$ ), median (range) BED10 was similar between cohorts: 87.5 Gy (33.6-125) in the solitary and 87.5Gy (37.5-125) in the bilateral cohort ( $p = 0.103$ ). Solitary kidney patients had a higher mean  $\pm$  SD eGFR at baseline (64.6  $\pm$  21.7 mL/min) than those with bilateral kidneys (57.2  $\pm$  21.6 mL/min;  $p = 0.016$ ). Post-SABR decline in eGFR was similar for solitary and bilateral cohorts with mean ( $\pm$ SD) decreases of -5.8 ( $\pm$ 10.8) and -5.3 ( $\pm$ 14.3) mL/min, respectively ( $p = 0.984$ ). No patients in the solitary cohort required dialysis versus six (4.2%) in the bilateral cohort. With median follow-up of 2.57 years, local control (LC), progression-free survival (PFS), cancer-specific survival (CSS), and overall survival (OS) at two years were 98.0%, 77.5%, 98.2% and 81.5%, respectively. No difference in local failure rate for solitary ( $n = 1$ ) versus bilateral ( $n = 2$ ) cohorts was observed ( $p = 1.00$ ). On univariable analysis, moderate chronic kidney disease (eGFR  $\leq$  60 mL/min) was associated with poorer PFS (HR 2.66,  $p = 0.043$ ) in the solitary cohort. **Conclusions:** Renal SABR appears to be a viable option for RCC tumours in patients with solitary kidneys and yields comparable local control, survival, and renal function outcomes to patients with bilateral kidneys. Pre-existing moderate chronic kidney disease may be predictive of poorer oncologic outcomes in patients with a solitary kidney, thus careful patient selection will be essential to optimize outcomes in this population.

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#### HYPOFRACTIONATED INTENSITY MODULATED RADIATION THERAPY PLUS WEEKLY GEMCITABINE FOR BLADDER PRESERVATION IN PATIENTS WITH INVASIVE BLADDER CANCER

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**Purpose:** Trimodality therapy (TMT) is an attractive alternative for bladder preservation in selected patients with muscle invasive bladder cancer (MIBC). We report results of hypofractionated IMRT (HypoRT) and weekly gemcitabine as components of a TMT regimen for patients with MIBC.

**Materials and Methods:** From June 2008 to June 2017, 49 patients with T2-3N0M0 bladder cancer underwent treatment with HypoIMRT with concomitant weekly gemcitabine following maximal transurethral resection of bladder tumour (TURBT). HypoIMRT delivered a dose of 50 Gy in 20 fractions to the whole empty bladder and 40 Gy to pelvic nodes in the same 20 fractions. Weekly gemcitabine at a dose of 100 mg/m<sup>2</sup> was given concomitantly. Response rate was assessed by cystoscopy evaluation and bladder biopsy.

**Results:** The median age was 76 years (range: 58-91). A complete TURBT

was achieved in 90% of patients. A complete response post-therapy was confirmed in 88% of the patients. At a median follow-up of 20 months, 20 patients had died, 10 of them from bladder cancer. Of those patients achieving a complete response, 29 patients (67.5%) have remained disease-free at a median follow-up of 21 months. The median time for either local or distant failure was 12 months. Eight patients (16%) failed in the bladder only (five with superficial disease only) with an actuarial local control projection of 75% at three years; 13 (26.5%) failed distantly. The three- and five-year cancer-specific survival rate was 77%. Treatments were well tolerated with all patients completing HypoMRT and gemcitabine. Grade 3 acute GU or GI toxicity was seen in 2% of patients (no Grade 4 or 5). Late Grade 2 or higher GI or GU toxicity was seen in 2% and 6% respectively (no Grade 4 or 5).

**Conclusions:** HypoMRT plus concurrent weekly gemcitabine post-TURBT is an effective, feasible and well-tolerated curative treatment strategy in selected patients with MIBC.

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### PROSTATE RADIOTHERAPY IS ASSOCIATED WITH IMPROVED SURVIVAL IN NEWLY-DIAGNOSED METASTATIC HORMONE-SENSITIVE PROSTATE CANCER

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**Purpose:** In patients presenting with metastatic prostate cancer, the role of local therapy is undefined. Recent registry analyses have suggested, however, that external beam radiotherapy (RT) directed at the prostate may improve overall survival (OS). We reviewed the experience of primary tumour-directed RT in this setting at our centre.

**Materials and Methods:** The study population consisted of men with newly-diagnosed metastatic prostate cancer referred to a comprehensive cancer centre between 2005 and 2015 and treated initially with androgen deprivation therapy. Patients were eligible for inclusion if they received 1) prostate RT with biologically effective dose at least that of a course of 40 Gy in 15 fractions; or 2) no prostate RT. The association between receipt of prostate RT and OS was studied. Descriptive statistics were used to characterize the study population. OS was estimated using the Kaplan-Meier method. Univariate and multivariate Cox regression were used to identify factors associated with OS.

**Results:** A total of 304 cases were eligible. Prostate RT was received in 105 cases. Median age at diagnosis was 75 years (interquartile range, 67-82). Median follow-up was 72.2 months. On univariate analysis, prostate RT was associated with improved OS (hazard ratio 0.62, 95% CI 0.46-0.84,  $p = 0.002$ ). Two-year and five-year OS was 74.7% and 41.8% respectively in those receiving prostate RT and 56.9% and 27.6% respectively in those not receiving prostate RT. Median OS was 48.3 months in those receiving prostate RT compared to 29.2 months in those not receiving prostate RT. In a multivariate Cox model taking account of age at diagnosis, year of diagnosis, presenting PSA level, clinical T stage, clinical N stage, and M1 subdivision, RT remained significantly associated with improved survival (hazard ratio 0.64, 95% CI 0.43-0.96,  $p = 0.033$ ).

**Conclusions:** To our knowledge, this cohort represents the largest single-centre experience of primary tumour-directed RT in metastatic prostate cancer reported to date. In this population, receipt of prostate RT was associated with improved OS. The observed 19-month absolute difference in median OS is clinically significant. This analysis could not account for performance status, volume of metastatic disease, co-morbidities, receipt of systemic therapies at the time of castration resistance, and other potential confounding factors. Only large-scale randomized trials, such as Arm H of the MRC STAMPEDE trial, will be able to definitively assess the value of prostate RT in this setting.

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### PATTERNS OF ADJUVANT RADIOTHERAPY AMONG LOW-, INTERMEDIATE-, AND HIGH-RISK GROUPS IN EARLY-STAGE ENDOMETRIAL CANCER

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**Purpose:** Endometrial cancer is the most common gynecological malignancy in Canada. Randomized prospective studies have shown that adjuvant radiotherapy (RT) following hysterectomy significantly improves loco-regional control among Stage I intermediate-risk patients. This study aims to elucidate the use of adjuvant RT among low-, intermediate-, and high-risk groups of Stage I endometrial cancer patients in current practice at our institution.

**Materials and Methods:** A single-centre retrospective chart review was conducted on FIGO Stage I endometrial cancer patients who have undergone hysterectomy at our institution between 2010 and 2015. Data on patient/tumour characteristics and radiation treatments were collected and analyzed among low- (Stage T1a all grade, or Stage T1b Grade 1), intermediate- (Stage T1b Grade 2-3, or Stage T1c Grade 1-2), and high-risk (Stage T1c Grade 3) groups, as defined by PORTEC-1. Patterns of adjuvant RT among these patients were compared to patients treated between 1998-2007 in a previously reported study.

**Results:** A total of 320 Stage I endometrial cancer patients were identified, and 184 (59.4%), 120 (38.7%) and six (1.9%) met criteria for low-, intermediate-, and high-risk groups, respectively. Among these groups, 22 (12.0%), 101 (84.2%) and four (66.7%) patients received adjuvant RT. A lower percentage (12.0%) of low-risk patients received adjuvant RT in the current cohort compared to previous study (20.4%), and a greater proportion of the adjuvant RT was given in the form of vaginal brachytherapy (VBT) (100.0%) compared to pre-2010 study (79.3%). In contrast, a higher percentage of intermediate-risk patients (84.2%) received adjuvant RT in the current cohort compared to the previous study (71.5%), and again, a greater proportion of the adjuvant RT was given in the form of VBT (81.2%) compared to previously (62.6%). Five-year overall survival (OS) and disease-free survival (DFS) rates among our current cohort of patients were 91.2% and 90.0%, respectively.

**Conclusions:** In current practice, compared to the approach used a decade ago, fewer Stage I low-risk endometrial cancer patients receive adjuvant RT, and more intermediate-risk patients receive adjuvant RT, mostly in the form of VBT among both groups, and the outcomes achieved remain excellent.

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### IMPACT OF EXTENDED FIELD AND/OR INTEGRATED BOOST USING VMAT ON ACUTE HEMATOLOGICAL TOXICITY IN PATIENTS WITH LOCALLY ADVANCED CERVICAL CANCER UNDERGOING RADIOCHEMOTHERAPY

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**Purpose:** Hematological toxicity (HT) due to radiotherapy in locally advanced cervical cancer (LACC) often results in delayed or missed chemotherapy cycles or prolongation of the overall treatment time (OTT), resulting in poorer outcomes. Recent evidence shows that V10 Gy or V20 Gy of the pelvic bone marrow is correlated with higher rates of G2 leukopenia and neutropenia, and with a higher rate of missed chemotherapy cycles. The aim of this retrospective analysis is to evaluate the impact of extended field radiotherapy (EFRT) ± simultaneous integrated boost (SIB) on acute HT, OTT and number of chemotherapy cycles in patients with LACC undergoing concurrent radiochemotherapy using VMAT.

**Materials and Methods:** Fifty-four consecutive patients with FIGO Stage IB-IVA, biopsy-proven squamous cell, adeno-, or adenosquamous carcinoma of the uterine cervix, undergoing radiation concurrently with weekly Cisplatin, followed by MRI-guided adaptive brachytherapy were analyzed. If pathologic lymph nodes were present in the para-aortic (PA) region, or if ≥ than 3 pathologic pelvic lymph nodes were involved, the PA region was included in the target volume. Enlarged/PET-CT avid lymph nodes were contoured for SIB. Target volumes and VMAT plans were created prospectively according to the EMBRACE II protocol. Bone marrow (BM) structures were retrospectively contoured as ileum (BM-IL), lower pelvis (BM-LP) and lumbosacral spine (BM-LS). Impact of PA ±SIB irradiation was evaluated on HT, OTT and missed chemotherapy cycles using linear mixed models and Welch's ANOVA. HT was scored using the common

terminology criteria for adverse events v.4.0. Dosimetric parameters (V10Gy, V20Gy, V30Gy, V40Gy, mean dose) were calculated for BM.

**Results:** Four groups of patients were identified: EFRT, no SIB (11%); EFRT +SIB (35%); pelvic, no SIB (46%), pelvic + SIB (8%). No significant differences on hemoglobin ( $p = 0.78$ ), leukocyte ( $p = 0.81$ ) or thrombocyte ( $p = 0.53$ ) counts amongst patients treated with or without SIB and/or EFRT were identified. Bone marrow doses were acceptable, irrespective of radiation field borders. Ninety-eight percent of patients had an OTT of less than 50 days (as aimed), 93% had  $\geq 3$  cycles of chemotherapy.

**Conclusions:** EFRT and SIB by means of VMAT planning in concurrent radiochemotherapy for LACC is feasible and safe, resulting in acceptable bone marrow doses, does not lead to increased HT, enables high compliance to concurrent chemotherapy and respects OTT.

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#### AN MRI-BASED RADIOMIC SIGNATURE FOR DISEASE-FREE SURVIVAL IN LOCALLY ADVANCED CERVICAL CANCER

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**Purpose:** Radiomics is an emerging area of discovery where quantitative imaging features are extracted from routine imaging and mined to identify prognostic imaging phenotypes. The majority of studies have focused on CT images and non-cervical cancer. We aimed to develop a MRI-based radiomic signature for disease-free survival (DFS) in locally advanced cervical cancer.

**Materials and Methods:** The study comprised a discovery dataset of 80 patients and an independent validation dataset of 81 patients with FIGO Stage IB-IVA cervical cancer treated with definitive chemoradiation between 2005-2014. Disease status was recorded prospectively. The primary end-point was DFS, defined as freedom from relapse or death measured from the date of diagnosis. A single observer retrospectively contoured the primary tumour on T2-weighted pre-treatment MRI. Radiomic features of the tumour were extracted using PyRadiomics. The stability of each feature was determined by calculating the Pearson correlation coefficients of radiomic features extracted from each of the following settings: 1) test-retest MR images acquired 15 minutes apart, 2) diagnostic and simulation MR images acquired <10 days apart, and 3) tumour delineation by two observers. Less stable features with an average Pearson correlation coefficient of <0.6 were excluded. A radiomic signature for DFS was built using the discovery cohort, with minimal redundancy maximum relevancy feature selection method and 10-fold cross validation. The radiomic signature was dichotomized by its median value into high- and low-risk groups. Uni- and multi-variable Cox regression analyses were performed to evaluate the performance of the radiomic signature in both datasets using the concordance index (CI).

**Results:** A radiomic signature comprising two features (based on shape and wavelet) was prognostic for DFS in the discovery cohort (HR 2.58, CI 0.65,  $p = 0.007$ ). The five-year DFS rates of patients in the high- versus low-risk radiomic groups were 73 versus 42%, respectively ( $p = 0.005$ ). Tumour volume, and a clinical model with stage and nodal status were moderately prognostic for DFS in the discovery cohort (CI 0.60,  $p = 0.03$ ; and CI 0.64,  $p = 0.08$ , respectively). The radiomic signature remained independently associated with DFS when added to tumour volume (HR for radiomic signature 2.29,  $p = 0.038$ , model CI 0.65), or the clinical model (HR 2.27,  $p = 0.02$ , model CI 0.69) in the discovery cohort. The radiomic signature was also prognostic for DFS in the independent validation cohort, both on univariable analysis (HR 2.39,  $p = 0.044$ , CI 0.63), and also when added to a clinical model with stage and nodal status (HR 2.65,  $p = 0.039$ , model CI 0.70).

**Conclusions:** A radiomic signature can be used as a prognostic biomarker for DFS following chemoradiation in patients with locally advanced cervical cancer. Further external validation is planned.

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#### OF MONSEL'S AND MRI: CAUTION REQUIRED FOR IMAGE QUALITY

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**Purpose:** Radiotherapy (RT) provides excellent hemostasis for bleeding tumours, such as those associated with gynecological malignancies. Other methods (packing, styptic agents) may be used, prior to or sometimes during RT. With increasing frequency of MRI in RT applications (planning, image verification), including for brachytherapy, we investigated how non-RT-mediated approaches to hemostasis, such as with Monsel's solution (MS; ferric subsulfate), impact MRI quality.

**Materials and Methods:** Hypothesizing that artifacts might be possible due to the iron component of MS, we added the solution to chicken eggs (a proven tissue-like phantom to test MRI relaxation sequences). Three scenarios were tested: MS directly administered on the egg contents, MS doused on thin versus thick gauze pieces (commonly used in clinical settings for packing/compression) placed within egg contents. Eggs with no MS served as controls for each scenario. Plated samples were scanned by MRI at 3T, using two different sequence weightings, resulting in a T1 and a T2 contrast. The T1 contrast was obtained using a spoiled-gradient echo (SGE) sequence with a TE and TR of 2.84 and 250 ms, respectively, and the T2 contrast was obtained using a turbo-spin-echo (TSE) sequence with TE and TR of 89 and 4000 ms, respectively. All scans were oriented coronally, with the read-encode direction aligned in the foot-head axis (vertical). Comparative scans repeated on CT (120 kV, 500 mA, 2 mm slices) were corrected using the metal artifact reduction algorithm. The MRI and CT scans were evaluated for variation in image quality.

**Results:** Both the SGE and TSE scans exhibited large artifacts (voiding and signal buildup) surrounding the MS, regardless of whether it was applied to gauze or administered directly. The signal voiding spanned a range of 2-4 cm on the SGE sequence and a little smaller (up to 3 cm) on the TSE sequence, as expected due to the spin-echo rephasing. The CT numbers for all three test scenarios ranged from 100 – 600 HU. Though CT images were not degraded with the presence of MS, faint streak artifacts were observed adjacent to the region of MS administration.

**Conclusions:** Regardless of sequence, the application of MS will likely null out any MRI signal from anatomy within a 1 to 2 cm radius. The persistence of MS-related image artifacts following application is not known, thus imaging in all cases should be interpreted with caution. If MS is clinically indicated prior to MRI, particularly near structures critical to accurate interpretation, alternative hemostasis approaches should be strongly considered.

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#### PATTERNS OF RECURRENCE BY TYPE OF ADJUVANT RADIOTHERAPY FOR STAGE II ENDOMETRIAL CANCER: A PROVINCIAL REVIEW

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**Purpose:** Optimal adjuvant treatment of FIGO Stage II endometrial cancer is controversial. As surgical practice evolves to include nodal resection, there may be a role for de-intensifying adjuvant therapy. In this province-wide retrospective review, patterns of recurrence were analyzed, alongside adjuvant radiotherapy (RT) practices including pelvic external beam (EB) RT, vaginal vault brachytherapy (BT), and small "minipelvis" (MP) EBRT fields, covering surgical bed, vaginal vault, and parametria, but not the classic elective nodal volumes.

**Materials and Methods:** We identified patients diagnosed with Stage II endometrial cancer between 2000-2014 who received adjuvant RT in Alberta. We collected demographics, disease characteristics, treatment details, and clinical outcomes. Recurrence-free survival (RFS) was calculated by Kaplan-Meier analysis, and factors associated with recurrence were determined by univariate and multivariate analysis.

**Results:** Two hundred and sixty-four patients (median age 62 [35-87]) met inclusion criteria. Eighty-three percent had endometrioid adenocarcinoma, 25% had Grade 3 disease, 56% had outer half myometrial invasion, and 44% had lymphovascular invasion (LVI). Nodes were surgically assessed in half: 130 (49%) pelvic and 26 (10%) para-aortic. Thirty-four patients (13%) had

chemotherapy. Adjuvant RT was predominantly full pelvis (FP) EBRT+BT (114), but included BT alone (63), FP-EBRT alone (42), MP-EBRT+BT (34), and MP-EBRT alone (11). Five-year RFS for the entire cohort was 87%, with median follow-up of 93.0 months [5.0-212.7]. Fifty-seven patients recurred (22%), including 25% of those treated with FP-EBRT+BT, 16% receiving BT alone, 14% receiving FP-EBRT alone, 21% receiving MP-EBRT+BT, and 55% receiving MP-EBRT alone. On multivariate analysis (reference: FP-EBRT+BT), no treatment group was significantly associated with recurrence. A trend was seen for MP-EBRT alone (hazard ratio [HR] 4.25,  $p = 0.052$ ). Mixed histology and presence of LVI were associated with recurrence (HR 3.73,  $p = 0.008$ ; and HR 3.38,  $p = 0.001$ , respectively). Chemotherapy was protective (HR 0.20,  $p = 0.012$ ). Pathologic nodal assessment was not correlated with recurrence ( $p = 0.90$ ). Median time to recurrence was 19.9 months [2.9-92.3]. Recurrence was loco-regional-only (not para-aortic nor distant) for a minority of patients ( $N=19/57$ , 33%), comparable for the FP-EBRT+BT ( $n = 8$ , 7.0%) and MP-EBRT+BT ( $n = 3$ , 8.8%) groups. One patient recurred in the pelvis outside of a MP-EBRT field. Among all patients, 62 (24%) had recorded late toxicity, most frequently gastrointestinal ( $n = 40$ ), including Grade 3-4 ( $n = 3$ ) and Grade 5 ( $n = 2$ ), with all Grades 3-5 having received FP-EBRT+/-BT.

**Conclusions:** No single best adjuvant treatment strategy exists for Stage II endometrial cancer. Careful risk stratification is suggested in selecting optimal adjuvant treatment. MP-EBRT+BT is an option for local treatment of the surgical bed, vaginal vault, and parametria, with potential to decrease toxicity.

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#### EVALUATION OF LARYNX PRESERVATION ON PATIENTS WITH LOCALLY ADVANCED LARYNGEAL CANCER IN THE ERA OF IMRT: RESULTS FROM A SINGLE TERTIARY CANCER CENTRE

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**Purpose:** Laryngeal cancer is the third most common head and neck cancer in Canada. Locally advanced laryngeal cancer can be treated with total laryngectomy (TL) or larynx-preservation (LP). TL is recommended for T4 disease, whereas LP is reserved for T3 disease. We hypothesize that patients with T3 disease, despite LP (T3-LP), have a better clinical outcome compared to those with T4 disease treated with TL (T4-TL).

**Materials and Methods:** A retrospective analysis was conducted on patients with T3 and T4 laryngeal cancer, treated between January 2007 and July 2015. Patients with history of other malignancies within three years of laryngeal cancer diagnosis, metastatic disease at diagnosis and/or palliative treatment were excluded. Intensity modulated radiotherapy (IMRT) was used as radiotherapy technique. Data on demographics, tumour characteristics and treatments were collected and correlated to clinical outcomes, including overall survival (OS), salvage laryngectomy-free survival (LFS), and failure-free survival (FFS).

**Results:** A total of 103 patients were eligible. Median age at diagnosis was 64 years (range: 37-93 years). Median follow-up was 36 months (range: 1-123 months) for total population, and 53 months for those still alive at last follow up. Among all patients, 68% had clinical T3 disease, among which 83% underwent LP, while 32% of patients had T4 disease, among which 70% underwent TL. N0 disease was found in 59% of patients. In T3-LP group, 31% of patients underwent salvage laryngectomy at median 11 months. No statistically significant difference was observed between T3-LP and T4-TL groups in three-year OS (66% versus 64%, respectively) or five-year OS (57% versus 47%, respectively). Three-year FFS rate was 52% in T3-LP group compared to 76% in T4-TL group ( $p = 0.08$ ). The findings were due to higher loco-regional failure rate in T3-LP group (RR = 5.53, 95% CI: 1-15.6,  $p = 0.025$ ). Three-year LFS was 68% in T3-LP group.

**Conclusions:** Many laryngeal cancer patients with T3 disease have intact larynx many years after larynx preservation. For those with recurrence, despite high loco-regional failure in T3-LP group, patients continue to perform well following salvage laryngectomy with clinical outcome comparable to patients with T4 disease treated with total laryngectomy. Therefore, larynx preservation remains a suitable option for patients with T3 disease.

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#### INFLUENCE OF COMORBIDITY ON THERAPEUTIC DECISION-MAKING AND IMPACT ON OUTCOMES IN PATIENTS WITH HEAD AND NECK SQUAMOUS CELL CANCERS: RESULTS FROM A PROSPECTIVE COHORT STUDY

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**Purpose:** High prevalence of comorbidity is seen in head and neck squamous cancer (HNSCC) due to the common use of tobacco and alcohol. These patients with comorbidity often receive suboptimal treatment resulting in inferior outcomes. The purpose of this study is to evaluate the presence of comorbidity, its impact on therapeutic decision-making, treatment compliance and overall survival.

**Materials and Methods:** Five hundred and eighteen patients seen at the multidisciplinary head and neck joint clinic at Tata Memorial hospital from August 2012-2015 with non-metastatic HNSCC, >18yrs of age, without any prior history of cancer or anti-cancer treatment in the last five years were evaluated for the present study.

**Results:** Of the 518 patients, 293 (56.6%) had comorbidity as per ACE-27 index. Of the total, 107 patients (20.6%) had deviation from the ideal treatment plan, with 74 (69.2%) patients having ACE 27 score  $\geq 1$ . Patients with higher grade of comorbidity were less likely to complete guideline-concordant therapy (moderate ACE 27 versus none: odds ratio (OR) 0.46, 95% confidence interval (CI) 0.26 - 0.82,  $p$  value < 0.01\*; severe ACE 27 versus none: OR 0.23, 95% CI 0.08 - 0.57,  $p$  value < 0.01\*). Patients who completed guideline-concordant treatment had the best outcomes as compared to those who could not receive or complete guideline-concordant therapy (median survival: not reached versus 9.56 months, Hazard ratio 3.66, 95% CI: 2.8-4.79;  $p < 0.01$ \*).

**Conclusions:** The presence of increasing severity of comorbidity in patients with HNSCC influences therapeutic decision-making. Survival outcomes are poorer in patients receiving guideline-discordant treatment.

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#### A COLLABORATIVE APPROACH TO CARE: THE DEVELOPMENT OF A MULTIDISCIPLINARY CLINIC FOR HEAD AND NECK CANCER PATIENTS IN NOVA SCOTIA

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**Purpose:** In 2017, the average wait time for head and neck cancer patients in Nova Scotia was 38 days from ready to treat date to the start of treatment compared to the standard of 14 days. Studies have shown that wait time correlates decreased loco-regional control and overall survival. Delays are compounded by multiple appointments to finalize a treatment plan. The Provincial Head and Neck Cancer Site Team recognized the need to improve patient care. A proposal was made for the implementation of a collaborative multidisciplinary clinic for this patient population based on evidence suggesting that a multidisciplinary approach can improve various outcomes.

**Materials and Methods:** Supported by the Nova Scotia Cancer Care Program senior leadership, a project manager and an industrial engineer were assigned. The Head and Neck Cancer Site Team, including patient and public representatives, determined the project structure and goals. This information was presented at an interprofessional stakeholder engagement meeting in June of 2017. This session solidified support for the project and refinement of the structure, goals and timelines. It was determined that a strong evaluation piece is needed to determine if the goals were achieved. A steering committee oversees the project and subcommittees address specific aspects of the plan. An implementation meeting with stakeholders is scheduled for April 2018. Outcome measures include: "Assessment of Interprofessional Team Collaboration Scale" (AITCS), access to care, wait times, and patient reported outcomes. This data will be used to define a baseline for the current treatment process which will be compared to the same data collected post intervention.

**Results and Conclusions:** The process of developing a multidisciplinary clinic has accelerated team dynamics leading to a goal driven group where patients and their families come first; in fact, patient advisors have become an integral part of this project. We anticipate that pre- and post-intervention data will confirm improvement of process efficiencies, space and human resource utilization, and patient and health care provider satisfaction. The pilot will start in April 2018 and we will report on the process design and implementation of multidisciplinary clinics with early data available.

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#### A BIOIMPEDANCE ANALYSIS OF HEAD AND NECK CANCER PATIENTS

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**Purpose:** Bioelectrical Impedance Analysis (BIA) gauges the malnutrition state of cancer patients by measuring the intra- and extracellular water content (ICW/ECW) and the phase angle (p) between the body's resistance and capacitance – quantities that are associated to the cellular membrane integrity and fluid balance and nutritional health of the patient.

**Materials and Methods:** In this study we are interested in the phase angle because it is a known prognostic factor for the morbidity and mortality of cancer patients. We are proposing univariate and multivariate hierarchical linear models correlating p with the weight (m), ICW (w) and time (t). The hierarchical model treats the slope and intercepts of the linear models as normal distributions whose means and variances are characteristic of the population. We followed a group of 18 head and neck cancer patients as a feasibility study, performing BIA measurements prior to the first fraction; at the midpoint; and at the end of their radiation therapy course. The univariate analysis shows statistically significant nonzero slopes of  $-0.00634^{\circ}$  per day for p versus t;  $0.299^{\circ}$  per % ICW for p versus t; and  $0.0588^{\circ}$  per % of the initial weight for p versus m. Multivariate analysis looks at the variation of one variable while accounting for the effect of the others. The population predicted phase angle is  $p = -6.579 - 0.002254t + 0.2072w + 0.01698m$  and all three slopes are significantly different than zero.

**Results and Conclusions:** This study demonstrates all three variables (t, w, m) have a significant correlation with the phase angle and the study of phase is essentially a multivariate problem. Future studies will require at least four repeated measures to estimate the three slopes and the intercept. Furthermore this work provides guidance regarding comparative studies of control groups and cancer patients.

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#### PATIENT REPORTED OUTCOMES DURING RADIOTHERAPY FOR HEAD AND NECK CANCER: A PROSPECTIVE OUTCOMES AND SUPPORT INITIATIVE

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**Purpose:** This study evaluates the feasibility of collecting head and neck cancer (HNC) patient reported outcomes (PROs) weekly during radiotherapy (RT) and analyzes HNC PROs and their association with clinical characteristics.

**Materials and Methods:** The 50-item Vanderbilt Head and Neck Symptom Survey 2.0 (VHNSS) Questionnaire was used to assess PROs with three questions added to evaluate chemotherapy side effects. Using an iPad, patients completed the full survey at baseline and post-RT follow-ups and a 12 item partial survey weekly while undergoing RT, the questions were selected to include potential symptoms that could be addressed by supportive care measures or allied health interventions. This study analyzed HNC patients treated with  $>50$  Gy Equivalent Dose in 2 Gy fractions (EQD2) who completed the baseline and  $\geq 1$  partial survey during RT. For each

patient, the average and maximum (max) scores for each question during RT was calculated. Chi square and logistic regression analysis were used to assess the association of clinical characteristics and a moderate-severe symptom score (defined in previous VHNSS studies as max score  $\geq 4/10$ ).

**Results:** The questionnaire was offered to 154 patients at baseline and once or more during RT; 140 completed both, 11 did not complete the baseline (two unfit, three no interpreter available, six declined) and three did not complete the survey during RT (one unfit, two declined). Four or more weekly surveys were completed by 115 patients. The cohort consisted of 80% males. The median age was 64 years (InterQuartile Range 56-70). Most (84%) were ECOG 0-1 at initial consult. At diagnosis, 31% were never, 31% current and 37% former smokers and 34% had 7+ alcohol beverages/week. The most common sites included oropharynx (41%), larynx (19%), oral cavity (10%) and nasopharynx (9%) and 77% had Stage 3 or 4 disease. The median EQD2 was 70 Gy (IQR 65-70). Almost half (46%) received concurrent chemotherapy; the most common regimes were Cisplatin 100mg/m<sup>2</sup> q3weekly (45%), Cisplatin 40mg/m<sup>2</sup> qweekly (42%) and Cetuximab (9%). Primary surgery was performed for 26%. The median average weekly score for nausea and vomiting was 1/10. The median max score was 2/10. The median average and max scores for trouble maintaining weight because of swallowing problems were 2/10 and 4/10, choking on liquids 1/10 and 2/10, choking on solids 1/10 and 3/10 and mucous causing choking/gagging 2/10 and 3/10. The median average and max scores for dysgeusia was 3/10 and 7/10, pain 4/10 and 6/10, pain causing difficulty sleeping 1/10 and 3/10 and painful mouth/throat sores 2/10 and 5/10. On multivariate logistic regression analysis, receiving q3weekly (OR 3.3, 95% CI 1.0-11.0,  $p = 0.05$ ) or weekly Cisplatin (OR 5.1, 95% CI 1.6-15.9,  $p = 0.005$ ) were associated with a higher risk of moderate to severe nausea and vomiting. Receiving EQD2 70 Gy+ (OR 2.7, 95% CI 1.1-6.9,  $p = 0.03$ ) and oropharynx or oral cavity tumour site (OR 2.6, 95% CI 1.1-6.0,  $p = 0.03$ ) were associated with moderate to severe weight loss due to swallowing difficulties. Oropharynx or oral cavity tumour site (OR 3.1, 95% CI 1.3-7.2,  $p = 0.008$ ) was associated with a higher risk of moderate to severe painful mouth/throat sores.

**Conclusions:** This study confirms the feasibility of collecting PROs during HNC RT with 91% of patients completing at least 1 baseline and 1 survey during RT, and 75% of all patients completing  $\geq 4$  weekly surveys. Scores were highest for dysgeusia, mucositis and pain. The VHNSS demonstrated an ability to detect differences in PROs by tumour and treatment characteristics.

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#### DOCUMENTATION AND INCIDENCE OF LATE EFFECTS AND SCREENING RECOMMENDATIONS FOR ADOLESCENT AND YOUNG ADULT HEAD AND NECK CANCER SURVIVORS TREATED WITH RADIOTHERAPY

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**Purpose:** Little research exists regarding late effects experienced by adolescent and young adult (AYA) survivors of head and neck cancer (HNC) treated with radiotherapy (RT). A retrospective review of AYA HNC patients treated at our institution was performed to determine the potential late side effects discussed at the initial radiation oncology consultation, the incidence of late toxicities and the screening recommendations provided to primary care providers (PCPs) at discharge.

**Materials and Methods:** Charts ( $n = 162$ ) were reviewed for all patients 15 to 35 years at diagnosis with HNC treated with RT at our institution between 1960 and 2010 and surviving  $\geq 5$  years after diagnosis. Sarcoma and lymphoma histology were excluded. Consultations, progress notes and discharge summaries were reviewed to assess clinical and treatment characteristics, late side effects, and screening recommendations.

**Results:** Median follow-up was 6.4 years. The median age at diagnosis was 31 years, 49% of patients were male and 51% female. The most common tumour subsites were nasopharynx (30%), salivary gland (22%), thyroid (19%) and oral tongue (9%). All patients had RT, the majority (98%) received 40 Gy or higher, 59% had surgery and 10% neoadjuvant or concurrent chemotherapy. The risk of potential long term side effects from RT was documented in the initial radiation oncologist consult for 85% of patients. Specific side effects

of RT were not outlined in 31% of consults. The most common specific late effects discussed included xerostomia (42%), jaw osteoradionecrosis (27%), chronic skin changes (20%) and second malignancy (17%). The majority of patients (77%) developed at least one reported late effect from RT persisting at >1 year after diagnosis. The most common late effects included xerostomia (44%), chronic skin changes (28%), neck fibrosis (22%), nasal crusting (16%), epistaxis (16%), dental decay (14%), trismus (12%), dysgeusia (11%), secondary malignancy (9%, 2% in the RT volume), dysphonia (8%), hypothyroidism (6%), chronic pain (6%), dysphagia (6%) and hearing loss (6%). In all, 65% of patients were followed for five or more years post-RT and 20% are currently followed or were followed up to the time of death. Of the 80% discharged, 58% were discharged in a progress note without a formal discharge summary of their care, 23% were lost to follow-up (had a scheduled appointment but did not attend), 14% had a formal discharge summary and 5% moved outside the province to be followed at another cancer centre. For those discharged, screening recommendations included regular dental care (34%), screening for hypothyroidism (6% of patients excluding those with pre-existing hypothyroidism) and screening for second malignancy (4%). At the time of analysis 77% of patients were alive, 23% died, the majority from cancer (92%).

**Conclusions:** The majority of AYA HNC patients treated with RT developed late side effects. Most PCPs were not sent a formal survivorship care plan at discharge. A recall of this cohort is underway to assess ongoing RT related late effects. Survivorship care plans will be developed to improve the transition of care of these patients in their community.

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#### LATE TOXICITY FOR EARLY GLOTTIS CANCERS TREATED WITH HYPOFRACTIONATED RADIOTHERAPY

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**Purpose:** Definitive hypofractionated radiotherapy provides good cure rates and voice preservation for patients with early glottis cancers. We analysed our late toxicity and second malignancy rates and intend to report our institutional experience.

**Materials and Methods:** We retrospectively reviewed consecutive patients treated with hypofractionated radiotherapy for T1-T2 glottis cancer between January 2006 and January 2013. Eighty-nine percent received 52.0 Gy in 20 fractions over four weeks. 82% were treated with 6MV photons and 18% with Cobalt using either wedged laterals or 3D conformal radiotherapy with 2-4 fields. Patients were treated supine with bolus, and immobilized with a thermoplastic shell. Patient information was collected and stored in our head and neck registry database. Descriptive statistics were calculated for all relevant demographic variables. Late toxicity was defined as adverse effects present three months after treatment. Cumulative incidence of second malignancy was calculated; death was a competing risk.

**Results:** Overall, we evaluated 114 patients, with a median age of 71 years at treatment. There were 92 men and 22 women included. Median follow-up was 4.6 years post-treatment. Most patients, 89%, had smoked more than 10 pack-years. Regular and heavy alcohol consumption was present in 30 and 23% of patients respectively. Occurrence of late toxicities was assessed in most patients. Late odynophagia was noted in 4%. Xerostomia rates at three and six months were 19% and 12%. Dysphagia was present in 8% and 6% at three months and beyond six months. Laryngeal edema persisting at three months was noted in 16%. Telangiectasia was noted in 60% of patients, of which 90% were noted along the laryngeal mucosa, 3% along skin surface and 3% on both skin and mucosa. Chronic hoarse voice was noted in 77% of patients at three months and 59% at six months. Voice quality recovered completely in 53%, improved mildly for 13%, and worsened in only 1%. Of 52 evaluated patients, 34 remained euthyroid, two were hypothyroid before treatment, six developed hypothyroidism post-radiation and 10 post-salvage surgery. Second malignancies were identified in 21 of 114 (18%) patients and included bladder (2), CLL (one), colorectal (three), lung (nine), prostate (three), and non-melanoma skin cancer (three). None were in-field and median time to second malignancy was 2.1 years, with cumulative incidence of developing second cancer of 17.3% (95% CI 0.100-0.264) at five years.

