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1

THE EMERGING ROLE OF STEREOTACTIC ABLATIVE RADIOTHERAPY IN PRIMARY RENAL CELL CARCINOMA: A SYSTEMATIC REVIEW OF THE LITERATURE

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Purpose: Stereotactic ablative radiotherapy (SABR) is a novel treatment option for primary renal cell carcinoma (RCC) for which evidence continues to emerge. The objective of this study was to systematically evaluate the literature on SABR for RCC primary tumours with respect to local control, toxicity, and renal function.

Materials and Methods: A PROSPERO-registered (ID#: 115573), PICOS/PRISMA-based systematic review was conducted, consisting of a structured, information scientist-supervised search of literature published from 1995-2019 plus secondary manual searches of meeting abstracts and article citations. The primary outcome was crude local control. Secondary outcomes included: toxicity reported as Common Terminology Criteria for Adverse Events (CTCAE) criteria, and renal function reported as change in estimated glomerular filtration rate (eGFR). Weighted averages were calculated for each characteristic and outcome of interest based on contributing study size.

Results: From 2,364 PubMed entries and 924 meeting abstracts screened, 26 studies (20 articles and six abstracts) from eight countries were identified (11 prospective, 15 retrospective), collectively enumerating n=390 mutually-exclusive patients. Follow-up duration was 27.9 months (range: 9-79.2). Tumour size was 4.6 cm (range: 2.3-9.5, n=208 in 15 studies). Dose-fractionation and treatment technique varied widely across studies: 26Gy single-fraction and 30-40Gy in 3-5 fractions regimens were common. Weighted crude local control was 91.8% (range: 43.5-100, n=357 in 24 studies). The CTCAE Grade 3 weighted event rate was 4.5%, with 2 (0.7%) Grade 4 events observed (duodenal ulcer, dermatitis) (n=298 in 24 studies). Renal function (eGFR) decreased by 8.9 mL/min (range: +6 to -18, n=181 in 15 studies) and six patients required dialysis (2.7%; all with baseline renal dysfunction).

Conclusions: Renal SABR is well-tolerated and locally effective for inoperable primary RCC, despite the treatment of relatively large tumours. Post-SABR dialysis is rare despite pre-existing renal dysfunction in most patients. Additional prospective studies with long-term follow-up are warranted.

2

ACURA

DRIVE: DEFINING RADIORECURRENT INTRAPROSTATIC TARGET VOLUMES

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Purpose: To characterize intra-prostatic recurrence volumes as defined by PSMA-PET and mpMRI to define an optimal imaging strategy for planning focal salvage among patients with local failure after primary radiation.

Materials and Methods: PICs (NCT02793284) is a prospective trial which enrolled men with biochemical failure after primary radiotherapy for localized prostate cancer. Patients underwent a clinical mpMRI pelvis followed by a research 18F-DCFPyL PSMA PET/CT (PET). PET was reported by nuclear medicine physicians at each cancer centre with central review, and a third read occurred when reports were discordant. We analyzed mpMRI and PET images of patients with localized prostatic disease. Qualitative assessment included quadrant (right superior, right inferior, left superior, left inferior) involvement as reported by the relevant Medical Imager. MIMfusion (MIM Software, Cleveland, OH) was used to co-register the mpMRI and PET/CT images for quantitative analysis. mpMRI lesions were delineated using manual contouring with reference to the clinical reports and with radiologist review. PET volumes were generated using a threshold of 30% of maximum SUV. Concordance between quadrant involvement and lesional volumes by mpMRI and PET were evaluated.

Results: Forty one out of 79 (52%) trial patients were found to have isolated intra-prostatic recurrence. mpMRI and PET detected intra-prostatic lesions in 33/40 (83%) and 39/41(95%) patients, respectively. There were seven patients with a lesion on PET but not MRI and two with a lesion on MRI but not PET. On mpMRI, 15/40 (38%) patients had suspected disease in one quadrant, 13/40 (33%) had involvement in two quadrants, 2/40 (5%) in had involvement in three quadrants, and 3/40 (8%) had involvement all four quadrants. In comparison on PET, 23/41 (56%) had involvement in one quadrant, 16/41 (39%) had involvement in two quadrants, 1/41 (2%) had involvement in three quadrants, and 2/41 (5%) had involvement in all four quadrants. Disease involvement by quadrants detected on PET and mpMRI were discordant in 20/40 (50%) patients. Lesion delineation using a 30% maxSUV threshold on PET delineated substantially larger lesion volumes (23.3cc) compared to mpMRI (2.4cc). PET contours frequently were non-contiguous and extended outside of the prostate. Low overall SUVmax and presence of brachytherapy seeds seemed to be associated with poorly defined lesional borders on PET.

Conclusions: Both PSMA-PET and mpMRI detected disease in the majority of patients. Most patients had involvement of less than half the prostate, suggesting a potential role of focal salvage. The quadrants involved as detected by mpMRI and PSMA PET were discordant in 50% of patients suggesting mpMRI and PET may be complimentary for planning salvage treatments. Further refinement of lesion delineation guidelines on PET beyond a fixed %SUV threshold is required.

3

ELECTROMAGNETIC RECONSTRUCTION OF CATHETER PATHS IN BREAST BRACHYTHERAPY

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Purpose: Accelerated partial breast irradiation (APBI) is an appropriate treatment option for women diagnosed with early stage breast cancer and treated with breast conservation surgery. Many techniques can be used for APBI, including multi-catheter interstitial breast brachytherapy (MCIBB). Catheter reconstruction can be a laborious process and may be prone to human error. To validate the position of the catheters post implantation, we propose using electromagnetic (EM) reconstruction to help with catheter identification. We evaluated the technology in two imaging suites where brachytherapy procedures are performed.

Materials and Methods: Twelve soft plastic phantoms were created, each with a simulated tumour bed visible on both CT and ultrasound. These phantoms were implanted with 7-10 catheters under ultrasound guidance. We tested our open-source EM reconstruction method in two breast brachytherapy rooms to best simulate working conditions. Each room had a CT scanner

from a different manufacturer.
The EM reconstruction procedure involved guiding a small electromagnetic sensor through each of the individual catheters and recording its positions. Using 3D slicer (www.slicer.org), an open source platform, we reconstructed the paths of the catheters. CT scans of the phantoms were acquired and superimposed over the reconstructed paths. The accuracy of the reconstructed paths was determined by measuring the distance between the EM reconstructed path to the catheter paths generated from the CT scans.

Results: We implanted 53 catheters in seven phantoms for room 1. The mean error in room 1 was 2.0 mm ±1.2 mm (median 1.8mm, interquartile range 1.1 [1.3-2.4] mm), which was higher than the voxel size of the CT scans (voxel size=1.2mm). In room 2 we implanted 48 catheters in five phantoms. For room 2, the average deviation between the planned and reconstructed catheters paths was 0.6 mm ±0.2 mm (median 0.5 mm, interquartile range 0.3 [0.4-0.7] mm). This was significantly lower than the voxel size for CT scans (p=0.001).

Conclusions: We have found that EM reconstruction can be as accurate as a CT for identifying catheter paths for MCIBB implants. This technology is valuable because it does not introduce additional radiographic exposure for patients and can be easily incorporated into clinical planning workflow. We have found that the surrounding environment may affect the accuracy of the reconstruction. The differences in the mean errors between each room was most likely caused by the presence of different imaging equipment and magnetic field distortions. However, this difference typically nears the resolution of CT-based planning. Further research is required to improve the robustness of EM reconstruction in preparation for evaluation on patients.

4
SAFETY AND EFFECTIVENESS OF STEREOTACTIC ABLATIVE RADIOTHERAPY FOR ULTRA-CENTRAL LUNG CANCER: A SYSTEMATIC REVIEW

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Purpose: The safety and effectiveness of stereotactic ablative radiotherapy (SABR) for patients with ultra-central lung tumours is currently unclear. We performed a systematic review to summarize existing data and identify trends in treatment-related toxicity and local control following SABR in patients with ultra-central lung lesions.

Materials and Methods: We performed a systematic review using the PRISMA guidelines. The PubMed and Embase databases were queried from dates of inception until September 2018. Studies in the English language that reported treatment-related toxicity and local control outcomes post-SABR for patients with ultra-central lung lesions were included. Ultra-central lung lesions were defined as lesion whose gross tumour volume (GTV) or planning target volume (PTV) abutted or invaded the proximal tracheo-bronchial tree (PBT) or other mediastinal structures such as the great vessels or esophagus. Guidelines, reviews, non-peer reviewed correspondences, studies focused on re-irradiation and studies with fewer than five patients were excluded.

Results: A total of 446 studies were identified, with 10 meeting all criteria for inclusion. A total of 250 patients with ultra-central lung lesions were included. All studies were retrospective in design. Radiotherapy dose and fractionation ranged from 30-60 Gy in 3-12 fractions, with median biologically-effective doses (BED_{10}) ranging from 78-103 Gy_{10} in individual studies. Median treatment-related Grade ≥3 toxicity was 10% (range: 0-50%). Median treatment-related mortality was 5% (range: 0-22%). The most common form of treatment-related mortality was pulmonary hemorrhage (55%). High-risk indicators for SABR-related mortality included gross endobronchial disease, maximum dose to the PBT ≥180 Gy_3 (BED_3, corresponding to 45 Gy in 5 fractions or 55 Gy in 8 fractions), peri-SABR Bevacizumab use, and antiplatelet/anticoagulant use. Median one-year local control rate was 96% (range: 63-100%) and two-year local control rate was 92% (range: 57-100%).

Conclusions: SABR for ultra-central lung lesions appears feasible with good local control outcomes. There is a potential for severe toxicity in patients receiving high doses to the PBT, those with endobronchial disease, and those receiving bevacizumab or anticoagulants around the time of SABR. Prospective studies are required to establish the optimal doses, volumes and normal tissue tolerances for SABR in this patient population.

5
PREDICTING RADIATION ADVERSE EFFECTS USING THREE-DIMENSIONAL DOSE AND FRACTIONATION DATA: RADIATION DERMATITIS

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Purpose: Predicting the radiation dose-toxicity relationship is important to patients, as iatrogenic toxicities affect patient's quality of life. Patients need accurate estimates of both treatment efficacy and toxicity risk to make informed decisions about a proposed treatment. QUANTEC uses point dose-volume, and mean doses to predict radiation induced toxicities. These models do not account for major factors known to affect organ toxicity, such as dose per fraction, radiation field volume, and anatomic location of the dose within the organ of interest. This study evaluates utilizing 3D dose images, and fractionation data to predict radiation dermatitis in patients undergoing whole breast radiotherapy.

Materials and Methods: One hundred and sixty patients underwent whole breast radiotherapy for ductal carcinoma in-situ or early stage breast cancer following breast conserving surgery. Patients were randomly separated into training or validation datasets. Three-dimensional radiation dose images, and fractionation data were used to train a modified three-dimensional squeeze excitation residual neural network to predict radiation dermatitis grade. Receiver operating characteristic analysis was used to assess the model's performance.

Results: Sixty-seven patients had Grade ≥2 radiation dermatitis, and 93 patients had Grade ≤1 radiation dermatitis. The predictive model discriminated between radiation dermatitis Grade ≤ 1 from Grade ≥2 with an area under the curve (AUC) of 0.80 on the training dataset, and an AUC of 0.81 on the validation dataset.

Conclusions: We have developed the first normal tissue complication probability model that utilizes 3D dose images and radiotherapy fractionation data to reasonably predict radiation dermatitis in patients undergoing whole breast radiotherapy. With advancements in 3D computer modelling, radiation oncologists will be able to better predict the probability and severity radiation toxicities compared to historical point dose-volume and mean dose toxicity models currently used in practice. With improved toxicity predictions, patients and physicians will be able to make more informed treatment decisions.

6

NOVEL X-RAY ACTIVATED PHOTODYNAMIC (RADIOPDT) NANOPARTICLES FOR DEEP SEATED TUMOURS

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Purpose: Current challenges in prostate radiotherapy (RT) involve balancing the benefits of higher dose with minimizing toxicity to nearby organs-at-risk. Photodynamic therapy (PDT) uses photosensitizers (PS) that, when exposed to light, generate reactive singlet oxygen species (ROS) to cause remarkable tumour cytotoxicity. The dependence on activating light limits PDT's use in deep seated cancers. RT has unlimited depth penetrance, making radiation-activated PDT (radioPDT) advantageous in treating deep seated tumours without increasing toxicity. Using nanoscintillators (NSC), X-rays is converted to light for PDT. High atomic number NSCs also have diagnostic potential with CT for image-guided RT (IGRT). We investigate our novel radioPDT nanoparticle (NP) for diagnostic and therapeutic effect in vitro and in vivo.

Materials and Methods: RadioPDT NP were synthesized by encapsulating LaF_3: Ce^{3+} NSCs and a clinically used PS (PPIX) into FDA approved nanocarriers (PEG-PLGA). NP toxicity was assessed with I.V. administration in C57/BL mice assessing for signs of toxicity and post-mortem analysis after 48 hours. RadioPDT therapeutic potential was evaluated via ROS yield and using PC3 prostate cancer cell viability assay under varying RT doses (0 to 10 Gy) using a Xstrahl orthovoltage irradiator (Camberley, U.K.). In vivo trials investigated PC3 flank tumour-bearing NSG mice treated with 6Gy x1 via an Xstrahl Small Animal Radiator (SARRP). Mice were grouped into control, RT only, NP injected intratumourally, and RT+NP, and following tumour size for 40 days or early mortality. Primary endpoint was tumour response and secondary endpoint was overall survival. Diagnostic tests used a Siemens Inveon CT (Erlangen, Germany) to scan phantoms and tumour-bearing mice, and compared Hounsfield Units (H.U.) between NPs versus Omnipaque 300® (GE Healthcare, Chicago, USA).