**Conclusions:** Radiation induced late side effects are minimal and acceptable. Our toxicity and second malignancy rates are comparable to that in the literature. Hypofractionated 3D conformal radiotherapy remains an excellent treatment option for early laryngeal cancer. In the future, we intend to use this study as a basis for comparison with a cohort treated with IMRT. It remains to be seen whether IMRT may further reduce late toxicity in a clinically significant manner.

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#### EARLY STAGE GLOTTIS CANCER: OUTCOMES AND EARLY TOXICITY

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**Purpose:** Radiotherapy (RT) alone has been the preferred treatment for early glottis cancers. We reviewed our institutional experience with hypofractionation and intend to report our outcomes and early toxicity.

**Materials and Methods:** We retrospectively reviewed consecutive patients treated with RT for T1-T2 glottis cancers at our centre between January 2006 and January 2013. Since 2006, all patients with early glottis cancer received hypofractionated radiation at our regional tertiary centre. Eighty-nine percent received 52.0 Gy in 20 fractions over four weeks. Eighty-two percent were treated with 6MV photons and 18% were treated with Cobalt using either wedged laterals or 3D conformal radiotherapy with 2-4 fields. Patients were treated supine with bolus, and immobilized with a thermoplastic shell. Baseline characteristics, outcomes, and toxicity data was compiled and stored in our head and neck registry database. Descriptive statistics were calculated for all relevant demographic variables. Overall survival and relapse-free survival were estimated using a Kaplan-Meier method.

**Results:** Overall, we evaluated 114 patients, with a median age of 71 years at treatment. There were 92 men and 22 women included. Most patients, 89%, had smoked more than 10 pack-years. Median follow-up was 4.6 years post-treatment. Overall survival at one, two, three, four and five years was respectively 98, 96, 91, 88 and 83%. Similarly, relapse-free survival rates were 91, 90, 88, 85 and 85%. In total, 16 patients relapsed, 12 locally, three in regional lymph nodes and one with distant metastases. Mean time to relapse was 17.3 months. Early toxicity was also rigorously assessed in the vast majority of patients. Odynophagia was present in 97% at the end of treatment and 58% described it as severe. However, it persisted in only 23% at one month and 4% at three months post-RT. Xerostomia was present in 56% of patients at the end of RT, 25% at one month and 20% at three months. Eighty-six percent developed dysgeusia during RT. 66% developed laryngeal mucositis by the end of treatment. Dysphagia occurred in 49% at the end of treatment, 18% at one month and 8% at three months. Skin reaction was noted in 97% of patients; 65% had erythema, 15% had dry desquamation and 16% had moist desquamation at the end of treatment. Seventy-one percent had no skin reaction at one month post-RT. Mild laryngeal edema was noted in 42% of patients, while 51% had no edema. Hoarse voice was noted at the end of treatment in all patients, this decreased to 88% at one month and 70% at three months.

**Conclusions:** Our survival and relapse rates are satisfactory and comparable to that in the literature. Early toxicity is tolerable and its rates are acceptable. Hypofractionated radiotherapy remains an excellent treatment for early laryngeal cancer. It remains to be seen if IMRT may further reduce clinically relevant early toxicity endpoints.

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#### COMPARISON BETWEEN POSTOPERATIVE TRUS-CT FUSION WITH MRI-CT FUSION FOR POSTIMPLANT QUALITY ASSURANCE IN PROSTATE LDR PERMANENT SEED BRACHYTHERAPY

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**Purpose:** Post-implant dosimetry is critical for the quality assurance (QA)

of permanent seed implants. CT-MRI fusion is the gold standard for post-implant dosimetry. However, MRIs are not always available and the majority of post-implant QA is performed using CT imaging only. Contouring the prostate after seed implant can be challenging and interobserver variability is large. Transrectal ultrasound (TRUS) is used for live procedure guidance and a set of TRUS images can be readily obtained at the completion of the implant. We hypothesized that prostate edge detection for contouring would be clearer on TRUS than on post implant CT, and that sufficient seeds would be visible to allow seed-to-seed fusion between post-implant TRUS and CT. **Materials and Methods:** Twenty consecutive patients with localized prostate cancer undergoing LDR prostate brachytherapy, either as monotherapy or a boost, were recruited. Post-implant TRUS images were recorded at the completion of their implant. Patients were scheduled for our standard post-implant QA procedure which includes a CT and an MRI at Day 30. These were co-registered; contoured and seed identification was carried out. The post implant TRUS was then contoured and registered to the uncounted Day 30 CT. Prostate volumes and relevant mean dosimetric parameters including D90, V100, V150 and V200 were compared. Patients served as their own controls. Comparisons were made through the use of descriptive and inferential statistics.

**Results:** Twenty patients were recruited between October 2017 and January 2018. Mean prostate volume was 33.8 cc (SD 11.3) on pre-implant TRUS, 35.2 cc (SD 10.8) on post implant TRUS and 35.7cc (SD 11.6) on MRI, showing good agreement between post implant TRUS and MRI, and x% edema compared to the preimplant TRUS. Comparing dosimetric parameters between contours based on post implant TRUS versus MRI, D90 was 114.1% (SD 10.9) versus 112.1% (SD 10.3), V100 was 95.4% (SD 4.3) versus 94.3% (SD 4.1), V150 was 56.4% (SD 11.7) versus 55.8% (SD 10.7) and V200 26.5% (SD 8.5) versus 26.4 % (SD 7.6) Student T-tests were used to compare each pair of dosimetric observations and no significant differences were found. **Conclusions:** Post-implant TRUS may be a valuable tool for quality assurance for post-implant dosimetry and may be a viable alternative to the more expensive post implant MRI, particularly if access to an MRI is limited. Contouring on post implant TRUS was surprisingly straightforward. We plan to repeat the contouring exercise with two additional independent observers and will present those results.

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#### OUTCOMES OF STEREOTACTIC ABLATIVE RADIOTHERAPY FOR PRESUMED EARLY-STAGE LUNG CANCER: THREE-YEAR RESULTS IN A 119 PATIENT COHORT

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**Purpose:** For non-operable Stage I non-small cell lung cancer (NSCLC), Stereotactic ablative radiotherapy (SABR) has emerged as a standard treatment option. However, in some cases obtaining pathological confirmation is not feasible due to either a patient's comorbidities or preference. We aimed to assess clinical outcomes among patients who received SABR for a pulmonary mass without tissue diagnosis.

**Materials and Methods:** Eligible patients presented with a pulmonary mass and a strong clinical suspicion of lung cancer. Patients were either not eligible for a biopsy or had an inconclusive biopsy. All patients had a PET-CT showing hypermetabolism, and documented growth of the mass. Patients had either significant comorbidity that precluded lobectomy, or refused surgery. We included masses that would have been clinically staged T1 or T2, N0, M0. The primary endpoint was progression-free survival (PFS). Secondary endpoint were overall survival (OS), local control (LC), regional control (RC) and distant metastasis-free survival (DMFS), evaluated by Kaplan-Meier analysis.

**Results:** A total of 931 lung SABR treatments were performed, on 878 patients from July 2009 to July 2017. Within this population 119 patients met our inclusion criteria. The median age of the patients was 74 years, and the median follow-up was 3.9 years (range 0.3 – 7 years). Median SUV of treated tumours was 4.9 (range 1.6 – 15.9). Estimated three-year overall survival and PFS were 65% and 55%, respectively. Estimated local control, regional control and metastasis-free survival at three years were 93%, 93% and 85%. Five patients (4%) presented Grade 3 treatment-related adverse-

events, and one a Grade 4 adverse event. There were no reported Grade 5 adverse events.

**Conclusions:** With a median follow-up of almost four years, we have found that SABR is both feasible and well tolerated in this fragile population for localized, non-pathologically proven, neoplastic lung disease.

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#### CAN THE NEUTROPHIL-TO-LYMPHOCYTE RATIO AND PLATELET-TO-LYMPHOCYTE RATIO PREDICT SURVIVAL IN PATIENTS TREATED WITH STEREOTACTIC BODY RADIATION THERAPY FOR NON-SMALL CELL LUNG CANCER? A SYSTEMATIC REVIEW

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**Purpose:** Markers of systemic inflammation are increasingly being recognized as prognostic indicators following lung cancer therapy. Two of these markers, the neutrophil-to-lymphocyte (NLR) and platelet-to-lymphocyte (PLR) ratios, are most commonly reported, yet their prognostic significance in the setting of stereotactic body radiation therapy (SBRT) in early stage non-small cell lung cancer (NSCLC) is unclear. Therefore, we conducted a systematic review of NLR and PLR as prognostic factors for overall survival (OS) of patients with Stage 1 NSCLC following SBRT with curative intent. **Materials and Methods:** Following PRISMA guidelines, the EMBASE, Cochrane library, MEDLINE, and Pubmed databases were searched from January 1996 until September 2017 for primary research studies and systematic literature reviews that reported both pre-treatment NLR and PLR of patients with Stage 1 NSCLC and OS of patients following SBRT. Screening, data extraction, and risk of bias assessment were performed by two independent reviewers.

**Results:** An electronic database search identified 292 articles that met our search criteria of which five (three published full-text and two conference abstracts) were determined to be eligible for inclusion. Studies were all retrospective chart or database reviews conducted in North America, and were published between 2015 and 2017. The dose fractionation schemes varied between studies, ranging predominantly from 30 Gy to 60 Gy in 3 to 5 fractions. A formal meta-analysis was not feasible due to the heterogeneity of published studies. Overall, there were variations as to whether NLR and PLR variables were analyzed as a continuous versus dichotomous prognostic factor. When dichotomized, cut-offs for a high NLR ranged from 2.18 to 3.16 while cut-offs for a high PLR ranged from 146 to 187.27. Four studies analyzed NLR as a dichotomous factor and all found a statistically significant association of high NLR with worse OS. Similarly, all three studies that examined PLR as a dichotomous prognostic factor found a statistically significant association between high PLR and worse OS. As a continuous variable, two of three studies found NLR to be a significant prognostic factor for OS while only two of four studies found PLR to be a significant prognostic factor for OS.

**Conclusions:** NLR and PLR appear to be relevant prognostic factors for OS following lung SBRT in Stage I NSCLC, particularly when NLR and PLR were dichotomized as high and low values. A minimum cut-off value of above 3.00 for NLR and 155 for PLR may be appropriate, but requires further prospective validation. NLR and PLR are readily accessible and inexpensive tests that can be performed in the clinic to aid in clinical decision-making on the appropriateness of SBRT for Stage 1 NSCLC.

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#### PROSPECTIVE EVALUATION OF QUALITY OF LIFE AND PULMONARY FUNCTION IN EARLY-STAGE NON-SMALL CELL LUNG CANCER PATIENTS TREATED WITH ROBOTIC SBRT: FIVE-YEAR RESULTS

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**Purpose:** To prospectively evaluate the quality of life (QoL) and pulmonary function of patients with early-stage non-small cell lung cancer (NSCLC) treated with robotic stereotactic body radiation therapy (SBRT).

**Materials and Methods:** Eligible patients had histologically confirmed T1-T2N0M0 NSCLC and were not surgical candidates. SBRT was delivered with CyberKnife® at a median dose of 60 Gy in 3 fractions for peripheral tumours and 50 Gy in 4 or 5 fractions for central tumours. QoL was scored using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 (QLQ-C30) and Lung Cancer-13 questionnaires. Pulmonary function tests (PFTs) included forced expiratory volume in 1 second (FEV1) and lung diffusion capacity of carbon monoxide (DLCO). Changes over time in QoL scores and PFTs were tested with nonparametric tests for longitudinal data. Tumour control and survival rates were estimated with the Kaplan-Meier method. Toxicity was assessed with the Common Terminology Criteria for Adverse Events version 3.0.

**Results:** From January 2010 to May 2013, 45 patients were enrolled. Median follow-up was 63 months. QLQ-C30 mean ( $\pm$ SD) baseline scores for global QoL and physical functioning were  $66 \pm 20\%$  and  $73 \pm 22\%$ . Multilevel analyses showed no statistically and clinically significant (10-point change) deterioration in any of the QoL scores after SBRT. Mean baseline PFTs were  $68 \pm 23\%$  for FEV1% and  $63 \pm 25\%$  for DLCO%. There was a progressive decline in mean PFTs of 1.2%/year for FEV1% and 2.3%/year for DLCO% that did not reach statistical significance. At five years, actuarial estimates for local control, disease-free survival, and overall survival were respectively 94%, 46%, and 59%. One patient with a history of idiopathic pulmonary fibrosis died of radiation pneumonitis three months after treatment. Grade 3 dyspnea occurred in three (7%) patients and four (9%) patients presented with grade  $\leq 2$  radiation-induced rib fractures.

**Conclusions:** In early-stage inoperable NSCLC patients, SBRT may achieve long-term tumour control while maintaining QoL and pulmonary function.

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#### DOSIMETRIC IMPACTS OF VARIATIONS IN ORGAN AT RISKS DELINEATION DURING LUNG SABR

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**Purpose:** The aim is to quantify the interobserver variations in delineation of thoracic organs at risk (OARs) and to evaluate its dosimetric impacts during lung stereotactic ablative radiation therapy (SABR).

**Materials and Methods:** This analysis included lung tumours treated with near-real-time tumour tracking using robotic SABR. Peripheral tumours were treated with 60 Gy in 3 fractions and central tumours with 50 Gy in 5 fractions. Gross tumour volume (GTV) and OAR delineations were performed by four experienced radiation oncologists on the end-expiration phase of the planning 4D CT scan. A 5 mm margin was added in all directions to obtain the final planning target volume. Delineations of selected treatment OARs including whole lung, trachea, proximal bronchial tree (PBT), esophagus and heart were retrospectively compared to reference contours blindly performed by a single radiologist as per Radiation Therapy Oncology Group (RTOG) thoracic atlas. Metrics used to compare contours included Dice similarity coefficient (DSC), absolute volumetric difference (AVD) and average surface distance (ASD). Treatment doses were projected on reference OARs contours to obtain maximum point dose (mPD) differences.

**Results:** Twenty early stage lung cancer patients including eight with central lesions were included. OARs with greatest mean ( $\pm$ SD) contours variations were PBT (DSC  $0.64 \pm 0.09$ , AVD  $47.3 \pm 12.3\%$ , ASD  $2.0 \pm 1.1$  mm), trachea (DSC  $0.72 \pm 0.09$ , AVD  $38.9 \pm 13.4\%$ , ASD  $1.4 \pm 0.5$  mm) and heart (DSC  $0.91 \pm 0.03$ , AVD  $9.1 \pm 4.6\%$ , ASD  $1.8 \pm 0.8$  mm). Variations in contours were mainly induced by 1) discordant identification of anatomic structures; 2) differences in the application of delineation guidelines; and 3) intentional modification of anatomical structures by the radiation oncologist (e.g. OARs dose sparing). Maximum differences in mPD were observed in centrally located tumours, ranging from -24.8 Gy to 31.2 Gy for PBT, -11.6 Gy to

13.0 Gy for heart and -2.5 Gy to 5.4 Gy for trachea.

**Conclusions:** Interobserver variation should be considered when implementing strict SABR OAR constraints. Although variations are typically in the order of a few millimeters, dosimetric impacts can be significant in the context of steep SABR dose gradients. The observed variations have lead us to further standardize our institutional delineation guidelines.

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#### THE IMPACT OF TUMOUR SIZE ON LOCAL TUMOUR CONTROL FOR PERIPHERAL LUNG LESIONS TREATED WITH STEREOTACTIC ABLATIVE BODY RADIOTHERAPY (SABR): A MULTI-INSTITUTIONAL STUDY

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**Purpose:** To determine if the Internal Gross Tumour Volume (IGTV) correlates with local tumour control.

**Materials and Methods:** We analyzed 208 patients who had primary lung tumours and received 48 Gy in 4 fractions in three oncology centres between 2012 and 2016. Patients were stratified into groups with IGTV below or above the median value. Recurrence data was obtained from follow-up notes and post-treatment CT images. Progression located within the 50% isodose volume of the initial treatment was defined as local recurrence. Kaplan-Meier analysis was used to calculate local control and the Log-Rank test was used for statistical analysis.

**Results:** Local failure occurred in 4% of the 208 patients included in this study. There were 100 patients in the small-IGTV group (below the median IGTV value of 7.5 cc) and 108 patients in the large-IGTV group (above the median IGTV value of 7.5 cc). Patients with small-IGTV had higher local control compared to patients with large-IGTV: 99% versus 93%, respectively. Local control rate at four years was 94% versus 70% for patients with small- versus large-IGTV respectively ( $p < 0.05$ ). The mean local control time was 55 (with 95% CI 52 and 57) and 51 (with 95% CI 45 and 57) months for small- and large-IGTV patients, respectively.

**Conclusions:** In this retrospective analysis, high local control was achieved for peripheral lung lesion using SABR. Smaller IGTV correlates with better local control.

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#### A DOSIMETRY COMPARISON AND LOCAL TUMOUR CONTROL ANALYSIS OF 3DCRT-SABR VERSUS VMAT-SABR FOR PERIPHERAL LUNG LESIONS

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**Purpose:** To determine if the differences in IGTV dose metrics between 3DCRT-SABR and VMAT-SABR for peripheral lung lesions are statistically significant and if these dose differences correlate with local tumour control.

**Materials and Methods:** We analyzed 237 patients who were treated at three centres between 2013 and 2016. The prescribed dose was 48Gy in 4 fractions. Ninety-eight patients were treated with VMAT and 139 were treated with 3DCRT. For dosimetric comparison, the maximum, mean and minimum dose and Internal Gross Tumour Volume (IGTV) for each case were obtained from the treatment planning system. For local control analysis, only patients with primary lung tumours were included. Recurrence data was obtained from a combination of follow-up notes and post-treatment CT images. Tumours located within the 50% isodose volume of the initial treatment were defined as local recurrence. Wilcoxon-Mann-Whitney rank test was used for statistical analysis and Kaplan-Meier analysis was used to calculate local control.

**Results:** There was a statistically significant difference between VMAT and 3DCRT in IGTV maximum dose (124.8% versus 129.0%,  $p < 0.001$ ), IGTV minimum dose (101.2% versus 106.6%,  $p < 0.001$ ) and IGTV mean dose (113.6% versus 120.2%,  $p < 0.001$ ) despite insignificant differences in IGTV volume (mean 13.26 cc (VMAT) versus 11.59 cc (3DCRT),  $p = 0.27$ ). The mean local control time was 43 and 47 months for VMAT and 3DCRT, respectively. Local control rate at two years was 95.2% versus 94.5% for VMAT and 3DCRT, respectively ( $p = 0.343$ ).

**Conclusions:** Within the three centres evaluated, 3DCRT resulted in higher IGTV dose metrics compared to VMAT. These dose differences did not have a statistical impact on local control.

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#### ARE HIGHER RADIATION DOSES BENEFICIAL IN LIMITED-STAGE SMALL-CELL LUNG CANCER? A PROPENSITY SCORE-MATCHED ANALYSIS

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**Purpose:** Hypofractionated thoracic radiotherapy may be advantageous in limited-stage small-cell lung cancer (LS-SCLC) due to short overall treatment times, decreased resource utilization, and patient convenience. However, there are no randomized data comparing hypofractionated radiotherapy (HFRT; defined as 40 Gy in 15 fractions or 45 Gy in 20 fractions) and high dose conventionally-fractionated radiotherapy (CFRT; defined as  $\geq 60$  Gy in 2 Gy fractions) in LS-SCLC patients. The objective of this study was to compare the survival outcomes and toxicities of these fractionation schemes using propensity score-matched retrospective data to simulate the setting of a clinical trial.

**Materials and Methods:** This retrospective study examined records of patients from our institution diagnosed with LS-SCLC between January 2000 and December 2013 who were treated with HFRT or CFRT. Propensity scores were estimated by logistic regression using age, performance status, concurrent chemoradiation usage and prophylactic cranial irradiation (PCI) usage. Nearest neighbour-matching was performed on a 1:1 basis using a caliper distance of 0.1, without replacement. Overall survival (OS) and progression-free survival (PFS) endpoints were estimated by the Kaplan-Meier method and compared with log-rank tests. Cumulative incidences of esophageal and pulmonary toxicity were compared with Fisher's exact tests. A two-sided significance level of 0.05 was used.

**Results:** Among 398 LS-SCLC patients reviewed, 57 patients treated with HFRT and 61 patients treated with CFRT were included in the unmatched analysis. Five-year OS was 26% for the HFRT cohort and 24% for the CFRT cohort ( $p = 0.82$ ). Five-year PFS was 22% for both cohorts ( $p = 0.79$ ). Significant differences in age, performance status, concurrent chemoradiation usage and PCI usage were noted in the unmatched cohorts. After propensity score-matching, the balanced cohorts each contained 37 patients. Five-year OS was 25% and 27% ( $p = 0.72$ ) and five-year PFS was 25% and 24% ( $p = 0.63$ ), respectively for the HFRT and CFRT cohorts. Incidence of any esophageal toxicity was not significantly different between the cohorts (92% HFRT, 84% CFRT,  $p = 0.60$ ), though there was a trend towards a higher incidence of any pulmonary toxicity in the CFRT cohort (59% versus 38%,  $p = 0.06$ ).

**Conclusions:** OS and PFS outcomes were similar between HFRT and CFRT in balanced cohorts. HFRT was associated with a potentially reduced incidence of pulmonary toxicity. These results suggest clinical equipoise and a prospective randomized study is needed to determine the optimal radiotherapy fractionation in patients with LS-SCLC.

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#### A NOVEL AND PRACTICAL PROGNOSTIC MODEL FOR LIMITED-STAGE SMALL CELL LUNG CANCER

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**Purpose:** There is currently no prognostic model designed specifically for patients with limited-stage small cell lung cancer (SCLC). The purpose of this study was to construct a novel prognostic model for this patient population using baseline characteristics readily available in clinic.

**Materials and Methods:** An institutional retrospective consecutive patient database was constructed by reviewing the charts of patients diagnosed with limited-stage SCLC between January 2000 and December 2013. Baseline patient characteristics, treatment details and outcomes were extracted. The primary endpoint for the prognostic model was overall survival (OS) and the secondary endpoint was progression-free survival (PFS). Univariable and multivariable Cox regression analyses were performed to identify variables associated with OS and PFS. Prognostic models were generated using recursive partitioning analysis (RPA).

**Results:** A total of 398 patients were eligible for analysis. Median follow-up was 8.2 years. The median age was 67 (range: 40-87). Overall, 94% of patients received chemotherapy, 82% received radiotherapy and 65% received both concurrently. Both hypofractionated (40 Gy in 15 fractions) and conventionally-fractionated (50-66 Gy in 25-33 fractions) radiotherapy were used. Prophylactic cranial irradiation was used in 45% of patients. The median OS for the entire cohort was 15.4 months, with a five-year OS of 19.7%. Overall median PFS was 9.3 months, with a five-year PFS of 14.1%. On multivariable Cox regression, age, Eastern Cooperative Oncology Group (ECOG) performance status, tumour location and baseline presence of any pleural effusion were prognostic of OS, while performance status and T-stage were prognostic of PFS. RPA model of OS divided patients into favorable (ECOG 0-2, no pleural effusion, middle/upper lobe location: five-year OS 31%), intermediate (ECOG 0-2, no pleural effusion, non-middle/upper lobe location: five-year OS 21%) and unfavourable (ECOG 3-4 or any pleural effusion: five-year OS 5-8%) groups (log-rank  $p < 0.001$ ). RPA for PFS divided patients into favourable (ECOG 0-2,  $\leq T3$ : five-year PFS 21%) and unfavourable (ECOG 3-4 or T4: 5-year PFS 5-9%) groups (log-rank  $p < 0.001$ ).

**Conclusions:** Novel prognostic factors for OS and PFS based on baseline patient characteristics were successfully identified for patients with limited-stage SCLC. RPA prognostic models were able to separate patients into distinct risk groups for OS and PFS. Our results will benefit from further external validation and can be useful in stratifying patients in future prospective studies.

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#### STEREOTACTIC ABLATIVE RADIOTHERAPY FOR A RARE CASE OF EARLY LUNG CANCER FOLLOWING DOUBLE LUNG TRANSPLANTATION

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**Purpose:** Development of primary lung cancer in donor lung post-lung transplantation is very rare. Herein, we present a case of a patient with a Stage IB adenocarcinoma arising from donor lung post-bilateral lung transplantation, which was performed due to advanced emphysema. Stereotactic ablative radiotherapy (SABR) was used as the primary treatment modality for this patient due to medical inoperability. A review of existing literature was performed to investigate the prevalence of lung cancer arising from donor lung.

**Materials and Methods:** The patient's chart was extensively reviewed for baseline patient status, tumour features, radiotherapy characteristics and post-SABR follow-up results. The patient's transplant physician was contacted to obtain donor characteristics and peri-transplant information. The Medline database was queried from inception to Dec 2017 to identify other reports of primary lung cancer arising from donor lung post-transplantation.

**Results:** Our patient is a 60-year-old female who received a double-lung transplant in 2008 secondary to emphysema. The donor was a 64-year-old female with a 25 pack-year smoking history. The patient's past history was otherwise significant for post-transplant lymphoproliferative disorder treated with chemotherapy and chronic lung allograft dysfunction, leading to significantly compromised pulmonary function. In 2016, the patient presented with a positron emission tomography-avid 12 mm right upper lobe lung nodule, which was biopsied to show adenocarcinoma, ALK and EGFR mutation negative. The patient was presented at multidisciplinary rounds and was deemed not operable due to poor pulmonary function. She consented to undergo SABR to a dose of 60 Gy in 8 fractions, which was delivered with volumetric modulated arc therapy. Maximum point dose was 75 Gy, mean lung dose was 3.3 Gy and V20 was 4.3%. The patient tolerated

treatment well and was alive without recurrence 12 months post-SABR. On literature review, the prevalence of primary lung cancer arising from donor lung ranged from 0.3% to 1% of lung transplant patients. Only one other case of SABR treatment for early lung cancer arising from donor lung was identified, also demonstrating good tolerance and durable control.

**Conclusions:** We demonstrate the feasibility and safety of full-dose SABR for an early-stage non-small cell lung cancer arising from donor lung in a double-lung transplant recipient. Treatment options are frequently limited for these patients and the effect of immune suppression on systemic therapy and disease progression is unclear. A larger repertoire of patients with adequate follow-up is required to determine SABR's oncologic effectiveness in this population of chronically immunosuppressed patients.

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### RADIOTHERAPY NEAR END OF LIFE IN A RAPID ACCESS LUNG CANCER CLINIC COMPARED TO STANDARD PRACTICE

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**Purpose:** The Rapid Access Lung Cancer Clinic (RALCC) at our institution is designed to deliver palliative radiotherapy (RT) to patients with symptomatic newly diagnosed incurable lung cancer. Potentially eligible patients are triaged in advance, with CT simulation and RT appointments pre-booked to start on the same day as their initial consultation. As the result of a prior analysis in 2014 identified that 13% of patients received RT in the last four weeks of life, we hypothesized that RALCC patients may be more likely to receive RT near end of life due to the short time-frame for treatment decisions and the pre-booked same day treatment appointments. The purpose of this study was to compare RT utilization near end of life in RALCC to that in standard practice (SP).

**Materials and Methods:** Patient demographic and treatment factors were retrospectively collected from the electronic records for all patients assessed in RALCC in 2014 and 2015 and a SP cohort (all newly diagnosed Stage IV lung cancer patients referred to a Radiation Oncologist at a neighboring cancer center during the same time period). Differences between RALCC and SP patient and treatment factors were compared using chi-square and t-tests. Kaplan-Meier analysis was used for survival statistics.

**Results:** One hundred and eighty-seven patients were assessed in RALCC and 284 in SP. There were no significant differences between the two groups for gender, age, performance status, histology or number of lines of palliative chemotherapy. RALCC patients were more likely to receive RT following the initial consultation (93% versus 80%,  $p < 0.001$ ), start RT on the same day as the initial consultation (77% versus 7%,  $p < 0.001$ ) and receive single fraction RT as their longest course (18% versus 11%,  $p < 0.05$ ). Anatomic sites treated were also similar between RALCC and SP (chest 52% versus 61%,  $p = 0.1$ ; bone 44% versus 37%,  $p = 0.2$ ; brain 30% versus 29%,  $p = 0.8$ ). Median survival from consultation was 12 and 18 weeks for RALCC and SP respectively ( $p = 0.4$ ). There was no difference in receipt of RT within four weeks (15% versus 12%,  $p = 0.4$ ) or two weeks of death (5% versus 7%,  $p = 0.4$ ) for RALCC patients compared to SP. However, 12 patients in the SP cohort spent more than half of their remaining days receiving RT, compared to only one patient in RALCC (4.2% versus 0.5%,  $p = 0.02$ ) and RALCC patients were more likely to complete the intended course of RT (98% versus 93%,  $p = 0.03$ ).

**Conclusions:** Despite the short time frame in which physicians have to make treatment decisions in RALCC, their patients are not more likely to receive RT in the last four weeks of life, but they are more likely to receive single fraction RT and spend less than half of their remaining days on treatment. This difference may be attributed to the multidisciplinary nature of RALCC, and the specialized interest in palliative care, which may influence methods of prognostication and choice in fractionation.

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### PALLIATIVE RADIOTHERAPY NEAR THE END OF LIFE IN LUNG CANCER PATIENTS: A POPULATION-BASED ANALYSIS

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**Purpose:** Palliative radiotherapy (PRT) can improve quality of life for patients with advanced lung cancer, but symptomatic relief may take up to a few weeks. PRT in the last four weeks of life is an emerging indicator of poor quality care. We sought to determine the patterns of PRT utilization in patients with advanced lung cancer in a population-based health care system.

**Materials and Methods:** All patients with lung cancer in a Canadian province treated with PRT in 2014 and 2015 were identified. Patient and treatment characteristics were extracted from a provincial cancer database. Chart review was performed for patients receiving potentially radical fractionation schedules to confirm palliative intent. Site of PRT was classified as bone, brain or chest; all other sites were excluded. Patients who received more than one course of PRT were considered independently for each course. Associations between starting a course of PRT within four weeks of death and patient/treatment characteristics were assessed using chi-square and t-tests. Multi-variable logistic regression analysis was subsequently performed.

**Results:** 4160 courses of PRT were delivered to 2571 patients. Median survival for the entire cohort was 17 weeks (95% CI 15.7-17.4) from start of PRT. Forty-one percent of PRT courses were delivered to chest, 39% to bone and 20% to brain. Fourteen percent of PRT courses were prescribed to patients in the last four weeks of their life, with significant differences by male versus female (17% versus 11%;  $p < 0.001$ ), performance status (ECOG 0, 1, 2, 3 and 4 were 8%, 9%, 11%, 19% and 39% respectively;  $p < 0.001$ ), histology (adenocarcinoma, squamous cell carcinoma, NSCLC NOS and small cell lung cancer were 11%, 15%, 19% and 16% respectively;  $p < 0.001$ ) and site of PRT (bone, chest and brain were 17%, 12% and 11%;  $p < 0.001$ ). These associations persisted on multi-variable analysis. Of PRT courses delivered in the last four weeks of life, the majority were planned using simple techniques (1-2 fields, 96%) and using short fractionation regimes (single fraction for bone, 71%;  $\leq 5$  fractions for brain, 92%;  $\leq 5$  fractions for chest, 91%).

**Conclusions:** This population-based analysis found that 14% of PRT courses for lung cancer were delivered in the last four weeks of life. Males, those with poor performance status, non-adenocarcinoma histology and bone metastases were more likely to receive PRT near end of life. Appropriately, simple planning techniques and shorter fractionation regimes were used more commonly closer to death. Although there is no consensus of what constitutes poor quality care with regard to PRT near end of life, the limited number of published series report 10-20% death within four weeks of PRT. While further clarification in this domain occurs, clinicians should be cognizant of the prognosis of their patients when considering indications and fractionation schedules of PRT.

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### FINANCIAL TOXICITY PREDICTS SURVIVAL FOLLOWING CHEMORADIOTHERAPY FOR LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER IN A SOCIOECONOMICALLY DIVERSE POPULATION

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**Purpose:** "Financial toxicity" (FT) describes the burden faced by patients from the out-of-pocket costs of cancer treatment. Our center serves a population including many patients with low socioeconomic status (SES), for whom even relatively small financial requirements may cause significant hardship. Here, we report on the association between survival and both patient-reported FT and SES for patients with locally advanced non-small cell lung cancer (NSCLC).

**Materials and Methods:** The study population includes patients treated with definitive concurrent chemoradiotherapy for locally advanced NSCLC in our department between 2015 and 2017 and enrolled on a prospective clinical trial that includes pre-treatment quality of life assessment using the EORTC QLQ-C30 questionnaire. One question asks about "financial difficulties" caused by illness or treatment, with responses ranging from 1 (indicating "not at all" experiencing financial difficulties) to 4 ("very much"). We tabulated FT scores and socioeconomic status (SES), which was based on home address using neighborhood-level data and dichotomized at the median value for survival analyses. Financial toxicity scores were compared

to SES using Spearman correlation. Financial toxicity scores and SES were tested as predictors of progression-free survival (PFS) using Cox proportional hazards modeling and log-rank testing. Median survival was calculated using the Kaplan-Meier method.

**Results:** Thirty-five patients met inclusion criteria. Prior to initiating treatment, 18 patients (51%) answered "not at all" regarding FT while 11 (31%) answered "a little," one (3%) answered "quite a bit" and five (14%) answered "very much." FT scores were not associated with SES (Spearman correlation  $p = 0.173$ ). With a median follow-up duration for surviving patients of 11 months, 16 patients (46%) experienced disease progression, and 11 patients (31%) have died. Cox proportional hazards modeling demonstrated that increasing FT score was associated with reduced PFS (HR = 1.80 per unit increase, 95% CI: 1.21 to 2.66,  $p = 0.003$ ). Median PFS was 11.7 months for patients who responded "not at all" regarding financial difficulty, and median PFS was 6.6 months for other patients (log-rank  $p = 0.023$ ). PFS was not associated with SES ( $p = 0.42$ ).

**Conclusions:** In our diverse patient population, patient-reported FT was associated with worse PFS while SES was not. Larger data sets are needed to validate these findings and to investigate the effect of FT in other cancer types. Future work should seek to clarify the underlying causes of FT and how it contributes to barriers to accessing care by means of more detailed financial data and patient reporting. Prospective trials should investigate the effect on survival of screening patients for FT at initial clinical intake and interventions such as support to help patients' access financial resources.

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#### ACCELERATED HYPOFRACTIONATED RADIOTHERAPY FOR CENTRALLY LOCATED LUNG TUMOURS NOT SUITABLE FOR STEREOTACTIC BODY RADIOTHERAPY (SBRT) OR CONCURRENT CHEMORADIOTHERAPY (CRT)

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**Purpose:** In our institution, accelerated hypofractionated radiotherapy is a treatment option for 1) Stage I lung non-small cell lung cancer (NSCLC) patients whose tumours are too bulky or too centrally located for SBRT; and 2) select Stage II-III NSCLC patients who are not candidates for concurrent CRT. The purpose of this project was to review the clinical outcomes of a large single institutional experience of treating such patients with a dose of 60 Gy in 15 fractions in an era when SBRT was routinely used in clinical practice for early stage lung cancer.

**Materials and Methods:** Central tumours were defined as the gross target volume being in contact with mainstem bronchi, trachea, esophagus, great vessels, or heart. All patients who received 60 Gy in 15 fractions treated between 2008 and 2017 were reviewed. Competing risk analysis was used to calculate the cumulative incidence of local failure (LF), regional failure (RF), and distant failure (DF). Kaplan-Meier methodology was used to calculate overall survival (OS). Univariate analyses were used to look for potential predictive factors.

**Results:** Eighty-nine patients were treated. Median follow up time was 24.0 months (range: 6.1-94.2 months). Median age of patients was 79.4 years and most tumours were adenocarcinoma ( $n = 47, 52.8\%$ ), followed by squamous cell carcinoma ( $n = 31, 34.8\%$ ). Thirty patients (33.7%) had Stage I disease, 47 patients (52.8%) had Stage II-III disease, and 12 patients (13.5%) had Stage 4 disease (mostly oligometastatic). Cumulative incidence of LF was 15.3% at two years. In those with Stage I-III disease, the cumulative incidence of RF and DF were 12.9%, and 28.5%, respectively at two years. OS was 74.9% at two years, with a median OS of 39.4 months for those with Stage I-III disease. In the subset of those with Stage II-III disease, the median OS was 38.1 months and two-year OS was 67.7%. Tumour stage, histology, EGFR mutation status, and location were not found to be statistically significant predictors for any outcomes, although tumour size  $> 3.5\text{cm}$  was borderline significant in predicting for a higher cumulative incidence of LF (subdistribution hazard ratio = 2.726; 95% confidence interval 0.995-7.469;  $p = 0.051$ ). The most common toxicity was radiation pneumonitis ( $n = 6, 6.4\%$ ). The cumulative incidence of any Grade 3 toxicity was 10.8% at  $\geq 1$  year. There were no deaths or hospitalizations directly attributed to treatment.

**Conclusions:** Accelerated hypofractionated radiotherapy to a dose of 60 Gy in 15 fractions resulted in favorable outcomes in NSCLC patients who

were not suitable for SBRT or concurrent CRT. Patients with Stage II-III disease had good OS despite not receiving concurrent chemotherapy. Severe toxicities were uncommon.

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#### UPSTAGING RATE IN LOCALLY ADVANCED LUNG CANCER PATIENTS AS A FUNCTION OF DELAY FROM DIAGNOSTIC IMAGING

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**Purpose:** Diagnostic F18-FDG PET imaging has become standard of care in the diagnosis non-small cell lung cancer (NSCLC) due to superior sensitivity and specificity compared to conventional helical CT scans. Due to the aggressive nature of NSCLC, upstaging of disease due to time elapsed between diagnosis and treatment is a concern for patients scheduled to undergo radical radiotherapy. We seek to review our institution's experience with treatment planning PET-CT scans and potential upstaging rates.

**Materials and Methods:** As part of a REB-approved study, PET-CT scans used for initial staging were compared with PET-CT images acquired for treatment planning purposes by two independent assessors. Patients' age at diagnosis, sex, tumour histology, stage and date at diagnostic PET-CT, stage and date at treatment PET-CT and survival/follow-up were collected prospectively. Patients were staged with the AJCC 7th edition TNM Staging System. Reported stages were compared and differences were reconciled by a third independent party. Descriptive statistics were calculated and the estimates of the upstage rates were obtained using the Kaplan-Meier product-limit method.

**Results:** Between October 2009 and February 2012, 28 patients were accrued to the study. The mean age was 64 years (range: 41-81). Eight were female and 19 were male. The majority of patients had Stage IIIA disease (15), with others having Stage IIIB (11), Stage IIA (one) and Stage IIB (one) disease. The most common tumour histology was adenocarcinoma (20). Median time between diagnostic and planning PET-CT scans was 21 days (range: 2-73). Overall upstaging occurred in 25% of patients. The TNM upstage breakdown was as follows: T-stage 7%, N-stage 14% and M-stage 11%. The three patients who had newfound metastatic disease were no longer candidates for radical treatment. New nodal stations were found in 32% of patients, thereby necessitating a change in the treatment volumes. The rate of overall upstaging increased with delay between staging and treatment planning PET-CT scans: 13% at 20 days (95% CI: 4%-95%), 33% at 40 days (95% CI: 14%-86%), and 56% at 60 days (95% CI: 29%-71%).

**Conclusions:** The use of a treatment planning PET-CT demonstrated upstaging which altered patients' treatment due to the detection of new nodal station involvement or metastatic disease. Our data is consistent with two published studies which showed similar upstaging rates.

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#### A PROSPECTIVE STUDY OF MRI ASSESSMENT OF POST-RADIATION CHANGES FOLLOWING STEREOTACTIC BODY RADIATION THERAPY FOR NON-SMALL CELL LUNG CANCER

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**Purpose:** Follow up computed tomography (CT) scans after lung SBRT are difficult to interpret due to the presence of benign fibrosis that can difficult the detection of local recurrence. The objective of this study was to determine the feasibility of a novel thoracic magnetic resonance (MR) imaging protocol incorporating diffusion-weighted imaging (DWI) and dynamic contrast-enhanced (DCE) imaging for the assessment of the treated lung parenchyma after SBRT.

**Materials and Methods:** On a prospective trial, post-treatment MR images were acquired in 30 patients treated with SBRT (divided into three different cohorts according to the likelihood of local recurrence as per an expert panel). These images were assessed by an expert thoracic radiologist blinded to clinical data, which indicated local recurrence in a dichotomous

fashion. Local recurrence was confirmed by biopsy or subsequent growth on follow up CT scans.

**Results:** Thirty patients underwent MR imaging as part of this study, and 27 out of 30 patients were analyzable for local recurrence. MR imaging was conducted at a median of 27.3 months (range: 6.5 to 71 months) from SBRT. No side effects resulted from either MR imaging or contrast administration. At a median follow up time of 45 months after treatment, three local recurrence episodes have occurred. MR assessment diagnosed seven patients as having a local recurrence that was later confirmed in three and did not miss any of the true local recurrences. When comparing ADC values according to local recurrence, mean ADC value for the local recurrence-free group was  $1770 \times 10^{-3} \text{mm}^2/\text{s}^2$  (range: 1038 to  $3105 \times 10^{-3} \text{mm}^2/\text{s}^2$ ) versus  $981 \times 10^{-3} \text{mm}^2/\text{s}^2$  (range: 926.6 to  $1065 \times 10^{-3} \text{mm}^2/\text{s}^2$ ) for the local recurrence group ( $p = 0.0014$ ).

**Conclusions:** A novel 3.0 T MR imaging protocol incorporating DWI and DCE was feasible and confirmed the suspicion of local recurrence in patients with highly suspicious CT scans. This imaging tool could potentially aid in selecting patients for salvage treatment after local SBRT failure. Future work should be pursued to validate these findings.

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#### CLINICAL IMPACT OF INCREASED COMPLEXITY OF TOTAL MARROW IRRADIATION TREATMENTS

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**Purpose:** Transitioning from open-field extended-distance total body irradiation to VMAT total marrow irradiation increases complexity of contouring, treatment planning, and quality assurance. These steps were practiced and studied before implementation to estimate time needed for each step and to establish booking guidelines for imaging and start of treatment. TMI treatments also increase the complexity of patient set-up, immobilization, daily imaging, and dose delivery at the treatment unit. This work provides an analysis of the clinical impact of daily TMI patient treatments in comparison with the previously used TBI technique.

**Materials and Methods:** Eligible patients were treated with TMI instead of TBI starting in December 2015, and each received 12 Gy in 6 fractions delivered BID over three days. Data was retrospectively reviewed using the Aria database to record the actual versus scheduled time of appointments, length of time used for patient set-up and imaging, the effect of any increase in treatment time on patients (e.g. need for breaks due to discomfort, nausea/vomiting, urination) and factors that lead to significant delays or prolonged appointments. Data was also recorded for patients treated with TBI during the three years before the switch to TMI for comparison.

**Results:** Thirty-one patients received TMI between December 2015 and January 2018. This led to averages of 1.5 and 1.1 patients treated per month in the 2016 and 2017 calendar years respectively. During our clinic's TBI era, the monthly average was 1.0 (2013), 1.8 (2014) and 1.4 (2015) patients treated. The percentage of appointments that either ended early or within 10 minutes of the scheduled end time was 67% for TMI and 68% for TBI. Fifteen percent of TMI and 9% of TBI treatments ended more than 20 minutes late. Daily BID treatments must be separated by at least six hours, so delays in the morning appointment can lead to delays in the subsequent afternoon appointment. A total of 101 (TMI) and 115 (TBI) afternoon appointments were reviewed and 46% of TMI appointments ended before 5pm, and another 9% ended before 5:30pm. For TBI, 80% finished before 5pm, another 11% by 5:30pm. In both cases there were three appointments that ended after 7pm. The main issues encountered during TMI that led to significant increases in appointment length were positioning and imaging of patients' arms and health status of patients. Some inefficiencies in scheduling of treatments were also identified.

**Conclusions:** While TMI introduces increased complexity at all stages of treatment compared to TBI, these differences can predominantly be accounted for during patient scheduling and booking. Daily treatment times were longer for TMI, however incidents of unexpected delays and prolonged appointments were similar in both TMI and TBI. Due to the length of the treatments, this more frequently led to patients finishing after the end of regular clinic hours for TMI. This analysis has led to some proposed changes in appointment booking as well the need for further

investigation into more reliable immobilization for patients' arms.

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#### TREATMENT OUTCOMES OF PATIENTS WITH LOW GRADE LYMPHOMA OF THE ORBIT OR CONJUNCTIVAE

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**Purpose:** Orbital lymphoma is a rare presentation low grade Non-Hodgkin's Lymphoma (NHL). Radiation therapy (RT) can be used with curative intent in Stage I and II or if the lymphoma is limited to the bilateral orbits (Stage 4AE). This study evaluated local control and survival outcomes of patients with unilateral or bilateral orbital lymphoma treated in a provincial population. The previous largest series to date is 81 patients.

**Materials and Methods:** Subjects were 179 patients referred between 1980-2016 with newly diagnosed low grade orbital or conjunctival lymphoma. Demographic, tumour and treatment characteristics were abstracted by chart review.

**Results:** Median follow-up time was 8.5 years (Range: 0.2-29 years). Median age at diagnosis was 66 years (Range: 20-97 years). Forty-two percent were male. The most common histologic subtype was MALT (74%). Most patients were Stage IAE (78%) or 4AE (20%). Orbital RT was used in 124 patients with Stage IAE (88%), 2 patients with Stage 2AE (100%) and 10 patients with Stage 4AE (28%). Ninety-four percent received 24-25 Gy/10-12 fractions. Other treatments were antibiotics (eight patients), chemotherapy (nine patients), radioimmunotherapy (six patients), surgery (three patients) and observation (seven patients). Within the group treated with orbital RT, there were no local recurrences, 6.4% had contralateral orbital relapse and 16% had distant relapse. In Stage IAE, the average time to progression was 4.75 years. In Stage 4AE, the average time to progression was 2.58 years. The local recurrence risk was high in patients who did not undergo RT to the orbit (53%). The risk of death in the entire cohort from lymphoma was 6%.

**Conclusions:** Radiation therapy for stage I-IIAE and 4AE (bilateral) orbital low grade NHL resulted in excellent local control in this population-based cohort. Patients who did not receive primary orbital radiotherapy had very high rates of local recurrence, even in the setting of other treatments.

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#### EFFICACY OF PALLIATIVE RADIATION THERAPY (RT) FOR DIFFUSE LARGE B-CELL LYMPHOMA: A POPULATION-BASED RETROSPECTIVE REVIEW

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**Purpose:** To investigate outcomes of palliative RT in patients with diffuse large B-cell lymphoma (DLBCL) and clinical factors that impact treatment efficacy. **Materials and Methods:** All patients with DLBCL who received palliative RT from 2001-2015 in the province were reviewed for patient characteristics, treatment details, and outcomes.

**Results:** Two hundred and seventeen patients who received 370 courses of palliative RT were identified. Median age at RT was 76 years, and 57% of courses were in male patients. Median equivalent dose in 2 Gy fractions (EQD2) was 19 Gy. Size of treated lesion was documented in 240 courses; median largest dimension was 5.8 cm. Irradiated sites were 22% skin, 18% head and neck, 14% spine, 13% abdomen, 10% pelvis, 7% bone, 6% thorax, 5% axilla, and 5% other. Indications for palliative RT were 42% pain, 22% enlarging mass, 20% obstruction or peripheral nerve compression, 9% spinal cord compression, 4% bleeding, 2% non-healing wound, and 1% pruritis. Clinical response assessment was available for 274 courses (74%), of which 42 courses had radiologic follow up; 2 had only radiologic response assessments. Symptom resolution was achieved in 42% of courses (114/274), symptom improvement in 40% (110/274), and stability in 13% (36/274); there was symptom progression in 5% (14/274). For courses given for pain relief, complete pain relief was achieved in 51% of courses (60/118) and partial pain relief in 36% (43/118). Factors associated with symptomatic benefit and/or radiological response were initial Stage I/II versus III/IV

(95% versus 78%,  $\chi^2 p = <0.0005$ ), response versus no response to initial chemotherapy (85% versus 70%,  $\chi^2 p = 0.01$ ), ECOG performance status 1-2 versus 3-4 (86% versus 73%,  $\chi^2 p = 0.04$ ), skin versus non-skin disease (97% versus 80%,  $\chi^2 p = 0.003$ ), and spinal versus non-spinal disease (62% versus 87%,  $\chi^2 p < 0.0005$ ). Local control (LC) at six months was 69% (95% confidence interval [CI] 61-76%). Six month LC was 76% versus 58% for extranodal versus nodal disease ( $p = 0.02$ ); 78% versus 63% when initial stage was I/II versus III/IV ( $p = 0.01$ ); 63% versus 82% when the time from diagnosis to first relapse or progression was  $<1$  year versus  $\geq 1$  year ( $p = 0.02$ ); and 76% versus 47% when initial response to chemotherapy was partial or complete versus none ( $p < 0.0005$ ). LC at six months was not significantly associated with age, skin disease, spinal disease, EQD2, lesion size, concurrent steroids use, or number of previous chemotherapy lines. On multivariable Cox regression analysis, response to initial chemotherapy (HR 4.6, 95% CI 3.8-5.3) and maximum lesion dimension  $<5.8$  cm (HR 1.9, 95% CI 1.2-2.5) were associated with improved LC.

**Conclusions:** Palliative RT for DLBCL is effective for symptom improvement and local disease control. In deciding upon RT for incurable DLBCL, factors to consider include lesion size, response to initial chemotherapy, and anatomical site.

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#### OUTCOME AND ROLE OF RADIOTHERAPY IN STAGE I-II MESENTERIC DIFFUSE LARGE B-CELL LYMPHOMA

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**Purpose:** Limited stage DLBCL in the mesentery is an uncommon presentation. There is debate on the role and technique of RT in this disease both in terms of the need for RT, and targeting a mobile mesentery. We examined the outcome and role of combined modality therapy (CMT) policy in Stage I-II DLBCL.

**Materials and Methods:** All patients presenting with Stage I-II mesenteric DLBCL at our centre between 2000 to 2016 were reviewed ( $n = 48$ ). The median age was 63 years (range 24-81) and 65% ( $n = 31$ ) were men. All patients were staged with CT and bone marrow biopsy and 8% ( $n = 4$ ) were staged with PET-CT. Stage II presentation was in 88% ( $n = 42$ ) with paraaortic (69%,  $n = 33$ ) and/or iliac (19%,  $n = 9$ ) nodal regional sites involved. International prognostic index (IPI) of 0-1 was documented in 38% ( $n = 18$ ). Bulky disease ( $\geq 7.5$ cm) was seen in 71% ( $n = 34$ ). Most patients ( $n = 40$ , 83%) received RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone), 10% ( $n = 5$ ) had CHOP and 6% ( $n = 3$ ) had mixed regimens. A total of 33 patients received consolidative RT and completed as planned. The median dose was 35 Gy in 20 fractions (range 30-36 Gy). Most patients had involved site RT (ISRT); planned target volume: median 1235 cc, range 317-4557cc) except two had whole abdominal RT. IMRT was used in 55% ( $n = 18$ ) following ISRT principles with CTV to PTV margin of 1-2cm. Treatment response was assessed based on the Lugano response criteria with PET-CT (42%,  $n = 20$ ) and International Working Group response criteria with CT.

**Results:** The median follow-up was 3.7 years (range 0.4-13). After initial chemotherapy, 35 patients (73%) had complete response (CR/CRu), eight (17%) had partial response (PR), one had stable disease (SD) and four had progressive disease (PD). Among those in CR/CRu, 25 (71%) received consolidation RT, and 10 did not due to referring physician/patient choice. All eight patients with PR underwent RT and remained disease free. Four out of five patients (80%) who had SD/PD after initial chemotherapy died of the disease within a short time (5 - 13 months). Among the 43 patients with CR/CRu/PR to initial chemotherapy, two (5%) relapsed of which one had CMT (one of 25 CR/CRu patients, zero of eight PR patients) and one had RCHOP only (one of 10 CR/CRu patients). The five-year overall survival, progression-free survival and local control rates were 81% (95%CI 68-95%), 81% (95%CI 68-93%) and 83% (95%CI 71-95%) respectively. Among the 33 patients who had consolidative RT, one had G3 acute toxicity (GI bleeding, small bowel involvement at presentation) and there was no G2 or above late toxicity.

**Conclusion:** Stage I-II mesenteric DLBCL has a favourable outcome similar to other sites when treated with combined modality therapy or chemotherapy

alone. ISRT for mesenteric lymphoma is feasible and well tolerated. We are unable to assess whether consolidative RT is required following a CR to chemotherapy due to small sample size, and low number of events.

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#### PERSONALIZED SKIN CANCER RADIATION THERAPY FROM REFERRAL TO FIRST TREATMENT

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**Purpose:** The radiation planning processes for patients with medically or technically inoperable skin cancer can be challenging for both patients and their family members/caregivers. These challenges can also cause burden on the radiation program that is already under pressure due to the workload for a large cancer patient population. Our goal is to increase efficiency and decrease appointments length by improving communications between resources and standardizing our practices throughout the radiation therapy process. **Materials and Methods:** Using multiple Plan-Do-See-Act (PDSA) our team has started to customize patient's radiation therapy experiences by implementing various changes in our current process. These changes were implemented between September 2017 and January 2018 and included (but not limited to) moving clinical markup sessions to clinic, having peer review done real time in clinic, and reaching out to patients before to understand patient's needs to allow for coordination of clinic visit and planning workup. We also implement a disease team huddle previous to patient clinic visit to outline a plan for each patient.

**Results:** When comparing Clinic Clinical markup and CT appointment length for 40 skin patients, those patients that were seen during the project PDSA cycles had an average of 52.8 minutes for the combined appointments, this is compared to 109.5 minutes for patients seen previously. We also looked at day 1 appointment length to ensure no increase in treatment time, this data was consistent.

**Conclusions:** With the changes made to the process from referral during the PDSA cycles, there has been a reduction in patient appointment length and coordination of some appointments where possible, this is being done for those patients most in need with a patient and family input.

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#### IMPLEMENTING A NEW TREATMENT OPTION: RADIOTHERAPY FOR EARLY STAGE DUPUYTREN'S CONTRACTURE

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**Results:** Dupuytren's Contracture is a benign condition causing thickening of the fascia in the palm of the hand. Early stage disease usually presents as palpable nodules on the palm. With progression, these nodules can develop into thickened cords causing contracture of the fingers. Advanced stage disease can be very debilitating. Traditional treatment options may include observation, injections or surgery. Early intervention may be beneficial to slow progression. Radiotherapy is a non-invasive, but less commonly used, option for patients with early stage disease (N or N/1). The intent of radiotherapy is to slow or stop disease progression.

**Materials and Methods:** Patients were seen by a radiation therapist and a radiation oncologist at the treatment markup appointment. The patient's hand was immobilized and nodules within the palm were delineated by the radiation oncologist. Involved field technique was used, defined by using margins of 1-2 cm distal/proximal and 1 cm lateral to the marked nodules. Patients were treated with a single direct field, using either orthovoltage (100kV) or electrons (6 or 9 MeV), depending on machine availability. Radiotherapy was delivered in two phases; each phase separated by six to eight weeks. Dose fractionation for each phase was 15Gy in 5 fractions, for a total dose of 30 Gy.

**Results:** The first patient was treated in 2013. To date, 19 patients have received treatment: six with orthovoltage and 13 with electrons. The relatively simple technique and ease of set-up resulted in short treatment times. Treatments were well tolerated with minimal patient reported side effects.

**Conclusions:** Implementation of radiotherapy for early stage Dupuytren's

Contracture has provided an alternative to traditional treatment for some patients. Simple set-up and treatment, and the non-invasive nature of Radiotherapy make it a desirable option.

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#### QUANTIFYING OPERATOR VARIABILITY IN CONTOURING MALE BOWEL BAG ON TREATMENT PLANNING AND CONE BEAM CT WITH EXPANDED AND REFINED RTOG GUIDELINES

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**Purpose:** Accuracy and consistency of bowel delineation, and differences in bowel location on daily set-up images can impact the correlation of bowel toxicity with dose-volume metrics. Bowel definitions vary by disease site group, are limited in axial extent, and are ambiguous in certain regions. The bowel bag has better potential for contouring consistency and automation than bowel loops. The purpose of this study is to expand and refine the RTOG male pelvis guidelines for bowel bag contouring, and to assess operator contouring variability using the new guidelines on treatment planning CT (TPCT) and on daily cone beam CT (CBCT) images.

**Materials and Methods:** The RTOG male pelvis guidelines were expanded to include the full abdominal bowel bag and refined to explicitly describe the retro-peritoneal and peri-renal fascial planes as boundaries. Operational rules were developed for use when limited structure visibility lead to ambiguity. For each of five male patients, one TPCT and one CBCT scan were used to evaluate intra- and inter-operator variability. Seven operators (four experienced physicians and three residents) contoured five times per scan with two days minimum between repeat contours on the same scan. The CBCT was contoured before its respective TPCT, and operators were blinded to all contours. The CERR computational package was used to create contour masks to assess operator variability using volume differences, Dice Similarity Coefficient (DSC), and Euclidean Surface Distance (ESD). The STAPLE algorithm was used to estimate the reference contour as a weighted mean for each set of five contours, and metrics were calculated relative to this reference.

**Results:** The refined and expanded RTOG guidelines are being made available as an online resource, with an interactive, annotated atlas. For the currently available contours (one operator, three patients), the mean reference volume for TPCT is 6296cc and 5016cc for the limited field-of-view CBCT, and the corresponding mean volume differences for repeat contours are  $75 \pm 33$ cc for TPCT and  $81 \pm 43$ cc for CBCT. The DSC (1.000 for completely overlapping contours) is  $0.978 \pm 0.004$  for TPCT and  $0.975 \pm 0.004$  for CBCT. For the ESD, the percent of repeat contour surface at a perpendicular distance of 5 mm (10 mm) or more from the reference is  $2.5\% \pm 1.6\%$  ( $0.8\% \pm 1.1\%$ ) for TPCT and  $2.0\% \pm 0.9\%$  ( $0.2\% \pm 0.2\%$ ) for CBCT. The lower ESD for CBCT over TPCT is because operational rules were always used on CBCT due to consistent invisibility of structures like fascial planes, whereas structure visibility on TPCT means these rules were only sometimes applied.

**Conclusions:** Initial results for the expanded and refined bowel bag guidelines show the potential for their utility on TPCT and CBCT images, with operator variability smaller than the expected magnitude of daily bowel mobility.

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#### BEHIND THE CURTAIN - ESTABLISHING MODELS OF CARE IN RT

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**Purpose:** The purpose of this pan-Canadian jurisdictional review was to identify practice trends, unique practices and, best practices for improvement. The aim is to establish provincial models of care for radiation therapy that optimize care delivery. The new model of care will ensure the right person provides the right care, in the right place, at the right time. The completed report along with recommendations will be reviewed by cancer centre leadership as they seek to establish models of care that optimize design and delivery in RT centres across the province.

**Materials and Methods:** An initial assessment of the provincial system was

completed in summer 2017 providing a baseline for the proposed change. A literature review of staffing models was also conducted reviewing literature from 2000- 2015. Then a nationwide jurisdictional review of RT centers was conducted to collect workforce data from across Canada via survey and interview. This information was collated for comparison of work force practice based on skill level, equipment, patient numbers and treatment needs. In addition to workforce data, the jurisdictional review sought information on research processes, best practices in staff and patient education; innovations in patient care or services offered in addition to cancer treatments.

**Results:** The objective was to complete a nationwide jurisdictional review of multiple RT treatment sites via questionnaire and interview to compare current Canadian RT Service Models. Determine benchmark levels of service deliver. Identify and select best practices processes to create a quality matrix used to develop recommendations for optimizing the RT service delivery model that would establish a new model of care for radiation therapy.

**Conclusions:** The jurisdictional review results will allow RT sites to provide the best patient care, at the right place, at the right time, by the right members of their care team meeting the needs of the Cancer Plan, as well as supporting the health authority's people first and patient centred strategy.

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#### REASONS FOR SCREEN FAILURE AMONG PATIENTS IDENTIFIED AS CANDIDATES FOR A PHASE 2 STUDY OF 5-FRACTION STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR OLIGOMETASTATIC CANCER

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**Purpose:** The term oligometastatic (OM) was introduced to describe patients with a limited number of clinically detectable metastases for which local ablative therapy could potentially provide improved disease-free survival or even cure. The incidence of an oligometastatic disease distribution is difficult to estimate. The purpose of this analysis was to describe the reasons precluding trial participation in our trial of SBRT for oligometastatic cancer. **Materials and Methods:** We retrospectively audited all patients who were screened for participation in a single-arm phase II trial designed for patients with OM cancer (up to five sites of extra-cranial metastases). Study participants received local ablative therapy to all known sites of disease and at least one index lesion was treated with 5 fraction SBRT (study intervention). Eligibility criteria required baseline computed tomography (CT)  $\leq 1$  month prior to enrolment, and all cases were discussed at peer-review rounds to confirm eligibility.

**Results:** Between March 7 2013 and November 17 2017, 236 patients were screened and 145 (61%) enrolled to the study. The reasons for screen failure included patients declining study participation in 4% (nine out of 236) [ $n = 9$ ; four with  $< 5$  mets, and five with uncertain number] and 12% (29/236) having  $> 5$  metastases upon restaging baseline scans. Of the remaining 53 patients who had  $\leq 5$  metastases but were not enrolled, reasons for screen failure included uncertainty that the primary tumour was controlled ( $n = 9$ ), lesions where alternative ablative therapy was recommended ( $n = 10$ ), not suitable for SBRT ( $n = 18$ ; size  $n = 3$ , non-SBRT strategy preferred  $n = 8$ , toxicity risk  $n = 4$ , previous RT field overlap  $n = 3$ ), high subjective risk of systemic relapse ( $n = 9$ ; progressive disease during restaging scans  $n = 4$ , not suitable for comprehensive ablative therapy  $n = 1$ , plan for systemic therapy  $n = 4$ ) or other reasons ( $n = 7$ ; e.g. index lesion resolution, index lesion was a primary tumour, presence of cranial metastases).

**Conclusions:** In our review of a cohort of patients flagged to be potential candidates for enrollment in a clinical trial of SBRT for OM cancer, 87% of patients were confirmed to have  $< 5$  metastases. The screen failure rate was high. The most common reason for exclusion was detection of  $> 5$  metastases (12%) while a small group of patients (5%) were deemed to be at high risk of systemic relapse based on clinical factors and peer review rounds. Reporting of the characteristics of screen failed patients are important in the interpretation of trial results.

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### RADIOTHERAPY IN THE LAST MONTH OF LIFE: CASE SERIES INCLUDING CAUSE OF DEATH

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**Purpose:** Mortality following radiotherapy delivered at the end of life has been increasingly described over the past several years. The radiation use rate has been reported in this setting, but to date, none have reported on the cause of death.

**Materials and Methods:** Twenty-five patients who died in the last 30 days of life following radiotherapy from January to June 2017 were identified. Their demographic and clinical data were extracted using the hospital, regional, and radiation medical records. The data collection included age, gender, primary cancer, stage, performance status, disease and treatment site, intent of treatment, indication, technique, and cause of death.

**Results:** Twenty-one patients received radiotherapy in the last month of life: 13 completed the prescribed course, and eight did not. Median age was 71 (range: 45-91). 56% were men, and 44% were women. The most common primary was non-small cell lung cancer (32%). 84% had Stage IV disease. Most had an ECOG status of 3 (68%). Forty-eight percent were treated for bone metastases, 20% for brain metastases, and 16% for lung metastases. Ninety-two percent were treated with palliative intent. The most common treatment indication for palliative RT was pain in 56%. 3D-conformal radiotherapy was the most common technique (84%), with a dose-fractionation of 8 Gy in 1 fraction in 40%. The most common causes of death were respiratory failure (36%) and failure to thrive (32%). There were no reported deaths from radiation toxicities.

**Conclusions:** Radiation treatment did not cause death when given in the last month of life in our case series. This is the first report including cause of death in this setting.

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### THE DEVELOPMENT OF A PREDICTION MODEL USING DEEP LEARNING FOR SHORT TERM PROGNOSIS IN PATIENTS SEEN IN A PALLIATIVE RAPID ACCESS CLINIC

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**Purpose:** Prognosis is an important component of oncologic assessment that enables optimal individualized care, but accurate prediction is challenging. Deep learning (DL) is an advanced subtype of machine learning whereby an algorithm creates layers of artificial neural networks to enable independent learning and decision-making. We used DL to develop a tool to predict the prognosis (less than or greater than three months) for patients seen at a palliative rapid access clinic.

**Materials and Methods:** We completed a retrospective, single-institution study of 769 serial, anonymized patients who were assessed at the radiation oncology rapid access clinic from May 2011 to April 2017. After excluding those lost to follow-up, 734 patients were included. The patients' consult notes were digitized, curated and entered into the DL algorithm. Prediction models were developed using three machine learning techniques: Long Short Term Memory (LSTM; a type of DL technique), Random Forests and Decision Tree. They were trained using randomly selected 70% of data (training set), and precision and accuracy were calculated using the remaining 30% (test set).

**Results:** The LSTM model best predicted survival of three months or greater compared to traditional machine learning algorithms such as Decision Tree and Random Forests. The accuracy of prediction of the LSTM model for the overall test set was 0.67 with the test set, and predictive accuracy further increased to 0.70 when the algorithm focused on the final three-quarters of each document.

**Conclusions:** This pilot study achieved accuracy of 0.70 for prediction of survival of three months or greater, by using a sophisticated DL technique analyzing consult notes from the palliative rapid access clinic. As an LSTM algorithm is designed to self-improve with additional data, we will continue to improve the model by further training with a larger dataset to achieve greater predictive power.

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### PATTERNS OF PRACTICE SURVEY: RADIOTHERAPY FOR EXTREMITY SOFT TISSUE SARCOMA

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**Purpose:** Neoadjuvant or adjuvant radiotherapy (RT) for extremity soft tissue sarcoma (STS) confers significant local control benefit. To determine patterns of practice, a survey of RT planning practices was undertaken.

**Materials and Methods:** The survey was sent to the members of the Connective Tissue Oncology Society and Canadian Association of Radiation Oncology to describe general practice patterns of RT for extremity STS, patterns of contouring and planning, and use of quality control measures such as guidelines, tumour boards, and quality assurance rounds.

**Results:** Fifty-eight radiation oncologists treating extremity STS from 12 countries responded. 89.7% worked in academically affiliated centres, and 55.2% saw at least 20 cases per year. Most (96.7%) held multidisciplinary sarcoma boards, 85.5% of whom reported discussing every sarcoma case. 78.6% held quality assurance rounds. Most (92.9%) used planning guidelines although there was no consistency in the type employed. Pre-operative RT was used nearly twice as much as post-operative RT. CT simulation with MR fusion was used by 94.6%, although average score for satisfactory fusion was only 67.0%. Patterns of CTV contouring for both superficial and deep STS were variable. 69.8% contoured a normal soft tissue strip, 13.5% without routine constraints and the remainder with various constraints. Most (91.1%) used 50 Gy in 25 fractions pre-operatively and 39.6% reported using post-operative RT boost for positive margins. Post-operative dose was more variable, ranging from 59.4 Gy to 70 Gy.

**Conclusions:** Major aspects of RT planning for extremity STS were similar among the responders, most of whom were academically affiliated. Over twice as many employed pre-operative versus post-operative RT. There was considerable heterogeneity in planning details such as use of: margins for contouring, normal healthy strip as an avoidance structure, and RT boost for positive margins. This survey shows variable patterns of practice and identifies areas that may require further research before consensus can be reached.

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### RADIOTHERAPY FOR EXTREMITY SOFT TISSUE SARCOMA: THE ROLE OF NORMAL SOFT TISSUE STRIP IN VMAT PLANNING

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**Purpose:** Most guidelines for extremity soft tissue sarcoma (STS) lack details for contouring and planning, largely due to lack of evidence. Many institutional protocols for extremity STS include a longitudinal strip of healthy soft tissue as an avoidance structure (hsOAR: healthy strip as an organ-at-risk), although its dosimetric significance has not been established.

**Materials and Methods:** We aimed to determine spatially variant normal tissue objectives (NTOs) that may confer an equivalent healthy strip sparing and to dosimetrically compare with plans that use hsOARs. Seventeen patients previously treated for extremity STS between 2015 and 2018 at a single institution were identified and anonymized. Optimization PTVs were derived from the original contours and used to contour hsOARs. Two separate plan optimizations via standard protocol (using hsOAR) and the NTO protocol (without hsOAR) were done for each patient. The 17 sets of plans were compared for PTV coverage, hotspots, and hsOAR V20Gy and analyzed using the Wilcoxon rank sum test. Various parameters of the hsOAR and PTV were calculated using the relative volumes (hsOARs:PTV).

**Results:** Average hsOAR volume in proportion of the corresponding limb segment was 43.6%. Overall, there was one plan that showed exactly equivalent V20Gy, three plans with better V20Gy for NTO protocols, and the remaining 14 plans achieved better V20Gy using the standard protocol, five of which with less than 10% difference between the two protocols. Mean Dmax for the two protocols were statistically different: 108.2% for the NTO

protocol and 106.5% for the standard protocol ( $p < 0.01$ ). V20 Gy values were not statistically different between the NTO and the standard protocol ( $p = 0.06$ ). Review of individual plans did not reveal any pattern among the plans that achieved significantly different V20 Gy between the two protocols. **Conclusions:** V20Gys achieved by NTO protocol were not statistically different from the ones with standard hsOARs although there appears a trend to favour the standard protocol. There was a small difference in Dmax favouring the standard protocol although still meeting the commonly used constraint. Given statistically uncertain dosimetric advantage, eliminating hsOARs in contouring and planning of extremity STS may be appropriate once an NTO protocol is optimized to allow more efficient workflow of RT planning.

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#### UTILIZATION RATES OF PALLIATIVE SINGLE FRACTION RADIOTHERAPY (SFRT) VERSUS MULTIPLE FRACTION RADIOTHERAPY (MFRT) FOR BONE METASTASES IN MANITOBA AND IDENTIFICATION OF RISK FACTORS ASSOCIATED WITH RECEIPT OF MFRT: A RETROSPECTIVE, POPULATION-BASED, COHORT STUDY

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**Purpose:** Considerable high quality evidence exists which demonstrates equivalent outcomes between SFRT and MFRT for the palliative management of bony metastatic disease. Furthermore, SFRT is more convenient for patients, and is more economically sustainable to deliver. We aimed to assess the utilization rates of SFRT and MFRT in Manitoba and identify risk factors associated with the use of MFRT.

**Materials and Methods:** A retrospective, population-based, cohort study was conducted where patients with metastatic disease who received palliative radiotherapy to bone were identified using the provincial cancer registry and ARIA RO database. Patient, disease, and treatment factors were extracted using electronic data queries of the ARIA MO database and manual review of individual records when necessary. Univariable and multivariable logistic regression analyses were carried out for the endpoint receipt of MFRT.

**Results:** From January 1 2015 to December 31 2015, a total of 916 patients received palliative RT to bone metastases. Of these, 38.1% of the cohort received SFRT and 61.9% received MFRT. Proportions of SFRT varied by disease site whereby 54.6% of prostate cancer metastases received SFRT and only 21.7% gastrointestinal metastases received SFRT  $p < 0.001$ . The most common anatomical sites treated were spine (43.9%) and pelvis (29.6%). After multivariable adjustment, variables associated with receipt of MFRT included younger age, ECOG performance status of 0 to 1, low Charlson Comorbidity Index scores, gastrointestinal primary site (OR 3.20, 95% CI 1.49-6.88), treatment to the spine, and presence of complicated bone metastases (OR 3.53, 95% CI 1.27 to 9.85).

**Conclusions:** Our study found that the use of SFRT in Manitoba during the study period was suboptimal. The results of this study will provide the framework to devise knowledge translation efforts designed to increase the use of SFRT in Manitoba.

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#### END OF LIFE CARE DISCUSSIONS IN PRACTICE: SURVEY OF CANADIAN RADIATION ONCOLOGISTS

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**Purpose:** Numerous studies have demonstrated that discussion of preferences for end of life (EOL) care with patients and their families improve patient satisfaction as well as quality and cost-effectiveness of care. However, studies also show that many radiation oncologists are unlikely to discuss EOL care issues until patients develop significant symptoms or families initiate the discussion. Barriers previously identified by oncologists include limited knowledge or training, sense of failure in not being able to provide curative treatment, belief that patient's outcome will be negatively impacted,

uncertainty about prognosis, ambiguity about which physician should initiate these discussions, and perception of lack of available time. There are no data indicating how often these discussions take place specifically in the setting of radiation oncology practice. The purposes of this study are: 1) to describe if and how Canadian radiation oncologists are incorporating End of Life (EOL) care discussions into their practice and to identify their perceptions of barriers to such discussions; 2) to assess the impact of MAID policies on EOL discussions; and 3) to provide reference data for CARO's Symptom Control Advisory Group to make future policy and educational initiatives. **Materials and Methods:** To the radiation oncology membership of The Canadian Association of Radiation Oncologists (CARO), we circulated an online survey consisting of 22 questions. Demographic information including age, gender, site of location and residency training, specialty sites, number of years in practice, and training in palliative were collected. End of life care discussion practice pattern, including frequency of discussion regarding prognosis, site of death, advanced directive, and goals of care were asked. Barriers, impact of MAID, and perception of importance of end of life care discussion, and further potential areas of training were elicited.