Results: Inactive radioPDT NP showed no toxicity in vitro and in vitro to normal tissue or cancer cells at doses up to 1000mg/kg. RT-activated radioPDT NPs showed increased ROS production and increased cell-killing by up to 50% ($p<0.001$) over RT alone. In vivo studies showed no difference in tumour growth between control and NP alone, and a two week delay in tumour progression with RT ($p=0.006$). RT+NP performed the best with near complete tumour response, which was significantly better than RT alone ($p=0.006$), and extended median survival to 56.5 days from 36 days, respectively ($p=0.010$). Diagnostic studies with a phantom showed similar contrast efficiency to Omnipaque (62.2 versus 46.01 H.U./mg/ml, ns). The NPs were easily seen intratumourally on CT studies, with average tumour signal increase of 20 H.U.

Conclusions: In vitro and in vivo studies show radioPDT significantly increases therapeutic effect of RT, with minimal toxicity increase. Good in vivo CT diagnostic performance also aided in IGRT using the SARRP. Future studies will look at NP biodistribution, dosing, and RT dose/fractionation schemes.

7

CARO ACURA 2013

MRI-GUIDED FOCAL SALVAGE HDR BRACHYTHERAPY FOR LOCALLY RECURRENT PROSTATE CANCER

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Purpose: Biochemical failure may occur in up to 40% of patients treated with external beam radiotherapy (RT) alone for localized prostate cancer. A proportion of these may be associated with intraprostatic disease recurrence alone. While efficacious, whole-gland salvage brachytherapy may be associated with significant morbidity as is the use of androgen deprivation therapy (ADT). Focal brachytherapy has recently gained more attention with the aim of reducing toxicity and may facilitate deferral of ADT. We report results of a prospective study of MRI-guided focal salvage brachytherapy.

Materials and Methods: This was a Phase II single-arm cohort study. Eligibility was pathologically proven locally recurrent prostate cancer visible on multi-parametric MRI (mpMRI) at least 18 months after primary RT with PSA-doubling time >6 months and ECOG performance status 0-1. All patients were treated with HDR brachytherapy under MR image guidance alone. Patients received a dose of 13Gy to a partial intraprostatic tumour-bearing region, repeated 7-14 days later. The GTV was defined on mpMRI (T2-weighted, diffusion-weighted and dynamic contrast-enhanced sequences). CTV margin expansion (5 mm in all directions) was restricted to adjacent organs at risk and 2 mm beyond the prostate boundary where applicable. PTV margins of 2 mm cranio-caudally and 1mm elsewhere were then applied. No patients were given ADT. Patients were followed with regular PSA, and mpMRI +/- prostate biopsy were performed after a minimum of two years. Toxicity was assessed using Common Terminology Criteria for Adverse Events (v4). Biochemical relapse was defined using Phoenix definition (nadir +2).

Results: A total of 29 patients (median age 71 years, range 62-85) were enrolled. Median PSA pre-salvage was 3.93 (1.68 – 14). Two patients had Gleason 6 disease on pre-salvage biopsy, 19 with Gleason 7, five Gleason 8 and three Gleason 9. Median follow-up was 41 months (6 – 68). Median PSA nadir prior to disease recurrence was 0.54 (<0.05 – 3.32) and time to nadir was 27.3 months (7 – 66). Crude rates of biochemical control at two years was 83% (19/23) and 58% (8/19) at three years. Seventeen patients were eligible and agreed to post-salvage MRI and/or biopsy. Of these, six (35%) had localized recurrence confirmed, four of which were within the treated salvage volume. GU and GI symptoms (<G2) were reported in eight and five of all patients respectively at one-month follow-up. Five reported continual GU and two GI symptoms of the 24 patients that had completed one year follow-up (≤G2). All patients are currently alive, five have confirmed metastases and seven are on ADT. Only three of the eight patients with Gleason 8/9 disease have disease control.

Conclusions: MR-guided focal salvage brachytherapy appears to provide good local disease control in selected patients with low rates of late toxicity. Further dose escalation to the tumour may be considered but other methods for appropriate patient selection beyond PSA dynamics and Gleason score are also needed.

8

STEREOTACTIC BODY RADIOTHERAPY AND PRECISION HYPOFRACTIONATED RADIOTHERAPY VERSUS SURGERY FOR STAGE I NON-SMALL CELL LUNG CANCERS: AN 11-YEAR REVIEW OF A PROVINCIAL CANCER REGISTRY

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Purpose: Surgery is currently the standard management for resectable Stage I non-small cell lung cancers (NSCLC). Stereotactic body radiotherapy (SBRT) and precision hypofractionated

radiotherapy (hypoRT) have shown promising outcomes. Large randomized trials comparing the modalities have yet to be completed. The objective of this study is to compare the provincial outcomes of patients treated with SBRT/hypoRT to those treated with surgery.

Materials and Methods: We conducted a retrospective analysis of all provincial patients with Stage I NSCLC who underwent surgery or SBRT/hypoRT (biological equivalent dose of at least 84 Gy), from 2006 to 2016. Baseline patient, tumour, treatment and clinical outcome data were collected from the British Columbia Cancer Registry. Overall survival (OS) and cancer specific survival (CSS) were analyzed using Kaplan-Meier method. We further analyzed patients based on age, with 75 as cut off for older population. Cox regression analysis was performed to identify predictors of outcomes.

Results: Among 1230 patients, 235 (19.1%) were treated with SBRT/hypoRT and 995 (80.9%) with surgery. 158 (12.2%) patients received 48Gy in 4Fx, 42 (3.4%) 60Gy in 8Fx, 35 (2.8%) 60Gy in 15Fx. 783 (63.7%) patients underwent lobectomy, 28 (2.3%) pneumonectomy, 184 (15.0%) sub-lobar resection. The median age was 69, with 339 (27.6%) age >75. The median follow-up was 26.2 months for SBRT/hypoRT and 29.4 months for surgery. The two- and five-year OS were 73.8% and 27.7% for SBRT/hypoRT, and 78.4% and 36.1% for surgery, with no significant difference between the groups (p=0.182). Differences in OS were not significant among the radiotherapy dose fractionations (p=0.653) or the surgery types (p=0.193). Comparing SBRT/hypoRT to surgery, significant differences in OS were not detected for patients age <75 (p=0.299) nor >75 (p=0.224). The two- and five-year CSS were respectively 85.2% and 54.3% for SBRT/hypoRT, and 81.1% and 42.2% for surgery, with improved outcomes in the SBRT/hypoRT group (p=0.004). Patients age >75 had greater CSS with SBRT/hypoRT (p<0.001), with no significant difference in patients age <75 (p=0.077). On multivariate analysis, there was no significant indicator of improved OS found for the SBRT/hypoRT group. For the surgery group, age <75 (p<0.001) predicted for better OS while ECOG (ref=0) 2 (p=0.041), 3 (p<0.001), 4 (p<0.001) predicted for worse.

Conclusions: At a registry level, SBRT/hypoRT achieves OS outcomes similar to surgery. Improved CSS is observed in the SBRT/hypoRT cohort, notably for patients age >75. Further evaluation in large randomized studies is warranted.

9 CARO FELLOWSHIP
KNOWLEDGE-BASED PLANNING TO IMPROVE AND AUTOMATE PATIENT-SPECIFIC RADIOTHERAPY QUALITY ASSURANCE PROCEDURES IN CLINICAL TRIALS - SECONDARY ANALYSIS OF CCTG HN6

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Purpose: Radiotherapy (RT) quality assurance (QA) is a critical component of clinical trials; current RTQA methods are rule-based and do not account for what dosimetry is achievable for a specific patient. To improve and individualize the RTQA process, we are developing a knowledge-based (KB) QA process utilizing RT plans submitted in the CCTG HN6 trial (NCT00820248), which was a multicentre Phase III study comparing standard-fractionation RT plus high-dose Cisplatin versus accelerated-fractionation RT plus Panitumumab in patients with locally advanced head and neck (H&N) cancers (Siu, JAMA Oncol 2017).

Materials and Methods: Eclipse Rapidplan™ KB planning software was utilized to replan the cases submitted in the HN6 trial. The planning target volume (PTV) coverage was normalized so the PTV_{70} $V_{100\%}$ was equivalent for the investigator-submitted (IS) and replanned cases. Dosimetric endpoints were compared for PTV's and organs-at-risk (OAR), and two-sided Wilcoxon signed rank test was used with a p value of <0.05 to determine statistically significant differences.

Results: The HN6 trial included 320 Canadian patients randomized between December 30, 2008 and November 7, 2011. Among the 315 cases submitted for protocol-specified RTQA review by the Quality Assurance Review Center (Rhode Island), a preliminary analysis was performed on 50 cases. All 50 cases were originally planned with IMRT or VMAT, and were replanned with 9-field IMRT using the WUSTL Rapidplan™ H&N model. Target coverage and homogeneity metrics were similar between the IS and KB plans, as measured by mean PTV70 $D_{99\%}$ (68.4 versus 68.8 Gy, p=0.014), mean PTV70 $D_{95\%}$ (70.4 versus 70.5 Gy, p=0.077), mean PTV70 D_{max} (78.2 versus 77.5 Gy, p=0.015), mean PTV56 $D_{99\%}$ (55.0 versus 55.9 Gy, p<0.001), mean PTV56 $D_{95\%}$ (56.6 versus 57.2 Gy, p<0.001), and mean PTV56 D_{max} (71.8 versus 70.9 Gy, p<0.001). OAR dosimetry was similar between the IS and KB plans for the following endpoints: brainstem D_{max} (43.0 versus 42.4 Gy, p=0.246), spinal cord D_{max} (43.4 versus 43.6 Gy, p=0.412), ipsilateral parotid D_{mean} (40.0 versus 37.4 Gy, p=0.079), contralateral parotid D_{mean} (28.1 versus 28.4 Gy, p=0.779), composite salivary gland D_{mean} (36.9 versus 35.5 Gy, p=0.119), larynx D_{max} (64.2 versus 65.1 Gy, p=0.184) and mandible D_{max} (73.4 versus 72.4 Gy, p=0.841). KB plans showed improved OAR sparing for the following endpoints: larynx D_{mean} (51.6 versus 42.3 Gy, p<0.001) and oral cavity D_{mean} (43.2 versus 35.1 Gy, p=0.002).

Conclusions: Preliminary analysis of the first 50 HN6 cases demonstrate the feasibility of KB planning to produce acceptable H&N RT plans with a high degree of automation, with comparable plan quality to IS plans. Further work is underway to analyze the entire dataset, and correlate suboptimal dosimetry with clinical toxicities observed in the HN6 trial. Based on the observed dosimetric variation and potential impact on clinical outcomes, case-specific criteria for protocol deviations will be proposed for a KBQA process in H&N clinical trials.

10
THE IMPACT OF DOSE TO BLADDER NECK ON URINARY TOXICITY IN PATIENTS TREATED WITH HDR BRACHYTHERAPY BOOST FOR PROSTATE CANCER

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Purpose: To evaluate whether the dose to bladder neck is a predictor of urinary toxicity after High Dose-Rate Brachytherapy (HDRB) for prostate cancer.

Materials and Methods: Between 2014 and 2016, 313 patients with intermediate and high-risk prostate cancer were treated in our institution and reviewed. They received external beam radiation therapy 37.5 Gy /15 to 44 Gy /22 (EBRT) and 15 Gy single fraction HDRB boost. Intraoperative CT scan-based inverse planning (CT) was performed in 173 patients and ultrasound-based inverse planning (US) was used in 140. The following structures were prospectively contoured: prostate, urethra, rectum, bladder and the bladder neck. The bladder neck is defined as 5 mm around the urethra between the catheter balloon and the prostatic urethra.

The dose to the bladder neck was only reported and no constraint was applied. The International Prostate Symptom Score (IPSS) at six weeks and six months and urinary obstruction rate were used to report acute and late urinary toxicity, respectively. Clinical and dosimetric factors associated with urinary toxicity were analyzed using multivariate generalized linear model including pretreatment IPSS, bladder neck D2cc and prostate volume as covariates.

Results: Mean age and median follow-up were 69.9 years and 25 months, respectively. The mean pretreatment PSA was 9.30 ng/ml. According to D'Amico definition 70% were intermediate risk and 30% high-risk. The mean prostate volume was 57.5 cc. The mean pretreatment, six weeks and six months IPSS were 8.35, 12.24 and 9.97 respectively. We observed 17 cases (5.34%) of GU obstruction in our cohort of patients. Pretreatment IPSS was significantly associated with acute and late urinary toxicity ($p<0.001$). Prostate volume was also associated with acute ($p=0.013$) and late urinary toxicity ($p=0.024$). The dose for the most exposed 2cc (D2cc) of bladder neck was not correlated with acute mean IPSS 12.24 ($p=0.737$) or late mean IPSS 9.97 ($p=0.785$). There was also no correlation between D2cc and urinary obstruction 8.5 Gy versus 7.5 Gy ($p = 0.191$). Even if the mean D2cc was higher in the US group 10.1 Gy versus 7.6 Gy CT $p < 0.00001$ it was also not correlated with GU acute/late toxicity and urinary obstruction.

Conclusions: The pretreatment IPSS and prostate volumes remained the only predictors of acute and late urinary toxicity after HDRB boost in our study. Although bladder neck D2cc was correlated with acute and late urinary toxicity after low-dose rate brachytherapy, bladder neck D2cc was not associated with urinary toxicity after HDRB boost. These results could be explained by the fact that the dose the bladder is not optimize in the LDR technique. These findings are not influenced by the HDR technique used (CT versus US).

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PROSTATE BED TREATMENT INTENSIFICATION WITH LONG TERM ANDROGEN DEPRIVATION AND PELVIC NODAL RADIOTHERAPY IS EFFECTIVE AND WELL TOLERATED: RESULTS FROM THE MCGILL 0913 PHASE II CLINICAL TRIAL

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Purpose: After radical prostatectomy (RP), pathological features of high-risk prostate cancer and a detectable prostate-specific antigen (PSA) signify an increased risk of recurrence. RTOG 9601 and SPPORT demonstrated further benefit in subsets of such patients by adding long-term androgen deprivation therapy (LTADT) or pelvic nodal radiotherapy (PNRT) to prostate bed radiotherapy (PBRT). However, toxicity increased with therapy intensification. McGill 0913 quantified the safety and efficacy of intensifying PBRT in high-risk patients with the combination of LTADT and PNRT.

Materials and Methods: Following RP, patients with a diagnosis of high-risk disease (pT3 or Gleason 8) were enrolled in this single-arm prospective Phase II trial. Patients received 24 months of LTADT and radiotherapy commenced 8-12 weeks into LTADT. Intensity modulated radiotherapy provided 44Gy in 22 fractions of PNRT then a 22 Gy in 11 fraction boost to complete PBRT. Primary endpoints were freedom from biochemical failure (FFBF) (PSA nadir + 0.3 µg/L) or clinical progression. Secondary endpoints included local and distant failure rates, toxicity as per Common Toxicity Criteria, and Quality of Life (QoL) as per the EORTCQL30's visual analog score. Statistical methods employed included a Kaplan-Meier analysis for FFBP, a Wilcoxon signed rank test for ordinal data, an unpaired t-test for continuous data, and a chi-square proportion test for binary data.

Results: From August 2010 to May 2015, 46 patients were enrolled, 43 were treated as per protocol and two were lost to follow-up. The median PSA was 0.30 µg/L (IQR 0.20-0.47), 52% had positive margins, 40% had at least Gleason 8 disease, and 19% had lymph node involvement. At a median follow-up of 5.2 years, FFBF was 97.1, 90.3, and 71.0% at three, four, and five years, respectively. No patients had clinical progression. Among the seven patients with biochemical failure, only two completed two years of LTADT and three maintained castrate levels of testosterone (<0.7 nM) on LTADT, with no statistical difference between the groups ($p=0.24$ and $p=0.23$, respectively). Univariate analysis appreciated no statistical relationship between FFBP and any baseline variable, including Gleason score, PSA, T stage, or N stage. Adverse effects (AEs) and severity included sexual dysfunction for all men on ADT, 14% Grade 2 endocrine AEs while on ADT, one incident of long term gynecomastia, 5% Grade 2 acute urinary AEs, 5% Grade 2 late urinary AEs, and no Grade 3 AEs. The average and minimum QoL reported during LTADT were statistically similar, though the minimum QoL was more heterogeneous (baseline = 8.2, $\sigma=1.2$; average = 8.1, $\sigma=1.5$; minimum = 7.6, $\sigma = 2.0$).

Conclusions: Salvage therapy was intensified with both PNRT and LTADT in a cohort of patients at high-risk of relapse with robust FFBP being observed. Few AEs and only minor decreases in QoL suggest treatment was well tolerated. Intensification of PBRT with PNRT and LTADT in high-risk patients was efficacious and well tolerated.

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IMPACT OF COMPLIANCE ON OUTCOMES FOR PATIENTS ON ACTIVE SURVEILLANCE FOR PROSTATE CANCER

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Purpose: Active surveillance (AS) is the standard of care for low-risk prostate cancer (PCa) to reduce the risk of overtreatment. Compliance with repeat biopsies required on AS is low. The purpose of this study is to determine the impact of compliance with biopsies on PCa-specific outcomes.

Materials and Methods: A review of a large, mature, single-institution prospective cohort of 1,275 patients on AS for PCa was performed to determine compliance rates with biopsies. Compliance with the confirmatory (one year) biopsy was used as a surrogate for overall compliance. The primary outcomes were recurrence after treatment and the development of metastases. Recurrence was defined as PSA > 0.2 after surgery, PSA > nadir + 2 after RT, subsequent treatment for progression or the development of metastases.

Results: Amongst the 1,275 patients included, 453 (36%) received treatment for their PCa, metastases were diagnosed in 36 patients (3%) and 22 patients (2%) died of PCa. Median follow-up was 7.8 years. Compliance rates with biopsies at years one, four and seven were 74%, 52% and 43%. Non-compliant patients (to the confirmatory biopsy) were older than compliant patients ($p<0.001$) but there was no difference in baseline PSA scores ($p=0.33$) or Grade Group ($p=0.14$). In the cohort of treated patients, non-compliance resulted in higher rates of recurrence (41% versus 26%, OR=2.0, $p=0.001$) even after accounting for age, PSA and Grade Group. The risk of developing metastases was impacted by non-compliance (OR=4.1, $p<0.001$) and Grade Group (OR=3.2, $p=0.001$) but not by age ($p=0.4$) or baseline PSA ($p=0.5$).

Conclusions: Non-compliance with the confirmatory biopsy leads to poorer oncologic outcomes including higher rates of recurrence and metastases for men on AS for PCa. Patients

should be counseled about these risks when enrolling in AS and during follow-up.

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COMPARISON OF FIDUCIAL MOTION IN LIVER STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR) PATIENTS USING 4DCT, AND FLUOROSCOPY

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Purpose: Information about tumour movement for liver SABR planning and treatment is obtained from a 4-dimensional CT (4DCT) and 2D fluoroscopy assessments of implanted fiducial (fid) motion at our centre. This information guides treatment planning, choice of treatment technique. This study compares liver fid motion during dynamic tracking treatments (DTT) with pre-treatment motion as assessed on 4DCT and fluoroscopy. Data is reported from 26 patients who received liver SABR DTT between October 2017 and February 2019.

Materials and Methods: Liver SABR patients have a pre-treatment fluoroscopic assessment on the Brainlab Vero linac. 3D motion statistics of the implanted fids are generated following automatic detection of the fids by the integrated Exactrac imaging system. All patients receive a respiratory correlated 4DCT that is retrospectively binned into 10 phases of the breathing cycle. The sup/inf motion of the fids over 10 phases is recorded. All sources of fid motion data is analyzed as follows: 1) 3D motion characteristics based on pre-treatment fluoroscopy; 2) pre-treatment fluoroscopy assessment motion compared to 4DCT; 3) pre-treatment fluoroscopy assessment motion compared to On-treatment DTT motion; and 4) intra-fraction variation in patient FID motion during DTT.

Results: 1) General 3D motion characteristics of the dynamic tracking patient population: From the pre-treatment VERO fluoroscopy assessment, fid motion ranged from 0.4 - 9.7 mm (avg 3.3+/-2.7 mm) left/right, 2.2 – 15.5 mm (avg 5.6 +/-3.4 mm) ant/post, and 9.0 – 32.0 mm (avg 17.8+/-5.8 mm) sup/inf for all patients. 2) Comparison of pre-treatment Vero fluoroscopy assessments and 4DCT fid motion statistics: The average discrepancy between the fluoroscopy and 4DCT fid motion in the sup/inf direction is -0.2+/-6.5 mm [min, max: -13.9, 13.0 mm]. 3) Comparison of pre-treatment Vero fluoroscopy assessment and On-treatment dynamic tracking motion statistics: The average discrepancy between the pre-treatment motion and the on-treatment motion is 0.3+/-6.8 mm [min, max: -19.5, 31.9 mm]. 4) Intra-fraction fid variation: The maximum intra-fraction variation (standard deviation) of fid motion over 26 patients is 3.8, 3.2, and 8.9 mm in the left/right, ant/post, and sup/inf direction respectively. In the sup/inf direction, 72% of patients had a standard deviation of < 5mm.

Conclusions: 4DCT and fluoroscopic assessments do not always accurately represent tumour motion trajectories over a treatment course of SABR radiation therapy. Employing a radiotherapy technique that can adapt to daily patient variation, such as dynamic tumour tracking, may be beneficial.

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CLINICAL OUTCOMES OF DEFINITIVE RADIATION THERAPY (RT) FOR OROPHARYNGEAL HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC) PATIENTS PLANNED WITH OR WITHOUT POSITRON EMISSION COMPUTER TOMOGRAPHY (PET-CT)

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Purpose: PET-CT is recognized for its potential to impact RT planning. Results of a previously published local study showed the use of PET-CT in the RT planning process resulted in a major change in radiation therapy plans in 40.6% of HNSCC patients. Despite the plethora of literature describing the impact of PET-CT on establishing a care plan for patients with HNSCC, the impact of incorporating a planning PET-CT in RT on clinical patient outcomes is still unclear. The purpose of this retrospective study was to elucidate the clinical value of PET-CT in comparison to CT-based RT planning alone, by examining the five-year overall survival (OS), locoregional control (LRC), and metastatic disease (MD), in two well-matched HNSCC patient groups who received definitive RT alone or combined radiation and chemotherapy (CRT).

Materials and Methods: Two databases consisting of similarly matched HNSCC patients treated with definitive RT or CRT were compared. Database 1 consisted of 83 patients who underwent CTsim and PET-CT planning scans (PET-CT group). Database 2 served as a control group, consisting of 69 patients who received CTsim planning scan only RT (CT-alone group). Both groups received MRI planning scans. To establish similarity between groups, categorical variables were analyzed with $\chi 2$ tests without continuity correction. For continuous variables both t-test and Wilcoxon rank sum test were utilized. Kaplan-Meier estimate (including censored observations) was used to examine OS and time to event (LRC & MD) for both groups.

Results: Statistical analysis showed that the two groups were homogenous with respect to patient characteristics (age, gender, disease stage, site of primary tumour, smoking, alcohol, and human papilloma virus (HPV) status), but not overall-treatment-time ($p < 0.01$) and referral-to-consult wait time ($p < 0.01$). Overall survival for both groups were similar at 57.8% and 58.0% for the PET-CT and CT-alone groups respectively. Rates of local recurrence (14.5% and 11.6%) and metastatic disease (17.4% and 19.2%) were similar for both groups respectively. Kaplan-Meier estimate for OS and LRC for the two groups showed their 95% confidence intervals overlap, indicating differences were not significant at $\alpha = 0.05$ ($p=0.7$ and $p=0.9$, respectively).

Conclusions: PET-CT has proven to significantly impact the RT planning process for HNSCC patients undergoing curative RT especially in delineating accurate TVs and upstaging of nodal status. However, our results show that PET-CT planning scans did not significantly affect OS, LRC and MD in HNSCC patients. Study findings did identify strong correlation between other variables (ie: smoking status and HPV) on patient outcomes. Further research is required to determine if nodal volumes that are indolent on CT but avid on PET-CT are perhaps sufficiently eradicated by low-risk dose levels.

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LEARNING TOGETHER; ESTABLISHING A PROVINCIALLY INTEGRATED SYSTEM FOR INCIDENT REPORTING AND LEARNING

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Purpose: In April 2018, the Provincial Health Authority adopted and imbedded the National System for Incident Reporting-Radiation Therapy Minimum Data Set (NSIR-RT MDS), into the existing reporting and learning system for two zone based radiotherapy

departments. Each department has a Radiation Treatment Quality Assurance Committee (RTQAC), reporting to the Provincial RTQAC, and subsequently into the provincial quality framework. Here we report on 10 months experience utilizing the NSIR-RT taxonomy within a provincial quality framework.

Materials and Methods: The 2017 NSIR-RT Minimal Data Set was populated as a stand-alone form within the RL Solutions incident reporting platform. Statistics were generated through the RL Solutions analytics tools based on: acute medical severity, dosimetric harm, problem type, and volume stratified by "technique" and "body regions treated". Following multidisciplinary review by the departmental incident reporting and learning team, incident analyses were completed, recommendations were captured using a provincial action items template, and shared learning was provided through case study presentations, workshops and new policy teaching sessions.

Results: Excluding the category of "other," the top three problem types were: "radiation therapy scheduling," "patient position, set-up point or shift" and "treatment accessories" related incidents. Acute medical severity coding triggered concise incident analyses which included: timelines, contributing factors and provincial and/or multidisciplinary recommendations. Combining volume trends based on "technique" and "body region treated" allowed for the rapid identification of incidents attributed to a change in treatment indications, resulting in a cascade of differing problem types, which led to policy and process revision and standardization. Four provincial and/or multidisciplinary shared learning events were created in response to incident reporting and learning.

Conclusions: We established a provincially integrated system for incident reporting and shared learning across departments. In the first 10 months of incident reporting using the NSIR-RT taxonomy, we have been able to successfully identify areas of interrelated process change, policy revision and standardization, requiring collaborative departmental action.

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THE USE OF MRI-BASED CONTOUR IN ASSESSING THE IMPACT OF HYDROGEL SPACER ON RECTAL DOSIMETRY IN PROSTATE STEREOTACTIC RADIOTHERAPY

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Introduction: The dosimetric impact of hydrogel spacer on rectum in prostate radiotherapy has been demonstrated by comparing two independent dose distributions generated based on contours delineated on CT acquired before and after its placement. However, despite using the same optimization objectives, the quality of two distributions can vary. There is also greater variability with delineation on CT. This retrospective planning study used MRI-based contours and a single dose distribution to assess the impact of hydrogel spacer on rectal dosimetry in prostate stereotactic radiotherapy.

Materials and Methods: MRIs acquired before and after the hydrogel spacer placement (MRI_{pre} and MRI_{post}), along with the CTs of 19 patients who received SBRT to the prostate were retrieved. After image registration, prostate, PTV (Prostate + 5mm), rectum and bladder were defined on both MRIs and propagated onto the corresponding CT to generate a VMAT distribution. The distribution was optimized based on the MRI_{pre} contours to deliver a total dose of 30Gy/5 while respecting the rectum constraint of V_{100} <1cm^3. Distances from the posterior surface of prostate to the anterior surface of rectum were measured at the base, midgland and apex of the prostate on both MRIs. Rectum of the MRI_{pre} and MRI_{post}, encompassed by the 95% and 50% prescription dose (V_{95} and V_{50}) were compared.

Results: In the absence of the hydrogel spacer, the range of rectum V_{100} was 0 – 2.5 cm^3, with four out of 19 patients violating the V_{100} <1cm^3 constraint. In contrary, max rectum V_{100} was reduced to 0.5cm^3 in its presence. The hydrogel spacer increased the distance (mm) between prostate and rectum by a mean of 7, 10 and 8 at the base, mid-gland and apex of the prostate, respectively. With this increased distance, the rectum V_{95} and V_{50} were reduced by a mean of 97% and 70%. In addition, eight patients had <1cm^3 of rectal wall exposed to 50% prescription dose.