**Results:** Data collection is in progress and will be available by July 2018.

**Conclusions:** The detailed results of the survey will be shared with CARO's Symptom Control Advisory Group and may enable it to advise CARO's Board on future policy and educational initiatives at the Annual Scientific Meeting.

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#### WHITE MATTER HYPERINTENSITIES ON MAGNETIC RESONANCE IMAGING AND THEIR EFFECT ON COGNITIVE FUNCTION AFTER WHOLE BRAIN RADIOTHERAPY (WBRT)

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**Purpose:** Our study aim was to assess whether pre-treatment white matter hyperintensities (WMH) would be associated with worse cognitive outcomes after WBRT in patients with brain metastases previously enrolled in a clinical trial (NCT01046123).

**Materials and Methods:** Forty-one patients treated with WBRT and radiosurgery had suitable pre-treatment MRIs, as well as serial Montreal Cognitive Assessments (MoCA) and Mini-Mental State Examinations (MMSE) after radiotherapy. Baseline T2-weighted fluid attenuation inverse recovery (FLAIR) imaging was independently assessed by two neuroradiologists for the presence of deep (dWMH) and periventricular (pvWMH) WMH using the Fazekas visual rating scale. WMH volumes were also manually contoured on the baseline T2 FLAIR imaging. For all analyses, patients were censored at the time of radionecrosis or progression of brain metastasis. Descriptive statistics and logistic regression modeling were used to investigate the relationship between WMH and cognitive scores.

**Results:** For a dWMH Fazekas score of 1-3 versus 0, there was a median drop of 3 points in total MoCA score between baseline and the lowest score at any time point. A 1.5-point median drop in MoCA score was also seen between baseline and last cognitive testing date. For pvWMH Fazekas scores of 2-3 versus 0-1, there was a median drop of 1 point in MoCA score between baseline and the lowest score at any time point. A 3-point median drop in MoCA score was seen between baseline and last cognitive testing date. These trends towards worse cognitive outcomes with increasing WMH were also seen in MMSE scores and in our analysis using the WMH volumes. Using logistic regression modeling, a non-significant increased risk of MoCA decline was associated with the presence of either dWMH (OR 2.20; 95% CI 0.57-8.6;  $p = 0.25$ ) or pvWMH (OR 3.73; 95% CI 0.67-20.7;  $p = 0.13$ ).

**Conclusions:** This small hypothesis-generating study outlines a methodology for investigating whether pre-treatment WMH is a risk factor for worse cognitive outcome after whole brain radiotherapy.

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### CLOSING THE LOOP: WOULD A POST-TREATMENT PHONE CALL IMPROVE THE PERCEPTIONS ABOUT QUALITY OF CARE FOR PALLIATIVE RADIATION THERAPY OUTPATIENTS?

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**Purpose:** Evaluations of the use of post-radiotherapy phone calls for curative cancer patients indicate that they provide a clinically meaningful opportunity for patients to discuss their concerns. The aim of this qualitative study was to investigate the use of a post-treatment phone call to improve palliative radiation therapy outpatients' perception of their quality of care. This simple and cost-effective method could be used to enhance the patients' and caregivers' feelings of being supported without requiring additional hospital visits, which can be particularly burdensome for palliative patients. **Materials and Methods:** Needs assessments surveys were distributed from November 2017 to January 2018 to all outpatients who had received previous palliative radiation within 12 months. Interviews were conducted with new palliative patients to gain insight into how they felt about the quality of their care. Interviews were framed using the salient belief question method, and responses were coded to identify common themes and indicators of importance. Post treatment phone calls were performed by one palliative radiation therapist at one week post-treatment for all new palliative patients or those who had previous palliative radiation more than one year ago, and had consented to receiving a phone call.

**Results:** Twenty-six needs assessment surveys were returned with a response rate of 47%. Quality of Care (QoC) ratings of "very good" during and after treatment were 81% and 58% respectively, showing a 23% decrease in QoC rating post-treatment. Approximately half of patients (46%) thought a phone call after completing treatment would improve how they felt about their QoC. There were 15 new palliative patients who consented to be interviewed. Their most important post-treatment concerns were: side-effects; experiencing anxiety or being overwhelmed emotionally; and not knowing what to expect. Post-treatment phone call data collection is ongoing, preliminary data suggests these phone calls were well-received and all of the patients who received a phone call said they found it useful.

**Conclusions:** A decrease in self-reported QoC after treatment is noted for palliative radiation therapy patients, which can be attributed to many factors. About half of patients who had previous palliative treatment felt a post-treatment follow up phone call would have improved their perceptions of QoC. The interviews revealed that new palliative patients still have many questions especially regarding side-effects, and a radiation therapist led post-treatment phone call would address those concerns in a timely manner.

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### FUNCTIONAL CRANIO-SPINAL IRRADIATION: A DOSIMETRIC COMPARISON AND EFFICIENCY ANALYSIS

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**Purpose:** Craniospinal irradiation (CSI) is a method used to treat various central nervous system malignancies including medulloblastoma. Although CSI improves clinical outcomes it comes with a cost of long-term endocrine and neuro-cognitive sequelae. We hypothesize that "Functional" CSI can reduce the dose to the hypothalamic-pituitary axis (HPA) and hippocampus below what was tried on ACNS0331 without sacrificing coverage of standard CSI care outside these two structures. In this abstract we compare the efficacy of Volumetric Modulated Arc Therapy (VMAT) and Helical Tomotherapy (HT) in delivering this novel technique.

**Materials and Methods:** Data from nine patients with medulloblastoma and ages 3-18 years were utilized. Five were supine and four were prone. All structures were contoured as per the published ACNS0331 Atlas and our local protocol. The HPA and hippocampus contours were verified with an experienced neuro-radiologist. All plans were generated by two dosimetrists to cover D95 with the prescribed dose of 23.4 Gy for CSI followed by a posterior fossa involved field boost of 30.6 Gy. A Dmean constraint of  $\leq 18$  Gy

was assigned to the HPA and hippocampus Planning Organ-at-Risk Volume (PRV). Treatment plans were compared using Velocity AI. Parameters of comparison included PTV coverage, mean dose to HPA and hippocampus, Conformity Index (CI) and estimated Treatment Time (TT). Descriptive statistics and two-sided t-test were used.

**Results:** Mean CSI PTV D95 coverage was 2302cGy (SD: 49.6) for VMAT and 2294cGy (SD; 19.9) for HT. PTV D95 was not statistically different between VMAT and HT for both the CSI ( $p = 0.65$ ) and boost ( $p = 0.06$ ) components, but was statistically significant in favour of HT with D2 for both CSI ( $p = 0.037$ ) and boost ( $p < 0.0001$ ). CI was improved with VMAT ( $p < 0.05$ ) in all components. The HPA CSI Dmean was 1399cGy (SD; 402) in VMAT and 1501cGy (SD; 385) in HT, but the combined CSI plus boost dose to the HPA was 2209cGy in VMAT and 2138cGy in HT ( $p = 0.71$ ). The CSI Dmean to the hippocampus was 1721cGy in VMAT and 1598cGy in HT. The boost location dictated the sparing of right or left hippocampus and was on average a total of 2773cGy in VMAT and 2745cGy in HT ( $p = 0.92$ ). VMAT had an estimated shorter treatment time (15 minutes versus 22 minutes).

**Conclusions:** Functional CSI is dosimetrically capable in achieving the required coverage while sparing the HPA and both hippocampi. However, the boost component will often exceed the mean dose of 18Gy and dictates which hippocampus gets spared more. We are currently evaluating a third arm using functional CSI with proton therapy.

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### DOSIMETRIC COMPARISON OF VMAT AND 3D CONFORMAL TECHNIQUES FOR CRANIO-SPINAL IRRADIATION IN PEDIATRIC PATIENTS WITH SCOLIOSIS

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**Purpose:** Delivering craniospinal irradiation (CSI) to patients with scoliosis presents unique dosimetric challenges where the curvature of the spine results in higher dose to non-midline critical structures. In pediatric patients, this is especially concerning due to the late effects on the heart, kidneys, and lung. In the current study, we compared 3D conformal radiotherapy (3D-CRT) and volumetric modulated arc radiotherapy (VMAT) CSI delivery techniques to investigate if there is a dose-sparing advantage with VMAT CSI.

**Materials and Methods:** CT simulation dataset from a four-year-old male patient with high risk medulloblastoma and spine scoliosis was used for the analysis. The patient was previously treated with 3D-CRT CSI with standard cranial fields and a single field-in-field posterior beam covering the spine. Dose prescription for the CSI portion of the radiotherapy plan was 36 Gy in 20 fractions. A VMAT CSI plan was created using a novel VMAT CSI technique developed at our centre with linear ramping dose profile removing the presence of junctioning and instead resulting in an overlap region. Three 360-degree arcs were used: 1 brain arc and 2 spine arcs; each arc was a separate isocenter along the length of the spine. Both plans met PTV objectives. Conformity index (volume of 95% isodose line divided by volume of PTV), dose to organs-at-risk, and non-target integral doses from the two plans were compared.

**Results:** The conformity index (95%) was 1.0 with VMAT CSI and 1.3 with 3D-CRT CSI. Mean heart and esophagus dose was 16.7 Gy (4.2 Gy versus 20.9 Gy) and 14.8 Gy (16.2 Gy versus 31.1 Gy) lower, respectively, with VMAT as compared to 3D-CRT CSI. Mean thyroid dose was 9.3 Gy higher with VMAT. VMAT CSI improved lung V20Gy by 18.7% (absolute) and reduced bilateral kidney V28Gy by 11.7% (absolute) although kidney V12Gy was higher for VMAT CSI. Stomach Dmax was reduced by 9.5 Gy (22.2 Gy versus 31.6 Gy) with VMAT CSI. Lower integral dose was achieved by the 3D-CRT CSI plan.

**Conclusions:** VMAT CSI provides equivalent PTV coverage with significant dose-sparing of most critical structures compared to 3D CRT CSI in this case of a pediatric patient with scoliosis. Higher thyroid mean dose and integral dose seen with VMAT may have implications for late effects with secondary cancers or hypothyroidism. VMAT CSI warrants consideration for scoliosis patients.

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### THE PROGNOSTIC IMPACT OF PD-L1 AND CD8 EXPRESSION IN ANAL CANCER PATIENTS TREATED WITH CHEMORADIOTHERAPY

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**Purpose:** The programmed death ligand-1 (PD-L1) and programmed death-1 (PD1) signaling axis is exploited by cancer cells as a mechanism to evade the host's immune surveillance. The expression of PD-L1 has been shown to be prognostic in many cancer types and expression status has been used in consideration of checkpoint inhibitor immunotherapy. However, there are very limited and conflicting data on the prognostic impact of PD-L1 in patients with anal cancer. The objectives of this retrospective study were to measure expression of PD-L1 and CD8 in patients with anal cancer treated chemoradiotherapy (CRT), and to correlate tumour expression with overall survival (OS).

**Materials and Methods:** One hundred and two patients with anal cancer treated with primary CRT at two tertiary care cancer centres between 2000 and 2013, with available pre-treatment tumour, were included. Tissue microarrays from tumour specimens were stained for PD-L1 and CD8. PD-L1 expression in tumour and in stroma was quantified using HALO image analysis software, and the results were interpreted using novel quantitative methods comparing average pixel intensity of the tissue sample normalized to reference cell lines. The density of CD8 cells within the tumour was interpreted by a specialist pathologist semi-quantitatively, using a 0-4 scoring system. Kaplan-Meier analysis with log rank was used to determine significance in association between tumour markers and OS. Cox multivariate analysis was used to explore independent predictors of OS.

**Results:** Of the 102 patients, 65 (64%) had sufficient tumour sample available for full analysis. There were no differences in baseline characteristics between tested and not tested cases. Mean follow up was 14.1 years; the female:male ratio was 2.5:1. Most patients had T2 disease; the majority were squamous histology (88%). We analyzed commonly used PD-L1 expression levels from the literature, and determined that the 5% cut-point was most strongly prognostic for OS. Approximately half the patients had tumoural PD-L1 expression  $\geq 5\%$ . Patients with tumoural PD-L1  $\geq 5\%$  had better OS versus PD-L1  $< 5\%$ , HR = 0.29 (CI 0.10-0.78),  $p = 0.009$ ; 10 years OS: 84% for PD-L1  $\geq 5\%$  versus 46% for PD-L1  $< 5\%$ . On univariate analysis, OS was associated with PD-L1 status, as well as T stage, N stage, ECOG status and gender. On multivariate analysis, PD-L1  $\geq 5\%$  remained statistically significant for better OS, HR=0.35 (CI 0.12-0.99),  $p = 0.047$ . 33 of 65 (51%) of tumours had high CD8 levels (3 or 4). There was no association between CD8 status and OS; further stratifying PD-L1 high patients by CD8 did not improve the prognostic impact versus PD-L1 status alone.

**Conclusions:** This is the first study reporting significant association of PD-L1 expression with OS in patients with anal cancer treated with CRT. PD-L1 status warrants consideration in the prognostication of patients with anal cancer. Future studies are required to determine the benefit of alternative treatment strategies based on PD-L1 status.

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### RESEARCH PRODUCTIVITY OF CANADIAN RADIATION ONCOLOGY RESIDENTS: A TIME-TREND ANALYSIS

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**Purpose:** Research productivity is encouraged in many Radiation Oncology (RO) training programs, and the Canadian licensing body of the Royal College of Physicians and Surgeons requires completion of a scholarly project during residency training. To our knowledge, the productivity of

RO residents in Canada has not been studied before.

**Materials and Methods:** A 12-year database of RO residents in Canadian training programs who completed residency between June 2005 and June 2016 was compiled. Resident names and dates of training were abstracted from Provincial physician databases (e.g. CPSP Physician Registry in Ontario), hospital and department websites, and online professional sites. Names were used to query PubMed. Productivity was measured by the number of PubMed publications during the time period of residency and six months thereafter. Abstracted data included training program, year of publication, publication journal, type of research, and authorship position. Residents were divided into four cohorts of three years each were created, representing graduates from 2005-2007 ( $n = 41$ ), 2008-2010 ( $n = 62$ ), 2011-2013 ( $n = 65$ ), and 2014-2016 ( $n = 59$ ). Descriptive statistics and linear trend analysis were used to analyze the data.

**Results:** A total of 227 RO residents graduating from Canadian programs between 2005 and 2016 were identified, collectively co-authoring 363 publications across more than 120 journals. The majority ( $n = 205$ ; 56%) were first-author papers. Forty-one percent of papers were published in journals with an Impact Factor  $\geq 4.0$ , most commonly *Int J Radiat Oncol Biol Phys* (20%) and *Radiother Oncol* (8%). Most papers were Original Research (77%), while Case Reports, Reviews, Systematic Reviews and Correspondence represented 10%, 8%, 4% and 2% respectively. Thirty-nine percent of residents had no publications during training. The majority of papers were published by senior residents, with 82% of first author, and 80% of all author articles were published in residency year 4 or higher. The mean number of first author publications per residency increased significantly over time from 0.61 (95% confidence interval: 0.35-0.87) to 1.17 (0.72-1.62; linear trend test  $p = 0.016$ ). Similarly, total publications increased from 1.24 (0.75-1.74) to 2.08 (1.25-2.92;  $p = 0.039$ ).

**Conclusions:** Canadian RO resident publication productivity nearly doubled over a 12-year period.

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### DO CANADIAN RADIATION ONCOLOGISTS CONSIDER GERIATRIC ASSESSMENT IN THE DECISION-MAKING PROCESS FOR TREATMENT OF NON-METASTATIC PROSTATE CANCER PATIENTS 80 YEARS OF AGE AND OLDER? - NATIONAL SURVEY

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**Purpose:** Clinical judgement may not be sufficient to detect problems specific to older cancer patients that may alter treatment. We investigated which Geriatric Assessment Tools (GA) are used by Canadian radiation oncologists (CRO) to treat non-metastatic prostate cancer patients 80 years and older.

**Materials and Methods:** A 27-item cross sectional survey was developed with input from a multidisciplinary team of radiation therapists, nurses, and geriatricians. The survey was distributed to Genitourinary (GU) CROs through the Canadian Association of Radiation Oncologists (CARO) via LimeSurvey. Survey content included: demographics, approach to treatment decisions based on factors in GA, and usability and comfort with GA in clinic. Descriptive statistics were used to analyze the data. Open-ended question responses were coded and analyzed for emerging themes.

**Results:** One hundred and seventy-two GU CROs were contacted, 44 responded (26%). Participants were from Ontario (38.6%), Quebec (25%), Alberta (11%), British Columbia (11%), Manitoba (9%), and Nova Scotia (5%). Active surveillance was the choice of therapy in low risk patients regardless of GA components (97-100%), whereas in intermediate and high-risk patients, results were more heterogenous. Functional status and comorbidities were the most important GA components in the decision-making process (73.2%, 65.9%, respectively). Sixty six percent of CROs do not use any GA; 77% felt comfortable to very comfortable treating older patients. Eighty-eight percent felt there were some to very few guidelines in helping them treat this patient population. Barriers to using GA included lack of time, support, resources, and lack of understanding on how to

interpret the results.

**Conclusions:** GAs are not commonly used by CROs, with most feeling comfortable treating this patient population. Heterogeneity in treatment choice in intermediate and high-risk patients based on GA components suggests a lack of consensus amongst CROs. Lack of evidence-based guidelines on treating older patients with prostate cancer may be indicative of a further investigation on how to best meet the needs of this patient population.

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### **RADONC RESIDENT GUIDE: PLACING RADIATION ONCOLOGY IN THE PALM OF YOUR HAND**

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**Purpose:** A Radiation Oncology on-call handbook for use by residents and staff was previously developed in printed format. However, the printed format was cumbersome, and there was a voiced need for an electronic version. Thus, a project to convert the content to an electronic app version was undertaken, specifically to make it accessible via a smartphone.

**Materials and Methods:** The content of the Radiation Oncology on-call handbook was updated and expanded to reflect the knowledge and information commonly utilized within the practice of Radiation Oncology. An undergraduate Computer Science student developed the app. The process involved transferring the material within the handbook into Xcode and Android Studio for iOS and Android platforms respectively. The material was designed into a mobile app format, and assets such as icons and buttons were created by the programmer during the process of development. To distribute the app, it will be published to the iOS App Store and Google Play Store. A pilot group of Canadian Radiation Oncology residents were invited to download the app and trial it for perceived usefulness. A questionnaire was created and will be distributed to the pilot group. Data from questionnaire will be analyzed to determine overall usefulness of this app, and guide future modifications prior to making it available publicly. Analysis of quantitative data will be carried out using an Excel spreadsheet and SPSS statistical software. Qualitative data and feedback will be aggregated, and grouped according to themes that emerge. Approval of the local research ethic board is in process.

**Results:** The mobile app was created for use on both iOS and android platforms. The app includes common medications and dosages, management algorithms for oncologic emergencies, common toxicities observed in Oncology and suggestions for their management, dose constraints for organs at risk and depth dose data for photons and electrons. Calculators (BED, EQD2, Glasgow Coma Scale) and prognostic tools (Spinal Instability Neoplastic Score, Mirels' Score of Bony Instability, GPA for brain metastasis) were included. **Conclusions:** Preliminary data from our residency programme indicates that the original handbook is useful to Radiation Oncology residents at all levels of their training. We anticipate that the mobile app version with expanded features will have even greater usefulness and applicability for both residents and staff.

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### **HUDDLE UP: CULTIVATING A CULTURE OF QUALITY IMPROVEMENT**

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**Purpose:** Quality and patient safety are ingrained in radiation medicine practice, built in to checks and balances used to ensure safe delivery of treatments. Continuous quality improvement (QI) is the responsibility of all healthcare providers to ensure a positive experience and improved patient outcomes. A Quality Conversation (QC) is a very short, weekly, huddle that provides an opportunity to engage staff in both strategic and local quality initiatives, rapid cycle improvements and ultimately equip staff with a QI skillset to become leaders in change. QCs were performed both in the planning and treatment departments of a busy radiotherapy program and assessed for impact on quality culture.

**Materials and Methods:** Multiple forums were engaged to raise awareness amongst teams with regards to, goals, purpose and benefits of engaging in these conversations. Weekly QCs, limited to 15 minutes were facilitated by a member(s) of the leadership team in both the planning and treatment departments. All members of the interdisciplinary team were encouraged to attend their respective QC. Each conversation was conducted before a custom designed board and was grounded in three guiding questions: "What are we currently working on?"; "How well are we doing?"; and "Are our change ideas working?" Initiatives were selected both from organizational targets and staff identified topics. QIs were monitored using rapid Plan-Do-Study-Act Cycles (PDSA). Throughout the introductory period key staff participants were identified as change initiative leaders and provided status reports regarding the status of in progress activities.

**Results:** QCs focused on a number of change initiatives, during the introductory period five large organizational initiatives identified for improvement including; smoking cessation; falls risk; vascular access; person centred care; symptom screening. In addition, staff identified six additional areas to focus improvement; therapist simulations; intravenous pager requests; booking efficiency; workflow and communication; new patient education; appointment changes and bookings. Through regular staff participation and input each of the 11 areas identified for improvement had identified increased and sustained performance during the introductory period. During the introductory period there was a shift from leadership driven initiatives and QCs to Radiation Therapist driven development (e.g. new patient teaching redesign) and QC delivery.

**Conclusions:** Quality Conversations bring a unique dimension to the practice of radiation oncology. QCs build a QI infrastructure on which practice issues can be identified by staff and solutions generated to improve (but not limited to) workflow improvements through to best practice adoption. Fostering this QI capacity beyond our existing safety culture can lead to improvements in both staff and patient experience.

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### **ALIGNING REQUIREMENTS OF TRAINING AND ASSESSMENT IN RADIATION PLANNING IN THE ERA OF COMPETENCY-BASED MEDICAL EDUCATION**

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**Purpose:** Radiation treatment planning is a unique skill that requires interdisciplinary collaboration among Radiation Oncologists (RO), Dosimetrists, and Medical Physicists (MP) to train and assess residents. With the adoption of competency-based medical education (CBME) in Canada, it is essential that residency program curricula focus on developing competencies in radiation treatment planning to ensure entrustment. Our study investigates how radiation oncology team members' perspectives on optimized experiential treatment planning training align with requirements of CBME, and implications for residency training.

**Materials and Methods:** This qualitative research study took place in one academic hospital RO Department in Southern Ontario. Through convenience sampling, focus groups were conducted with ROs (n = 11), dosimetrists (n = 7), MPs (n = 7), and residents (n = 7). Thematic design was adopted to analyze the transcripts through open coding resulting in three overarching themes.

**Results:** The results identified existing strengths and weaknesses of the residency program, and future opportunities to redesign the curriculum and assessment process with a CBME paradigm. Stakeholders were optimistic that CBME was helping to enrich resident learning with the increased frequency and quality of competency-based assessments. All participants believed greater communication about residents' developmental progress was required between educational stakeholders. Dosimetrists and MPs were interested in participating directly in assessing and coaching residents. Participants across all stakeholder groups suggested building a library of cases so as to provide a safe environment to develop skills in contouring, dosimetry, and plan evaluation, in accordance with CBME training.

**Conclusions:** The interdisciplinary residency education stakeholder consultations approach yielded rich results and common themes emerged. In support of a CBME environment, it is important that all team members

communicate effectively, participate in formative assessments, and play a role in coaching residents. These findings inform the modification of treatment planning competency development to better align training and assessment of RO residents in the era of CBME.

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### CREATION OF AN EDUCATIONAL QUALITY IMPROVEMENT PROGRAM FOR RADIATION ONCOLOGY RESIDENTS

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**Purpose:** Quality Improvement (QI) is a pillar of good clinical governance and is at the center of modern health care. The Royal College of Physicians and Surgeons of Canada mandated, in CanMeds 2015, that QI should be taught and the competencies assessed in all post-graduate residency programs. The objective is to report on the feasibility and impact of teaching QI to radiation oncology residents at a single institution.

**Materials and Methods:** A QI team consisting of a clinical fellow and three staff physicians as well as an expert in QI methods was created within the Department of Radiation Oncology. QI teaching took place in a longitudinal manner with approximately 12 hours of direct faculty teaching. A mandatory curriculum divided into foundation, and intermediate and advanced competencies was devised. Phase 1 teaching, delivered during two academic half days, consisted of didactic lectures, practical workshops and self-directed online modules. Phase 2 required intermediate year residents to complete a nine-month QI project. A QI day hosted by the Department invited QI experts to teach and enabled residents to present their work with merit prizes awarded. Our program evaluation used validated assessment tools (self-assessment, QI-knowledge based assessments (QI-KATs), and balanced score cards) before and after curriculum implementation and answers quantified using satisfaction indices (SI).

**Results:** Subjective and objective assessments demonstrated improvements in resident's QI knowledge acquisition following curriculum implementation. Those who had completed a project (n = 4) had greater confidence with QI methodology compared to those who had completed Phase 1 (n = 2) alone (mean SI 53% pre-curriculum to 66.5% and 90%). The majority lacked previous QI teaching and knowledge but learner attitudes improved (SI 50 to 70%) and 91% of colleagues were enthusiastic about the program being implemented.

**Conclusions:** We have demonstrated that implementation of a QI curriculum for radiation oncology residents is feasible and that early results suggesting improvements of attitude and knowledge are positive. We anticipate that the QI skills gained will enable the residents to elevate the quality of their practice throughout their subsequent careers.

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### COMMUNICATING THE EXTERNAL BEAM RADIATION EXPERIENCE (CEBRE): A NOVEL GRAPHIC NARRATIVE PATIENT EDUCATION TOOL

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**Purpose:** Effective communication with patients decreases anxiety, pain, and psychological distress. National guidelines recommend readability of patient education materials be at or below a 6th grade level. However, radiation oncology materials average a 10th grade level. The Communicating the External Beam Radiation Experience (CEBRE) discussion guide, a novel graphic narrative educational tool, was developed. A pilot study evaluated perceived benefits of CEBRE.

**Materials and Methods:** CEBRE was designed as a collaboration between physicians and designers. Designers conducted structured interviews of patients, family members, and radiation oncology clinic staff. Interviews

were coded for themes to uncover stakeholder based insights, leading to design principles driving the design of CEBRE. The CEBRE discussion guide comprehensively covers the external beam radiation care path from consultation through follow-up. A "My information" section includes patient-specific information to facilitate a tailored discussion. Readability was measured using the Flesch-Kincaid (FK) test. A pilot perceived benefits study utilized a survey to determine usability and effect on anxiety in patients. Modified versions of the Systems Usability Score (SUS) and Spielberger State-Trait Anxiety Inventory short form (STAI) along with questions unique to CEBRE were included. Patients receiving treatment or in active follow-up and practicing radiation oncologists were asked to review CEBRE and complete separate patient and physician perceived-benefit surveys. Likert-type scores are reported as median [interquartile range].

**Results:** The CEBRE guide scores a 5.4 FK grade level, meeting national guidelines. Thirty-four patients and 12 radiation oncologists completed perceived benefits surveys. Patients completed a high school/GED (18%), a two-year degree or some college (50%), or at least four years of college (32%). Patient and physician responses were concordant. On a scale of 1-5 for the modified SUS and 1-4 for the modified STAI ("strongly disagree" to "strongly agree") the median modified SUS is 4[4-5] for each cohort and modified STAI scores were 3[3-4] and 3[3-3.5] for patients and providers, respectively. Both cohorts "agree" CEBRE is usable and would decrease patient anxiety. Compared to a text only pamphlet, the graphic narrative component of CEBRE was rated as "quite" helpful 4[4-5] by both cohorts. Patient qualitative responses revealed that presentation of the CEBRE guide by a care provider would make them feel even more comfortable. Providers reported the CEBRE guide would be "quite helpful" 4[4-5] compared to a text-only pamphlet, that with CEBRE "patients will understand more" 4[4-5], and providers are "extremely likely" 5[3-5] to use CEBRE at initial consultation.

**Conclusions:** The CEBRE discussion guide is a patient accessible and practical education tool that warrants further investigation in the radiation oncology clinic.

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### YOU AIN'T SEEN NOTHING YET: INTEGRATING THERAPEUTIC MRI INTO RADIATION THERAPY PRACTICE

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**Purpose:** With its superior soft tissue visualization, Magnetic Resonance Imaging (MRI) has increasingly been integrated into radiation oncology practice for diagnosis, staging and assessment of treatment outcomes. Within radiation therapy (RT) practice, MRI currently assumes a vital role in treatment planning for central nervous system, head and neck, gynecological, urological and gastrointestinal malignancies. Given its high contrast, MR-guided radiation therapy represents the next evolution of image guided RT with the potential for dose escalation and margin reduction. The seamless adoption of MRI into the RT workflow is not trivial as there are significant challenges extending beyond the additional safety requirements of MRI. The focus of diagnostic MRI is to optimize image acquisition to facilitate a differential diagnosis, but in RT, the application of MRI takes more of a therapeutic approach. To ensure safe practice and successful implementation of therapeutic MRI, the gap in knowledge, skills and training requires immediate attention.

**Materials and Methods:** To better understand the landscape of therapeutic MRI, an investigation was initiated to evaluate the current state and projected utilization of MRI within RT departments across Canada. An electronic survey was circulated to Canadian RT managers to determine: 1) proportion that currently have a dedicated MRI; 2) proportion who anticipate acquiring a dedicated MRI simulator and/or integrated MRI-linear accelerator (MRL) in the next five to 10 years; and 3) current and/or anticipated staffing models for these units. The survey also provided an opportunity for RT managers to comment on anticipated training needs with the integration of therapeutic MRI.

**Results:** The survey was completed by 23 of 39 RT managers (56%) with respondents from 10 of 12 provinces. Dedicated MRI simulators exist in 17% of the RT departments and 26% of the RT departments anticipate

acquisition of a dedicated MRI-simulator in the next five years and of those, half also anticipate acquiring an integrated MRL. An additional 13% of the RT departments anticipate acquiring only an integrated MRL in the next five to 10 years. There was a large variation in staffing models, whereby the units may be operated by: dual certified RTT/RTMRI, RTT with specialty MRI training, or a team comprised of individual RTT and RTMRI. There was general consistency regarding anticipated departmental training needs with 30-39% agreement on the need for training on: MR safety; MR-based anatomy; MR image quality, scan optimization/ interpretation; and QA requirements and procedures.

**Conclusions:** A comprehensive snapshot of MRI in RT across Canada has been collated and the results demonstrate that RT departments recognize the value and anticipate the integration of therapeutic MRI, however there is currently no consensus as to the optimal staffing model or requisite training. The opportunity exists to respond to this paradigm shift by exploring new staffing models to maximize resources and the scope of practice of Radiation Therapists. Concurrently, it is vital that education and training solutions for therapeutic MRI are established to meet the needs of RT departments efficiently and effectively and to ensure the seamless integration of therapeutic MRI to ultimately benefit cancer patients across Canada.

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#### IMPROVING RESIDENT SELECTION PRACTICES IN RADIATION ONCOLOGY USING A MULTIPLE MINI INTERVIEW FORMAT

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**Purpose:** It is highly important to residency programs that resident selection procedures identify the best possible candidates for training. Selection procedures must also be fair and transparent to candidates. Bandiera et al (1) have published guidelines for resident selection (Best Practices in Admission and Selection; BPAS). We sought to improve the quality of the selection procedures in our Radiation Oncology residency training program by applying the BPAS recommendations.

**Materials and Methods:** The BPAS recommendations were reviewed together with our existing selection procedures for candidates applying to our training program through the Canadian Resident Matching Service (CaRMS). Our residency program committee (RPC) developed and approved goals and objectives for resident selection, including definition of criteria for candidacy and ranking. A novel selection procedure was developed, including the Multiple Mini Interview (MMI) format to incorporate evaluation of the candidate's non-cognitive skills.

**Results:** The overarching goals of the selection process were to identify candidates likely to succeed in residency training and practice in Radiation Oncology, prioritizing strong interpersonal skills, professionalism, ability to work as part of a team, and interest and motivation in Radiation Oncology. A scoring system was developed to evaluate the candidate's submitted application. The MMI format was designed to take the place of the traditional interview; stations were developed to assess candidate's skills through situational assessments and role play, evaluating the factors identified in the goals and objectives. This format has been fully implemented and used for four cohorts of candidates. The selection procedure has allowed us to function in better accordance with the BPAS recommendations.

**Conclusions:** We have developed a resident selection procedure which improves our agreement with the published BPAS recommendations. We have implemented an objective assessment of non-cognitive skills using the MMI format, which in our opinion provides an assessment more in line with the defined goals of the selection process and is more fair to applicants. We plan to present more detailed information about these selection procedures and how they are applied in our program.

1 Bandiera et al, *Acad Med* 2015;90;1594-1601.

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#### BURNOUT AND RESILIENCY IN CANADIAN ONCOLOGY RESIDENTS: A NATIONWIDE RESIDENT AND PROGRAM DIRECTOR SURVEY

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**Purpose:** To measure burnout rates and resiliency scores in Canadian Oncology residents and to describe the existing resiliency and wellness content in Canadian Oncology residency programs.

**Materials and Methods:** Online surveys were circulated to all Canadian Radiation Oncology, Medical Oncology and Hematology residents and program directors. Oncology resident burnout rates and resiliency scores were measured using the abbreviated Maslach Burnout Inventory (aMBI) and Connor-Davidson Resiliency scale (CD-RISC). Information regarding pre-existing resiliency and wellness training programs as well as interest in and suggestions for potential resiliency and wellness activities was collected.

**Results:** The resident survey had a response rate of 30% (57/187). The average resiliency score (CD-RISC) was 65.4 (95% CI 62.2-68.6). 42.1% (24) of residents met defined burnout criteria. High resiliency was significantly associated with a lower rate of burnout ( $p = 0.01$ ), which suggests that activities aimed at fostering resiliency could lead to less burnout in this population. No specific demographics predicted low resiliency or high burnout, indicating this training should be offered to all oncology residents. 58% (33) of residents felt that they had not received adequate resiliency and wellness training. The program director survey had a response rate of 48% (20/42). Fifty percent of program directors indicated they had no formal resiliency and wellness training.

**Conclusions:** Canadian Oncology residents demonstrate high rates of burnout and low resiliency when compared with the general population, and similar burnout rates when compared with American Radiation Oncology residents and other resident groups. This is the first study to comprehensively report rates of burnout and resiliency in oncology residents and establishes a baseline for studying resiliency and burnout in this population. The development of resiliency and wellness curricula is warranted in this population, and will be a mandatory component of the accreditation standards for Canadian residency programs from 2018 onwards.

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#### DESIGN OF A "TRANSITION TO PRACTICE" ROTATION FOR RADIATION ONCOLOGY RESIDENTS

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**Purpose:** Implementation of Competence By Design (CBD) will require residency training programs to develop formalized "Transition to Practice" (TTP) experiences. We have previously reported the results of an interprofessional survey assessing the relative importance of various skills required by residents transitioning into independent practice in Radiation Oncology. The purpose of this abstract is to present the design and structure of a formalized TTP rotation in Radiation Oncology.

**Materials and Methods:** TTP rotation objectives were developed using the previously reported interprofessional survey results, our program goals and objectives for senior residents, and draft CBD documents outlining expected competencies to be acquired in the TTP stage.

**Results:** The TTP rotation will occur in the final 12 weeks of the PGY-5 year. The rotation is designed to allow the resident to refine their independent decision-making skills and medical expertise, and places an emphasis on the elements of practice related to the intrinsic CanMEDS roles. Specific tasks include completing a project related to Radiation Oncology practice, taking a leadership role in quality assurance rounds or other administrative meetings, developing a relationship with a mentor, and providing mentorship to, and evaluating, junior residents. Residents are expected to complete a self-evaluation portfolio. The proposed TTP rotation has been approved by our residency program committee, and the first cohort of residents will pilot this rotation in the 2017-18 academic year.

**Conclusions:** A TTP rotation has been developed to assist Radiation Oncology residents with transitioning to independent practice. The rotation content and experiences after the first cohort of residents have completed

this rotation will be presented.

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#### DEVELOPING A GLOBAL HEALTH SCHOLARSHIP FOR YOUNG LEADERS IN RADIATION ONCOLOGY: RESULTS OF A PILOT PROGRAM

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**Purpose:** Surveys conducted by CARO's International Communications Workgroup (CIC) revealed that half of Canadian radiation oncology residents were interested in Global Health electives, yet only one resident had completed such an elective between 2007-2013. Studies frequently identify a lack of financial resources and difficult-to-find information on potential placements as important barriers to address. In order to promote personal and professional development, a unique perspective on global cancer control, and international collaboration, our objective was to increase the number of trainees completing electives in Global Health.