Conclusions: Using the patient as their own control, use of hydrogel spacer was demonstrated to improve rectal dosimetry. The magnitude of improvement varied and further investigation is needed to identify patients who can benefit the most from this intervention.

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DEVELOPMENT AND IMPLEMENTATION OF A GROUP PEER REVIEW PROCESS TO IMPROVE QUALITY CULTURE AND FULL PLAN REVIEW COMPLIANCE

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Background: Peer review (PR) is an important tool in improving the quality and safety of radiation oncology treatment. Within our tertiary, academic radiation oncology department, PR occurs in two stages: target contour PR (tcPR) by another physician only, and full plan multidisciplinary PR (fpPR). In conjunction with several national/regional PR initiatives, the department began to track and report rates of tcPR in 2015. tcPR tasks were part of the workflow in the electronic medical record (EMR) and occurred for most curative cases. At that time fpPR was conducted weekly in rounds and one-on-one settings for about 20% of curative cases in a department treating approximately 2,500 cases per year. A model to improve plan PR for all curative cases was developed and implemented in early 2017.

Objectives: 1) To establish fpPR as a critical part of the treatment planning process and department culture; and 2) to improve the rate of PR of radiation treatment plans by building PR activities into the EMR workflow and tracking PR rates and outcomes using EMR.

Materials and Methods: A multidisciplinary group, with representatives from Radiation Oncology, Radiation Therapy, Dosimetry, and Medical Physics, developed a model of group plan PR which was implemented in January 2017. Each disease site established weekly group fpPR meetings. fpPR meetings were led by a Radiation Oncologist (RO). A questionnaire was developed within ARIA® in order to guide and document important elements of fpPR. Issues were flagged to the attending RO, for minor or major revisions. Relevant statistics including response to suggested revisions were captured via ARIA®.

Results: From 2015 to 2018, overall fpPR for curative plans increased from 20% (estimated) to 71%, ranging from 23% to 81% based on site. In terms of timing, 90% of completed reviews occurred prior to treatment or before 25% of treatment was delivered. Of the 990 plans subject to fpPR in 2018, 22 plans were flagged for changes and 10 cases were re-planned. The most common reasons for this were suggestions to edit the Clinical Target Volume, add a boost, or re-plan for a specified dose constraint. Multidisciplinary fpPR session continue weekly, and quarterly results are reported to the provincial Cancer Care Quality Assurance Committee.

Conclusions: PR is becoming integrated into department culture, through scheduled site group sessions and integration of tasks into the general workflow. Creating PR tasks as compulsory parts of the ARIA® Carepath increased compliance and provided a means of retrieving information on when and how PR occurred, and whether recommended changes were implemented. Time constraints may limit the attendance of fpPR rounds. Quarterly statistics are generated and reviewed by the local quality assurance committee, guiding future developments such as implementing a provincial PR approach, extending PR to palliative cases, following up on recommendations made during PR, and monitoring impact on outcomes.

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PILOT STUDY TO ASSESS SAFETY OF THE NOVEL CARA BREAST SUPPORT FOR SUPINE ADJUVANT BREAST RADIOTHERAPY

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Purpose: A carbon-fiber adjustable reusable accessory (CARA) for breast positioning was designed to reduce the inframammary fold (IMF), and thereby moist desquamation, for breast radiotherapy (RT) patients with large, pendulous breasts treated in the supine position. Here we report on a twenty patient pilot investigating the safety of this device.

Materials and Methods: Eligible patients received supine breast +/- regional lymph node RT and had a treatment position IMF of >= 1 cm. Patients were simulated with and without the CARA, and were treated with the CARA. Standard dose constraints were used. Treatment delivery was performed using a step and shoot IMRT technique for prescribed doses of 42.5 Gy in16 fractions or 50 Gy in 25 fractions. Skin folds and dose volume statistics with and without the CARA were compared. Skin reaction was assessed using a modified 7-point scale derived from NCI CTCAE V 4, to quantify the area of moist desquamation in folds, during and up to two weeks post-RT.

Results: In the nine eligible, consented patients to date, body mass index ranged from 26 to 52 and five were left breast patients. All IMF folds were eliminated with the CARA, as confirmed on imaging. Skin remained intact without moist desquamation in the IMF for 34% of patients assessed. For those experiencing moist desquamation, the affected area was <25 % of the unsupported breast skin fold area. V107% body was reduced in six of nine of cases with CARA. Planning constraints were met for heart in nine of nine cases, lung in eight of nine cases, and breast and nodal coverage in nine of nine cases. In the single breast + regional lymph node case where the lung dose constraint was not met with the CARA, this was also true for the plan without the CARA.

Conclusions: This study shows that patients were safely treated with the CARA and the IMF was reduced in all cases. The degree of moist desquamation was reduced in comparison with historical data for this patient population. Further testing of the device in a randomized trial is supported.

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STEREOTACTIC BODY RADIOTHERAPY FOR LARGE PRIMARY LARGE RENAL CELL CARCINOMA: A REPORT FROM THE INTERNATIONAL RADIOSURGERY ONCOLOGY CONSORTIUM FOR KIDNEY (IROCK)

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Purpose: Thermal ablation is an established option for small renal cell carcinomas (RCC). However, patients with larger (T1b, >4cm) RCC not suitable for surgery have few treatment options as thermal ablation is less effective in this setting. This study evaluates clinical outcomes after stereotactic body radiotherapy (SBRT) in this cohort.

Materials and Methods: Individual patient data from nine IROCK institutions in Germany, Australia, USA, Canada and Japan were pooled. Outcomes from larger RCC were compared to small RCC. Patients with metastatic disease or urothelial histology were excluded from the database (n=31). Demographics, treatment, oncologic and renal function outcomes were compared between cohorts using the Chi-square test, Fisher's exact test, two-sample T-test, or Wilcoxon rank sum test as appropriate. Kaplan-Meier estimates and univariable and multivariable Cox proportional hazards regression were generated for oncologic outcomes.

Results: There were 95 patients with larger RCC identified from 192 eligible patients. Median follow-up was 2.5 years. Median tumour size in the larger RCC group was 4.9 cm compared to 2.9 cm in the small RCC group. In the overall cohort, normal renal function (eGFR >90mL/min) at baseline was recorded in 9.0% of patients, with 26% having moderate to severe dysfunction (eGFR <45mL/min). Patients with large RCC were of poorer performance status (ECOG 0-1 in 81.1% versus 93.8%, p=0.008) and were older (mean age: 75 years versus 69 years, p<0.001). Toxicities ≥ Grade 2 occurred in 12 patients (6.3%) with no differences in toxicity rates between cohorts (p=0.526). Median baseline eGFR was lower in the larger RCC cohort (59.0 mL/min versus 68.5 mL/min, p=0.013), and demonstrated a median reduction post-SBRT of -5.8 mL/min versus -2.9 mL/min, p=0.073). There were eight recurrences (8.4%) in larger RCCs, compared to one recurrence (1.0%) in the small RCC cohort. Local control at one year was 100% in both cohorts, and at three years was similar at 96.6% versus 98.5%, respectively (log-rank p=0.512). Distant control was worse in larger RCC at one and three years, at 97.8% versus 100% and 87.0% versus 100% respectively (log-rank p=0.006). Cancer-specific survival (CSS) at three years was 91.4% versus 96.2% (log-rank p=0.224). Overall survival (OS) at three years was 72.3% versus 84.6% (log-rank p=0.294). On multivariable analysis, higher pre-SABR creatinine (hazard ratio [HR] per 10 µmol/L: 1.08, p=0.002) and poor performance status (HR: 3.85, p=0.004) were associated with inferior OS. Increasing tumour size (HR per 1 cm: 1.18, p=0.028) was associated with inferior CSS.

Conclusions: SBRT for larger RCC appears tolerable and similarly locally effective as in small RCC, although associated with a higher likelihood of metastatic progression and death. Efforts to reduce risk of distant recurrence, such as adjuvant systemic therapy, should be further investigated.

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CARO ACURA
PRELIMINARY RESULTS OF A TWO STAGE PHASE II STUDY OF 18F-DCFPYL PET-MR FOR ENABLING OLIGOMETASTASES ABLATIVE THERAPY IN SUBCLINICAL PROSTATE CANCER
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Purpose: Despite maximal local therapies (MLT) (radical prostatectomy followed by radiotherapy [RT]), 20-30% of men will have incurable progression of prostate cancer (PC). Most recurrences in this scenario are characterized by continuous PSA rises and failure of standard imaging (bone scan [BS] and computed tomography [CT]) to detect recurrence sites. We conducted a Phase II trial for men with rising PSA after MLT using 18F-DCFPyL PET-MR/CT followed by targeted ablation of PET positive foci. We report the results of our pre-defined analysis.

Materials and Methods: Patients with rising PSA (0.4 – 3.0 ng/mL) after MLT, negative BS/CT and no prior salvage ADT were eligible. All patients underwent 18F-DCFPyL PET-MR followed by immediate PET-CT acquisition. Those with limited disease, where possible, underwent stereotactic ablative RT (SABR) or surgery. No ADT was used. The primary endpoint was biochemical response rate (complete [undetectable PSA] or partial [PSA decline ≥50% compared to baseline]). A Simon's two stage study design was employed. Stage 1 included 12 response-evaluable patients, requiring one or more responses in the absence of Grade 3+ toxicities to proceed to Stage 2 (additional 25 response-evaluable patients).

Results: After a median of 58 months (range 29-120) post MLT, 20 patients underwent PET-MR/CT to have 12 response-evaluable patients. Median PSA at enrollment was 1.3 ng/mL (range 0.4-2.8). Three patients had negative PET-MR/CT, while 17 had positive scans, of which 12 (60%) were amenable to response-evaluable ablation. The median number of detected lesions in those treated was 2 (range 1-5). Ten patients underwent SABR (27-30 Gy / 3 fractions) and two had surgery. One patient (8%) had complete and four (33%) had partial PSA responses at a median of 3.3 months (range 2.8-6.0) after ablation, while the remaining seven (59%) did not have biochemical response. No Grade 3+ toxicities were observed.

Conclusions: 18F-DCFPyL PET-MR/CT has high detection rates in men with rising PSA after MLT. We observed favorable early results with SABR or surgery (41% RR; no Grade 3+ toxicities). Accrual completion and preliminary results on the entire cohort are expected for Q1 and Q3 2019, respectively. Our study will uniquely inform if ablative approaches offer potential for cure in an early molecularly-defined PC oligometastatic state.

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THE ELDORADO STUDY: A PHASE II RANDOMISED STUDY OF CHEMO-RADIATION AND LONG-TERM ANDROGEN DEPRIVATION IN PATIENTS WITH HIGH-RISK PROSTATE CANCER. A RE-ANALYSIS OF THE PRIMARY ENDPOINT
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Background: Treatment intensification is warranted for high-risk prostate cancer. Docetaxel (DO) and radiotherapy (IMRT) may provide biological dose-escalation, but could also potentially cause dose-limiting GI or GU toxicity, necessitating dose reductions or dose omissions of the chemotherapy. Treating the whole pelvis last (WP-L) versus the whole pelvic lymphatics first (WP-F) could reduce the number of dose delays or reductions of DO.

Materials and Methods: We performed a double-blind, randomized trial, in patients with high-risk non-metastatic prostate cancer who had any one of the following: 1) ≥ T2c TNM category, 2) Gleason score ≥ 8, or PSA ≥ 20 and ≤ 50 µg/L, OR have a greater than 50% risk of recurrence after radical prostatectomy (RP), as predicted by the Kattan nomogram, with no evidence of metastatic disease. Patients received 2.5 years of leuprolide acetate 45 mg sc q six months, and after four months of neoadjuvant ADT, received IMRT and concurrent DO 20 mg/m^2 x 8 weekly infusions. Patients were randomized to receive WP-F followed by a boost to the prostate/prostate bed, or to have WP-L. The primary outcome was to compare the number of DO dose reductions, delays or omissions due to GI or GU toxicity, between arms. Target sample size was 86 patients.

Results: Ninety-eight patients were registered, 88 were randomized, two withdrew consent. Forty-two patients were randomized to WP-F, and 44 patients to WP-L. 81.8% of Patients treated with WP-L received all eight weeks of DO versus 78.6 % of patients treated with WP-F. Fifteen patients in the WP-F arm experienced delays or reductions in DO due to GI or GU toxicity versus five patients in the WP-L arm, and when analyzed by Poisson regression, there were significantly less delays or reductions in DO dose in the WP-L arm (p-value = 0.0266). Actuarial overall survival at four years is 96% (WP-F versus WP-L: 94% versus 97%, p=0.6). Biochemical relapse-free survival at four years is 96.7% (WP-F versus WP-L: 98% versus 97%, p=0.92). Two patients have needed surgical intervention for Grade ≥ 3 GU toxicity. Cumulative treatment-related Grade 3 or 4 GI or GU toxicity was 36%. When patients were last seen, only two out of 84 (2.3%) patients had ongoing Grade 3 GI or GU toxicity.

Conclusions: Concurrent use of DO and IMRT is feasible with reasonable toxicity. Sequence inversion reduces events that cause dose reductions or delays in concurrent chemotherapy, and can be a model for future studies where there is overlapping toxicity between radiotherapy and concurrent systemic therapy.

Trial registration: ClinicalTrials.gov ID: NCT00452556

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OUTCOMES AND PROFILES OF ELDERLY PATIENTS RECEIVING DEFINITIVE RADIOTHERAPY FOR MUSCLE-INVASIVE BLADDER CANCER AT A TERTIARY MEDICAL CENTER IN U.S.A.
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Purpose: To examine the profiles and outcomes of elderly patients with muscle-invasive bladder cancer (MIBC) treated with definitive radiotherapy (RT) +/- chemotherapy (CHT) at a tertiary medical centre in USA

Materials and Methods: A retrospective study was conducted for elderly patients with MIBC who were ≥ 70 years old and underwent definitive RT +/- CHT between January 2000 and December 2016. Overall survival (OS) and progression-free rate (PFR) were estimated using the Kaplan-Meier method. Patterns of tumour recurrences were examined. Univariate analyses were performed to identify variables associated with OS and PFR, using the Cox proportional hazards model.

Results: A total of 84 patients underwent definitive RT +/- CHT. Only 24 (29%) were deemed to be medically fit to undergo radical cystectomy (Group1), while the remaining 60 were medically unfit or surgically inoperable (Group 2). Sixty-one percent, 29%, and

11% had Stage II, III, and IV. Median age was 80.8 year [range 70.1, 94.3]. 66 (79%) were male. Seventy-two (86%) underwent maximal TURBT prior to RT. Sixty (71%) received concurrent CHT. All but 11 received platinum-based regimens. RT was directed to the bladder and regional pelvic lymph nodes in 69%, and to the bladder only in 31%. The median doses to the bladder tumour and pelvic lymph nodes were 6490 cGy and 4500 cGy, respectively. The median follow-up was 5.7 years. Median OS was 23 months. OS at one, two, three and five years was 69%, 49%, 42% and 25%, respectively. OS was significantly better for Group 1 (versus Group 2, p<0.01; 79%, 75%, 70%, and 37% for Group 1 versus 65%, 38%, 31%, and 20% for Group 2), and those that were able to receive concurrent CHT (p=0.01). PFR at one, two, three and five years was 75%, 63%, 56%, and 51%, respectively. Twenty-three, seven, and 26 patients had a relapse in the bladder, pelvic lymph nodes, and distant sites, respectively. Of 23 local relapses, 11 were MIBC, six with superficial disease, and six with no biopsy due to palliative setting. Local control at one, two, three and five years was 83%, 76%, 72%, and 71% respectively. Maximum TURBT was significantly associated with better local control (p=0.02), whereas concurrent CHT had no impact. Freedom from pelvic nodal relapse at one, two, three, and five years was 95%, 92%, 92% and 91% respectively. Freedom from distant failure at one, two, three and five years was 88%, 79%, 74%, and 67%, respectively. Acute, Grade ≥ 2 urinary and gastrointestinal (GI) toxicity was seen in 38% and 26% of patients, respectively. Late Grade ≥ 2 urinary and GI toxicity was 33% and 5%, respectively. No patients died from treatment-related causes.

Conclusions: Elderly patients with MIBC referred for RT were often medically unfit or surgically inoperable. Definitive RT+/- CHT yielded encouraging results for these elderly patients.

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IMPACT OF CONCOMITANT MEDICATIONS ON OUTCOME IN PATIENTS WITH LOCALIZED PROSTATE CANCER TREATED WITH DOSE-ESCALATED EXTERNAL BEAM RADIOTHERAPY AND ANDROGEN DEPRIVATION THERAPY: A POOLED ANALYSIS OF TWO PROSPECTIVE TRIALS

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Purpose: Several retrospective studies have investigated the impact of commonly-prescribed concomitant medications (ConMeds) on oncologic outcomes in patients with prostate cancer (PCa). Notably, receipt of metformin, statins, or COX-inhibitors concurrently with anticancer therapy has been found to be associated with overall outcome. Few studies, however, have assessed the impact of these ConMeds in patients with localized PCa (L-PCa) treated with external beam radiotherapy (RT). We conducted a pooled analysis of two single-institution randomized controlled trials (RCTs) to evaluate the impact of ConMeds on biochemical failure-free survival (BFFS) of patients with L-PCa treated with RT and androgen deprivation therapy (ADT).

Materials and Methods: In the first RCT, patients with L-PCa with clinical Stage T1b-T3, PSA <30 and Gleason score (GS) ≤7 (but excluding low-risk patients) were treated with RT (76 Gy/38 fr/7.5 wks) and six months of ADT initiated either four months prior to RT or concurrently with RT. In the second RCT, patients with high-risk localized PCa were treated with RT (76 Gy/38 fr/7.5 weeks) and three years of adjuvant ADT. BFFS was estimated using the Kaplan-Meier method. Cox regression model was used to analyze the association between BFFS and clinicopathologic factors including age at diagnosis; performance status; pre-treatment PSA; T-stage; GS; risk group; RCT protocol; and classes of ConMeds. Factors with p <0.05 were included in a multivariate regression model (MVR) to calculate the adjusted cause-specific hazard ratio (aHR) with 95% confidence intervals. Cumulative incidence of BF (CIBF) was estimated using non-PCa related deaths as a competing risk and compared using Gray's statistics with p-values. Subdistribution HR (SHR) was estimated using the competing risk regression method for factors found to have Gray's p <0.05.

Results: A total of 486 patients were evaluable, of which 388 were from the first RCT and 98 from the second RCT. Median age was 70 years. Median PSA was 9.8 ng/mL. Median follow-up was 105 months. For the entire cohort, 10-year BFFS was 83.7%. BFFS at 10 years for patients receiving metformin (n=39) and not receiving metformin (n=447) was 73% and 85%, respectively (p=0.02). On MVR, the aHR of BFFS for receipt of metformin was 2.25 (1.1-4.6, p=0.03). There was no significant association between BFFS and receipt of ConMeds from all other classes. CIBF at 10 years was 24% and 13% in those receiving and not receiving metformin, respectively (p=0.04). The adjusted SHR for receipt of metformin was 1.87 (0.86-4.05, p=0.11).

Conclusions: In this pooled analysis of two RCTs, use of concomitant metformin was independently associated with inferior BFFS and a higher 10-year CIBF in L-PCa patients treated with a combination of RT and ADT. It is noteworthy that the metformin association identified here is directionally opposite to that seen in majority of studies in advanced PCa and patients with L-PCa treated with radical prostatectomy. These findings merit validation in an independent dataset.

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SUBSEQUENT ANDROGEN DEPRIVATION THERAPY AFTER INITIAL TREATMENT IN INTERMEDIATE RISK PROSTATE CANCER: PROSPECTIVE DATA FROM A PHASE III TRIAL

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Purpose: Using prospective data from a phase III randomised trial in intermediate risk prostate cancer (IRPC) treated initially with androgen deprivation therapy (ADT) plus radiotherapy (RT) versus RT alone, we report ADT duration per arm and ADT timing (early or late) post-treatment failure.

Materials and Methods: From December 2000 to September 2010, 600 patients with IRPC were equally randomized in a three-arm trial: six months of ADT given neo-adjuvantly and concomitantly (NAC) to prostate dose of radiotherapy of 70 Gy (ADT+RT70) versus ADT and prostate dose escalated RT of 76 Gy (ADT+DERT76) versus prostate DERT alone at 76 Gy (DERT76). After biochemical failure (BF) and/or prostate cancer progression (PCP), ADT use was left at the discretion of the treating physician. We compared ADT duration (in months) and timing amongst the three arms.

Results: Patient characteristics were well balanced between the three arms. Median follow-up was nine years (IQR 7.5-11.2). Based on the treatment patients actually received, NAC ADT was given to 195/200 in ADT+RT70, 196/200 in ADT+DERT76 and 7/200 in DERT76. One hundred and twenty-three of the 600 patients presented BF (33, 28 and 62 patients respectively, p<0.001). Eighty-nine patients (72%) received subsequent ADT (SADT) (24, 19 and 46 patients respectively, p<0.001). Intermittent SADT after BF (varying from 1-5 cycles) was used in significantly more patients in DERT76 (20, 15 and 33 patients respectively,

p=0.02). After PCP, SADT was given to significantly more patients in DERT76 (seven, five and 21 patients respectively, p=0.001). Thirteen patients who received intermittent SADT for BF were treated subsequently for PCP. SADT began within six months of BF in 44% of patients, within one year in 65% and within two years in 82%. SADT started later after baseline for patients with ADT+DERT76 than patients with ADT+DERT70 or DERT76 alone (median (range): 70 (31-133), 93 (60-158) and 64 (6-184) months respectively, p=0.051). No statistical difference was observed between ADT+DERT70 and DERT76 alone. There was no significant difference in the total usage of SADT (median (range): 23 (0-107), 9 (0-24) and 9.5 (0-31) months respectively, p=0.25). Of note, 69% (140/202) of all patients treated with RT alone (five in ADT+RT70, four in ADT+DERT76 and 193 in DERT76) did not fail and never received SADT.

Conclusions: In IRPC, patients receiving dose-escalated RT alone developed more BF and PCP than those treated with RT combined with neo-adjuvant and concomitant ADT. When ADT was used after BF or PCP, it was mostly timed as an early intervention.

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STEREOTACTIC BODY RADIATION TREATMENT OF SYNCHRONOUS EARLY STAGE NON-SMALL CELL LUNG CANCERS

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Purpose: Synchronous early stage non-small cell lung cancers are rare but increasingly seen, providing a diagnostic and therapeutic challenge. Stereotactic body radiation therapy (SBRT) is shown to be effective in the treatment of early stage lung cancers, though only few studies have focused on its use in the treatment of synchronous primaries. This study reviews outcomes from SBRT treatment of synchronous primaries and characterizes this population.

Materials and Methods: A review of an ethics-approved database of Stage I NSCLC patients treated between 2009 and 2015 at The Ottawa Hospital Cancer Center identified 445 consecutive patients treated with SBRT alone for curative intent. From this population, there were 28 (6.3%) patients with two synchronous primaries at diagnosis. Their survival outcomes were analyzed using Kaplan-Meier Estimate and compared to patients with a single lesion via Log-Rank Test.

Results: The mean age of patients with synchronous primaries was 72.8. They were all smokers or ex-smokers with a mean of 37.2 pack-year history. 64.3% had both lesions on the same lung. Mean primary tumour diameter was 2.07cm. Of the 56 tumours from the 28 patients, 80% were individually biopsied yielding 71% adenocarcinoma, 20% squamous cell carcinoma and 9% others. 76.8% of these tumours were at the periphery of the lungs. SBRT dose fractionation to the individual tumours consisted of 57-60Gy/8 (66.1%), 60Gy/5 (30.3%) and 45-54Gy/3 (3.5%). The mean overall survival (OS) time for patients with two synchronous primaries was 49.7 months which was equivalent to the 51.6 months seen in patients with a single lesion. Three-year OS rate was 63.5% in the synchronous primary group. The respective mean progression free survival was 40.7 versus 47.7 months (p=0.344). Eight patients developed subsequent local, regional and/or metastatic disease in the synchronous primaries group.

Conclusions: SBRT treatment resulted in similar survival outcomes in patients with synchronous primary lung cancers as those with single primaries. Our study supported its role in the management of this subpopulation of early stage lung cancer patients.

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RADIATION-INDUCED BRAIN INJURY IN MENINGIOMA PATIENTS TREATED WITH PROTON OR PHOTON THERAPY

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Purpose: Proton therapy is often used to treat meningioma given its advantage to achieve a lower integral brain dose, compared to the photon therapy. However, it is unclear whether the difference in the rate of brain injury is due to uncertainties in the end-of-range effects. The purpose of this study is to characterize and compare brain injury as a consequence to proton or photon therapy.

Materials and Methods: We retrospectively reviewed 38 consecutive patients treated with proton therapy between 2014 and 2017 and 39 patients treated with photon therapy between 2008 and 2018 at two high-volume tertiary cancer centres. Patients with history of previous radiotherapy or follow-up period less than three months were excluded. Radiation-induced brain injuries were categorized into white matter lesions (WML), defined as newly detected abnormal T2 signal intensities, or radiation necrosis (RN), defined as newly detected abnormal T2 and T1 post-contrast signal intensities. Follow-up imaging was reviewed by an experienced neuro-radiologist and a radiation oncologist. Abnormal MRI scans were then reviewed after fusion with initial radiation plans. Toxicity was graded as per the common terminology criteria for adverse events (CTCAE v4.03).

Results: Median follow-up time was 18 months for the proton arm and 24 months for the photon arm. There was no significant difference in WHO grade, radiation dose, clinical target volume (CTV) volume, history of diabetes, or history of stroke between the two groups. The median dose was 54 CGE (Cobalt Gray Equivalent) in 30 fractions (range: 50.4-60 CGE) in the proton arm and 54Gy in 27 fractions (range: 50.4-61.4Gy) in the photon arm. Nine of the 39 patients on the photon group received an additional 7.5-9Gy radiosurgical boost. In the proton group, 23 of 38 patients were treated with pencil beam scanning and 15 with uniform scanning. The cumulative incidence of WML at two years was 38.3% after proton and 45.0% after photon therapy (p=0.60). The cumulative incidence of RN at two years was 17.9% after proton and 4.2% after photon therapy (p=0.01). In the proton group, Grade ≥2 toxicity was recorded in seven (18.4%) patients and one (2.6%) patient had a Grade 4/5 event. In the photon group, Grade ≥2 toxicity was recorded in three (7.7%) patients and one (2.6%) patient had a Grade 4/5 event.

Conclusions: Patients treated with either proton and photon beam therapies have high rates of developing parenchymal T2 signal intensity abnormalities. However, in our series, patients were more likely to develop parenchymal T1 post-contrast abnormalities after the proton therapy. The rate of Grade 4/5 events was the same between the two groups. Further study on developing strategies to decrease the risk of brain injury is warranted to optimize treatment of meningioma.

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PROGNOSTIC ASSESSMENT OF INTERIM FDG-PET IN ESOPHAGEAL CANCER TREATED WITH CHEMORADIATION WITH OR WITHOUT SURGERY

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Purpose: The aim of this study was to evaluate if the FDG-PET

response after two weeks of chemoradiation for locoregionally advanced esophageal cancer (T3 and/or N+ M0) was linked to the pathologic response for patients undergoing surgery, to disease-free survival (DFS) or overall survival (OS).

Materials and Methods: Between March 2006 and October 2017, 40 patients were prospectively enrolled in our study, gave IRB-approved written consent and were planned to have PET scans performed prior to treatment and after two weeks of chemoradiation. One patient did not undergo his two-week PET and was excluded from analyses.