**Materials and Methods:** The CIC created a Radiation Oncology Global Health Scholarship, available to residents (PGY 2-5) and fellows. It provides \$2500 in travel and lodging expenses for oncology-related Global Health electives, requires applicants to reflect on CanMEDS competencies, supports pre-departure training, and encourages familiarity with the ethics of Global Health. Recipients are encouraged to present their experience at CARO's annual meeting and complete an exit evaluation. Potential applicants are provided with resources to find opportunities, including a network of previous participants, and access to a worldwide elective database through GlobalRT.org. The scholarship is supported by an industry-supported unrestricted educational grant.

**Results:** Three scholarships were awarded from 2014-2017. A PGY-3 resident traveled to Accra, Ghana, collaborating on cervical cancer research and helping establish a distance learning program. A PGY-3 traveled to Zambia for a clinical elective focused on gynecological malignancies, and a PGY-2 conducted research on access to radiotherapy in Nunavut. Preliminary data from exit evaluations suggest electives have contributed to personal and professional development, provided unique perspectives on global cancer control, developed CanMEDS competencies, and fostered international collaboration.

**Conclusions:** Between 2014-2017, the CIC Radiation Oncology Global Health Scholarship has increased the number of radiation oncology trainees completing Global Health electives in Canada and abroad. In exit evaluations, electives have met defined goals for the Scholarship.

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#### CREATION AND IMPLEMENTATION OF HIGH-FIDELITY COMPUTER-BASED SIMULATION TO IMPROVE RESIDENT COMPETENCY IN RADIOTHERAPY TREATMENT PLAN EVALUATION

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**Purpose:** Treatment plan evaluation is a core competency for radiation oncology (RO) and medical physics (MP) residents. Gaps in teaching and assessing plan evaluation have been identified in residency training. The purpose of this project was to create and implement an interactive plan evaluation case bank for RO and MP residents to improve competency.

**Materials and Methods:** A needs assessment was performed to inform case selection, case bank development and accompanying software. Current and former residents were asked to assess their confidence in various aspects of plan evaluation using a 10-point Likert scale (1=least confident, 10=most confident). In parallel, a list of clinically unacceptable plans (with corresponding acceptable plans) from January 2011 - June 2013 was compiled and categorized by clinical site, reason for rejection, detectability and

relevance. Cases were reviewed for consensus by two ROs and two MPs. An interactive web-based DICOM-RT tool was used to query and interact with the case bank database. A companion software tool, acting as an interactive simulation platform, was created to allow user interaction with the database. **Results:** Thirty participants (68%) responded to the needs assessment: 13 current RO (six junior, seven senior), 10 former RO, three current MP and four former MP residents. Opportunities for improving plan evaluation were identified with the following mean confidence scores: assessment of target coverage (6.6 + 2.5), doses to OARs (6.2 + 2.4), conformity (5.7 + 2.5), overall plan acceptability (5.5 + 2.3) and ability to suggest improvements (4.9 + 2.1). Extracted themes for case bank development included incorporating diverse clinical sites, common cases, target coverage and OAR assessment, DVHs, conformity and provision of immediate feedback. Of the 218 clinically unacceptable plans, 50 were included in the case bank. These cases were categorized, anonymized and imported into the case bank database. Additional acceptable and unacceptable plans were generated to augment the case bank where required. The companion simulation software platform was implemented and tested to ensure proper functionality. The simulation platform describes each clinical scenario and allows residents to enter their assessment, error classification and suggested corrective action (if applicable). The simulation platform then provides immediate feedback, including error description, correction strategy and link to the corrected plan.

**Conclusions:** An innovative, interdisciplinary plan evaluation case bank has been created to address an identified learning gap in RO and MP training. The format improves fidelity of the simulation by allowing interaction with the images and plan in 3D, incorporation of feedback to residents and visualization of the corresponding clinically acceptable plan. This case bank can be leveraged as a teaching and assessment tool in competency based medical education. Future work will evaluate resident satisfaction with and effectiveness of the case bank as a learning tool.

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#### EVOLVING MENTORSHIP NEEDS FOR RADIATION ONCOLOGY RESIDENTS DURING TRAINING: IMPLICATIONS FOR PROGRAM DESIGN

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**Purpose:** Mentorship in academic medicine guides professional and personal development. This translates into enhanced career success and productivity as well as decreased stress and burnout. Despite this, formal mentorship programs within postgraduate medical education, in general, and radiation oncology training programs, in particular, are uncommon. The objective of this qualitative, exploratory study was to assess the mentorship needs of radiation oncology residents to facilitate the design of a formal mentorship program.

**Materials and Methods:** Radiation oncology residents and faculty from a single university were invited to participate in one-on-one semi-structured interviews to learn and understand the mentorship experiences with and needs of residents during training. Interviews were audiotaped and transcribed verbatim. Data analysis involved a coding process, with assistance of NVivo Pro version 11, to derive key themes. A second coder was used for collaborative analysis. A constant comparative and iterative approach was used. Data collection occurred until saturation.

**Results:** Twenty interviews took place (10 residents, 10 faculty). Participants were balanced according to gender (10 females, 10 males) and seniority (four junior residents, six senior residents; five junior faculty, five senior faculty). Three major themes emerged during the coding process. First, both faculty and residents believe mentorship needs change throughout training. Junior residents typically seek mentorship in general aspects of training, such as program logistics and establishing research, whereas senior residents look for specific advice regarding networking, fellowship and jobs. Second, ideal mentee and mentor characteristics were identified. Residents feel engagement, approachability, availability and advocacy as ideal mentor characteristics; faculty feel engagement, initiative and active listening as ideal mentee characteristics. Third, residents may benefit from exposure to multiple mentors throughout their training, both faculty and

peer, to address specific areas and their changing needs.

**Conclusions:** Junior and senior radiation oncology residents have differing needs regarding mentorship. Juniors seek general guidance, whereas seniors pursue more focused advice. Active engagement by both mentors and mentees was identified an important characteristic for creating and maintaining successful relationships. Multiple mentors may be the most appropriate way to address resident needs. These results will inform the design and implementation of a formal mentorship program in our department and can be modified for use in other institutions.

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### EXPLORING THE EDUCATIONAL NEEDS OF WOMEN WITH GYNECOLOGICAL CANCERS POST-BRACHYTHERAPY

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**Purpose:** Brachytherapy (BT) plays a fundamental role in the treatment of women with gynecological cancers. Patient education around self-management post-BT involves an interdisciplinary team of healthcare professionals (HCPs), including radiation oncologists, brachytherapists and specialized oncology nurses. There is a paucity of guidelines regarding patient education and the teaching of self-management behaviours post-BT. The objective of this study was to evaluate the current post-BT education provided to gynecological cancer patients, determine the educational needs of patients surrounding self-management and to determine the enablers and barriers to the provision of this education.

**Materials and Methods:** This prospective cross-sectional study recruited English-speaking women with gynecological cancers receiving external beam radiotherapy and BT for curative intent. Patients completed a one-time questionnaire at their first follow-up appointment post-BT to assess the perceived importance for self-management education (16-items) and details of teaching received (12-items). The preferred education modality (paper, digital, one-on-one with HCP) was also assessed. HCPs, (radiation oncologists, brachytherapists and oncology nurses), completed a one-time questionnaire that assessed: patient factors influencing teaching (4-items), HCP perception of important topics (5-items), self-report of self-management teaching (12-items), perceived patient satisfaction with current teaching (1-item) and involvement of the patient's partner (1-item).

**Results:** Between May 2016 to February 2017, 18 patients and 55 HCPs were approached for the study. Of these, 12 patients (67%) and 53 HCPs (96%) consented to participate. Education related to vaginal care (cleansing, bleeding, pain etc.) and symptom management were rated as very important/important by 100% of responding patients. Education related to sexual health, intimacy and impact on relationships was rated as very important/ important by 87%. Detailed information pertaining to vaginal stenosis prevention techniques was desired by 76% of patients and 58% wanted their partner involved in the education. Although education regarding prevention of vaginal stenosis and dilator use was provided to 75% of patients, only 50% reported routine dilator use. Qualitative data revealed that patients are very appreciative of the one-on-one education provided by HCPs, in addition to receiving education pamphlets. They also expressed the importance of a follow-up phone call from a HCP upon BT completion to reinforce important information. HCPs (73%) indicated that providing detailed instructions to patients is important for engaging them in self-management behaviors. 60% reported that they always provide vaginal self-management education and 59% reported that they always discuss dilator use patients. Involvement of the patient's partner in the education was more limited, with 20% of HCPs indicating that they always involve the partner, 62% sometimes and 28% never. Only 39% of HCPs felt that they have adequate knowledge in providing post-BT vaginal self-management and sexual health education.

**Conclusions:** The majority of patients receive teaching in vaginal self-management and dilator use. Patients highly value the education provided and prefer to have education done one-on-one with their HCPs alongside their partner. However, a mismatch was found as most HCPs feel they do not have adequate knowledge to provide this education. Future work will involve developing a standardized post-BT patient education program to address patient and HCPs needs.

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### EXTRACTING FROM PATIENT EXPERIENCE: THE USE OF VIRTUAL SOFTWARE FOR RADIATION THERAPY EDUCATION FOR BREAST CANCER PATIENTS

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**Purpose:** Education regarding radiation treatment and management of side effects is essential to cancer care. While treatment technology has evolved, little attention has been made to bring patient education inline with modern techniques. Most radiotherapy education is delivered using videos, written materials, and one-to-one information sessions. Virtual simulation is commonly used in medical education for learners, yet there has been little research to explore its role in patient education. This project aims to evaluate a virtual radiation simulation program as a supplement to the standard educational process for breast cancer patients, and assess its impact on patient knowledge, satisfaction, and anxiety.

**Materials and Methods:** Breast cancer patients undergoing curative intent radiation therapy at a large academic oncology centre were randomized to: 1) current radiation therapy education with videos, written materials, and one-to-one information sessions (CM); or 2) current method supplemented with simulation (CMS). Patients completed a paper-based survey with closed and open questions at three time points (after CT Simulation, first week and last week of treatment). The survey, based on a needs analysis, assessed patient anxiety, knowledge and satisfaction. Anxiety levels were based on the State-Trait Anxiety Inventory (STAI). Data were interpreted using mixed methods.

**Results:** Two hundred and thirty patients with breast cancer completed the study (115 in each arm) from February 2016 to January 2018. The majority of the patients had post-secondary education (77% CM, 73% CMS) with the average age of 51-65 years (50% CM, 44% CMS). The groups were similar with regard to educational attainment and baseline state and trait anxiety scores. Both arms observed a decrease in state (situational) anxiety scores from CT simulation to the last week of treatment. Baseline knowledge satisfaction for both arms resulted in a high level of satisfaction with the information provided (92% CM, 98% CMS). Both arms (90% CM, 97% CMS) felt well-informed about treatment and management of side effects at CT sim. Despite this, patients (17% CM, 13% CMS) wanted more information about radiation therapy treatments. Notably, CM reported the need for more information consistently higher at all three time points. Analysis of narrative comments confirmed the supportive role therapist plays in providing technical and side-effects management information, and patients need of a visual representation to "preview" the experience. Supplementing the information session with simulated software provided an opportunity for patients to visualize and understand special techniques, such as deep inspiration breath hold.

**Conclusions:** The results of this study indicate that there may be a role for virtual simulation to supplement current radiation teaching methods. Results show simulation resulted in higher perceived levels of patient understanding. The influence of virtual software to supplement patient education session did not appear to affect a patient's anxiety level. Qualitatively, the addition of simulation improved the ability for a subset of breast cancer patients to visualize more complex techniques and understand specific instructions such as deep inspiration breath hold. As such, simulation may be best employed for specific patients requesting more detailed information or receiving more complex treatments.

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### PRE-LAUNCH FEEDBACK FOR EFFECTIVE TRANSITION TO PRACTICE TRAINING WITH COMPETENCY-BASED MEDICAL EDUCATION IN RADIATION ONCOLOGY

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**Purpose:** While entering independent practice is associated with a sense of achievement with most new specialists reporting a high level of competence in the Medical Expert domain, they also express apprehension in other aspects, particularly practice management and leadership. These concerns have been recognized, and under the new Royal College Competence by Design (CBD) medical education platform, a Transition to Practice (TtP) component will be incorporated as the last stage of residency training. This study aims to determine the learning environments and content that would be most beneficial to inform and optimize the TtP curriculum for Canadian radiation oncology (RO) residents.

**Materials and Methods:** We conducted focus groups with each of four groups of stakeholders involved in the TtP for Canadian Radiation Oncologists: senior residents, fellows, new to practice radiation oncologists, and residency program directors. Focus groups contained 5 – 12 participants, lasted 30 – 60 minutes and were audio recorded. Each group was asked to: 1) describe the current state of TtP education in RO; 2) identify gaps that currently exist in the TtP in RO; 3) suggest essential competencies, skills, knowledge and attitudes that should be incorporated into the TtP curriculum; and 4) propose how trainees can acquire these competencies. Interview transcripts were assessed by two observers and coded for common themes using NVivo qualitative data analysis software, v11.0. Thematic disparities were resolved through group consensus.

**Results:** Half of the participants reported having a TtP curriculum that varied from 2-12 months in length with differing learning objectives. All stakeholders emphasized a paucity of exposure to the business, administration and practice management aspects of independent practice and the benefit of mentorship. Program directors focused on cultivating opportunities for leadership roles, and providing support for the TtP both during residency and through onboarding programs for new physicians. New radiation oncologists focused on the need for training on practice logistics, triaging consults, institutional differences in practice management, and contract negotiation. Senior residents described a strong interest in mentorship and increased exposure to treatment planning evaluation and approval. Suggestions for a TtP phase included a longitudinal clinic, simulation labs, a simulation/treatment issues rotation, contract negotiation seminars and managing a physician's practice with less oversight.

**Conclusions:** There are perceived gaps in current TtP training of Canadian RO resident with opportunities for enrichment with CBD. Our data is informative for the development of an evidence-based TtP curriculum in advance of the first CBD cohort that will enter the TtP residency training stage in 2023. This work also establishes quality improvement measures to compare stakeholders' feedback following the introduction of TtP with the CBD education model.

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#### EMPATHIC PATIENT-ORIENTED COMMUNICATION IN CANCER CARE COURSE: PROGRAM DESIGN AND EVALUATION

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**Purpose:** Sensitive and effective communication skills are critical for successful health professional (HP) and patient/caregiver interactions. There is a lack of effective training for HPs in approaching and managing challenging communication. The purpose of this study was to evaluate the impact of a blended curriculum in communication on trainee competence and knowledge.

**Materials and Methods:** Following a needs assessment using a 1-5 likert scale on perceived competence in various aspects of communication, an interprofessional, blended curriculum was developed to advance competence and training in challenging conversations in cancer. The blended curriculum consisted of 5 eLearning modules: communication styles, speaking in plain language, principles of breaking bad news, principles for incident disclosure and fundamentals of resilience and coping. Two patient experience videos were recorded. A reflective practice forum was created for the video vignettes to foster resilience skills. Following this asynchronous training a three-hour in-person, facilitated, skills development session with standardized patients was held. Trainees participated in four standardized scenarios. A pre-/post-

evaluation design was used to evaluate self-perceived competence (4-items) and knowledge acquisition (13-items). The McNemar-Bower Chi Squared test was used to compare self-assessed competency scores and paired T-Tests were used to compare knowledge acquisition scores pre and post course. Learner satisfaction was collected post course.

**Results:** Sixty-one interprofessional trainees completed the needs assessment. The overall perceived competence for breaking bad news was 2.3 (1-5) and the importance was 3.7 (2-4), for incident disclosure was 2.2 (1-4) and importance 3.6 (2-4) and for highly emotional encounters 2.5 (1-5) and importance 3.6 (2-4). The top needs identified were greater knowledge in these areas and opportunities for simulation. Thirty-one trainees completed the pre and 18 the post-assessment. There was a significant increase in self-perceived competency following course completion in two of four competency domains: disclosing an incident to patient/family (p-value = 0.046), and breaking bad news (p-value = 0.011). There was a trend towards a significant difference in knowledge acquisition scores pre (M = 7.47, SD = 2.36) and post (M = 6.50, SD=2.31); t(14) = 2.12, p = 0.053). Course satisfaction was high with 79% (26/33) (reporting that they were "confident" to "totally" confident that they have mastered the techniques in difficult conversations. Seventy-nine percent (26/33) reported they "likely" to "definitely" intend on using these techniques in their work. 93.76% (30/33) stated they "intend to" "are likely to" or will "definitely" continue to practice communication skills after the training. Overall, 100% said they would recommend this course to a colleague.

**Conclusions:** A blended curriculum to advance HP competence and training in challenging conversations in cancer can build HP perception of competence and knowledge.

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#### EXPLORING THE ROLE OF PROSTATE CANCER SURVIVORS IN MANAGING SURVIVORSHIP CARE

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**Purpose:** New models of follow-up care are needed to meet the demands of the growing numbers of prostate cancer survivors. These models should leverage shared-care between primary care physicians and oncologists and maximize patient self-management. The purpose of this prospective study is to explore the role that prostate cancer survivors can play in their survivorship care.

**Materials and Methods:** This prospective cross-sectional study recruited patients who completed treatment >2 years ago at Princess Margaret Cancer Centre. Participants completed a one-time questionnaire including demographics (7-items), cancer health literacy (CHL) (6-items with >4 indicating adequate CHL), self-efficacy (6-items; 1-10 Likert scale), symptom severity (27-items; arithmetic mean of items rated 1-not severe to 10-very severe), and readiness for self-management (8-items). Descriptive statistical analysis, univariable (UVA) and multivariable (MVA) logistic regression analysis were conducted.

**Results:** Two hundred and six patients were recruited from May-November 2017. Median age 72 (range: 47-89), 33% were working, 61% were college/university educated, 78% were Caucasian, 82% were married, and 78% had adequate CHL. Self-efficacy score was high (8.3, range 1.6-10), while symptom severity score was low (1.8, range 0-6.5). Mean readiness for self-management score was 24 (range 20-97.5). On UVA, low income 4.37 (1.93,9.89; p = <0.001), being single (marital status) 2.31 (1.07,5.02; p = 0.034) and symptom severity 1.33 (1.05,1.69; p = 0.018) were significantly associated with readiness to self-manage. On MVA, only low income 3.99 (1.71,9.35; p = 0.014) and symptom severity 1.38 (1.07,1.78; p = 0.013) remained significantly associated with readiness to self-manage. Higher readiness to self-manage was predicted for patients with household income less than \$49,999/year and patients with higher symptom severity scores. Sixty-two percent of survivors agree/strongly agree that improving their engagement in their survivorship care is important while 50% agree/strongly agree that they'd like to know more about symptoms and what they can do about them. The most frequently identified barriers to accessing survivorship care were "transportation to appointments" (10.6%), and "lack of communication with doctors" (9.7%).

**Conclusions:** Prostate cancer survivors are willing to engage in self-management activities with healthcare providers. Support is needed to build self-management skills.

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#### THE PREVALENCE AND NATURE OF UNMET SURVIVORSHIP NEEDS OF PROSTATE CANCER PATIENTS

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**Purpose:** The purpose of this prospective study is to explore the prevalence and nature of unmet survivorship needs in prostate cancer patients.

**Materials and Methods:** This prospective cross-sectional study recruited patients who completed treatment >2 years ago for prostate cancer at Princess Margaret Cancer Centre. Participants completed a one-time questionnaire including demographics (7-items), cancer health literacy (CHL) (6-items with >4 indicating adequate CHL), self-efficacy (6-items; 1-10 Likert scale), symptom severity (27-items; arithmetic mean of items rated 1-not severe to 10- very severe), and cancer survivor unmet needs measure (CaSUN) (35-items; max unmet needs score 70). Univariable (UVA) and multivariable (MVA) logistic regression analyses were conducted with unmet needs score as the outcome.

**Results:** Two hundred and six patients were recruited from May-November 2017. Median age 72 (range: 47-89), 33% were working, 61% were college/university educated, 78% were Caucasian, 82% were married, and 78% has adequate CHL. High self-efficacy mean scores were observed (M=8.3, range 1.6-10) while symptom severity scores were low (M = 1.8; range: 0 - 6.5). The median unmet needs score was 9 (range: 0-49). The most common unmet supportive care needs were "more accessible hospital parking" (n = 34, 18.5%), "help addressing problems with my sex life" (n = 28, 15.6%), and "ongoing case management" (n = 21, 11.6%). On UVA only age and symptom severity score were significantly associated with unmet needs. On MVA, age was not a significant predictor of having unmet needs (age 0.96 (0.92,1) p = .077; symptom severity 1.81 (1.35,2.41) p < 0.001). For a one-unit increase in symptom severity score, there is likely an 81% increase in the odds of having unmet needs, when adjusted for age.

**Conclusions:** Prostate cancer survivors have multiple unmet needs and those with greater symptom severity have a greater chance of having unmet needs.

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#### LEARNING IN 360 DEGREES: A PILOT STUDY ON THE USE OF VIRTUAL REALITY FOR RADIATION THERAPY PATIENT EDUCATION

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**Purpose:** Due to the uniqueness of radiotherapy treatment, most new patients have little knowledge of radiotherapy treatment procedures. Patient education for external beam radiation therapy (EBRT) is traditionally delivered in verbal and/or written form. These education methods may not provide a full picture of the technical aspects of treatment. The purpose of this pilot study was to create and evaluate a prototype 360degree Virtual Reality (VR) video outlining the technical aspects of EBRT to the pelvis as a supplement to traditional education methods.

**Materials and Methods:** A prototype VR video was filmed to simulate the delivery of one fraction of image-guided EBRT to the pelvis from the patient's point of view. Storyboarding and scripting were used to ensure the technical aspects of treatment and standard new patient education protocols at our institution were addressed. The video overlaid with an audio narration track, edited for time and formatted for viewing through a smartphone VR headset. Patients having a radical course of image-guided EBRT to the pelvis were approached in clinic to participate in a focus group evaluating the prototype VR video. Focus groups led by an independent facilitator allowed participants to view and discuss the prototype VR video with relation to the patient education they received prior to treatment. Discussions were

recorded, transcribed and subjected to thematic analysis.

**Results:** All patients were accrued from a single academic cancer centre in a large metropolitan area. In total, 15 patients were approached, nine consented to participate and two were withdrawn (unable to attend a focus group). Of the remaining seven participants, three were male and four were female, ranging in age from 54 to 67 years ( $\mu = 61$ ,  $SD = 4.89$ ). Thematic analysis revealed 71% (five out of seven) of participants felt the traditional patient education met their needs. However, 86% (six out of seven) mentioned the education did not capture all the elements of treatment. Participants identified potential benefits could include an increased understanding of the treatment process, specifically the spatial and acoustic aspects of treatment, as well as the potential to reduce anxiety in new patients. Participants also recommended changes, such as including 2-dimensional elements in the VR video and improvements which would make the viewing experience more realistic. Timing was also important, with 86% (6/7) of participants recommending VR video viewing prior to the first day of treatment.

**Conclusions:** Overall, patient education at our centre was found to be adequate by most participants. Supplementing traditional education with VR video has the potential to improve upon existing methods, increasing understanding of treatment and decreasing anxiety. Next steps include implementing participant feedback and testing the VR video in the setting of a randomized controlled education study.

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#### MONITORING THE SITUATION: IMPLEMENTATION OF A PATIENT INFORMATION MONITOR IN A RADIATION THERAPY DEPARTMENT WAITING ROOM

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**Purpose:** The waiting room experience can impact patient satisfaction and affect outlook on encounters with healthcare professionals and quality of care. Patient education initiatives in waiting areas have been shown to improve overall patient experience in the primary care setting. A survey conducted by the Radiation Therapy Patient Experience Group (RTPEG) in a large metropolitan cancer centre revealed patients and their families were dissatisfied with the waiting room experience. Lack of distraction and a desire for more information on available resources were cited as sources of dissatisfaction. The aim of this initiative was to evaluate the impact of implementing a patient information monitor, with content developed in response to the RTPEG survey, on the experience of patients and families visiting the radiation therapy department.

**Materials and Methods:** This initiative was executed by a working group consisting of RTPEG members with representation from different areas within the department including administration, treatment delivery, specialty areas, research and education. A brainstorming session was held and five categories of content were identified, ranging from patient resources to brain teasers. Categories were assigned to RTPEG members for content development. Template pages were created to ensure consistency and uniformity of messaging. Where possible, information from existing patient education and information materials was used verbatim. Sample pages were sent to various stakeholders for review, including patient education experts, patient representatives and interprofessional groups. Post monitor activation, 50 patients and caregivers were approached for their feedback on the content. **Results:** A convenience sample of 50 patients, family and care givers was approached for feedback over the course of one week. Only 42% (21/50) of those approached were aware of the monitor in the waiting area. However, 29% (6/21) of these respondents found the Organizational and Resource content informative and helpful while 48% (10/21) enjoyed the distraction provided by the Scenic Photos, Trivia and Brain Teasers.

**Conclusions:** The introduction of a patient information monitor aligns with institutional and provincial strategic goals to improve cancer care by enhancing the experience and care of our patients and their families. The waiting room experience in the radiation therapy department is an important component of the overall patient experience. The monitor provides an easily accessible source of information and distraction. Quality improvement

initiatives, such as the monitor, provide cost effective services that are truly person-centred improving the quality of care provided.

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### RESULTS FROM THE 2017 SURVEY OF RADIATION ONCOLOGY RESIDENTS IN CANADA

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**Purpose:** Previous pan-Canadian surveys of Radiation Oncology (RO) residents performed in 2003 and 2009 identified job availability as a major concern and characterized a perceived decline in employment opportunities for radiation oncologists in Canada. The Canadian post-MD education registry indicates that Canadian RO trainee levels rose from 130 in 2003 to reach a peak of 209 in 2009 before declining to approximately 130 in 2017. Recognizing that RO has entered another period of transition, we investigated resident perspectives among a more contemporary cohort of RO trainees in Canada.

**Materials and Methods:** Surveys were distributed electronically to residents at each RO training program in Canada. Surveys consisted of 116 multiple choice and open-ended questions assessing center demographics, motivations for choosing RO, clinical experiences, didactic learning, research experiences, professional relationships, resident satisfaction, and career aspirations. Questions were constructed based on the 2003 and 2009 Canadian survey, and on previous Association of Residents in Radiation Oncology reports from the United States. Anonymized, aggregate responses from completed surveys were abstracted, and descriptive statistics were calculated.

**Results:** Out of 128 eligible residents, 84 completed the survey (65.6% response rate) with representative sampling from each training year (17.1% - 22.4% each year). Demographics reveal 52.6% were male, 68.4% were Canadian medical school graduates (CMGs), 22.4% held either a master's degree or doctorate, and 2.6% held additional medical certification. Nearly all respondents (97.9%) were satisfied with their specialty and training program. The most frequently perceived weakness in training was feeling unprepared to be competitive in the job market (42.6%), and 78.7% plan to pursue a post-residency fellowship. Most CMGs (86.1%) plan to practice in Canada, but only 12.8% of respondents believe there is strong demand for RO in Canada. Few respondents believe they can obtain staff positions treating their preferred tumour sites (38.3%), and at their preferred geographic location (27.7%). The job market was perceived by 40.4% to be less competitive than it was five years ago, and 59.6% predict it will be less competitive five years from now.

**Conclusions:** Canadian RO residents feel adequately trained as competent physicians, and a majority of trainees pursue post-residency fellowships, similar to prior surveys. Although current perceptions of the Canadian job market remain guarded, RO residents are highly satisfied with their choice of specialty and training program, and are more optimistic about their future job prospects. Our survey update provides continued insights into RO residency training in Canada, and identifies opportunities for improvement that could be addressed by the incoming competency-based medical education model for RO.

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### DISTRACTED DRIVING? AN EXAMINATION OF CONSOLE INTERRUPTIONS DURING RADIATION THERAPY TREATMENT

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**Purpose:** The risks associated with workplace distractions are well documented. Distracted working can lead to an increase in workplace injuries and errors. Errors in radiation therapy treatment delivery by radiation therapists (RTTs) are relatively rare, but when they do occur can lead to serious consequences.

In the radiation therapy environment distractions can stem from interruptions during treatment, for example by co-workers, patients and other sources. The problem of distraction in radiation therapy departments during treatment has not been well examined. Focused attention by RTTs is particularly important during the time that the treatment machine is delivering a beam of radiation. Inattention due to distraction or interruptions can result in errors, for example, a mismatch between patient set-up information and the identity of the patient on the treatment couch or targeting errors due to unexpected patient movement. This study quantifies the amount and types of treatment interruptions found in three cancer centres.

**Materials and Methods:** A non-participant observation study of the types of distractions occurring during treatment was carried out using a standard checklist plus field notes (e.g. to capture an unusual interruption). The process and tool were piloted before use.

**Results:** Of 94 treatments observed, 51 experienced interruptions (54%). Thirty-two were interruptions by RTTs (either team members or RTTs from different units), 15 were from a patient or family, seven were from another healthcare professional, seven were "other" and four were phone calls. Field notes indicate that console area design and patient flow can impact on the amount and types of interruptions.

**Conclusions:** It is hoped that data capturing the typical distraction events, and how often these occur, will lead to measures to improve the working environment of RTTs.

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### BREAST CANCER PATIENTS' PERCEPTIONS OF ADJUVANT RADIOTHERAPY: AN ASSESSMENT OF PRE-TREATMENT KNOWLEDGE AND INFORMATIONAL NEEDS

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**Purpose:** Through media, Internet, and supportive community programs, patients are able to share cancer-related experiences. It can be difficult for patients to assess if the information about radiation that they encounter is accurate and relevant to one's own situation. In order for physicians to recognize patients' concerns and help them make decisions about breast radiotherapy (BRT), a better understanding of how patients are educating themselves and the types of information they have encountered is valuable. The purpose of this study is to assess breast cancer patients' information-seeking behaviours, needs and perceptions of BRT prior to radiation oncology consultation.

**Materials and Methods:** Breast cancer patients referred for adjuvant BRT at BC Cancer, > 18 years, without a history of prior BRT, were asked to complete an anonymous survey prior to their radiation oncology consultation. Likert scale, multiple choice and open-ended questions were used to assess information sources, knowledge, and perceptions of BRT.

**Results:** The response rate was 88%; 46/52 patients approached agreed to participate in the study. Most patients were >50 years old (65%) and 71% had a post-secondary degree or diploma. The most commonly reported sources of information about BRT were healthcare providers (HCP, 57%), family or friends treated with BRT (50%), family or friends treated with radiation for a different cancer (43%) and Internet websites (39%). Few received information about BRT from traditional media (11%), scientific articles (9%), social media (7%), and support groups (4%). HCP were considered the most trusted resource by the majority of patients (33%), followed by family or friends treated with BRT (26%), Internet websites (13%), and family or friends treated for a different cancer (10%). Most patients reported having little or no knowledge about BRT (80%). This was true even among those whose most trusted source of information was HCP (85%). Most (67%) were a little or moderately concerned about the side effects of BRT, while 27% were very concerned. Most were unsure (60%) about the benefit of BRT and 40% thought BRT would provide a moderate to significant benefit. While educating themselves about BRT, a wide range of topics were encountered, and the most common ones were fatigue (70%), skin problems (52%) skin care (48%), effects on healthy body tissues (43%), effects on the immune system (35%), and radiation as a cause of cancer (33%). Several other topics were encountered, including BRT and bone health (28%), pain (26%),

recommended activity during BRT (24%), dietary recommendations (22%), radioactivity (22%), and problems with lungs (22%), heart (22%), hair loss (20%) and arm swelling (20%). Of these topics encountered, those patients considered the most important for the radiation oncologist to address were BRT effects on healthy body tissues (22%) and radiation as a cause of cancer (20%). Although commonly encountered topics, relatively fewer patients indicated skin care (15%), skin problems (13%), and fatigue (13%) as important issues to be addressed at their consultation.

**Conclusions:** Breast cancer patients encounter a broad range of information about BRT from a variety of sources prior to their radiation oncology consultation and many are concerned about the potential side effects. Patients surveyed felt that BRT effects on healthy body tissues and second malignancies were the most important for radiation oncologists to address during consultation.

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#### ESTABLISHING A ROLE FOR TUMOUR GENOMICS IN RADIATION MEDICINE: AN ANALYSIS OF HEAD AND NECK CANCER PATIENTS ENROLLED IN THE PERSONALIZED ONCO-GENOMICS (POG) INITIATIVE

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**Purpose:** The role of personalized onco-genomics is not well established in radiation oncology. This study evaluated head and neck cancer (HNC) patients enrolled in the Personalized Onco-Genomics (POG) clinical trial, assessing if DNA repair gene expression (DRGE) or specific mutation signatures were correlated with time to progression after treatment with radiotherapy (RT).

**Materials and Methods:** Twelve patients with HNC and documented progression after RT for presumed localized disease were enrolled on the POG trial. Clinical characteristics were assessed retrospectively. DNA and RNA libraries were prepared from tumour biopsies (eight metastatic and four primary) and peripheral blood followed by Illumina sequencing. Hierarchical clustering of 134 DNA repair genes was performed using the Ward.D2 method to identify clusters of differentially expressed DNA repair genes, and the Manhattan method was used to determine the distance between samples. Somatic mutations were assigned to the COSMIC (Catalogue of Somatic Mutations in Cancer) mutation signature reference set using the non-negative least squares method, and represented as exposure scores, defined as the number of mutations attributed to the signature divided by the total number of mutations, for each tumour sample. Comparison of mutation signature scores between DRGE groups was assessed using the Wilcoxon test. Kaplan-Meier curves were created to assess progression free survival (PFS).

**Results:** The population comprised a heterogeneous group of tumour pathologies, including two adenoid cystic carcinomas, three other salivary gland tumours, and two thyroid cancers. The median age at diagnosis was 50 years. Four were female, and eight were male. Five were prior smokers. Four received curative intent RT, seven adjuvant RT, and one palliative RT. Total RT dose received was 50-70 Gy in 2-2.4 Gy fractions. Seven progressed locally, three distantly, and two locally and distantly. Gene expression clustering analysis revealed a subset of 17 genes, belonging to multiple DNA repair pathways, stratifying tumour into two groups, one with low DRGE and one with high DRGE. Although not statistically significant, patients with low DRGE tumours were younger (median age 36 versus 56 years,  $p = 0.09$ ) with a longer median PFS (27 versus 16 months,  $p = 0.30$ ), compared to those with high DRGE.

Mutation signature analysis revealed tumours characterized by low DRGE were associated with a higher number of mutations attributed to signature 5 (mean score 0.29, 95% CI 0.18-0.40) compared to tumours characterized by high DRGE (mean score 0.03, 95% CI 0.0-0.07). In contrast, tumours with high DRGE were associated with a higher signature 8 score (mean score 0.18, 95% CI 0.12-0.24), compared to tumours characterized by low DRGE (mean score 0.08, 95% CI 0.0-0.17). Two tumours were characterized by high signature 7 (scores 0.61 and 0.39), a mutation signature associated with UV light exposure. Patients with tumours characterised by high signature 5 scores ( $> 0.09$ ) had a trend towards improved PFS (median PFS 32 versus

12 months,  $p = 0.04$ ).

**Conclusions:** This exploratory study demonstrated a trend towards longer PFS after RT in HNC patients with low DRGE and higher signature 5 expression. Given the small numbers in our study and varied pathologic subtypes of HNC, larger scale, prospective studies are needed to validate these results.

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#### PROMOTING CAREER SELECTION THROUGH A COMPREHENSIVE ENRICHMENT EXPERIENCE: A REVIEW OF THE CARO-CROF SUMMER STUDENTSHIP

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**Purpose:** The impact of early clinical exposure to radiation oncology on medical student's understanding of oncology and career choice is not known. This study aims to review the experience and outcomes of medical students who participated in the Canadian Association of Radiation Oncology (CARO)-Canadian Radiation Oncology Foundation (CROF) summer studentship.

**Materials and Methods:** Medical students who participated in the studentship from 2014 to 2017 completed a survey at the end of their program. The survey queried radiation oncology exposure prior to the studentship, student satisfaction with the studentship (scale 1-5, 5 = outstanding, 3 = meets expectations, 1 = unsatisfactory) and willingness to recommend it to other students (scale 1-10, 1 = strongly disagree, 5 = neutral, 10 = strongly agree). Effect of studentship on their interest in the specialty was assessed (scale 1-10, 1 = strongly disagree, 5 = neutral, 10 = strongly agree) including intent to direct their career toward radiation oncology. Descriptive statistics were used to analyze the data. Match rates to radiation oncology from within this cohort are reported.