Results: Median age at diagnosis was 62 years old. 72 % of patients had N+ disease. Median OS for the entire group was 24 months. Five-year overall survival was 17%. Survival curves for patients with no PET response, moderate PET response or important PET response overlapped and were not statistically different. For the 25 patients who underwent surgery, the PPV (positive predictive value) of the PET response relative to the pathologic response was 75% and the NPV (negative predictive value) was 62%. In study patients, the crude recurrence rate was 69% and there was no correlation between PET response and DFS.

Conclusions: In our study, interim PET response after two weeks of chemoradiation for locoregionally advanced esophageal was not predictive of outcome or pathologic response. Based on our data and current literature, interim PET should not be used to alter treatment (whether to escalate neo-adjuvant treatment or omit surgery).

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MRI-GUIDED BRACHYTHERAPY PLAN OPTIMIZATION WITH THREE VERSUS FOUR FRACTION TREATMENT FOR LOCALLY ADVANCED CERVICAL CANCER

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Purpose: MRI-guided brachytherapy (MRgBT) has become the standard treatment for locally advanced cervical cancer. The ability to optimize target and organ-at-risk (OAR) doses with three-dimensional image-based planning has improved toxicity profiles and local control. MRgBT, however is considerably more resource-intensive than the classical 2D planning and most of the available data on MRgBT has been based on a four-fraction protocol of 7 Gy per fraction (7x4). A potential alternative to minimize resource utilization is a three-fraction regimen of 8 Gy per fraction (8x3). However, there is limited data on MRgBT using the 8x3 protocol. The ability of this higher dose per fraction treatment to meet EMBRACE II planning aims has not been extensively studied. This study aims to compare optimized 8x3 versus 7x4 plan dosimetry.

Materials and Methods: Ten patients with locally advanced cervical cancer (FIGO IB2 – IVA) treated at a single institution between July 2018 and January 2019 were included in this planning study. Clinical plans that were optimized and treated using a prescription 7x4 and the EMBRACE II planning aims (CTV_{HR} $D_{90\%}$ 90-95 Gy, rectum D_{2cm3} < 65 Gy and bladder D_{2cm3} < 80 Gy) were retrieved. Plans were then scaled to 8x3 and adjusted using graphical optimization. Three scenarios were evaluated: (1) The CTV_{HR} $D_{90\%}$ EQD2 dose was adjusted to be equivalent to the 7x4 plans; while limiting doses to organs at risk. Bladder and rectum D_{2cm3} doses and GTV $D_{98\%}$ doses were recorded. (2) The bladder D_{2cc} EQD2 dose was adjusted to be equivalent to the 7x4 plans (3) The rectal D_{2cc} EQD2 dose was adjusted to be equivalent to the 7x4 plans. An a/b of 10 was used for the tumour bioequivalent dose calculations and an a/b of 3 for the OAR calculations. Doses were compared using Mann-Whitney-Wilcoxon.

Results: The median GTV_{res} and CTV_{HR} volumes were 13.42 cc (1.02 – 92.2) and 32.5 cc (10.99 – 120.4). For the 7x4 plans optimized for clinical treatment, median CTV_{HR} $D_{90\%}$, rectum and bladder D_{2cm3} EQD2 doses were 93.7Gy (87.4 – 104.4), 58Gy (51.3 – 83.7) and 77.7Gy (72.2 – 89.1). For scenario 1, where CTV_{HR} $D_{90\%}$ was made equivalent, median rectum and bladder D_{2cm3} were 58.5Gy (51.3 – 84.6) and 77.1Gy (73.1 – 90.0), respectively, with no significant differences compared to the 7x4 plans (p=1.0, p=0.85). Median GTV_{res} $D_{98\%}$ for 8x3 plans versus 7x4 was 105.1Gy (84.5 – 150) versus 110.2Gy (86.4 - 144.4), p=0.63. When bladder and rectum in 8x3 were set equal to 7x4 plans (scenarios 1 and 2), there was no significant difference in CTV_{HR} $D_{90\%}$ doses (p=0.63, P=0.91) or GTV_{res} $D_{98\%}$ (p=0.53, p=0.53) .

Conclusions: In this study, planning optimization with the 8x3 fraction protocol yields similar EQD2 doses for CTV_{HR} $D_{90\%}$, bladder and rectum D_{2cm3} when compared with the 7x4 fraction protocol. The EQD2 GTV $D_{98\%}$ is marginally lower for 8x3 when compared to 7x4; however, remains clinically acceptable. Further evaluation in a large cohort of patients is underway.

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BONE-ONLY DUAL-ENERGY STEREOSCOPIC X-RAY IMAGING FOR SPINE SBRT

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Purpose: Owing to a-priori CT data and digitally reconstructed radiographs (DRR), our novel patient-specific pixel-based weighting factor dual energy (PP-DE) algorithm was previously proven to be a compelling technique for effective bone suppression throughout the image to enhance the soft-tissue-only image quality and to overcome the limitation of the conventional DE algorithm with constant weighting factor, which is restricted to regions with uniform patient thickness [1]. The purpose of this work is to exploit this technique to develop the PP-DE algorithm for efficiently suppressing soft-tissue across the image to enhance the bone-only image quality.

Materials and Methods: A step phantom was constructed consisting of slabs of solid water (5 to 30cm) and average bone (0 to 6cm) materials, creating 7 by 7 regions of interest (ROIs). The slabs were stacked on a custom-made stand, angled at 42°, such that the central axis of the x-ray beam was perpendicular to the phantom surface. Using Brainlab's ExacTrac system, projection images were acquired at 60 kVp and 140 kVp. Using an in-house Matlab code, the optimal pre-calculated weighting factors (ω) were found by varying values from 0 to 2 for each ROI such that soft-tissue contrast-to-noise ratio (CNR) reached zero. CT images of Rando phantom were acquired using thorax protocol. Using Ray tracing technique, the bone and soft-tissue DRRs were calculated. The ω image for Rando phantom was generated, using the pre-calculated weighting factors. By applying the ω image into the DE algorithm and utilizing noise suppression algorithm, the bone-only DE image was generated and compared to the clinical single energy x-ray image and conventional DE image, which uses a constant ω throughout the image. Signal-to-noise ratio (SNR) of regions with different soft-tissue and bone thicknesses in step phantom was evaluated for both DE techniques. To investigate the impact of different patient thicknesses, Rando phantom was wrapped with layers of the superflab bolus.

Results: The optimal pre-calculated ω values were found to be in a range [0.82, 1.19] depending on the region thickness in step phantom. The ω values that cancels 25 cm (ROI1) and 10cm (ROI2)

soft-tissue overlapped with 3cm bone were calculated as 0.93 and 0.83, respectively. The SNR of DE image for ROI1 and ROI2 of the step phantom was 45 and 674 for PP-DE compared to 43 and 203 for conventional DE, respectively. The effectiveness of the PP-DE algorithm compared to the clinical single energy x-ray image and conventional DE images, as well as the impact of patient size will be presented explicitly.

Conclusions: This study proved the feasibility of the bone-only PP-DE algorithm, which could potentially have clinical interests for image guidance for spine SBRT patients. This innovative method improves visualization of bony anatomy during, e.g., planar or stereoscopic image guidance of radiotherapy.

[1] Darvish-Molla et al., 2018, Medical Physics, DOI: 10.1002/mp.13354

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RETROSPECTIVE EVALUATION OF THE EFFECTS OF INTEROBSERVER CONTOURING PRACTICES IN CLINICAL PRACTICE

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Purpose: To assess the contouring practices of radiation oncologists during everyday clinical practice and their impact on patient DVHs at a population level.

Materials and Methods: The DVHs of 560 prostate cancer patients who had undergone hypofractionated treatment (60Gy in 20 fractions) were exported from the Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA) into a custom DVH registry at our institution along with structure volumes and lengths. Patients were separated into intermediate (prostate only) or high-risk (additional 44Gy boost to pelvic lymph nodes) cohorts and further categorized based on primary radiation oncologist (RO). Structure volumes, lengths, and DVHs were compared between oncologists using 2-tailed Student's t-tests.

Results: PTV coverage was consistent across ROs and risk levels. In intermediate risk patients, no differences in contouring habits or DVH distributions were observed. However, in high-risk patients, one radiation oncologist achieved significantly more sparing of the rectum and bladder than their peers. The root cause was determined to be an inconsistent pelvic lymph node contour definition between ROs. The RO achieving better sparing contoured significantly smaller lymph node CTVs than their peers, and two other ROs adhered to different cranial-caudal limits than others. In light of these findings, we presented our results to the oncologists at our institution, prompting the selection of a universal pelvic lymph node contour definition.

Conclusions: Systematic interobserver contouring practices in regular clinical practice are detectable through statistical analysis of past treatment plans. Retrospective revision of these practices is recommended as a quality assurance measure to ensure consistent quality of care across an institution.

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A MULTI-INSTITUTIONAL RETROSPECTIVE CLINICAL AND DOSIMETRIC ANALYSES OF 1033 OLIGOMETASTATIC PATIENTS TREATED WITH SBRT FROM THE CONSORTIUM FOR OLIGOMETASTASES RESEARCH - CORE

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Purpose: An international consortium of academic radiation oncology centres was formed to pool outcomes for patients with oligometastases (OM) treated with stereotactic body radiotherapy (SBRT). We sought to evaluate overall survival, progression-free survival, Grade 3 acute/late toxicities and the clinical factors that impact prognosis.

Materials and Methods: This study was a retrospective review of a multi-institutional cohort of patients treated with SBRT for oligometastatic (OM) disease (≤6 lesions) without brain metastases at presentation. Patients where other treatments led to a cytoreduction to an OM state were excluded. Patients were identified from databases at each institution and clinical and dosimetric data was collected through retrospective chart review. Survival statistics were calculated using a Kaplan-Meier product-limit method was used. A multivariate analysis was used to define the association of these outcomes to clinical parameters.

Results: 1033 patients were included in the analysis with 84 breast, 235 colorectal, 260 lung, 132 prostate, 63 kidney, 37 melanoma, 50 head and neck and 172 other cancers. Median age was 68 (18-94). Median follow-up was 24 months with 228 (22%) patients having undergone prior definitive (non-SBRT) metastases-directed therapy. Also, 754 patients had a metachronous presentation of OM while 279 presented with synchronous OM. At presentation, 596 (58%), 245 (24%), 105 (10%), 55 (5%), 32 (3%) patients had 1,2,3,4,5 metastatic lesions respectively and 875 (85%), 140 (13%), 18 (2%) patients had 1, 2 and 3 or more organs involved. All known sites of disease were treated in 981 (95%) patients. 663 (64%) of patients had systemic therapy before SBRT. OS was 83% and 67% at one and two years. Progression free survival at one and two years was 52% and 30%. Multivariate analysis for OS identified primary site ($p<0.001$), synchronous versus metachronous presentation ($p=0.01$), metastases confined to the lung only ($p<0.001$) and nodal/soft tissue metastases only ($p=.0.01$). Notably, age, pre-SBRT chemotherapy, number of metastatic lesions and gender were included in the prognostic analysis and were not statistically significant for OS. There were 31 and 35 reports of ≥Grade 3 acute and late toxicities were recorded, including one Grade 5 pneumonitis and one Grade 5 bile duct stenosis.

Conclusions: In a large multi institutional cohort of selected patients with OM disease at presentation, SBRT appears to be an effective treatment for OM cancer patients with favourable long term outcomes and low rates of severe toxicity. Multivariate analysis identified primary site, synchronous versus metachronous presentation, metastases confined to the lung only and to nodal/soft tissue only as prognostic for OS.

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LONG TERM RESULTS OF 120 CASES OF VESTIBULAR SCHWANNOMA TREATED WITH CYBERKNIFETM ROBOTIC STEREOTACTIC RADIOSURGERY AT THE OTTAWA HOSPITAL CANCER CENTRE

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Purpose: Stereotactic radiosurgery (SRS) is a safe and effective alternative to microsurgery in the management of acoustic neuromas. The excellent outcomes from such treatments are well documented with Gamma Knife therapy in literature. The CyberKnife (CK) Robotic Stereotactic Radiosurgery (SRS) is an

alternative, delivering the same quality but also have the benefits of a frameless treatment system. However, the body of evidence in its use is less robust. This study characterized the mature outcomes of a substantial population of acoustic neuroma patients treated with CK at The Ottawa Hospital Cancer Centre.

Materials and Methods: This study consisted of 100 patients treated with CK from September 2010 until April 2015. Patients with complete hearing loss were treated with a single 12Gy fraction (six patients). Those with hearing preservation or moderate to large tumours were treated with 18Gy in 3 fractions (94 patients). They were followed clinically and with imaging at standardized intervals. Follow-up T2 axial MRIs (0.50mm slice) were performed to evaluate tumour response and pseudo-progression. To obtain volume information, MRI images were contoured on PACs imaging station using Aquarius Net version 4.4.13 by a single radiation oncologist.

Results: Patients range in age from 15 to 91 with a mean of 59. The median follow-up time was 53 months. Mean tumour size was 2.6 cm^3 (range 0.1 cm^3 to 17.07 cm^3). Progression occurred in three patients (local control rate of 97%). One progression failed to respond to treatment and continued to grow in size while the other two had initial tumour shrinkage. Pseudo-progressions were seen in 12 cases and all were treated with 18 Gy in 3 fractions. Mean time to the maximum imaged tumour volume post treatment was 5.17 months (range of 3 to 12 months) with an average volume increase of 12% (Range 2-31%). Mean time to subsequent regression to pre-treatment size was 14.83 months (Range of 10 to 23 months). No pseudo-progression led to subsequent local recurrence. Toxicities were minimal with one patient who progressed suffering CN VII palsy prior to salvage surgery. All other patients had preserved facial nerve function.

Conclusions: Cyberknife offered excellent local control for acoustic neuromas with local control rate of 97%. Pseudoprogression was seen in 12% of patients and was not a predictor for treatment failure.

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EFFICACY AND TOXICITY OF STEREOTACTIC BODY RADIATION THERAPY FOR LOCALIZED PROSTATE CANCER: AN ELEVEN YEAR STUDY

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Purpose: This is the first study of prostate stereotactic body radiation therapy (SBRT) to have patients with 11-year followup. In this study, we report outcomes for prostate robotic SBRT in 560 patients, with NCCN low-, intermediate- and high- risk disease. We report on biochemical disease-free survival (bDFS), toxicity and Quality of Life (QOL).