**Results:** A total of 24/24 (100%) students responded to the survey over the four-year period. The students' previous exposure to radiation oncology varied with lectures being their most common 70.83% ( $n = 17/24$ ). Students rated their studentship experience positively: noting inclusion of a broad range of clinical problems (mean = 4.58/5), the opportunity to learn assessment, investigation, and management (mean = 4.04/5), and high educational value (mean = 4.83/5). Most students' interest in oncology ( $n = 18/24$ ), and specifically radiation oncology ( $n = 21/24$ ) increased from pre to post-studentship and all students would strongly recommend this program to another medical student (mean = 9.80/10). All students responded to plan to do electives in other oncology-related specialties (e.g., medical oncology, surgical oncology). The percentage (32%,  $n = 6/19$ ) of these students entering a radiation oncology career was higher than national residency match rates in radiation oncology (0.5%).

**Conclusions:** Clinical exposure to radiation oncology through a nationally funded CARO-CROF summer studentship positively impacted medical student learning, student interest in oncology, and career selection. This study suggests that there was a potential effect of the studentship program on career selection.

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#### BUILDING COMMUNITY AMONG PROVINCES, PROFESSIONS AND PATIENTS THROUGH THE DEVELOPMENT OF PATIENT AND CAREGIVER RESOURCES

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**Purpose:** To foster patient-centred care initiatives and improve patient education materials within a Radiation Therapy (RT) program, a multicentre, multi-disciplinary collaboration was sought in partnership with patients and families.

**Materials and Methods:** Three patient education/engagement initiatives were undertaken through collaboration across six RT centres, four provinces and multiple disciplines (radiation therapy, physics, radiation oncology,

nursing, nutrition, and speech language pathology): quality display board, skincare and head and neck RT patient education. Patients and caregivers were involved through membership in the committees, completion of surveys and development of the proposed tools.

**Results:** The quality display board has been visible in patient waiting areas of three regional RT centres since September 2016. Greater than half of the surveyed patients and caregivers reported that the information displayed on the quality display boards made them feel more comfortable with their oncology treatment. Ninety-three percent answered “somewhat or very interested” to the question: Are you interested in our slide show? When asked: Do you think other patients and family members would be interested in our slideshow, 96% responded “somewhat or very interested”. A standardized evidence-based skin care guideline including a patient and caregiver resource has been used in five cancer centres since October 2015. The committee for the management of head and neck RT side effects is currently in the process of amalgamating resources to create a standardized patient education tool to be used in all six centres.

**Conclusions:** These three patient education initiatives provide evidence of the feasibility of patient centred care initiatives that can be fostered through multi-disciplinary, multicentre collaborative efforts. Partnership with patients and caregivers was an integral component of these collaborative initiatives.

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#### THE ROLE OF PARTIAL BREAST IRRADIATION IN THE PREVIOUSLY IRRADIATED BREAST

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**Purpose:** Partial breast irradiation (PBI) is being considered increasingly as a treatment option in early breast cancer. However, its role in the management of previously irradiated breast tissue is unknown and rarely reported. We analyzed breast cancer patients who previously had mantle field or breast radiation (RT) followed by re-treatment with external beam PBI.

**Materials and Methods:** Women with early breast cancer treated with breast conserving surgery and PBI between 2007-2017 that had previously received RT were analyzed. Eleven were recorded; eight (73%) received prior treatment with mantle field RT for Hodgkin's lymphoma and 3 (27%) patients for prior ipsilateral breast cancer diagnosis.

**Results:** Median age at initial and second diagnosis was 28 years (range, 16-54) and 48 years (41-69) respectively. Patients (eight) treated for lymphoma received a dose of 35 Gy in 16-20 fractions to a classic mantle-upper abdomen field. Patients (three) with an initial diagnosis of breast cancer received whole breast RT (two with 50 Gy/25fractions, one with 40 Gy in 16 fractions). Median time from initial to second diagnosis was 22.6 years (range, 13.5-32.6). All with early stage (I-II) invasive ductal carcinoma, eight (73%) ER positive, three (27%) triple negative. All patients were treated with lumpectomy or repeat lumpectomy and external beam partial breast irradiation. Four received a dose of 45 Gy/25 fractions, four - 50 Gy/25 fractions and three - 42.4 Gy/16 fractions. Seven (64%) patients had adjuvant endocrine treatment and four (36%) had adjuvant chemotherapy. One patient had Grade 2 fat atrophy and Grade 1 fibrosis (one patient had valvulopathy secondary to first mantle field radiation). One patient developed a contra-lateral breast cancer. No loco-regional recurrences were reported with median follow up of 4.6 years (0.6-10.5).

**Conclusions:** External beam PBI after lumpectomy appears to be a safe and effective RT treatment option for selected patients with prior radiation and localized early-stage recurrent breast cancer.

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#### MANAGEMENT OF LOCO-REGIONAL RECURRENT BREAST CANCER AFTER PRIOR RADIATION TO THE BREAST OR CHEST WALL

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**Purpose:** To report the outcomes of radiotherapy (RT) re-treatment to the breast or chest wall in women with loco-regional breast cancer recurrence.

**Materials and Methods:** Between 2009-2017, 55 women with clinically non-metastatic loco-regional recurrence of breast cancer were re-irradiated (reRT) with curative intent after repeat local surgery. Initial breast cancer diagnosis was between 1980-2013. Twenty-nine (53%) patients received re-RT to the chest wall (CW) or breast +/- regional nodes (25 to the CW, three to partial breast and one to partial CW), 26 received RT to the regional nodes alone. Documentation of initial breast cancer diagnosis, first recurrence and second recurrence (where applicable) were recorded. Median follow up from the initial diagnosis to first recurrence and then from first recurrence to last survival date was 10.3 (range, 6.6-14.4) and 4.1 (range, 0.3-9.8) years, respectively.

**Results:** At time of initial breast cancer diagnosis, the median age was 48 years (28-86), 46 (84%) patients had Stage I-II disease, six (11%) were Stage III and 3 (5%) had carcinoma in-situ. Forty-eight (87%) underwent lumpectomy and seven (13%) had mastectomy. All patients received radiation to the breast/CW and eight to the regional lymph nodes.

First recurrence: twenty-three (42%) patients had regional nodal recurrence (axillary, supraclavicular or internal mammary), 19 (34%) had local breast/CW recurrence and 13 (24%) had simultaneous loco-regional recurrence. The most frequently used re-treatment dose was 45 Gy in 25 fractions (68%) for CW recurrence and 50 Gy in 25 fractions (71%) for nodal recurrence. Thirty-two (58%) patients received chemotherapy, half in the adjuvant setting, and half in the neo-adjuvant setting, 35 (64%) patients had endocrine treatment and 16 (29%) had both. Five-year survival rates for regional, local and simultaneous loco-regional recurrences were 93%, 86% and 73%, respectively (p-value = 0.148). Overall survival rates at five and eight years for the entire cohort were 86% and 63%, respectively.

Recurrence after retreatment: Eight (15%) patients had a subsequent breast cancer recurrence, with a median time of 1.6 (range, 0.6-6.1) years.

Only nine patients had Grade 2 or more toxicity recorded (fibrosis (four), lymphedema (two), fat atrophy (one), brachial plexopathy and hyperpigmentation (one), skin ulceration (one)).

**Conclusions:** Aggressive management of loco-regional breast cancer recurrences with surgery and repeat radiation is feasible with tolerable toxicity and good outcomes.

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#### THE HUMAN SIDE OF ARTIFICIAL INTELLIGENCE IN HEALTHCARE: DO WE KNOW WHAT'S COMING AND WHAT TO DO ABOUT IT?

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**Purpose:** As artificial intelligence (AI) strategies are increasingly implemented in healthcare, there will likely be a significant social and professional impact on relevant healthcare providers. It implores fields such as radiation medicine (RM) to explore the nature and extent of this impact in order to harness the capability in a responsible manner. To appreciate existing academic insight into how relevant professional groups will be forced to evolve with AI, a scoping literature review was performed.

**Materials and Methods:** Six databases were searched; Ovid MEDLINE, Ovid MEDLINE ePub ahead of Print, Embase, PsycINFO, CINAHL, and SCOPUS. “Artificial intelligence” was used as an umbrella term, encompassing related terms such as “deep learning”, “big data”, and “automation”. “Professional role” and “professional practice” were used to filter out more technical AI-related articles in favour of honing in on the social impact of AI. Citations were reviewed for duplicates, then by title and abstract for relevance based on consideration of high-skill professional groups (doctors, nurses, engineers, lawyers), and focus on AI technologies as they impact roles of humans. Full-text was sought and reviewed for identified citations. An iterative process was used to map themes and concepts across relevant articles, focusing on ways in which AI was considered to impact on professional practice and roles, and the approaches and response proposed or taken by impacted professions.

**Results:** 741 unique citations were identified, with only 46 deemed relevant based on abstracts, reduced to 18 after full-text review. Three more were identified through reference list review. With the exception of a cross-sectional and survey study, all included articles were short editorial pieces. One article

was published as early as 1984, but almost half (47.6%) were published only in the past two years. No articles suggested any profession would be made obsolete with AI. Most focused on the supportive role of AI in augmenting care. Others highlighted the greater likelihood that current roles would be “displaced” rather than “replaced”, primarily through outsourcing of manual, repetitive, or mundane tasks to AI, freeing time to focus on tasks requiring higher cognition or skills assumed not to be within reach of AI. Education to build technology literacy was thought to be important, as was professional engagement in defining novel workflows and roles. No themes were addressed in all articles and many were only mentioned tangentially, with little depth of analysis or supporting evidence.

**Conclusions:** Professionals, including those in RM, will be increasingly faced with AI. Little empirical attention has been paid to its impact or how to work proactively moving forward. There is also little written about shifting approaches to education and redefinition of professional roles or departmental workflow with AI. Future work should inform how best to equip an optimal workforce to maximize AI potential.

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#### PHYSICIAN AND FACILITY DRIVERS OF SPENDING VARIATION IN LOCALIZED PROSTATE CANCER

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**Purpose:** Prostate cancer is the most common male cancer and it is well-recognized that patients and physicians can pursue a wide range of treatments. Although payment reform designed to reduce unnecessary variation is an important strategy to improve quality and reduce spending growth, drivers of spending variation within prostate cancer are unknown. The objective of this study is to analyze spending variation amongst men with localized disease.

**Materials and Methods:** We examined contributions to variation in total medical spending excluding pharmacy in the year following diagnosis, focusing on within and between physician- and facility-level factors using the 2010-2013 Surveillance, Epidemiology, and End Results-Medicare linked database. We partitioned variation using multi-level regression with physician and facility random effects and examined drivers of variation using sequential models that included patient characteristics, disease risk, and treatment choices. Physicians were then sorted into quintiles of adjusted patient-level spending and practice patterns differences of the highest and lowest physician quintiles were reported.

**Results:** Mean annual spending per patient was \$30,444 (SD \$19,283) for patients who saw a urologist and \$34,377 (SD \$15,592) for those who also saw a radiation oncologist (RO). Variation in spending due to between-physician differences within facility was similar to between-facility differences (for urologists, 5% between-physician and 6% between-facility; for ROs, 7% versus 6%, respectively). For a patient treated by a urologist with annual spending one standard deviation above the mean, this is equivalent to \$7,860 higher annual spending (25.8% above mean); and \$7,760 higher spending (22.6% above mean) for patients seen by ROs. Greater between-physician variation was explained by differences in treatment choices (69% for urologists, 20% for ROs) than by differences in their patients' demographic/disease characteristics (1% for urologists, 15% for ROs). Urologists with the highest spending spent 71% more on patients undergoing active surveillance, had 27% longer inpatient stays, used 27% more imaging, and were associated with 43% greater radiotherapy spending compared to the lowest spending urologists, with no differences in robotic surgery. Highest spending ROs had more office visits and used more intensity modulated radiation and proton therapy versus the lowest.

**Conclusions:** Spending variation within geographic region is associated with meaningful differences in prostate cancer spending and is driven by differences between physicians within facility and between facilities. Different treatment choices for similar patients within the same insurance system

explain the greatest proportion of variation. These findings can establish targets for collaborative efforts aimed at improving value and can be used to design interventions that target the treatment decision-making process to improve the affordability of prostate cancer treatment.

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#### IMPROVING CLINICAL QUALITY BASED ON PATIENT'S PERSPECTIVE

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**Purpose:** The patient-centred care aims to incorporate patient preferences and needs into the clinical workflow. In this study, our radiation-oncology department conducted focus groups interviews in order to implement changes that would address patients' concerns and enhance overall patient experience. **Materials and Methods:** Three groups (breast cancer, prostate cancer and other cancers treated with concomitant chemotherapy) of eight participants (patients and their relatives) were consulted during 120 minutes meetings. These patients all received curative radiation therapy treatments in the past year at our facility. To structure these interviews, five open-ended questions were asked to the participants: 1) what does quality of care and service mean to you?; 2) did the information you received about your treatments and side effects meet your expectations?; 3) how did you deal with the different steps prior to your radiation therapy treatments and what were your preoccupations?; 4) how could our team give you a better clinical support?; and 5) how could we improve appointment booking?

**Results:** The majority of comments received from the patients during these interviews were positive. Several topics were recurrent among the groups such as the large amount of information given to the patient, the moment at which it was given and the clarity. Other areas of improvement were the parking management, the schedule layout and the waiting room atmosphere. More than a year after these focus group interviews, most of the issues raised by the patients and their relatives were addressed and changes have been implemented. We also formed an interdisciplinary team that created personalized information documents for the patients.

**Conclusions:** Collecting patient opinions through focus groups allowed us to properly identify potential modifications that would enhance their clinical experience. Follow-up of these adjustments is ongoing through anonymous satisfaction survey and iterative feedback from Patient Partners.

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#### TARGETING THE AREAS OF CARE THAT REQUIRED IMPROVEMENT IN PARTNERSHIP WITH PATIENTS

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**Purpose:** The Canadian healthcare system has undergone a significant shift in regards to patients' involvement in their own care. This patient-centred paradigm requires a thorough review of every single step from diagnosis to post-treatment follow-up. In partnership with our patients, we identified the areas of care that required improvement.

**Materials and Methods:** By bringing together a workgroup of various health professionals, communication advisor and former radiation therapy patients, we first identified possible clinical improvements that would benefit the patients. Anonymous surveys, focus group interviews and Patient Partner testimonials within this workgroup have allowed us to select a specific problem we would address. A literature review and a search for already existing tools from other cancer facilities in our region were performed. We then selected the appropriate tools that would meet the needs of our patients, and personalized via a survey given to patients who have completed their treatments within the last year.

**Results:** A recurring topic was the lack of support and information in the post treatment setting. No longer having daily appointments with health care professionals can create anxiety to some patients and put them in a state of limbo. We identify the most suitable resources and tools such as personalized post-radiotherapy treatment information leaflets, conferences and peer-support groups. Another survey has been created by the workgroup in order to target the exact content, topics and format that these tools should include.

**Conclusions:** By doing a step-by-step iterative approach involving the patients, we were able to target a specific issue affecting a majority of them. We are now better equipped to address our patients' needs in the post-treatments period and together with them, we are working on the creation of personalized support documents.

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#### DISPARITIES IN ACCESSIBILITY TO RADIOTHERAPY IN A HIGH-INCOME COUNTRY: THE CASE OF CANADA

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**Purpose:** Canada is a high-income country with universal healthcare. However, Canada's large geographic area and small population density creates challenges in accessibility to oncologic treatment, such as radiotherapy. We sought to explore regional variations in cancer outcomes across Canada and the potential associated variables, including distance to nearest radiotherapy centre, sociodemographic factors, and the impact of any spatial relationships.

**Materials and Methods:** We conducted spatial autocorrelation using the global Moran's I statistic to detect non-random spatial patterns in age standardized all-cancer mortality-to-incidence ratios (MIRs) across health regions in Canada, from 2010 to 2012. Global ordinary least squares (OLS) regression and geographically-weighted regression (GWR) were then applied to examine relationships between distance to nearest radiotherapy facility, sociodemographic factors, and the observed spatial patterns.

**Results:** All-cancer MIRs by health region across Canada exhibited positive statistically significant global Moran's I index values, with a tendency towards clustering (Moran's I = .346,  $p = .001$ ). Mapping of clusters showed one high-MIR cluster (range .45-.88) involving two of three Canadian territories (Nunavut and Northwest Territories) and the north of certain provinces (Manitoba, Ontario and Quebec). A second cluster of low-MIRs (range .40-.41) was observed in the southern region of British Columbia. In both regression models, health regions with longer Euclidean distance to nearest radiotherapy centre, higher rates of smoking and lower rates of food security were significantly associated with higher MIR ( $r_2 = .70$  with OLS and  $r_2 = .74$  with GWR).

**Conclusions:** Disparities in cancer outcomes exist in Canada and exhibit a north-south gradient, with poorer outcomes in the more northern regions. Differences in accessibility to radiotherapy may explain these regions' poorer outcomes, along with other sociodemographic factors. Further work is required to better understand how best to improve access to radiotherapy in Canada for regions with poorer accessibility.

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#### ACCESS TO RADIOTHERAPY AMONG INDIGENOUS POPULATIONS IN CANADA

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**Purpose:** To explore disparities in accessibility to radiotherapy among indigenous populations in Canada, and its impact on cancer outcomes.

**Materials and Methods:** We initially conducted univariate and multivariate analyses across health regions (HR) in Canada, using age-standardized all-cancer mortality-to-incidence ratios (MIRs) from 2010-2012 as the dependent variable, and proportion of self-identified Aboriginals, shortest Euclidean (straight-line) distance to nearest radiotherapy facility, and other sociodemographic factors as independent variables. High multicollinearity was observed between the proportion of Aboriginals variable and other sociodemographic factors; therefore, a multiple linear regression model was not possible. We stratified our two independent variables of interest (proportion of self-identified Aboriginals, and distance

to radiotherapy centre) using an exploratory recursive partitioning approach, and compared the resulting groups with respect to their impact on MIR.

**Results:** HRs with <23% versus  $\geq 23\%$  Aboriginals had significantly lower MIR (0.42 versus 0.53, respectively;  $p < .01$ ) and shorter distance to nearest RT center (121km versus 799km, respectively;  $p < .01$ ). In a significant one-way ANOVA considering both distance and proportion of Aboriginals ( $F = 33.07$ ,  $p < .01$ ), HRs with  $\geq 23\%$  Aboriginals had higher MIR compared to those with <23%, regardless of whether they were located less or greater than 37km away (both  $p < .01$ ), and HRs with <23% Aboriginals located  $\geq 37$ km from nearest radiotherapy center had higher MIRs versus those <37km away ( $p < .01$ ). A sub-analysis on HRs located 150-750km from nearest RT center revealed that HRs with  $\geq 23\%$  Aboriginals had higher MIR versus those with <23% Aboriginals ( $p = .03$ ), despite no significant difference in distance to nearest RT center ( $p = .43$ ).

**Conclusions:** Regions inhabited by a larger proportion of indigenous populations are located further away from the nearest radiotherapy centre, but distance does not completely explain these regions' poorer oncologic outcomes. Further exploration and identification of other contributing factors to this population's high MIR is required.

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#### EVALUATION OF A WEB-BASED TOOL HELPING PROSTATE CANCER PATIENTS BECOME ACTIVE PARTNERS IN THEIR CARE. A PILOT STUDY

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**Purpose:** Barriers to effective communication in cancer care have been identified at initial oncology consultations. Let's Discuss Health (LDH) is a website designed to help patients become active partners in their care. The objectives of this pilot are to assess; 1) the feasibility of referring patients to LDH before initial radiation oncology consultations; and 2) the impact of its use on radiation oncologists (RO)-patient communication.

**Materials and Methods:** Design: observational and comparative study. Participants: Five RO and 30 prostate cancer patients. Patients were recruited successively into two distinct groups: 1) Group 1 received care as usual; 2) Group 2 was invited to prepare their consultation with LDH. Instruments: consultations were audio recorded and analysed using MEDICODE (instrument to analyse verbal exchanges on treatments in terms of themes, dialogue and initiative), RO and patient questionnaires, and patient focus groups. Outcomes: perception of the LDH's usefulness and its impact on RO-patient communication.

**Results:** Demographic characteristics were fairly similar in both groups. However, the rate of participation was higher for Group 1 (68% versus 54%). Group 2 reported a favourable evaluation of the website: easy of navigation (86%), readability (77%) and suitability of links to others cancer resources (75%). The RO reported that Group 2 patients were better prepared (61%) and better informed about prostate cancer (64%). In terms of content discussed, the average number of themes discussed was similar in both groups ( $p > .05$ ), however the pattern differed between groups for discussions of "treatment adverse effects" (Group 2: 2.33 versus Group 1: 1.86). Participation indicators were on average similar in both groups ( $p > 0.05$ ) but certain themes presented with clinically significant differences in terms of dialogue: "Treatment main effect" (Group 2: 23% versus Group 1: 12.6%) and "Treatment-related attitudes and emotions" (Group 2: 52% versus Group 1: 42.5%).

**Conclusions:** This study confirmed the acceptability for prostate cancer patients to be referred to a website before their consultation with the RO. Using LDH before seeing the specialist enabled the patient's voice to be heard on themes recognized as important for them. Results will inform the conceptualization of a pragmatic randomized controlled trial with this cancer population.

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### LYMPH NODE RATIO AS A PREDICTOR OF DISTANT METASTASES IN MAJOR SALIVARY GLAND CARCINOMAS

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**Purpose:** To investigate the prognostic value of lymph node ratio (LNR, number of positive lymph nodes[LN]/total number of excised LN) on distant metastases (DM) and overall survival (OS) in patients (patients) with major salivary gland carcinoma (SGC).

**Materials and Methods:** REB-approved retrospective review was conducted for SGC patients treated at our institution with curative surgery and neck dissection (>=6 dissected LN)+/-adjuvant treatment in 2000-2015. Patients, treatment and outcomes data were collected from our institutional maintained databases. Staging was reviewed according to the AJCC-UICC 8th edition. High risk pathology was defined with histologic grade and WHO histologic subtype criteria, and included: adenoid cystic carcinoma (ACC), salivary duct carcinoma, SCC, G2/3 adenocarcinoma, G2/3 mucoepidermoid carcinoma (MEC), G2/3 carcinoma ex-pleomorphic adenoma, carcinosarcoma, undifferentiated (small-, large-cell or lymphoepithelial) carcinoma and G3 of other histologic subtypes. Distant control (DC) and OS were analyzed with competing risk and Kaplan-Meier methods respectively. LNR (continuous variable) was subjected to multivariable analysis (MVA) for DM and OS (adjusted for age, gender, primary SGC subsite, pathologic stage, high-risk pathology, lymphovascular invasion [LVI], perineural invasion [PNI], extranodal extension [ENE] and surgical margin status). The optimal cutpoint of LNR that maximized the difference in outcomes was determined using maximally selected rank statistics. Subgroup analysis was performed for patients with pN+.

**Results:** A total of 204 patients were identified: median age: 56 year (16-91); median follow-up: 5.2 year (0.4- 17.6); parotid gland primary tumour location: 168 (82%); high risk pathology: 151 (74%); pT3-4: 132 (65%), pN+: 99 (44%); LVI: 49 (26%); positive microscopic surgical margin: 103 (52%); ENE: 37 (19%). PORT was used in 195 patients (96%); and adjuvant concurrent chemotherapy in 11 (5%). Of 2,725 LNs evaluated, 328 (12%) were pN+. The median number of dissected LN was 23 (6-101). For pN+ patients, the median number of involved LN was 3 (1-65) and median LNR was 14% (1%-100%). High-risk pathology and LVI were associated with high LNR ( $p < 0.001$  for both). On MVA LNR was independently correlated with DM (HR:1.18, 95%CI: 1.07-1.30,  $p < 0.001$ ) and OS (HR:1.16; 95%CI: 1.06-1.28,  $p = 0.002$ ) and so did LVI+ (DM: HR:2.54, 95%CI: 1.38-4.70,  $p = 0.003$ ) and OS (HR:2.50; 95%CI: 1.33-4.70,  $p = 0.004$ ), positive margins (DM: HR:2.47, 95%CI: 1.31-4.65,  $p=0.005$ ) and OS (HR:2.59; 95%CI: 1.35-4.95,  $p = 0.004$ ). The optimal cut-off point for LNR was 8%; 5-yr DC: 42% versus 88%,  $p < 0.001$ ; 5-yr OS: 44% versus 89%,  $p < 0.001$  for LNR  $\geq 8\%$  versus  $< 8\%$ . In a subgroup analysis of patients with pN+, LNR remained predictive for DM (HR:1.24, 95%CI: 1.14-1.35,  $p < 0.001$ ) and OS (HR 1.27, 95%CI: 1.16-1.38,  $p < 0.001$ ).

**Conclusions:** High LNR is associated with a higher risk of DM and lower OS. LNR should be evaluated in future prospective studies for intensified therapy or surveillance schedule in patients with SGC.

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### EVALUATING THE NECESSITY OF RADIOTHERAPY DOSE ESCALATION FOR INFLAMMATORY BREAST CANCER (IBC) IN THE CONTEXT OF MODERN MULTI-MODALITY TREATMENT: A MULTI-INSTITUTION RETROSPECTIVE REVIEW, 2000-2011

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**Purpose:** Previous retrospective studies showed that dose escalation of post-mastectomy radiation therapy (PMRT) improved loco-regional control for IBC patients. However, modern multi-modality therapy for IBC has broadly improved outcomes, and most previous retrospective studies included patients not treated with anthracycline/taxane based chemotherapy. The purpose

of this study was to determine loco-regional recurrence rates following modern multi-modality treatment including PMRT for non-metastatic IBC. Secondary objectives were to identify predictors of loco-regional relapse which could be used to identify candidates for dose-escalated radiotherapy, and to assess the impact of hypofractionation.

**Materials and Methods:** All patients diagnosed with non-metastatic IBC (T4d, M0 at diagnosis) at four institutions in Alberta between 2000 and 2011 were identified from the Alberta Cancer Registry. Patients treated with triple modality therapy (chemotherapy, surgery, and PMRT) were included in the analysis. Actuarial five-year outcomes were calculated, and survival distributions were compared with the log-rank test.  $\hat{I} \pm = 0.05$ .

**Results:** One hundred and sixty-eight patients met eligibility criteria, all of whom received anthracycline and/or taxane based chemotherapy. Median follow-up was 58 months. At five years, overall survival was 55%, loco-regional control was 70%, and distant metastasis free survival was 49%. Eighty patients received hypofractionated RT (HypoF; 40-45 Gy in 16-25 fractions, 61 patients received conventionally fractionated RT (CF, 50 Gy in 25 fractions), and 27 patients received other regimens. Outcomes were not statistically different between HypoF and CF regimens, including five-year overall survival (51% versus 60%,  $p = 0.896$ ), five-year loco-regional control (74% versus 67%,  $p = 0.108$ ), and five-year distant-metastasis free survival (48% versus 52%,  $p = 0.649$ ) for HypoF versus CF, respectively.

Among the 81 patients who recurred, first sites of failure were loco-regional (47%) or distant (46%), with 7% being simultaneous. Patients with triple-negative (TN) disease more frequently first failed loco-regionally (77% versus 43% in all other patients,  $p = 0.016$ ), and five-year loco-regional control was significantly inferior for TN patients (53% versus 73% in others,  $p = 0.015$ ). In contrast, patients with hormone receptor (HR)-positive, HER2-negative disease were less likely to first fail loco-regionally (35% versus 58% in other patients,  $p = 0.067$ ).

**Conclusions:** Patients with IBC who completed triple-modality therapy in the past decade still had poor local control and frequently first failed loco-regionally, but outcomes were independent of fractionation among the regimens used. Escalation of PMRT dose may still be of benefit in this high-risk population in the era of modern chemotherapy, especially for HR negative patients.

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### HIGH DOSE STEREOTACTIC ABLATIVE RADIOTHERAPY (HD-SABR) FOR RADIORESISTANT LUNG METASTASIS: ASSESSING THE ACCURACY OF COMMERCIAL DOSE ALGORITHMS FOR A FUTURE CLINICAL TRIAL

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**Purpose:** The application of SABR for early stage lung cancer has resulted in local control rates (LCR) competitive with surgery (87.2% at three years). However, for radioresistant metastatic lung cancer LCRs are lower (72% at two years for metastasis from colorectal cancer), and dose escalation may improve local control. Previously we developed high dose SABR (HD-SABR), which exploits lateral electron disequilibrium (LED) to enhance steep dose gradients at the tumour/lung interface, and increase tumour dose relative to normal lung. Dose calculations for HD-SABR require accurate modelling of electron transport in regions of low density. Here, we compare the dosimetric accuracy of commercially-available algorithms versus the Vancouver Island Monte Carlo Arc (VIMC-Arc) system (as the gold standard).

**Materials and Methods:** Ten early stage lung cancer patients were retrospectively selected at random. 4D-CT image sets were acquired with a Philips 16-slice Helical CT scanner. For each patient, an internal target volume (ITV) was created to account for tumour motion due to breathing. The planning target volume (PTV) was generated by expanding the ITV by 5mm. HD-SABR plans were created using VMAT within the Pinnacle3 TPS (with a small average open field area of 2.4 cm<sup>2</sup>). Dose was initially calculated and optimized using the collapsed cone convolution (CCC) algorithm such that 95% of the PTV received at least the prescription dose (e.g. D95 = 54 Gy or 60 Gy). Each plan was then transferred to the Eclipse TPS and VIMC-

Arc system for recalculation of the dose distribution using the analytical anisotropic algorithm (AAA), Acuros XB (AXB), or MC algorithms.

**Results:** The average percent changes for PTV Dmean, Dmax, Dmin, and D95 were calculated relative to VIMC-Arc results for all ten patients  $[(X-VIMC)/VIMC \times 100\%]$ . The change in these PTV parameters were the smallest for AXB: 1.2+/-2.0%, -0.5+/-7.0%, 5.0+/-2.7%, and 3.4+/-2.4%; mid-range for CCC: 4.0+/-2.6%, 2.4+/-6.4%, 7.9+/-4.0%, and 6.5+/-2.7%; and largest for AAA: 8.7+/-7.0%, 0.3+/-6.4%, 8.7+/-7.2%, and 10.1+/-7.6%. Similar dosimetric trends were observed for doses in the ITV.

**Conclusions:** HD-SABR relies on very small field sizes to create severe LED and establish steep dose gradients necessary for dose escalation of the tumour. These dose effects are challenging to model even with modern day TPS algorithms. Results from this study suggest AAA and CCC algorithms are prone to significant dose errors, while AXB offers accurate dose calculations comparable to Monte Carlo results. This study will guide the selection of an appropriate dose calculation algorithm for HD-SABR of early stage lung cancer in a future clinical trial.

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### HIGH DOSE STEREOTACTIC ABLATIVE RADIOTHERAPY (HD-SABR) FOR DOSE ESCALATION OF RADIORESISTANT LUNG METASTASIS

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**Purpose:** SABR for early stage lung cancer has resulted in local control (LC) competitive with surgery (87.2% at three years). However, SABR of radioresistant pulmonary metastatic lesions including melanoma, renal cell carcinoma, or colorectal carcinomas, LC is significantly lower (72% at two years for colorectal cancer). Dose escalation has the potential to improve LC of SABR for these tumours. Previously, we introduced the technique of high dose SABR (HD-SABR), which exploits lateral electron disequilibrium (LED) to enhance steep dose gradients at the tumour/lung interface, and increase tumour dose relative to normal lung. This work aims to characterize HD-SABR for implementation in a potential clinical trial.

**Materials and Methods:** 3D-CT images of a CIRS thorax phantom were acquired using a Philips CT scanner. Spherical gross tumour volumes (GTVs) of different size were simulated within the Eclipse TPS. A planning target volume (PTV) was generated for each GTV using an expansion of 5 mm. HD-SABR plans were created using 10 MV arcs with asymmetric jaws corresponding to equivalent square field sizes (EQFS) ranging from 0.9 cm up to 4 cm. Dose was calculated using the Acuros XB algorithm such that 95% of the PTV received at least the prescription dose (D95 = 54Gy). For the patient study, ten early stage lung cancer patients were retrospectively selected at random. 4D-CT image sets were acquired for each patient, and an internal target volume (ITV) was created to account for tumour motion. The PTV was generated by expanding the ITV by 5 mm. The Pinnacle3 TPS was used to create two plans for comparison: 1) a standard 6 MV VMAT plan (control), and 2) a 10 MV HD-SABR plan (EQFS  $\approx$  2.4 cm). Dose was calculated and optimized such that 95% of the PTV received at least the prescription dose (e.g. D95 = 54 Gy or 60 Gy).

**Results:** PTV dose escalation can be controlled by manipulating the extent of LED, which is enhanced for the smallest EQFS. For example, in the phantom study, decreasing the EQFS from 2.0 cm, to 1.5 cm, down to 0.9 cm, increased the PTV Dmax/Dmean from 80.5Gy/62.3 Gy, to 119.2Gy/74.2Gy, and up to 204.9Gy/85.9Gy. In the patient study, the average percent change  $[(HDSABR-VMAT)/VMAT \times 100\%]$  for PTV Dmax and Dmean was 81.7+/-21.1% and 30.5+/-5.4%, while lung Dmean changed minimally by -1.9+/-5.5%. Importantly, the ratio of PTV Dmean to lung Dmean increased from 19.4+/-3.0 using VMAT to 25.9+/-4.3 for HD-SABR, implying HD-SABR more effectively increased PTV dose relative to normal lung compared to VMAT. **Conclusions:** Step-wise dose escalation of the PTV, as is commonly done in clinical trials, is possible using HD-SABR with incrementally smaller EQFSs (<3x3 cm<sup>2</sup>). This technique will require IGRT, tumour tracking/gating, and accurate dose calculation algorithms. HD-SABR will be tested in a planned Phase I study in the near future.

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### CHARACTERIZATION OF INTRA-FRACTION PATIENT MOTION FOR HYPO-FRACTIONATED TREATMENTS OF THE CENTRAL NERVOUS SYSTEM AND THE PROSTATE

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**Purpose:** Patient intra-fraction motion can be caused by pain, patient relaxation, bladder/rectal filling, and reaction to a rotated treatment couch if rotational set-up corrections are used, which is typical for hypo-fractionated treatments. The purpose of this study is to characterize patient intra-fraction motion during a time interval representative of the duration of a linac-based hypo-fractionated treatment, and to correlate the magnitude of this motion with rotational set-up corrections.

**Materials and Methods:** Data from the Cyberknife radiosurgery system were extracted to take advantage of the frequent imaging (every 20 – 60 seconds) that allows for characterizing patient motion during treatment. Patients with disease sites suitable for linac-based stereotactic treatments were included: glioblastoma (54 patients, 281 fractions), spine metastases (71 patients, 186 fractions), and prostate (53 patients, 266 fractions). The Cyberknife log files for those patients were analyzed to identify the first ten-minutes of uninterrupted treatment for each patient. The couch rotational angles during the ten-minutes, as well as the patient position at the start and end of this period were extracted. The intra-fraction displacement and the change in rotational orientation were calculated as the difference between the initial and final corrections. The accuracy of the image-based skull tracking and spine tracking was characterized over a realistic range of translational and rotational corrections using fiducial tracking as ground truth in an anthropomorphic phantom.

**Results:** The phantom study showed that the corrections determined using skull and spine tracking agree on average with those from fiducial tracking at the  $0.2 \pm 0.2$  mm/ $^{\circ}$  level. The 5th to 95th percentile of intra-fraction displacements fall within:  $\pm 1.0$  mm and  $\pm 1.0^{\circ}$  for glioblastoma treatments;  $\pm 1.0$  mm (A/P and S/I),  $\pm 2.0$  mm (L/R) and  $\pm 1.0^{\circ}$  for spine treatments;  $\pm 1.0$  mm (L/R),  $\pm 3.0$  mm (A/P and S/I); and  $\pm 3.0^{\circ}$  (pitch) and  $\pm 1.5^{\circ}$  (roll and yaw) for prostate treatments. The number of patients exhibiting displacements > 3 mm in at least one direction for at least one fraction were 0/54, 4/71 and 19/53 for glioblastoma, spine and prostate treatments, respectively. Clinically inconsequential correlations (e.g.  $R2 < 0.2$ , slopes and intercepts within  $\pm 0.3$  mm/ $^{\circ}$  and  $\pm 0.8$  mm) were found between the intra-fraction displacements and couch rotation angles for all sites.

**Conclusions:** Appreciable intra-fraction motion was observed, which was compensated for in Cyberknife treatments through frequent imaging. However, this motion is comparable to the margins used for hypo-fractionated treatments on conventional linacs, suggesting that more informed image guidance, patient immobilization, and motion management strategies are required to deliver these treatments safely.