Materials and Methods: We studied 515 patients with organ-confined prostate cancer, treated with SBRT to dose of 35-36.25Gy in 5 daily fractions between 2006-2009. We included 45 high-risk patients who received a 18-21 Gy SBRT boost after 45Gy to the pelvis with EBRT. Median follow-up was 114 months. The median age was 69 years, and median PSA was 5.58. 324 patients were low-risk, 153 were intermediate-risk and 83 were high-risk. ADT was administered to 102 patients. Patients were further stratified into low-intermediate risk versus high-intermediate risk, with high-intermediate risk criteria of Gleason 4+3=7 or >1 intermediate risk factors (cT2b-c, PSA 10-20, Gleason 7). Biochemical failure was assessed using the Phoenix criterion. Cox regression analysis was used to determine which risk factors were significantly associated with increased risk of biochemical failure.

Results: Eleven-year disease-free survival was 92.8, 79.5 and 64.0% for low-, intermediate- and high-risk group patients, respectively. Local control was 97.8, 92.4 and 88% respectively. Favourable intermediate-risk patients had excellent outcomes, with no significant difference compared to low-risk patients (11-year DFS 89.8 versus 92.8%, respectively). Unfavourable intermediate-risk patients had outcomes similar to high-risk patients, with 11 year bDFS of 67 and 64% respectively. For low and intermediate risk patients, Gleason score was the only significant factor predicting for biochemical failure on multivariate analysis (p=0.0003), with ADT, dose and PSA not significant. For high-risk patients, PSA was the only significant predictor of bDFS, with Gleason score, ADT or EBRT not significant.
Toxicity was mild. 36.25 Gy was associated with more Grade 2-3 late urinary toxicity than 35Gy (13% versus 6%) p=.01. Patients receiving EBRT had a higher rate of late Grade 2 late rectal toxicity. Mean EPIC QOL urinary and bowel domains for all patients declined during the first three months and then returned to baseline, where they remain. Mean sexual QOL scores have slowly declined by 39%.

Conclusions: This study suggests that early excellent control rates for SBRT for prostate cancer are durable over 11 years. Similarly, toxicity rates remain low and QOL scores remain high over that period. For patients receiving SBRT alone, 35Gy is as effective as 36.25Gy with less urinary toxicity, suggesting 35Gy may be the optimal dose. For high-risk patients, use of EBRT and ADT do not appear to increase long term control rates.

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DOSIMETRIC COMPARISON AND TOXICITY ANALYSIS OF STEREOTACTIC RADIOTHERAPY FOR HIGH-RISK PROSTATE CANCER

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Purpose: FASTR was designed to provide a compact treatment course for high-risk prostate cancer patients but was discontinued because of excess toxicity.(1) FASTR-2 employed a lower dose to the prostate (35Gy versus 40Gy), smaller PTV margins and omitted nodal radiation in order to lower the volume of rectum receiving high and intermediate doses compared to FASTR. Here we compare the acute toxicity and rectal dosimetry between our FASTR and FASTR-2 patients.

Materials and Methods: Eligibility for FASTR-2 included high-risk prostate cancer (cT3/4, PSA>20 or Gleason Score ≥ 8), age ≥ 70 or refused standard treatment, no evidence of extra-prostatic disease. Patients received 18 months of ADT starting two months prior to radiation. CTV was defined as prostate plus proximal 1cm seminal vesicles. PTV was a non-uniform expansion around CTV (4mm posteriorly, 5mm in all other directions). Volumetric arc therapy was used for treatment delivery (1 fraction/week x 5 weeks) and cone beam CT with soft tissue matching (no fiducial placement) was used for daily image guidance. Toxicity was assessed at six weeks, six months and one year according to Common Toxicity Criteria.

Results: Fifteen patients were enrolled in the original FASTR study; 30 patients were enrolled in FASTR-2 between 2015 and 2017. Two patients were withdrawn due to ineligibility following enrollment. One patient (3.7%) reported Grade 2 GI toxicity at six weeks. There were no reported Grade ≥2 GI toxicity at six months or one year. There were no reported episodes of rectal bleeding. Four patients (14.8%), five patients (17.9%) and five patients (21.7%) reported Grade 2 GU toxicity at six weeks, six months and one year, respectively. The most common toxicities were nocturia and urinary frequency/urgency. Rectal maximum point dose, D20

and D50 decreased from 40.7Gy, 29.6Gy and 20.8Gy in FASTR to 35.0Gy, 22.2Gy and 11.1Gy in FASTR-2 (p<0.001). Bladder point dose, D20 and D50 decreased from 40.9Gy, 28.1Gy and 21.5Gy in FASTR to 35.7Gy, 15.7Gy and 6.3Gy in FASTR-2 (p<0.001).

Conclusions: FASTR-2 was more tolerable than FASTR, with no Grade ≥ 3 toxicities reported, in keeping with expectations based on our previous FASTR analysis. (2) Advantages to FASTR-2 include image guidance without fiducials and a weekly treatment schedule which is more convenient for some patients. Trade-offs with FASTR-2 include a lower dose to the prostate (but still in keeping with ASTRO guidelines) and elimination of pelvic nodal irradiation (but need for routine pelvic radiotherapy still remains debated). Long-term follow-up is necessary to ensure disease control is comparable to conventional high-risk treatment paradigms.

1. Int J Radiat Oncol Biol Phys. 2015 Jul 15;92(4):856-62.
2. Pract Radiat Oncol. 2017;7(6):e457-e46.

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PROSPECTIVE CASE SERIES IN THE USE OF ABDOMINAL AND PELVIC SBRT IN THE CONTEXT OF OLIGO-PROGRESSIVE DISEASE

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Purpose: There is emerging evidence for the "Oligometastatic" state where local therapy for a limited number of metastatic lesions may have benefits for progression-free survival (PFS), overall survival (OS) and potentially quality of life. The "Oligo-progressive" state occurs when a patient has several metastatic deposits in which a small number are progressing either on systemic therapy or having just completed a line of treatment. Controlling such lesions with Stereotactic Body Radiotherapy (SBRT) is theorized to extend PFS by either extending an existing chemotherapy course or by delaying the need for commencing a new course. Limited information has been published for treating such lesions in the abdomen and pelvis.

Materials and Methods: We analyzed all oligo-progressing patients treated with 5-fraction SBRT to the abdomen and pelvis 2014-2018. Patients were treated with VMAT using Varian planning software over two weeks with abdominal compression employed to reduce breathing amplitude for upper abdominal targets. Patients were categorized in terms of primary diagnosis, target location, target size, dose delivered, PFS and OS from SBRT and time to next treatment. Oligo-progression was defined using an in-house protocol as metastatic patients who progressed radiologically in 1-2 lesions on systemic treatment or within six months of completing a course. Local control was evaluated using cross–sectional imaging. Toxicity assessment used CTCAE version 4. Data analysis was conducted as part of an institutional Quality Assurance Process.

Results: A total of 35 patients with 42 SBRT courses met inclusion criteria, mean age 62 (range 31–87 years). Their primary tumour types included colorectal 11 (31%), breast eight (23%), endometrial four (11%), lung four (11%), and other types eight (23%). SBRT target organs included liver 26 (62%), para-aortic lymph nodes five (12%), adrenal gland four (9%), iliac nodes four (9%) and others three cases (7%). Median PTV prescription dose was 40Gy in 5 fractions (range 25-50Gy) with mean ITV size 98cc (range 0.73-613cc). Median follow-up 300 days. Estimated local control rate was 69% at one year and 51% at two years, respectively. Median PFS following SBRT was 111 days (95% CI 60-161 days), with estimated one-year PFS 25%. Median OS was 663 days (95% CI 281-1044 days), with estimated one-year OS of 67%. Median chemotherapy-free time following SBRT was 133 days (95% CI 61-205 days). One patient developed a Grade 4 GI toxicity with a gastro-hepatic fistula, resolved with conservative management. No other Grade ≥3 toxicities were observed. There was no association between local control rate or PFS with cancer type, ITV size or prescribed dose.

Conclusions: Abdominal and Pelvic SBRT to oligo-progressive targets was well tolerated in this series and could allow either a period of time off chemotherapy or the continuation of existing systemic therapy thereby potentially increasing the remaining chemotherapy options.

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EVALUATING RESPIRATORY MOTION OF THE BONY THORAX IN THE CONTEXT OF STEREOTACTIC BODY RADIATION THERAPY (SBRT): IS IT NECESSARY?

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Purpose: There is a growing interest in using stereotactic body radiation therapy (SBRT) for local treatment in patients with metastatic cancer, especially in the oligometastatic setting. Bone is one of the most common sites of metastases but very little has been published on the technical considerations. The impact of respiratory motion in lung and liver SBRT is well established but it is unknown if the effect is similar in thoracic bone metastases. The purpose of this study was to quantify respiratory motion in thoracic bone metastases and to determine if the motion differs based on anatomic location.

Materials and Methods: The first 70 patients treated with thoracic bone SBRT and planned with four-dimensional computed tomography were identified from a prospective institutional database. To quantify motion, a region of interest representative of the treatment target was contoured by a single user in Pinnacle on the 0% (inhale) and 50% (exhale) datasets using fixed autocontour threshold values to eliminate subjectivity. A point of interest was placed in the centroid of each volume and the relative positional difference of these points was calculated to measure the lateral (LR), anterior/posterior (AP) and superior/inferior (SI) motion. A total linear distance (LD) vector was calculated from these values. Rib lesions were further categorized as anterior, lateral or posterior based on axial position as well as superior (1-4), middle (5-7) and inferior (8-12) depending on rib location. Rib motion was compared using analysis of variance (ANOVA); if it was significant (p<0.05) a post hoc analysis was done to evaluate pairwise comparisons amongst the groups.

Results: There were 15/16 sternal lesions assessed as one patient had significant bone destruction and could not be reliably contoured. Mean (SD) sternum motion in the LR, AP and SI was 0.2 mm (0.2), 1.2 mm (0.9) and 0.1 mm (0.1) respectively and the LD 1.2 mm (0.9). Forty-seven rib lesions were assessed for motion; 7 were excluded due to bone destruction preventing use of auto contour tool. The mean (SD) motion for all rib lesions in the LR, AP and SI was 1.1 mm (1.0), 2.4 mm (2.2) and 0.1 mm (0.1) respectively and LD 2.8 mm (2.3). When categorized by rib location, there were 9 superiorly, 22 middle and 16 inferior located rib lesions. The mean (SD) LD was 3.2 mm (2.3), 3.5 mm (2.6) and 1.6 mm (1.5) for superior, middle and inferior lesions respectively. There was a significant difference between the groups, with the inferiorly located lesions moving less in terms of AP motion (p=0.02) and LD (p=0.04). In terms of axial position, there were 6 anterior lesions, 27 lateral lesions and 14 posterior lesions. The mean (SD) LD was 3.6 mm (2.7), 3.3 mm (2.3) and 1.3 mm (1.7) for anterior, lateral and posterior lesions respectively. There was significantly less motion for posteriorly located lesions in the AP direction (p=0.005) and with LD (p=0.02).

Conclusions: This data suggests that respiratory motion of the bony thorax is variable but not trivial in the context of high precision radiation therapy techniques with small margins. It appears that lesions located in the sternum and posterior and/or inferior aspect of the ribs move less; however, contouring guidelines, margin recipes and image guidance strategies need to be strongly considered before eliminating motion assessment from thoracic bone SBRT planning.

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DEVELOPMENT OF AN IN VIVO RADIATION DOSIMETER FOR RADIOTHERAPY

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Purpose: Precise and accurate in vivo dosimetry – that is, direct calibration of the dose received by patients during radiotherapy treatment – is currently not possible without perturbation of the beam trajectory. The ideal dosimeter should have a small sensitive volume, be suitable for quality assurance and in-vivo dosimetry and measure the dose to a tissue-equivalent material. The aim of this study is to develop a novel dosimeter with tissue-equivalent material and sensitive volume smaller than the cross-section of a human hair, relying on hydrated electron absorption spectrophotometry. This will facilitate in-vivo compatibility and excellent spatial resolution.

Materials and Methods: Radiation-induced ionization affects the optical absorption of water [Jou and Freeman 1979], however the optical path required to measure this effect is on the order of meters. The proposed dosimeter enables detection of absorption changes in a few micrometers by folding the optical path back on itself thousands of times in a resonant fibre microcavity. To verify the operation mechanism, a macroscopic water-based multipass absorption experiment was developed. A 45 mW laser diode (660 nm) was used as the light source and biased silicon photodetectors were used for rapid transmission readouts. The cell was irradiated with a 10 MV FFF photon beam with a Varian TrueBeam™ linear accelerator at the highest dose rate. The absorbance was monitored over time.

Results: Examination of the absorbance profiles indicates clear absorption changes in the water when radiation is delivered to the system. Both the amplitude and the decay time of the signal are consistent with the characteristics of hydrated electrons stated in the literature. On average, the absorbance changes correspond to a dose of 0.36 mGy absorbed on the optical path.

Conclusions: This work confirms the potential of hydrated-electron absorption spectrophotometry as a dosimetry method in radiotherapy. By compressing such signals into micron-scale optical cavities, we aim to open a new avenue of research for precision in vivo dosimetry.

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EARLY DOSIMETRIC FINDINGS FROM THE LEARNING FROM ANALYSIS OF MULTICENTRE BIG DATA AGGREGATION (LAMBDA) CONSORTIUM

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Purpose: Looking beyond clinical trials, it is difficult to develop clinically relevant evidence-based recommendations for radiotherapy (RT) practice guidelines due to lack of comprehensive "real world" data. To address this knowledge gap, we formed the LAMBDA consortium. The first phase of this "Big Data" study aimed to show feasibility of comparing organs-at-risk (OAR) doses across large numbers of patients using technical approaches to amalgamate aggregated data of nomenclature standardized as per recently released TG263 guidelines.