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### NEUROLOGICAL DEATH IS COMMON IN PATIENTS WITH EGFR MUTANT NON-SMALL CELL LUNG CANCER

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**Purpose:** Patients with EGFR mutant non-small cell lung cancer (EGFRmNSCLC) have a high incidence of brain metastases (BM). We sought to determine the rate of neurologic death in EGFRmNSCLC patients diagnosed with brain metastases.

**Materials and Methods:** A single-institution prospectively managed database identified 204 patients with EGFRmNSCLC treated for brain metastases between 2000 and 2016. We estimated actuarial survival rates using the Kaplan-Meier method. The incidence of neurologic death (ND) was determined using a competing risks analysis. ND was correlated to clinical and treatment variables using Fisher's exact test. Survival was calculated from the date of BM diagnosis. We defined neurologic death as death due to brain metastases or leptomeningeal disease.

**Results:** Fifty-six percent of patients had BM at the time of initial diagnosis.

The initial BM treatment was up front stereotactic radiosurgery (SRS), whole brain radiation therapy (WBRT), or tyrosine-kinase inhibitor (TKI) alone in 22, 60, and 18 percent of patients, respectively. Two-year rates of OS in these subgroups were 64%, 38%, and 50%, respectively ( $p = 0.016$ ). The five-year rate of neurologic death was 38%. Thirty-four percent died of non-neurologic causes, 8% died of unknown causes, and the remaining patients were alive at last follow-up. Median survival (MS) was 19 months; MS in patients who died of non-neurologic causes and neurologic causes was 23, and 15 months, respectively. Of age, staging, BM at diagnosis, history of TKI therapy, initial treatment of BM, staging at diagnosis, and leptomeningeal disease at diagnosis (LMD), only LMD was significantly associated with ND ( $p = 0.047$ ).

**Conclusions:** Neurologic death due to EGFRmNSCLC BM was more common in our cohort than has been previously reported, highlighting the need for dedicated studies focused on the best management of BM in this population.

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#### COMMISSIONING AND CLINICAL IMPLEMENTATION OF AN ENDOBRONCHIALY IMPLANTED TRANSPONDER (CALYPSO) SYSTEM FOR LUNG STEREOTACTIC BODY RADIATION THERAPY

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**Purpose:** Stereotactic lung treatments require accurate target localization and treatment delivery due to uncertainties associated with respiratory motion. Though traditional CBCT-based IGRT is useful for patient set-up, real time tumour motion data is not available. Endobronchially implanted beacon transponders implanted near the tumour provide real-time positional information during irradiation. In this work we describe our commissioning experience with the Calypso system implemented on a Varian EDGE Linac. **Materials and Methods:** The commissioning work was divided into two phases: 1) basic and 2) lung-specific testing. Basic commissioning included: Calypso localization and tracking accuracy, adaptive couch repositioning, array attenuation and spatial accuracy measurements. A daily Calypso QA phantom was used for stability and positional accuracy checks. Translational and angular motions were introduced to determine the localization and tracking accuracies of the system. For lung specific commissioning, 4D-CT images of CIRS thorax phantom were acquired using a Philips CT scanner. The phantom holds a removable lung rod that contains a 1 cm tumour and Calypso beacons. The rod also accommodates either film or an ion chamber for dosimetry. A programmable actuator was used to drive the lung rod with 2 cm of sup-inf motion to simulate patient breathing. For planning purposes, an internal target volume (ITV) was generated from target contours in exhale phases of the 4D-CT (e.g. 40-70%). A planning target volume (PTV) was created from the ITV using an expansion of 3 mm. Eclipse TPS was used to create 10 MV (FFF) RapidArc plans for treatment delivery. The Calypso system was used in EDGE Linac to deliver gated treatment in exhale phases of the breathing cycle. Gating accuracy, localization comparison with CBCT and Calypso completed the other checks. First lung SBRT patient with implanted anchored transponders was treated to 54 Gy in 3 fractions. The tracking data was collected during imaging and treatment for all 3 fractions and analyzed.

**Results:** The maximum localization offsets in lateral, longitudinal and vertical directions for static positional increments from 0.5 mm to 50 mm were 0 mm, 0.5 mm and 0.5 mm, respectively. The maximum translational and rotational offset in the presence of motion in any direction was 0.5 mm and 1° deg. The array transmission factor for 5x5 cm<sup>2</sup> field size was 0.982. 2D gamma analysis of the film revealed that 98.5% of all points passed a criterion of 3%/3mm. For an absolute point dose comparison, the percent difference between the measured and calculated dose was 1.7%. Calypso data during treatment showed a mean inter-transponder variation of 1.9 mm.

**Conclusions:** We have clinically implemented the Calypso system for lung SBRT that provides real-time information of the tumour location. This is expected to improved treatment accuracy and reduce PTV margins.

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#### INCIDENCE OF RADIONECROSIS IN SINGLE VERSUS HYPOFRACTIONATED STEREOTACTIC RADIOSURGERY TREATMENT FOR BRAIN METASTASIS

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**Purpose:** Radiation-induced brain necrosis, or 'radionecrosis' (RN) is a relatively uncommon (5-20%) but potentially severe adverse effect of stereotactic radiosurgery (SRS) for brain metastasis. RN may be an incidental radiographic finding, however in some cases symptoms may be severe and mimic tumour recurrence requiring steroids and potential surgery. While dose, volume and other factors have been suggested to affect RN rates, it is difficult to clearly delineate this risk given the patient and treatment variability in this population. Hypofractionation of SRS treatment, particularly to larger lesions, has been used in attempt to minimize RN risk at our centre. We attempted to establish the effect of hypofractionation on RN rates by reviewing patients having simultaneous multi-fraction and single fraction treatment at our centre.

**Materials and Methods:** Patients receiving simultaneous (within one month) 1 or 3 fraction SRS treatments to from 2012 to 2015 were identified in our institution's Cyberknife database. Serial post-SRS MRIs were reviewed to determine the lesion quotient (LQ), or maximum cross sectional area on T1 plus gadolinium divided by T2 FLAIR sequences. LQ less than 0.3 was considered RN, and LQ greater than 0.6 with corresponding T1 cross sectional growth was considered recurrence. Treatment and clinical data were also collected.

**Results:** Of 90 patients identified, twenty-two patients had at least six month MRI follow up. Median follow up was 320 days, and all patients died during this time. The most common tumour type was non-small cell lung cancer, followed by breast and rectal cancer. For the three fraction and single fraction groups, the median lesion volume was 6585cc and 98cc, isodose line was 74% (range 67-87) and 72.9% (range 65-86), and maximum dose was 3020 cGy (range 2325-3802) and 2868 (2350-3750)cGy respectively. Sixteen patients developed radionecrosis in 21 of 62 lesions (33%), four of which were symptomatic (20%). Eleven of these lesions received 3 fractions and ten received one fraction, and fourteen were frontal lobe lesions, five were occipital lesions and one was cerebellar. All patients with symptomatic RN were treated with dexamethasone, and symptoms resolved in two of the four patients. Radiographic RN, however, did not clear in any patients who developed it. Eight patients developed a local recurrence (12%), six of which occurred in the single fraction group.

Radionecrosis is a serious adverse event which may result in significant clinical symptoms following SRS for brain metastasis. Surprisingly, in our cohort those patients receiving hypofractionated treatment were at higher risk for RN, while those receiving a single fraction developed more local recurrences. One must also consider that this may be confounded by volume effect.

**Conclusions:** Overall, our results indicate patients receiving SRS for multiple brain metastasis have a higher rate of radionecrosis than the literature and poorer survival despite having equivalent local control. Further investigation will help delineate the optimal dose and fractionation to minimize RN and optimize local control in this patient group

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#### ATTITUDE AND BELIEFS TOWARDS STEREOTACTIC BODY RADIOTHERAPY FOR OLIGOMETASTATIC BREAST CANCER- A SURVEY OF CANADIAN MEDICAL ONCOLOGISTS

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**Purpose:** While patients with metastatic breast cancer are typically considered incurable, those who present with limited, or oligometastatic (OM) disease may have an improved prognosis. While systemic therapy remains the standard of care in this setting, local therapy such as stereotactic body radiotherapy (SBRT) may also have a role in improving progression-free and overall survival. Currently, the role of upfront SBRT in newly diagnosed OM breast cancer in addition to systemic therapy is not clear, yet it is being increasingly utilized within the radiation oncology community, and

therefore prospective investigation is critical. The key stakeholders to drive increased SBRT utilization in this setting have been shown to be the referring medical oncologists (MO), and so a better understanding of their perceptions regarding SBRT will help delineate the appropriate context for SBRT use in a clinical trial.

**Materials and Methods:** A 31-item questionnaire was distributed by e-mail to MOs in Canada registered with the Canadian Association of Medical Oncologists (CAMO), regarding beliefs, opinions, and referral practices as it pertains to SBRT for OM breast cancer.

**Results:** Thirty MOs participated, the majority of whom were based at academic institutions (76.7%), and reported seeing up to eight OM breast cancer cases per year (60%), yet most referred 0-1 of these patients for consideration of SBRT. A majority of MOs reported a lack of comfort with the literature (63.3%), uncertainty on patient eligibility of SBRT treatment of OM (56.7%), concern for delaying systemic treatment (53.3%) and preference of initiating hormonal therapy prior to SBRT (63.4%) as possible reasons affecting SBRT referral. Most MOs, however, preferred SBRT to surgery as local therapy (60-86%), felt patients would be interested in SBRT referral (80%), believed their center had adequate resources for multi-site SBRT (80%), and felt SBRT could help prevent tumour growth and delay future symptoms in OM breast cancer (79.3%). Generally MOs felt that all subtypes of breast cancer should be considered, that patients should have a disease-free interval of at least six to 12 months from primary treatment (58.6%), yet most felt comfortable with SBRT upfront at the time of OM diagnosis (65%).

**Conclusions:** In general, there appears to be interest and feasibility from MOs to refer patients for SBRT in the setting of OM breast cancer. This interest is likely to be strengthened within the context of a clinical trial that is designed with appropriate eligibility and guidance regarding use of systemic therapy. MOs are important stakeholders that should be involved when designing trials evaluating optimal local therapy for patients with OM disease.

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#### DOES MODERN MEDIASTINAL IRRADIATION CAUSE ACUTE SUBCLINICAL CARDIAC DAMAGE? THE RESULTS OF THE MEDICATE STUDY (MEDIASTINAL IRRADIATION AND CARDIO-TOXIC EVENTS)

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**Purpose:** Radiation-induced heart disease (RIHD) is a late effect of cardiac irradiation (RT), and has been demonstrated in Hodgkin and non-Hodgkin lymphoma (HL and NHL), as well as in other thoracic cancers. There is no established measurement tool to detect acute cardiac damage, however high sensitivity troponin I and T (HsTnI and HsTnT) and imaging modalities such as echocardiograms have shown promise in some studies. We conducted a prospective trial to characterize acute and subacute cardiac damage in patients with thoracic cancers receiving at least 30 Gy to 5% of cardiac volume or a mean dose of 4 Gy.

**Materials and Methods:** Patients were recruited from Hematology and Lung clinics at the Juravinski Cancer Center. Following consent and CT simulation, conformal (3D) and intensity modulated radiotherapy (IMRT) plans were created and cardiac structures were contoured. Patients had blood drawn for C-reactive protein (systemic inflammatory marker), HsTnI, HsTnT prior to RT and at two and four weeks into radiotherapy and completed 3D echocardiograms (3D) prior to RT and one year post-RT. Serum markers levels, imaging results and cardiac RT dose-volume data were analyzed for association.

Twenty patients were recruited (including one who withdrew consent). The median value for "mean LV dose" was 3.1 Gy, and the median value for "mean total cardiac dose" was 8.6 Gy. Statistically significant positive associations between HsTnI and HsTnT at all time points, with an apparent decrease in mean value over time, and there was a positive association between HsTnI increase between week 2 to 4 and maximum cardiac LV dose ( $\rho = 0.66$ ,  $p = 0.027$ ). Although overall the mean change in LVEF for the whole cohort was non-significant (57.57 pre-RT and 56.4 post-RT), the mean dose to the left ventricle was associated with decrease in ejection fraction from

pre-RT to one year echocardiograms ( $\rho = -0.46$ ,  $p = 0.054$ ). An association was also seen between increase in left ventricular strain (LVS) and cardiac mean dose ( $\rho = 0.46$ ,  $p = 0.058$ ), and cardiac dose to maximum 5% volume ( $\rho = 0.48$ ,  $p = 0.043$ ).

**Results and Conclusions:** Our study suggests that HsTnI and HsTnT are intimately related, but detection of acute cardiac damage was not demonstrated potentially due to limitations of these markers, or low radiotherapy doses using modern techniques. Our results also suggest 3D echocardiogram findings may detect subacute damage at one year depending on dose to cardiac volumes. Given limitations of our study, we suggest that techniques to measure subacute cardiac damage including serum biomarkers and imaging modalities require further characterization to optimize their use. Identification early damage could facilitate the ability to closely monitor and intervene in patients at risk for RIHD. The current study is reassuring that modern quality-assured radiation techniques can prevent acute cardiac damage, even after anthracycline chemotherapy.

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#### CONSENSUS GUIDELINES FOR TARGET VOLUME DEFINITION OF THE SACRUM IN SPINAL STEREOTACTIC BODY RADIATION THERAPY (SBRT)

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**Purpose:** To develop consensus contouring guidelines for spinal stereotactic body radiation therapy (SBRT) for metastatic disease to the sacrum to improve uniformity in clinical target volume (CTV) delineation.

**Materials and Methods:** Nine radiation oncologists with spinal stereotactic radiotherapy expertise representing nine international centres in three countries independently contoured gross tumour volume (GTV), CTV and neural elements (cauda equina, thecal sac or sacral canal) for 10 representative clinical scenarios in metastatic disease to the sacrum. Contours were imported into in-house software developed in MATLAB, version 8.1.0.604 (The MathWorks, Inc., Natick, MA), and agreement between physicians calculated with an expectation minimization algorithm using simultaneous truth and performance level estimation (STAPLE) and with kappa statistics (<0, poor agreement; 0.01-0.20, slight agreement; 0.21-0.40, fair agreement; 0.41-0.60, moderate agreement; 0.61-0.80, substantial agreement; 0.81-1.00, almost perfect agreement). Optimized confidence level consensus contours were obtained using a voxel-wise maximum likelihood approach. Clinicians completed an 18-question survey about sacral metastatic disease SBRT practice including dose/fractionation schedule, margin expansion for GTV to CTV and CTV to planning target volume (PTV), the practice of contouring the sacral plexus/peripheral nerve roots and acceptable dose constraints for neural elements and small/large bowel.

**Results:** Mean STAPLE agreement sensitivity and specificity was 0.73 (range, 0.59-0.86) and 1.00 respectively for GTV and 0.59 (range, 0.47-0.69) and 1.00, respectively for CTV. Mean kappa agreement was 0.76 (range, 0.60-0.89) for GTV and 0.60 (range, 0.45-0.72) for CTV ( $P < .001$  for GTV and CTV in all cases). Different dose/fractionation schedules included 16-24 Gy/1 fraction, 24 Gy/2 fractions, 24-27 Gy/3 fractions, 30-36 Gy/4 fractions and 35 Gy/5 fractions, primary histology of the tumour was a factor in certain cases when choosing a schedule. Six experts applied an anatomic approach to the CTV, in some cases adding an extra margin for soft tissue extension/extra-osseous disease. Median PTV expansion was 1 mm (range, 0 - 3 mm). Six experts contoured the thecal sac as a surrogate for the cauda equina. In the majority of cases the sacral plexus and peripheral nerves were contoured however the lack of consensus contouring guidelines and low rates of clinical plexopathy observed in practice were reasons why contouring these critical

normal structures wasn't universal practice.

**Conclusions:** There was substantial agreement for GTV and moderate agreement for CTV contours with the majority of international experts applying an anatomic approach when contouring the CTV. Final consensus guidelines will be demonstrated in illustrations at the meeting.

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#### STEREOTACTIC BODY RADIATION THERAPY (SBRT) FOR THE TREATMENT OF LIVER METASTASES: A SINGLE INSTITUTION EXPERIENCE

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**Purpose:** To report on the outcomes of stereotactic body radiation therapy (SBRT) for liver metastases in a single institution.

**Materials and Methods:** All patients with liver metastases treated with stereotactic body radiotherapy (SBRT) between June 2010 and July 2017 were retrospectively reviewed. Prescribed doses were 35 Gy to 54 Gy/3 – 5 fractions, according to the tolerance of adjacent normal tissues.

**Results:** Forty-five patients with liver metastases, 26 women (58 %) and 19 men (42 %), were included in the analysis. Median age at diagnosis was 64 years (range, 33 - 86) and the median age at SBRT treatment was 68 years (range, 37-89). In 34 cases (75.5 %) the primary histology was colorectal cancer, four (9 %) breast, two (4.5 %) sarcoma and one case each for oesophageal, lung, renal cell cancer, pancreatic neuroendocrine tumour (pNET) and oropharyngeal cancer. In 23 cases (51%) there was metastatic disease at the time of diagnosis and in 13 cases (29 %) there was disease outside of the liver at the time of SBRT treatment. Twenty-five patients (56%) had prior liver directed therapy (LDT); 21/25 (84%) had a previous surgical resection and 14/25 (56%) had ablative therapy (radiofrequency/microwave ablation). The median number of LDT prior to SBRT was 2, (range, 1 – 4). The median number of lines of systemic treatment prior to SBRT was 1, (range, 0 - 7).

The median volume of the PTV was 132.85 cm<sup>3</sup> (range 29.8 – 639.5 cm<sup>3</sup>). In 64 %, the prescribed biologically equivalent dose (BED10) was < 100 Gy. With a median follow-up period of 59 months (range, 17-176 months), the two-year overall survival (OS) from SBRT treatment was 53% with median OS of 27 months. The two-year progression-free survival (PFS) from SBRT to progression in field was 39% with a median PFS of 17 months.

**Conclusions:** SBRT for liver metastases is a locally effective treatment. Further analysis is needed to determine if local control is significantly associated with higher delivered dose.

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#### OVERLAP BETWEEN TUMOURS AND ABLATION ZONES AFTER MR-GUIDED PROSTATE FOCAL LASER ABLATION THERAPY

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**Purpose:** Prostate cancer is the most common non-cutaneous cancer among men in the USA1. MRI-guided focal laser thermal ablation (FLA) therapy is an alternative to whole gland treatments which aims to eliminate small, low-risk lesions while preserving healthy tissue. This minimally invasive procedure has potential to reduce patient morbidity and maintain urinary and erectile function by leaving the neurovascular bundles and urethral sphincters intact. During FLA therapy, needles with an optical fiber are inserted by the physician to identified targets in the prostate. It is important that needles are guided accurately to ensure complete ablation of the lesion while avoiding critical structures. Multi-parametric magnetic resonance images (mpMRI) are acquired before, during, and following procedures to assist in identifying targets, guiding needles, and assessing treatment outcome. In this study, we evaluated the location of ablation zones relative to targeted lesions in 23 patients who underwent FLA therapy.

**Materials and Methods:** Pre-operative mpMRI were acquired for each patient

two to three months before the procedure and the prostate and lesion(s) were manually contoured on 3T T2-weighted axial images. The prostate and ablation zone(s) were also manually contoured on post-ablation 1.5T T1-weighted contrast-enhanced axial images acquired intra-operatively. The lesion surface was registered to the post-ablation image using an initial affine registration followed by non-rigid thin-plate spline registration of the prostate surfaces. The margins between the registered lesion and ablation zone were calculated using a uniform spherical distribution of rays in 2,048 directions, and the volume of intersection was also calculated. Each prostate was contoured five times on both images to determine the segmentation variability and its effect on the margins and intersection volume between the lesion and ablation zone.

**Results:** Our study showed that the boundaries of the segmented lesion and ablation zone were close. Of the 23 lesions that were analyzed, eleven had 100% overlap with the corresponding ablation zone and the rest were partially overlapping. A shift of 1.0, 2.0, and 2.6 mm would result in 19, 21, and all lesions within the ablation zone, respectively. The median unablated lesion volume across all lesions was 0.1 mm<sup>3</sup> with an IQR of 3.7 mm<sup>3</sup>, which was 0.2% of the median lesion volume (46.5 mm<sup>3</sup> with an IQR of 46.3 mm<sup>3</sup>). The median extension of the lesions beyond the ablation zone, in cases which were partially ablated, was 0.9 mm (IQR of 1.3 mm), with the furthest lesion extending 2.6 mm.

**Conclusions:** In many cases, the ablation zone did not completely cover the lesion it was intended to destroy. This suggests that more accurate imaging and needle guidance methods are required to deliver focal therapy to cancer. References

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#### ASSESSING COMBINED ERRORS IN IMAGE REGISTRATION AND GEOMETRIC ACCURACY FOR CT, MRI AND 3D ANGIOGRAPHY IMAGES FOR RADIOSURGERY PLANNING WITH THE CYBERKNIFE SOFTWARE

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**Purpose:** In addition to the primary treatment planning CT (TPCT) image, images from multi-modalities are utilized to aid in contouring and planning in stereotactic radiosurgery (SRS). For accurate combination of anatomical information from multiple imaging modalities, carefully executed image registration is essential—a task that has become heavily automated. We investigate the magnitude of image registration and geometric accuracy errors introduced by CyberKnife's (CK) MultiPlan Software's image registration tool using CT, MRI and 3D angiography images.

**Materials and Methods:** Two phantoms were used: for all CTs; CK's E2E Skull Phantom (containing 6 gold fiducials), for MRIs; an in-house built cubic (6.3 cm to a side) phantom with 30 parallel air-filled rods embedded in an H<sub>2</sub>O NiSO<sub>4</sub> solution. TPCT and 3T fast-SPGR MRIs (both with 1 mm slice spacing), as well as 3D helical and CBCT angiography scans were acquired using our CK brain SRS imaging protocols. For each phantom, images were registered to a reference TPCT. Automated determination of 3D fiducial positions (min. of 3 measurements/ scan) on coregistered and resampled image sets were performed using tools available in MultiPlan. The 2D centre-of-rod positions were assessed using an in-house written MatLab script. For external validation, 3D fiducial locations for CT images were analyzed with an intensity based thresholding algorithm implemented in MatLab. To isolate image registration and geometric accuracy errors, variations in imaging protocols, scan set-ups and time of scan were studied on additional CTs. Positions of fiducials/ rods along all imaging axes were found, with the TPCT's positions taken as reference. For a total of 24 scans, we report the largest mean difference in position ± standard deviation across all fiducials/ rods and the imaging axis (right-left (RL), antero-posterior (AP), superior-inferior (SI)) where the largest mean difference was observed. **Results:** CK's image registration tool showed CT fiducial position differences

as follows: intra- modality & observer repeatability tests:  $-0.2 \pm 0.3$  mm (RL); historical TPCs between 2012-2017:  $-0.3 \pm 0.9$  mm (RL); Varying mAs (100) and kVp (90):  $-0.5 \pm 0.3$  mm (RL and AP); transverse/ axial resolution changes and intentionally skewed set-up:  $-0.2 \pm 1.0$  mm (RL); post-processing (smoothing filter and reconstruction volume):  $-0.4 \pm 0.3$  mm (RL and AP); helical CT angio:  $-0.5 \pm 0.1$  mm (RL), and CBCT angio:  $-0.9 \pm 0.2$  mm (RL). External validation showed differences in fiducial/ centre-of-rod positions in all directions were  $-0.2 \pm 0.3$  mm for all CT and MRI scans, with the exception of CBCT angio (1.0 mm).

**Conclusions:** The largest fiducial position differences were observed RL with respect to the CT scan, followed by AP. The registration software performed consistently in the slice direction. Compared to MatLab, CK's clinical software showed greater discrepancy in fiducial positions post-registration for all modalities. Since this tool is routinely for quality assurance and motion management tracking, the impact of this discrepancy should be further investigated.

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### SYSTEMATIC REVIEW OF THE INCIDENCE OF CHEST WALL TOXICITY FOLLOWING STEREOTACTIC BODY RADIATION THERAPY FOR EARLY STAGE NON-SMALL CELL LUNG CANCER

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**Purpose:** Stereotactic body radiation therapy (SBRT) is well tolerated with high local control rates in patients with Stage I and Stage II medically inoperable non-small cell lung cancer (NSCLC). Radiation-induced chest wall pain (CWP) and rib fracture (RF) are unique late adverse effects after hypo-fractionated SBRT, however there is variability in the literature on the true incidence and risk factors for CWP and RF in patients with long-term follow-up. We performed a systematic review to determine the pooled incidence of CWP and RF in patients with early stage NSCLC treated with SBRT.

**Materials and Methods:** A comprehensive literature search following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines of English-language published records from 2001-2017 was undertaken using MEDLINE and EMBASE. Titles and abstracts were screened independently by a primary and secondary reviewer. A third reviewer resolved discrepancies. Full-text publication review and data extraction were performed by the primary reviewer. Observational studies and randomized controlled trials were included, while case reports, case series of <20 patients, letters and commentaries were excluded.

**Results:** A total of 548 records were identified through database search. Following abstract exclusion, 73 full-text articles were assessed for eligibility. Of these, 24 were excluded as they did not meet inclusion criteria. Forty-nine full text publications comprising 5919 patients met the inclusion criteria. The median patient age was 67-81 years and median follow-up varied from 12-84 months. The majority of the studies were retrospective in nature. The number of patients evaluated in these studies varied from 22-772. Radiation doses ranged from 16-70 Gy in 1-10 fractions. Results across studies were heterogeneous due to differences in grading, tumour location and the observational nature of the studies. Nonetheless, the pooled incidence of reported CWP was estimated to be 6.8%, and the estimated pooled incidence of reported RF was 4.5%. A total of 24 studies reported grade of CWP toxicity; of these, 57 of 313 patients with CWP (18.2%) reported Grade 3 and 4 pain (no Grade 5 reported). A total of 18 studies reported RF toxicity grading; of these, Grade 3 and 4 toxicity was observed in 13 of 114 patients (11%) who had RF. In the studies that reported SBRT dosimetry, a high chest wall V30 was an important common predictor of CWP and RF.

**Conclusions:** Results from this review demonstrate low rates of CWP and RF following SBRT across a broad spectrum of Stage I and II NSCLC patients. However, tumour location, accurate reporting of toxicity and dose-fractionation schemes may relatively increase or decrease these rates. Prospective correlation with dose/volume metrics and assessment of quality of life will further improve the understanding of the effects of CWP and RF following SBRT.

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### CORRELATING EARLY CHANGES IN MAGNETIC RESONANCE BIOMARKERS WITH DOSE FOLLOWING SRS OF BRAIN METASTASES WITH AND WITHOUT EVIDENCE OF RADIONECROSIS

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**Purpose:** To investigate potential correlations between magnetic resonance (MR) biomarker changes and dose on a direct voxel-wise basis for brain metastases both within the GTV and in the surrounding high dose regions > 12 Gy following SRS. Specifically, we quantified changes in apparent diffusion coefficient (ADC) computed from diffusion-weighted imaging (DWI), and contrast transfer coefficient (Ktrans) and volume of extracellular extravascular space (ve) extracted from dynamic contrast-enhanced (DCE) MRI to help provide insight into early physiological responses to SRS.

**Materials and Methods:** We examined 18 patients (29 brain metastases, five with evidence of radionecrosis) imaged on a 3T MRI at day 0, 3 and 20 following single fraction 15 – 21 Gy SRS as part of prospective clinical trials. Primary sites included: two renal, seven lung, two head and neck, one cervix, four breast and two melanoma. The ADC maps were generated by the scanner from DWI. We used the modified Tofts model with an in-house-developed robust 4-D temporal dynamic analysis to extract Ktrans and ve values from DCE-MRI data. To enable voxel-wise analyses, we developed an image registration pipeline using the Python interactor in 3D Slicer. We used the pipeline to register MR biomarker volumes to the planning MRI volume, thus putting the biomarker data in the same coordinate system as the dose and contours. For each voxel, we computed  $\Delta$ ADC,  $\Delta$ Ktrans and  $\Delta$ ve for day 3 and 20 post-SRS relative to day 0, allowing us to perform voxel-wise analyses. First, we interrogated biomarker differences between days 0, 3 and 20 using the non-parametric Kruskal-Wallis test in the GTV and > 12 Gy non-target region. Second, we performed linear regressions for  $\Delta$ ADC,  $\Delta$ Ktrans and  $\Delta$ ve versus dose within GTV and surrounding > 12 Gy region. Third, we repeated the linear regression analysis for metastases with evidence of radionecrosis.

**Results:** The Kruskal-Wallis test only revealed significant differences for ve in the GTV between day 0 and 20 ( $p < 0.005$ ) and day 3 and 20 ( $p < 0.05$ ). Significant negative correlations existed between  $\Delta$ Ktrans and  $\Delta$ ve with dose at day 20 within the GTV and > 12 Gy region ( $r = -0.04$  to  $-0.16$ ,  $p < 0.001$ ), but not ADC. However, we found significant positive correlations between  $\Delta$ ADC and dose in the GTV of brain metastases with evidence of radionecrosis at day 3 and 20 ( $r = 0.11$  to  $0.19$ ,  $p < 0.001$ ).

**Conclusions:** We found that dose-correlated decreases in Ktrans and ve at day 20 post-SRS both within the GTV and in the surrounding high dose region, likely reflecting underlying vascular responses. Although only a small sample, we observed dose-correlated ADC increases in the GTV of metastases. In future, we plan to explore potential value of MRI biomarkers for assessing early treatment response in a larger cohort with less variability primary sites and metastasis size.

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### CHEST WALL PAIN FOLLOWING STEREOTACTIC BODY RADIATION THERAPY (SBRT) TO THE LUNG USING 48 GY IN THREE FRACTIONS: A SEARCH FOR PREDICTORS

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**Purpose:** Chest wall (CW) pain, believed to be neuropathic and unrelated to rib fracture, is an uncommon but bothersome toxicity following SBRT to the lung. The majority of publications on predictors of CW pain after SBRT have limitations including analysis of a mix of patients treated with different dose and fractionation regimens, less than six-month follow-up times, and analysis of patients treated without heterogeneity correction during dose calculation. In addition, there remains no clear consensus on what the CW dose-volume constraints should be. Our goal is to report on our institutional experience with CW pain and the search for CW pain dose constraints in a group of patients treated with the same SBRT technique, dose and fractionation, at least six months of follow-up, and planned with

heterogeneity correction.

**Materials and Methods:** One hundred and twenty-two patients treated with SBRT were analyzed. CW pain was scored according to CTCAE v3.0. All patients had the CW (2 cm pleural expansion) retrospectively contoured. Patient (age, gender, diabetes, osteoporosis), tumour (volume of PTV, PTV/CW overlapping volume) and CW dosimetric parameters (V30Gy, V40Gy, V50Gy, D1cc, D2cc, Dmax) were collected. The correlation between CW pain (Grade 2 or higher) and the different parameters was evaluated using univariate and multivariate logistic regression.

**Results:** Median follow-up was 19 months (6-56). 12/122 patients expressed CW pain of any grade during follow-up (seven patients with Grade 1, 3 with Grade 2 and 2 with Grade 3). In univariate analysis, only V30Gy ( $p = 0.034$ ) and the overlapping volume between the PTV and the CW ( $p = 0.038$ ) were of statistical significance in terms of correlation with CW pain (Grade 2 or higher). The dosimetric variables V40Gy, V50Gy, D1cc, D2cc, D5cc and PTV volume, as well as all clinical parameters failed to show any statistical significance. In multivariate analysis, none of the parameters remained predictive for CW pain.

**Conclusions:** Considering the wide range of differing results from the literature and the lack of significant predictors found in our current study, a reasonable conclusion is that the ideal constraint for CW pain, if any, is yet to be defined.

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#### SYSTEMIC THERAPY AS A PREDICTOR OF PAIN AND VCF AFTER SPINE SBRT

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**Purpose:** The benefits of stereotactic body radiation therapy (SBRT) for spinal metastasis in pain control await confirmation in two large North American trials (RTOG0631 and CCTG SC24). Spinal SBRT is already commonly used to improve local control. We hypothesized that systemic therapy may influence the efficacy of spine SBRT in controlling pain and increase the risk of vertebral compression fracture (VCF).

**Materials and Methods:** We retrospectively reviewed the clinical data of 155 patients treated with SBRT between June 2009 and June 2016. In the current analysis, we included the 127 patients for which SBRT was administered in a context of oligometastatic or oligoprogressive disease (either alone or postoperatively). Outcomes were calculated actuarially and comparisons were performed using log-rank tests (significance set at  $<0.05$ ).

**Results:** The mean age was 64 (range: 22.67-81.82). Forty-nine patients (39%) had cancers considered radioresistant (kidney 16%, thyroid 9%, melanoma 3%) and 63 patients had breast (26%), prostate (14%) or lung (13%) cancers. Prior to SBRT, 33%, 63% and 3% had stable (SINS 0-6), potentially unstable (SINS 7-12) and unstable vertebrae (SINS 13-14). Postoperative SBRT was administered in 41%. Pain was present in 78% of patients prior to SBRT. Forty-two percent of the patients received systemic therapy during or within 7 days of SBRT, including chemotherapy and immunotherapy. The median BED10 was 48. Median local recurrence free survival, distant progression-free survival and overall survival were 20.5 months, nine months and 25 months, respectively. There were 14 VCFs. No case of radiation myelopathy was reported. On univariate analysis, patients who were receiving systemic treatment were significantly at a higher risk of developing VCF ( $p = 0.014$ ) or pain recurrence ( $p = 0.001$ ). SINS score, Bilsky scale and pre-SBRT stabilization surgery were not significantly associated with VCF, local recurrence or pain.

**Conclusions:** In our single center retrospective review, we observed that patients on systemic treatments prior to spine SBRT were at high risk of developing VCF and pain recurrence/progression. These results suggest that pain response analyses in ongoing trials need to take into account concurrent systemic treatments as a potential confounding factor. Patient and clinician expectations in the pain response to spine SBRT need to be adapted according to the patient's systemic disease status as to the risk of VCF may also need to be modulated.

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#### STEREOTACTIC ABLATIVE RADIOTHERAPY FOR UPPER TRACT TRANSITIONAL CELL CARCINOMA: A SYSTEMATIC REVIEW

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**Purpose:** Urothelial carcinoma of the upper urinary tract is a rare entity, consisting of only 5% of urothelial malignancies. The role of radiotherapy in treating upper tract transitional cell carcinomas has been very limited, mostly because there is a lack of evidence to support its use. The primary modality of treatment is surgical, namely radical nephroureterectomy. However, for patients who are poor surgical candidates, stereotactic ablative body radiotherapy (SABR) or stereotactic radiosurgery (SRS) might provide an acceptable alternative treatment for localized urothelial carcinoma of the upper ureter or renal pelvis.

**Materials and Methods:** We conducted a systematic review of literature on SABR or SRS as treatment for urothelial carcinomas of the upper tract. We followed a PRISMA protocol for systematic reviews, searching online databases including MEDLINE and EMBASE. Duplicates were removed. Articles were included if they were authored from 2000 to present, English language, primary malignancy was transitional cell carcinoma (TCC) of the upper tract, any T stage, any grade, patients were aged 18 or older, and primary treatment was SABR or SRS, not surgery. Outcome measures were disease free, progression free or overall survival or quantitative criteria such as RECIST. Excluded articles involved primary pathology other than TCC, non-SABR or SRS treatment, or constituted commentary, editorials, non systematic reviews, expert opinion, or consensus guidelines.

**Results:** A total of 302 articles were retrieved by the initial database search, of which 48 were duplicates and removed. After applying the inclusion and exclusion criteria, nine articles were included in the final group. Of those articles, none were meta-analyses, randomized controlled trials or prospective studies. Most were case series (level IV evidence) or retrospective studies (level III to IV). Articles generally concluded that SABR or SRS for upper tract TCC provided good local control with relatively little toxicity.

**Conclusions:** Stereotactic ablative radiotherapy for localized proximal urothelial carcinomas is a promising alternative to radical nephroureterectomy in non-surgical candidates, but more studies are needed, especially of higher evidential quality than case series or small retrospective studies can provide.

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#### RADIOSURGERY DOSIMETRIC COMPARISON BETWEEN BRAINLAB NOVALIS AND ECLIPSE VMAT FOR A LARGE PATIENT POPULATION

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**Purpose:** In stereotactic radiosurgery (SRS), a single high dose of ionizing radiation is delivered to a small stereotactically localized target using multiple non-coplanar photon irradiation beams. Dynamic conformal arc (DCA) therapy and volumetric modulated arc therapy (VMAT) are both well-established techniques and have been used for SRS treatment in brain metastases at the Tom Baker Cancer Centre (TBCC). This study retrospectively investigates the difference in dosimetry between the two techniques for a large population of patients (>40) treated for single brain metastasis at the TBCC.

**Materials and Methods:** A treatment planning comparison study was carried out to evaluate the dosimetric characteristics and treatment efficiency of VMAT and DCA based planning techniques. The DCA plans were generated using BrainLAB iPlan® RT Dose v4.5.5 and delivered with a 6 MV photon beam using a Novalis Classic linac with Brainlab microMLCs. The VMAT plans were generated using Varian Eclipse™ v13.6, and delivered with a flattening filter free 10 MV photon beam using a TrueBeam Edge with HD-MLCs. For each technique, treatment plans for 21 patients were studied. The size of targets varied from 0.1 to 38.5 cc. Prescription doses varied from 15 to 22 Gy prescribed to the 80% isodose line. In order to evaluate the plans, mean values of dosimetric indices scoring the conformity (CI-RTOG), homogeneity (the ratio of the maximum PTV dose to the prescription dose), and gradient (defined as the radial difference between V50% and

V100% equivalent spheres) were calculated and compared. Additionally, the correlation between V10Gy and target volume was assessed.

**Results:** It was found that VMAT is able to achieve better dose conformity ( $1.21 \pm 0.04$  compared to  $1.52 \pm 0.05$ ). This improvement was more pronounced for cases with smaller brain lesions ( $< 1$  cc). Dose homogeneities were comparable in both techniques ( $1.26 \pm 0.04$  for VMAT and  $1.28 \pm 0.02$  for DCA). However, VMAT plans resulted in higher gradients. V10Gy normalized to the prescription dose increased linearly with the target volume ( $R^2 > 0.97$ ) for both techniques, though less rapidly for VMAT. For all PTV volumes larger than approximately 6 cc, values of normalized V10Gy were lower for VMAT planning, whereas for PTV volumes less than 6 cc, values of V10Gy were comparable. This could potentially have important implications as the literature has shown that the development of tissue necrosis is correlated with V10 Gy. Lastly, the mean beam-on-time decreased by 59% for VMAT plans.

**Conclusions:** Based on our study, it was found that VMAT is able to achieve better dose conformity and comparable homogeneity compared to DCA plans with superior delivery efficiency. VMAT based SRS has now been adopted in our clinic as the alternative to the conventional DCA technique.

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#### A MULTIDISCIPLINARY CLINICAL EXPERIENCE IN SEXUAL HEALTH CARE FOR ONCOLOGY PATIENTS

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**Purpose:** Sexual health remains an under-addressed area in oncology care, implicating often long-term functional and psychosocial impairment for patients. With the goal of improving the quality of sexual health care provision at our tertiary cancer centre, we developed, implemented, and assessed a multidisciplinary sexuality program, to identify patient needs and apply interventions that could be effective in a broader oncology care context.

**Materials and Methods:** The establishment of our institution's first oncology-focused sexual health program is described. A complementary retrospective chart review was performed to evaluate clinicodemographic data, including responses to validated sexual health questionnaires, from a two-year clinical pilot.

**Results:** A sexual health program was introduced for any cancer patient identified by their health care provider or self-referred, receiving 130 referrals and conducting 64 consultation and 75 follow-up visits within a two-year pilot period. Patients attending the program were 75% female, of mean age 52 years, and had most often breast (33%) or hematologic (30%) malignancies. Most (84%) had completed curative-intent treatment, with no evidence of disease. 34% continued on endocrine therapy. The most frequent reasons for referral were pain (38%), decreased libido (35%), and vaginal dryness (27%). One hundred percent of female patients demonstrated sexual dysfunction on the Female Sexual Function Index (FSFI) and 80% of male patients demonstrated moderate or severe erectile dysfunction on the Sexual Health Inventory For Men (SHIM). Patients waited a median of 63 days (SD 107, range 3-516) from referral to consultation, suggesting that demand for multidisciplinary sexual health care overwhelmed existing resources.

**Conclusions:** We have demonstrated unmet sexual health needs across a diverse oncology patient population and have presented a framework for addressing these issues. Insights emerging included the role of group-based sexual health support to improve accessibility, the need for staff education to encourage proactive intervention, and the importance of integration with existing community expertise to expand our resource base.

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#### LONG-TERM HEALTH-RELATED QUALITY OF LIFE IN SURVIVORS OF INTRACRANIAL GERM CELL TUMOURS

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**Purpose:** The purpose of this study is to investigate health-related quality of life (HRQOL) in survivors of intracranial germ cell tumours (IGCT).

**Materials and Methods:** Survivors of IGCT were invited to attend the clinic and were asked to complete the 36-Item Short Form Survey Instrument (SF-36). The SF-36 is scored from 0-100, with a higher number representing a more favourable HRQOL. SF-36 scores of the study cohort were compared with that of the general population.

**Results:** The study cohort consisted of 12 survivors of IGCT, six males and six females. Median age was 13 years at diagnosis (range, 10-18 years), and 26 years at time of study (range, 7-34 years). Median follow-up was 11 years. Five patients had germinomas, and seven had non-germinomatous germ cell tumours. All 12 patients received radiation therapy (RT), 10 to the craniospinal axis, one to the whole ventricles and one to the tumour bed alone. Nine patients received chemotherapy. Mean SF-36 scores were 67.9 (standard deviation [SD] 33.2) for physical functioning, 58.3 (SD 37.4) for role limitations due to physical health, 77.8 (SD 32.8) for role limitations due to emotional problems, 43.1 (SD 18.4) for vitality, 74.3 (SD 15.3) for mental health; 62.5 (SD 32.0) for social functioning, 74.2 (SD 33.4) for pain, and 57.1 (SD 24.0) for general health; mean scores were  $\geq 1$  SD lower than that of Canadian normative data for vitality, social functioning and general health. Physical component summary score was 43.6 (SD 13.9) and mental component summary score was 47.6 (SD 11.2), normalized to a United States' population with mean scores of 50 and SDs of 10.

**Conclusions:** Long-term HRQOL for survivors of IGCT is lower than that of the overall population, particularly in vitality, general health, and social functioning. Physical and psychosocial supports should be considered for IGCT survivors. Larger studies would be worthwhile to determine factors associated with HRQOL, which may improve treatment decision-making and informed consent for patients and families affected by IGCT.

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#### OUTCOMES OF TRI-MODALITY BLADDER-SPARING THERAPY FOR MUSCLE-INVASIVE BLADDER CANCER

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**Purpose:** Although radical cystectomy is considered the standard of care for muscle-invasive bladder cancer (MIBC) in North America, the resultant urinary diversion or neobladder construction is a morbid and life-altering outcome for patients. Recent data has shown comparable survival results for bladder-sparing tri-modality therapy (TMT) involving complete transurethral resection of bladder tumour (TURBT), radiotherapy (RT), and chemotherapy. As there remains paucity in data to change clinical practice, we conducted a retrospective analysis of patients in our institution to better define clinical outcomes of TMT in the setting of MIBC.

**Materials and Methods:** A retrospective chart review was performed of adult bladder cancer patients assessed by a multi-disciplinary team consisting of uro-oncologists, medical oncologists, and radiation oncologists. Included patients were diagnosed with MIBC (T2-T4) in the past six years and underwent curative intent treatment with maximal TURBT followed by concurrent chemoradiation ( $\geq 50$  Gy; platinum-based agent or fluorouracil + mitomycin). Patients who underwent radical RT alone following TURBT were also included. Clinical and treatment data were summarized including resection status, pathological features, response to treatment, and salvage cystectomy rates. Overall survival (OS) and disease-specific survival (DSS) were estimated using the Kaplan-Meier method.

**Results:** Of 116 included patients, 54 underwent TMT and 62 underwent radical RT alone following TURBT. The median age at diagnosis was 79 years and the median follow-up was 1.9 years. Clinical T-stage was T2 in 84% of patients and maximum TURBT was performed in 72% of patients. Complete response rates in those receiving TMT and RT alone were 70% and 50%, respectively. The overall local recurrence rate was 12%. The local recurrence rates in the TMT and RT only groups were 11% and 13%, respectively. In the TMT cohort, 4% of patients had Grade 3 or higher late toxicity and 2% of patients underwent salvage cystectomy. For TMT patients, median OS and DSS were 57.2 and 28.1 months, respectively. Two-year OS and DSS were 74.5% and 51.5%, respectively.

**Conclusions:** Based on our data, TMT remains a safe and effective alternative to radical cystectomy and should be offered to appropriately selected patients with MIBC. This multi-disciplinary approach appears to yield similar survival outcomes with minimal toxicity, while avoiding the morbidity of surgical

intervention especially in older patients. Confirmation in larger patient cohorts with longer follow-up is required.

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#### A PROSPECTIVE EVALUATION OF HEALTH-RELATED QUALITY OF LIFE OUTCOMES AFTER SKULL BASE RE-IRRADIATION

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**Purpose:** Health-related patient reported quality of life outcomes (HR-PRO) after skull base re-irradiation (re-RT) have never previously been reported. The aim of this prospective study was to assess early HR-PRO after highly conformal re-RT to the skull base.

**Materials and Methods:** Patients with a past history of skull base radiotherapy (RT) and dispositioned to receive a course of re-RT to a recurrent or new primary tumour of the skull base were prospectively enrolled. HR-PRO were assessed at baseline, two weeks (2W) post-RT, and at three, six, nine and 12 months post-RT using the MD Anderson Symptom Inventory Brain Tumour (MDASI-BT) and the anterior skull base surgery QoL (ASBQ) questionnaires. MDASI-BT scores ranged from 0 to 10, with higher score indicating worse outcome, while ASBQ scores ranged from 0 to 5, with lower scores indicating worse outcome. HR-PRO were analyzed using linear mixed models, with  $p < 0.05$  considered statistically significant. As per previous work, MDASI-BT score difference of  $\geq 1$  was considered clinically significant. Kaplan Meier analysis was used for secondary outcomes of local control (LC), progression free survival (PFS) and overall survival (OS).

**Results:** Forty-nine patients with a median age of 60 year-old (range = 33-85) were enrolled. Median interval between past RT and re-RT was 2 years (range = 1- 47 years). Most common primary sites were paranasal sinuses (41%), parotid gland (22%), and nasopharynx/retropharynx (20%). Fifty-one percent of patients were treated with conventionally fractionated intensity modulated radiotherapy or proton therapy to a median dose of 62 Gy (range = 40-70) in 30 fractions (range = 20-33) while 39% were treated with stereotactic body radiotherapy (SBRT) to a median dose of 45 Gy (16-45) in 5 fractions (range = 1-5). Thirty-five percent of patients had surgery before re-RT, while 29% and 51% had induction and concurrent chemotherapy, respectively. Median follow-up was 11 months. Actuarial LC, PFS and OS at one year were 81%, 60% and 89%, respectively. At two weeks post-RT, MDASI-BT score showed mild worsening of fatigue (baseline mean score = 3 versus 2W post-RT mean score = 4,  $p=0.03$ ) and appetite loss (1.8 versus 2.7,  $p = 0.008$ ). There was a worsening of ASBQ score 2W post-RT compared to baseline for the physical function domain (3.8 versus 3.4,  $p=0.04$ ) and specific symptoms domain (3.9 versus 3.5,  $p=0.04$ ); these scores returned to baseline for all subsequent time points. There was no significant deterioration in all other HR-PRO scores. ASBQ emotional domain showed improvement at 3 months compared to baseline (3.5 versus 3.8  $p = 0.015$ ), which was maintained on subsequent time points. There were no significant differences in HR-PRO scores between conventionally fractionated and SBRT re-RT.

**Conclusions:** Skull base re-RT is associated with minimal, immediate post-RT deterioration in fatigue and appetite loss (MDASI-BT) as well as physical function and specific symptoms (ASBQ), which returned to baseline at three months post-RT. This study shows overall excellent tolerance of patients to highly conformal re-RT to the skull base.

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#### IMPROVEMENT IN PATIENT-REPORTED DISTRESS AFTER CHEMO-RADIATION IN CERVICAL CANCER PATIENTS

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**Purpose:** Curative treatment of cervical cancer with definitive chemoradiotherapy (CRT) can be associated with significant morbidity impacting quality of life and causing distress. Our objective was to evaluate the clinical

utility of prospectively collected patient-reported distress over time in cervical cancer patients treated with definitive CRT using the Edmonton Symptom Assessment System (ESAS) questionnaire.

**Materials and Methods:** Between 2011 and 2016, consenting cervical cancer patients treated with definitive CRT who completed  $> 2$  questionnaires at routine clinical visits, including baseline, were included. The ESAS is a validated 10-item patient-reported symptom screening tool. Items are scored 0-10 and summed to a total score with higher scores indicating higher distress. Mean total scores were calculated at all time points and compared to baseline using a paired t-test. For each patient, a slope was created using linear regression. A one-sample t-test was performed on the slopes to determine whether the degree of change differed from zero. The minimal clinically important difference (MCID) for total ESAS score was defined as a change of 3-points for improvement and 4-points for deterioration. A mixed model was used to evaluate the longitudinal change in the MCID from baseline.

**Results:** Of the 98 patients initially identified, 68 met inclusion criteria. Median (range) follow-up was 16 mos (2-57) and compliance at 12 months was 57% (39/68). The median (range) age at diagnosis was 46 years (30-77) and 32%, 53%, 15% were FIGO Stages IB, IIA-B, and IIIA-B respectively. All patients received external beam radiation with concurrent Cisplatin followed by MR-guided PDR (47%) or HDR (53%) brachytherapy with 59% intracavitary and 41% combined intracavitary/interstitial techniques. There was no difference in total score at baseline compared to end of treatment ( $p = 0.50$ ), but reductions in distress were observed at six weeks, three months and six months after treatment compared to baseline ( $p = 0.03$ ,  $p = 0.008$  and  $p = <0.001$ , respectively). There was a significant improvement in distress over time for each patient reflected in the change in slope (mean slope: -0.79; 95% confidence interval: -1.31, -0.27;  $p = 0.004$ ). There was also a significant improvement in the MCID for total score from baseline over time ( $p = 0.04$ ).

**Conclusions:** Cervical cancer patients experience significant distress at diagnosis and during definitive CRT that significantly improves over time after treatment to an extent that is expected to be clinically meaningful for patients as defined by the MCID. Prospective collection of cervix cancer specific patient-reported outcomes should be incorporated into routine clinical practice to better inform areas of need and survivorship planning.

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#### RE-ENGAGING SURVIVORS OF CHILDHOOD CANCER IN AFTERCARE: A QUALITY IMPROVEMENT INITIATIVE

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**Purpose:** Survivors of Childhood Cancer (SCC) have to contend with lifelong cumulative late effects of their treatment. There are evidence based guidelines that recommend these patients should be followed by specialized AfterCare clinics to screen for and address late effects of childhood cancer treatment (Children's Oncology Group (COG) Survivorship Guidelines, 2014). A recent report from the St Jude Lifetime Cohort Study of 3010 SCC showed a 99.9% rate of chronic health conditions (CHCs), including a 37% incidence of second neoplasm by 50 years of age (Bhakta et al, 2017). Anthracycline doses  $> 250$  mg/m<sup>2</sup> were associated with higher cumulative burden of CHCs and higher brain and chest radiation doses were associated with more severe CHCs. A cohort of SCC were known to be lost to follow-up from our centre's AfterCare clinic. We aim to re-engage SCC in AfterCare at our centre as part of a quality improvement project.

**Materials and Methods:** We will report on our technique for locating and recruiting adult survivors of childhood cancer previously lost to follow-up back to the Aftercare clinic. The first iteration of this process involved identifying patients at highest risk for late effects. Patients with  $>300$  mg/m<sup>2</sup> of doxorubicin equivalents or who had received any radiation as part of their treatment were deemed highest risk.

**Results:** There are currently 674 patients in the AfterCare clinic electronic database. Three additional sources of patient information were accessed: paper medication administration charts ( $n = 953$ ), historical paper AfterCare chart repository ( $n = 513$ ), and paper records of deceased and discharged patients ( $n = 735$ ). From these records, 767 unique patients were identified that were not known to be deceased and were not already accounted for

in the electronic database. The available paper charts were evaluated for these 767 patients to establish doxorubicin dose and whether patients had received radiation therapy. Without accessing contemporary electronic health records, we were able to identify a total of 221 patients who had received > 300 mg/m<sup>2</sup> of doxorubicin or any radiotherapy. Locatable patients will be contacted by letter to invite them to participate in AfterCare at our centre. We will report on our preliminary numbers regarding patients we were able to identify and make contact with, and rates or re-engagement in AfterCare. **Conclusions:** We hope that by re-engaging SCC in survivorship care that we will improve the health and well-being of those previously lost to follow-up, and decrease the burden on the health care system of late presentation of chronic toxicities of therapy. We aim to provide a framework for other AfterCare programs looking to re-engage survivors lost to follow-up.

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### LOCAL RELAPSE AND SURVIVAL OUTCOMES IN PATIENTS WITH SCALP SARCOMA

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**Purpose:** There is limited literature on the optimal treatment of sarcoma arising in the scalp. This study evaluates local relapse and survival outcomes of patients with scalp sarcoma treated at a provincial cancer care institution. **Materials and Methods:** Subjects were 95 patients referred between the years 1990-2015 with a primary diagnosis of scalp sarcoma. Chart review was performed to extract data on demographics, tumour and treatment characteristics. Kaplan-Meier (KM) statistics were used to estimate local relapse-free survival (LRFS) and overall survival (OS). Survival curves were compared using log-rank tests.

**Results:** Median follow-up time was 33.1 months (range 1.5 to 255.8 months). Median age at diagnosis was 77 years (range 19 to 96 years). The most common histologic subtypes were Pleomorphic Sarcoma/Malignant Fibrous Histiocytoma (36%), Angiosarcoma (27%), and Atypical Fibroxanthoma (11%). Excisional biopsy was performed in 61% of patients as initial surgery. Among 54 patients who underwent re-excision after initial biopsy, 16 (30%) required tissue flap and 28 (52%) skin graft. Final margin status were: 36% (n = 34) positive, 28% (n = 27) close <3 mm, 31% (n = 29) negative, and 5% (n = 5) unknown. Median survival was 54 months (range 1.5 to 256 months). Five-year KM LRFS was 56.0% (95% CI: 42.1-67.7%) and OS 48.3% (95% CI: 36.9-58.8%). On subset analysis, five-year KM LRFS estimates were 36.8% (95% CI: 16.4-57.5%) with positive margins, 81.4% (95% CI: 56.7-92.8%) with close margins, and 59.4% (95% CI: 35.3-77.0%) with negative margins, log-rank p = 0.008. Patients with close or positive margins who received pre- or postoperative RT (n = 19) had similar LR risk compared to patients who did not receive RT (n = 34) (five-year KM LRFS 41.8% versus 69.1%; log-rank p = 0.145). On univariate analysis, angiosarcoma was significantly associated with higher LR risk compared to other histologies (HR 4.81, 95% CI 2.34-9.87, p < 0.001). Age, re-excision surgery, and RT use were not significantly associated with LR. A trend for higher LR was observed with close/positive margin compared to negative margin but this was not statistically significant (HR 1.48, 95% CI: 0.69-3.18, p > 0.05).

**Conclusions:** Patients with scalp sarcoma have high risks of local relapse, particularly in cases with positive margins. Adjuvant radiation was not associated with improved local control for close or positive margins. Complete surgical excision establishing negative margins remains the primary standard treatment for patients with this rare disease.

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### INTERNATIONAL REFERRAL FOR PROTON BEAM THERAPY - A PATIENT AND CAREGIVER PERSPECTIVE

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**Purpose:** The purpose of this presentation is to examine the Ontario process for out-of-country referral for proton beam therapy (PBT) from the patient and caregiver perspective. PBT is an advanced type of external-beam radiation therapy that uses proton rather than photon beams to deliver radiation

doses to a tumour. Proton therapy offers a high degree of precision, which allows radiation oncologists to target an escalated dose of radiation directly on a tumour and spare nearby healthy tissue. There are no PBT treatment centres in Canada, except for one specialized research facility in British Columbia. Patients requiring treatment may be referred to out-of-country facilities. Alberta, Saskatchewan, Ontario, Quebec, and Nova Scotia will refer patients out of country; the remaining provinces do not. Fewer than 50 Canadian patients per year are estimated to be referred out of country to receive PBT. For children, and especially children with medulloblastoma, PBT has a number of advantages over traditional photon therapy because of the physics of the beam: reduced unintentional irradiation of surrounding tissue can reduce damage to other areas, and prevent negative effects such as hearing loss and cognitive dysfunction. When patients are referred out of country, they along with their caregivers may be away from home for up to eight weeks to receive treatment.

**Materials and Methods:** Evidence is principally first-person experience of a juvenile medulloblastoma patient and his caregivers. This is supplemented by discussions with administrators and a survey of parents of children treated for medulloblastoma.

Questions under examination:

- 1 What is the experience of requesting or seeking a referral following diagnosis?
- 2 What is the experience with the referral process itself?
- 3 What is the experience travelling and receiving treatment?

**Results:** International referrals provide Canadians with access to advanced treatments not available in Canada. Some provinces have negotiated standard terms for some treatments, streamlining decision making. The referral process creates additional anxiety and stress on the patient and caregivers at an already challenging time. The process in Ontario could be made more transparent, for example with online tools. Receiving treatment away from home removes both patients and caregivers from their existing support networks. Patients and caregivers are willing to relocate and spend time away from home in order to access treatments with better anticipated outcomes.

**Conclusions:** A cancer diagnosis is an emotional and distressing event. In cases where rapid intervention is required, decisions must be made quickly. Options and opportunities should be made clear to patients and caregivers, and referral decisions should be timely and efficient. Systems that are put in place to streamline the relocation and adjustment process help ease the emotional burden associated with being away from home for patients and caregivers. Patients and caregivers should be actively consulted on referral processes and opportunities

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### IS THERE A DIFFERENCE IN COMPLETION RATES? PILOT VERSUS PROVINCIAL IMPLEMENTATION OF EXPANDED PROSTATE CANCER INDEX COMPOSITE FOR CLINICAL PRACTICE (EPIC-CP) IN ONTARIO

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**Purpose:** The first disease-specific oncology patient-reported outcome (PRO) for prostate cancer patients (EPIC-CP) was pilot tested in 2014. The EPIC-CP is a 16-item validated symptom screening tool that asks about sexual function, vitality, and urinary and bowel problems. The EPIC-CP pilot was implemented along with support tools/resources in four Regional Cancer Centres (RCCs). Based on pilot results, EPIC-CP was implemented province-wide in 2016. The objective of this analysis is to examine whether the EPIC-CP completion rates for the pilot (May-November 2014) and the provincial implementation (October 2016 - November 2017 in 11 RCCs) were statistically significant.

**Materials and Methods:** The target population for the EPIC-CP was early-stage prostate cancer patients undergoing radiation or surgery. The hypothesis was that there would be no difference in question completion rates between the pilot and provincial implementation; since the pilot was structured to be generalizable and process improvements were made before provincial roll-out. To examine variances in completion rates by question,

hierarchical logistic regression models (implemented in PROC GLIMMIX, SAS 9.4) were applied.

**Results:** A total of 928 EPIC-CP assessments (n = 332 patients) were completed by patients during the pilot, compared to 10,801 (n = 5807 patients) in the provincial implementation. Provincial completion rates were lower than corresponding pilot results (ranging 2.7% to 7.3% for individual questions), which resulted in a statistically significant decrease in all EPIC-CP inventory questions (all ps < 0.001). Statistically, the largest decrease was observed for the “hot flashes/breast symptoms” (96.9% versus 90.4%, respectively;  $\beta$  = 1.28, SE = 0.22, t(5677) = 5.97, p < 0.001) and “overall sexual function” domains (91.9% versus 84.7%, respectively;  $\beta$  = 0.91, SE = 0.17, t(5677) = 5.33, p < 0.001).

**Conclusions:** The decrease in EPIC-CP question completion rates is undesirable and indicates the need for further investigation into the factors associated with question completion, which may include patient, process, or item-specific challenges.

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### ADJUVANT RADIATION THERAPY IMPROVES PFS OF WHO GRADE II MENINGIOMA RESULTING IN IMPROVED LONG TERM SURVIVAL: A SINGLE INSTITUTION EXPERIENCE

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**Purpose:** Meningiomas are the most common type of primary intracranial tumour, composing more than 35% of all. The World Health Organization's (WHO) classifies meningioma into Grade I (benign) 90%, Grade II (atypical) 5–7%, or Grade III (malignant or anaplastic) 1–3%. This study evaluated prognostic factors influencing the local recurrence rate (LRR), progression-free survival (PFS) and overall survival (OS) rates of meningioma, focused on the adjuvant radiotherapy role.

**Materials and Methods:** The retrospective analysis included 128 patients treated for meningioma at our institution from 2008 to 2017. The three, five, 10-year OS and three, five-year PFS rates were performed using Kaplan-Meier analysis, comparisons were performed using log-rank tests.

**Results:** Twenty (15.6%) patients were follow up by observation, 64 (50.0%) were treated with surgery, 33 (25.8%) with radiotherapy (RT) after surgery and 11 (8.6%) only RT. The three and five year PFS rates were 66 and 41% in the observation group, 83 and 66% in patients treated with surgery, 68% for the group treated with RT after surgery and 80% RT alone. To compare whether adjuvant radiotherapy provided a benefit, we analyzed the survival curves by WHO grade and treatment. The three and five year PFS rates were 84 and 69% for Grade I surgery, 33% and 0% for Grade II surgery, 80% for three and five year PFS Grade I surgery plus RT and 62% for Grade II surgery plus RT. Statistical analysis showed differences \*p value < 0.001. Patients who underwent to gross-total resection (GTR), afforded better survival compared with subtotal resection (STR).

**Conclusions:** Adjuvant radiotherapy had a positive impact on PFS in patients with meningioma WHO Grade II with improved and maintained five and 10 years OS rates. Additionally, the extent of surgical resection improved long term survival and STR patients experienced benefit in the PFS and OS.

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### INTEGRATION OF ONGOING QUALITY ASSURANCE MEASURES IN COLORECTAL CANCER SURVIVORSHIP CARE PLANS

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**Purpose:** A follow up program for patients with Stages II or III colorectal cancer (CRC) after completion of their treatment was initiated in 2014 at our institution, a provincial mandate that may lead to decreased wait times for new patients. Stable patients, with no disease or treatment related issues and not participating in a clinical trial were discharged to their primary care

providers (PCP). A dictated discharge letter, surveillance protocol, and a receipt of information sheet (RIS) were sent to PCP. An institutional quality assurance (QA) measure was started to monitor the return of the RIS. The RIS allowed the PCP to indicate they received this information and they would be responsible for managing surveillance. A dictation code triggered the QA process associated with this program that included sending reminders if RIS was not received in a timely manner. This study was conducted to assess if surveillance was completed according to the guidelines.

**Materials and Methods:** Research ethics board approval was obtained and 282 patients were identified as new referrals between April 1 2014 and June 30 2016 with Stage II or III CRC. After a chart review 125 patients were excluded due to treatment elsewhere, repeat charts, developing recurrent or metastatic disease, patient's refusal or death. In this cohort 157 patients were identified as eligible for discharge to their PCP. An additional 64 patients with a returned RIS who completed treatment prior to April 2014 were included. A total of 221 patients were included in this study who were either eligible or were discharged to PCP. The dates of one year follow-up endoscopy (from date of original surgery), computed tomography (CT) scans, and Carcinoembryonic Antigen (CEA) tests were determined after a chart review.

**Results:** Overall, 83.3% of eligible patients were discharged to their PCP, and by December 31 2017, 99.0% had completed follow up endoscopy, 84.1% CT scan, and 63.2% CEA tests. The systematic chart review identified 59 patients discharged to their PCP who were missed in the department QA process based on monitoring the return of the RIS. There was some variation in practice where one oncologist preferred continuing follow up at the cancer centre. Four patients were lost to follow up while continuing follow up at the cancer centre. Fifteen patients developed recurrent or metastatic disease and were repatriated to the cancer centre.

**Conclusions:** A well follow-up program for select CRC patients conducted by PCP is feasible. However, a carefully designed QA component of this program is essential. About 32% of discharged patients in this study were not identified in the department RIS based QA process. Since earlier detection of oligo-metastatic disease or a recurrence has a curative potential follow up testing should not have gaps. To identify the issues related to process ongoing feedback from patients, PCP, and specialists, as well as a periodic review, is recommended.

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### A SINGLE INSTITUTION RETROSPECTIVE ANALYSIS OF ADULT HEAD AND NECK RHABDOMYOSARCOMA (HN RMS) FROM 1984-2017

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**Purpose:** Head and Neck Rhabdomyosarcoma (HN RMS) in adults is an aggressive and challenging to manage malignancy. Our goal was to describe the presentation, treatment, outcomes, patterns of failure, and prognostic factors of HN RMS patients treated at our institution between 1984 and 2017.

**Materials and Methods:** A retrospective chart review of adult (>16 years of age) HN RMS patients registered in the multidisciplinary Sarcoma Clinic who received majority of their treatment here was performed. Survival analyses were performed using the Kaplan-Meier Method. Prognostic variables including age, anatomic location, histologic subtype, radiation, and TNM stage were analyzed in univariate (UVA) Cox analyses.

**Results:** Fifty-eight patients were identified, with a median age of 32 years (ranged 16 to 81); 26 were male. Seventy-six percent of tumours (n = 45) were parameningeal and 88% (n = 51) were >5cm. Fifty percent of patients (n = 29) had clinical node positive disease and 15% (n = 9) had distant metastases at the time of diagnosis. Local treatment consisted of surgery and radiotherapy (RT) versus RT alone in 9% (n = 5), and 91% (n = 53) patients respectively; and 76% (n = 45) received chemotherapy. Local and regional control at five years was 64%, and 73%, respectively. With a median follow-up of 18 months, five-year overall survival (OS) was 34% (95% CI: 20%-48%) for non-metastatic, and 29% (95% CI: 17%-42%) for metastatic patients. Patterns of failure were further analyzed in 49 non-metastatic patients. Sixty-seven percent (n = 30) patients relapsed, with median time to progression of 15 months. Median time to distant failure (DF) was 20 months. On UVA, concurrent chemotherapy (HR 2.3, p = 0.029) and tumour size (HR 2.6,

$p = 0.01$ ) were associated with worse survival. Distant metastasis was the predominant mode of first failure ( $n = 16$ , 33%). This population was also enriched for patients with metastases in unusual locations, including testes ( $n = 2$ ), breasts ( $n = 2$ ), leptomeninges ( $n = 12$ ), and bone marrow ( $n = 9$ ).  
**Conclusions:** Adult HN RMS of the head and neck is an aggressive malignancy with an unfavorable prognosis, despite intensive treatment, but is potentially curable, particularly with modern radiotherapy techniques and chemotherapy.

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#### TOTAL BODY PHOTON IRRADIATION WITH ISLAND-BLOCK ATTENUATORS: DOSE DISTRIBUTIONS GENERATED WITH A MONTE CARLO TREATMENT PLANNING SYSTEM

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**Purpose:** Our primary photon total body irradiation (TBI) technique uses multiple overlapping 6 MV arcs. Patients lie in the prone and supine positions on a floor stretcher at 200 cm SSD and are treated AP/PA. Obtaining organ (lung) doses lower than prescription dose, as sometimes required by protocol, is achieved using island-blocks placed on a tray above the patient. We investigated the feasibility of using a CT-based Monte Carlo (MC) treatment planning system (TPS) to calculate these complex geometries and provide dosimetric data on shielded organs.

**Materials and Methods:** Island-blocks (cerrobend or other eutectic alloy) are incorporated into TBI arc treatment by placing the block over the target organ on a static tray several cm above the patient. The sweeping arc creates complex geometries that blur the block shadows and are difficult to calculate with our CT-based TPS. We hypothesized that MC dose calculation was more amenable to our TBI technique using island-blocking, therefore we carried out a feasibility study to compare calculated versus measured dose, and to investigate the logistics of incorporating this system into clinical practice.

**Results:** A 90x24x30 cm<sup>3</sup> solid water phantom with an island-block was CT-scanned. Radiochromic film was placed both under and away from the island-block. Measurements were performed in water- and lung-equivalent phantoms. In all cases, the MC TPS agreed well with these measurements. A sample patient with simulated block position and appropriate block electron density was recalculated using the MC system. The block's impact on the shielded organ and neighboring structures was well demonstrated by the MC system.

**Conclusions:** MC treatment planning provides sophisticated capabilities for calculating complex geometries such as sweeping overlapping arcs for extended SSD photon TBI. Both geometric and dosimetric results compared favourably to measurement, thus promising to be a valuable tool in evaluating prescription compliance.

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#### EVALUATION OF INTRAFRACTION MOTION AND TREATMENT TIME IN RELATION TO IMMOBILIZATION AND BEAM ARRANGEMENT IN STEREOTACTIC BODY RADIOTHERAPY FOR EARLY STAGE LUNG CANCER

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**Purpose:** When entering into stereotactic body radiotherapy (SBRT), early stage lung cancer remains the most common tumour that radiotherapy programs use to introduce and develop their treatment techniques. Changes in immobilization, imaging, treatment beam arrangement and therapist training have occurred over time and may lead to a reduction in treatment length and intrafraction motion.

**Materials and Methods:** A cohort of patients treated early in the trajectory of SBRT program development was compared to a later cohort that used more comfortable immobilization and dynamic conformal arcs in place of ten static beams. A third cohort using volumetric modulated arcs (VMAT) was also analyzed. All three groups were compared for length of treatments and intrafraction motion as determined by post-treatment cone-beam CT (CBCT) imaging. Other parameters such as tumour location and size were also taken into account.

**Results:** While a change to conformal arc treatments and a more cushioned immobilization device led to decreased mean treatment times, the results were not statistically significant. Increased efficiency may have also been influenced by improvements in therapist training and competence in completing the tumour match on CBCT. Treatment times increased again with the implementation of VMAT treatment techniques, but further skill in tumour matching and elimination of post-treatment imaging except for the mock set-up day kept total appointment lengths within the same range. Intrafraction motion was small for the vast majority of patients no matter the treatment technique, but small improvements were observed with the use of arc treatments and a less rigid immobilization apparatus.

**Conclusions:** The use of SBRT continues to increase with its application to more primary and metastatic sites. Improvements in staff experience, immobilization, imaging and treatment processes can yield small changes that can improve treatment accuracy by decreasing intrafraction motion. The need for less linear accelerator time can also make it easier to implement this resource-intensive technique for more patients and tumour sites.

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#### AN EXAMINATION OF NEEDLE DEFLECTION IN HIGH DOSE RATE PROSTATE CANCER BRACHY THERAPY

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**Purpose:** High dose rate (HDR) brachytherapy (BT) is a common treatment technique for prostate cancer that involves irradiating the entire prostate by passing a high activity radioactive source through multiple hollow needles inserted within the prostate. Typically, a whole-gland approach is used where the goal is to deliver as uniform a dose as possible to the entire prostate, with a maximum deliverable dose limited by toxicities to nearby organs-at-risk. To improve tumour control while maintaining acceptable rates of toxicity, tumour-targeted HDR-BT has been proposed to escalate dose to the intra-prostatic lesion, which is the most common site of local prostate cancer recurrence. In this scenario, accurate and reliable needle placement is critical; however, ideal needle placement within the prostate is often hampered by unintended needle deflection, thus limiting how well a specific region within the prostate can be targeted. The purpose of this work, therefore, is to examine the magnitude and direction of needle deflection in HDR-BT procedures.

**Materials and Methods:** Post needle implant 3D ultrasound images have been taken for 11 prostate cancer patients who underwent HDR-BT, giving the final inserted position for a total of 173 needles. A medical physicist manually segmented the needles, thus determining the actual needle tip and trajectory. Needle deflection was quantified by assuming the radiation oncologist intended to insert the needle perpendicular to the template and at the left-right (X) and anterior-posterior (Y) position of the needle's associated template hole. Any deviation from this assumed path was characterized as a needle deflection. Tip error due to deflection was calculated as the Euclidian distance between the intended and the actual needle tip, while trajectory error was calculated as the angle between the intended and actual needle trajectory. Correlation between insertion depth and tip and trajectory error was also determined using the Pearson product-moment correlation coefficient.

**Results:** Mean tip and trajectory error due to deflection, plus or minus standard deviation, were  $6 \pm 3$  mm and  $2 \pm 1$  deg respectively. There was no significant correlation between insertion depth and tip or trajectory error ( $r = .11$  and  $r = .01$  respectively). Qualitatively, most needles bent away from the prostate, with increased deflection observed near the edge of the prostate.

**Conclusions:** We present an examination of the magnitude and direction of needle deflection in HDR-BT procedures. This information may be used by the radiation oncologist on a case by case basis to better guide needles to their intended target, which is especially important for needle insertion in tumour-targeted treatments. Future work includes completing analysis of the remaining 11 patients and completing analysis of the dosimetric effects of this needle deflection.