Materials and Methods: The consortium aggregates data on a range of patient, treatment and outcome parameters. A developed script automates extraction/packaging of RT details into a common database. Statistical dose volume histogram (DVH) curves were constructed. Distributions of medians and quantiles were compared by institution as well with statistical DVH curves. A Bayesian Network (BN) was used for possible structure-dose surrogates when not all structures were contoured. Student's t test was used for significance ($p<0.05$) tests.

Results: Plans were compared for 1,055 patients with head and neck (H&N) cancer treated with RT at three (A,B,C) of five current LAMBDA centres across Canada and the United States. Patients were treated to a mean dose of 66[55.7,68.7]Gy in 33[30,34] fractions. No significant difference in median volumes of parotid 27.1[20.8,35.2]cc or submandibular glands 7.9[5.8,10]cc was observed among centres. Parotid Mean was similar for ipsilateral 23.1[13.5,25.5]Gy, but significantly different for contralateral parotid A-20.5[5.9,24.8]Gy versus B-25.3[21.6,26.1]Gy. Differences were much larger for submandibular glands e.g. Ipsilateral A-29.4[21.7,41.2] versus B-57.8[39.0,67.2]Gy . Larynx doses and volumes were significantly different among centres A-19.3[18.3,24.6]Gy, 20.3[13.7,32.7]cc; B-43.7[34.6,54]Gy, 32.4[22.4, 47.2]cc; C-40.9[33.6,48.1]Gy, 38.6[27,45.7]cc. Statistical DVH curves showed larger differences throughout the curves. Esophagus doses and volumes also showed significant variation A-18.3[14.2,19.5]Gy, 8.8[6.2,12.6]cc; B-22.2[15.3,31.6]Gy, 15.8[11,21.2]cc; C-14.8[10.8,20.7]Gy, 16.8[12.8,22.3]cc. Although dose metrics for superior and inferior constrictor muscles have been shown to be significant for reducing dysphagia, only one institution consistently segmented these muscles for evaluation.

Conclusions: This multinational collaborative project has shown feasibility of amalgamating aggregated H&N RT plan data of standardized TG-263 nomenclature for high volume extraction of DVH curves in multi-centre comparisons. Observed differences among centres for OAR structures are the launching point for next steps to investigate potential relationships between DVH parameters and outcomes of physician or patient reported outcomes.

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DETERMINATION OF THE IMPACT OF INTRATUMOURAL HETEROGENEITY ON PROGNOSTIC BIOMARKERS IN LOCALIZED PROSTATE CANCER

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Purpose: Localized prostate tumours show remarkably diverse clinical courses after curative-intent radical prostatectomy (RP) or radiotherapy. Genomic-based biomarkers have been developed to predict these divergent behaviors, highlighting those harboring lethal disease. However, the clinical validity of these biomarkers remains uncertain, in part because of the susceptibility to be confounded by the spatial heterogeneity of

prostatic adenocarcinomas: most are multi-focal and harbour multiple sub-clonal populations. Herein, we determined the robustness of three validated DNA-based genomic biomarkers to intratumoural heterogeneity, and their association with the respective clinical phenotype.

Materials and Methods: After obtaining Institutional approval, we queried a prospective registry including 1,054 patients with high-risk prostate cancer who underwent RP between 2001-2013. A case-control cohort (n=42) risk-matched by clinicopathologic prognostic indices was derived, comprising 21 patients that developed early biochemical recurrence (eBCR; <18 months after RP), and 21 with long-term control (LTC; >48 months after RP). Then, we dissected multiple distinct tumour foci per patient (average 3 foci), leading to a total of 119 samples for genomic profiling. For each focus, three genomic DNA-based biomarker scores were calculated: percentage of genome with a copy number aberration (PGA), a 100-loci biomarker, and an optimized 31- loci biomarker derived from the previous. For each patient and biomarker, we considered three scenarios: sampling of only the lowest-score region, the highest-score region, or sampling of all foci and use the mean score across them.

Results: We observed high intra-patient genomic divergence between the least and most altered tumour sample, in average representing 6.15% of the genome (i.e. gain or loss of approximately an entire chromosome). Nevertheless, all three biomarkers successfully distinguished eBCR from LTC in this case-control cohort, regardless of which focus, or way of summarizing foci was used: PGA, 100- and 31-loci scores separated the two clinical phenotypes with an AUC ranging from 0.75-0.80, 0.76-0.85 and 0.76-0.80 respectively. No statistical difference between AUCs was observed. Similarly, on time-to-event analyses (Cox proportional hazards modeling) all three biomarkers were significantly associated with BCR-free survival independent of how different foci were summarized.

Conclusions: Genomic heterogeneity within patients is very large, and translates in differences in DNA-biomarker scores. Nonetheless, despite the theoretical impact on prognostication, all three genomic biomarkers evaluated were spatially robust and accurately predicted eBCR. Our study provocatively suggests that individual samples may be adequate in patients with high-risk disease. The validity and implications of this findings in patients with low- and intermediate-risk disease, and other genomic biomarkers warrants further investigation.

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CANAGLIFLOZIN, A NEW ANTI-DIABETIC AGENT TARGETING CELLULAR METABOLISM, SUPPRESSES SURVIVAL AND ENHANCES THE RESPONSE OF NON-SMALL CELL LUNG CANCER (NSCLC) TO RADIOTHERAPY

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Purpose: Non-small cell lung cancer (NSCLC) is highly resistant to radiotherapy (RT). Metabolic pathways involved in glycolysis, lipogenesis and protein synthesis determine tumour survival and response to RT. These events are modlated by the metabolic stress sensor AMP-activated protein kinase (AMPK), a key regulator of cell metabolism that also responds to cytotoxic therapy. Canagliflozin (CANA) is a new diabetes agent developed to control glycemia through inhibition of the Na^+-glucose co-transporter 2 expressed in the proximal renal tubule. We showed that clinically relevant doses of CANA activate AMPK and suppress survival of NSCLC. In this study we examined the anti-tumour effects of CANA in combination with RT.

Materials and Methods: Adenocarcinoma (A549, H1299, H1975) and squamous cell carcinoma (SK-MES-1) NSCLC cells were subjected to proliferation, clonogenic survival and metabolic assays after combined CANA (0–30mM) and RT (0–16Gy) treatments. Immunodeficient nude mice were grafted with H1299 cells and treated with Canagliflozin (100 mg/kg/day by oral gavage) and/or RT (10Gy). Cell and tumour lysates are analyzed with immunoblotting and immunohistochemistry.

Results: CANA, at low micromolar doses which are achieved routinely in diabetic patients, inhibits proliferation and clonogenic survival of NSCLC cells and enhance NSCLC response to RT. This is associated with inhibition of histone H3 phosphorylation and de-novo lipogenesis. CANA blocks effectively mitochondrial complex I activity, activates AMPK and mediates inhibitory phosphorylation of Acetyl-CoA Carboxylase (ACC) and suppression of the mammalian target of rapamycin (mTOR) pathway. Importantly, CANA also inhibits HIF1a expression and blocks early signaling events of the Epidermal Growth Factor Receptor (EGFR) pathway such Shc, Gab and PLCg1 phosphorylation. On-going experiments analyze in tumours proliferation, angiogenesis, cell death and microenvironment markers.

Conclusions: CANA, is a new widely-used diabetes drug, which suppresses survival and radio-resistance pathways and improves NSCLC response to RT, at doses well within its therapeutic window. This suggests a strong potential for clinical development of CANA in combination with RT for the treatment NSCLC.

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PARTNERSHIP INITIATIVE FOR THE EVALUATION OF TECHNICAL INNOVATION IN RADIOTHERAPY (PERA): PILOT PERFORMANCE OF A NOVEL TRIAL METHODOLOGY

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Background: Randomized controlled trials (RCTs) focused on evaluating the impact of technology are time consuming and costly, whereas trial efficiencies are outpaced by innovation.

Objectives: We piloted the cohort multiple randomized clinical trial (cmRCT) model as a strategy to
accelerate pragmatic clinical research in radiotherapy (RT), where patients were randomly selected to be offered an experimental intervention.

Materials and Methods: Consent forms were provided to physicians for registry enrolment at the time of RT consent (NCT03378856). Subjects were then registered online, with automated emailed survey schedules to physicians and patients. Following baseline data entry by the treating physicians, patients meeting eligibility criteria were randomly selected and approached by a clinical research associate for consent to participation in an interventional study cohort (PSMA-PET guided intensification of radiotherapy NCT03525288).

Results: The PERa-Prostate registry accrued 140 patients between April 2018 and January 2019, 38% of which were eligible for random

selection to the interventional trial, and all consented to their study arm assignment. Three percent of patients refused registry enrolment, and 3% of enrolled patients refused to receive electronic patient-reported outcome (ePRO) surveys. For those patients consenting to ePROs, baseline completion rates was 68%. Patients assigned to the control or interventional study arms were further prompted by phone once, increasing ePRO completion rates to 89%. Physician acceptance improved over time, as demonstrated by a rising proportion of patients consented to the registry (30% rising to 60%), and 98% of baseline data entry completed.

Conclusions: Our electronic, registry-based cmRCT methodology is promising for the efficient conduct of a randomized trial evaluating the impact of a desirable experimental intervention. PERa will now proceed to the next phase of deployment, evaluating its performance in the context of multiple institutions, disease sites, and interventional trials.

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CIRCULATING TUMOUR CELLS PREDICT OUTCOME IN TRIMODALITY MANAGEMENT OF ADVANCED NON-METASTATIC ESOPHAGEAL CANCER

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Purpose: Circulating tumour cells (CTC) correlate with poor prognosis in metastatic esophageal cancer, but there are few data describing the importance of CTCs in patients with non-metastatic disease. Our aim was to establish if CTCs predicted worse outcome in patients with non-metastatic esophageal cancer.

Materials and Methods: We prospectively collected CTC data from patients with operable non-metastatic esophageal cancer from April 2009 to November 2016 enrolled in our QUINTETT esophageal cancer clinical trial (NCT00907543). Patients were randomized to receive either adjuvant or neoadjuvant chemoradiotherapy plus surgery. CTCs were enumerated with the CellSearch® system (Menarini Silicon Biosystem, Philadelphia, PA) before the initiation of any treatment (surgery, or chemoradiotherapy) as well as at six, 12, and 24 months post-treatment. CTC findings were correlate with standard tumour characteristics, including tumour size, and grade. Oncological outcomes were examined using Kaplan Meier estimates and Cox proportional hazards regression.

Results: CTCs were identified in 26 of 74 patients (35%) at a median follow-up of 12.7 months (interquartile range: 6.8-23.9 months). Detection of CTCs at any follow-up visit was significantly predictive of worse disease free survival (p=0.004), regional control (p=0.042), distant control (p<0.001) and overall survival (p=0.034). After adjusting for receiving neoadjuvant versus adjuvant chemoradiotherapy, the presence of CTCs at any follow-up visit remained significantly predictive of worse overall survival (hazard ratio:1.82[HR];95% confidence interval [CI]:1.03-3.22; p=0.04) and disease free survival (HR: 2.26 ;95% CI: 1.29-3.97; p=0.005). Similarly, any observed increase in CTCs was significantly predictive of worse overall survival (HR: 2.70; 95% CI: 1.30-5.62; p=0.008) and disease-free survival (HR: 2.92; 95% CI: 1.43-5.95; p=0.003).

Conclusions: Patients with positive CTCs post trimodality therapy was associated with significantly poorer disease free and overall survival regardless of timing of chemoradiotherapy. Further investigation is warranted for the role of CTCs as a prognostic indicator in management of advanced non-metastatic esophageal cancer.

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USING COMMUNITY CONSULTATION TO MAINTAIN RELEVANCE AND PROMOTE UPTAKE OF THE QUALITY ASSURANCE GUIDELINES FOR CANADIAN RADIATION TREATMENT PROGRAMS: A QUALITY IMPROVEMENT PROCESS

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Purpose: The Canadian Partnership for Quality Radiotherapy's (CPQR) Quality Assurance Guidelines for Canadian Radiation Treatment Programs (QRT) has served as a gold standard benchmarking tool for Canadian radiation oncology programs (ROP) since 2011, with many of the key quality indicators (KQI) included in Accreditation Canada's 2017 refresh of Cancer Care Standards. The current CPQR-supported initiative sought to measure pan-Canadian ROP compliance and assess perceived barriers to uptake and relevance as quality improvement (QI) tool.

Materials and Methods: QRT self-audits and surveys were conducted with ROPs in 2015 and 2018, providing a report of compliance to the responding ROP and feedback to CPQR on QRT use and perceived barriers and relevance of each KQI. Quantitative and qualitative data was gathered from ROP KQI self-audits and survey responses pertaining to perceived barriers and relevance. A comparative and thematic analysis of the QRT and Accreditation Canada's Cancer Care Standards (CCS) informed further decision making.

Results: KQI self-audits were performed by 44 and 30 ROP in 2015 and 2018, respectively. In 2015, 81.8% of programs used the QRT document as a benchmark for programmatic guidance. In 2018, all responding programs recognized the QRT document's continued relevance to achieving quality radiotherapy. Of the 45 KQIs measured, four had a sustained compliance of less than 75%, nine saw an increase in compliance of more than 10% and a further four had a decrease in compliance of more than 10%. As in 2015, the 2018 survey continued to identify the most challenging KQIs as being those related to patient outcome data collection and use. In the 2018 survey, responding ROP made a total of 25 suggested changes to the QRT document that involved to improve clarity, reflect a change in practice or support a more granular approach to measuring compliance. The thematic analysis of the QRT and CCS provided further insight into possible barriers of KQI compliance or potential for modernization of the QRT. One example of an emerging theme was the complex nature of legislated quality standards across provinces and potential to better align such regional expectations with the more rigorous CPQR-developed pan-Canadian guidelines.

Conclusions: Since its first iteration in 2011, the QRT has maintained relevance as a tool allowing ROP to perform self-assessments of KQI, benchmarking and direct QI efforts locally. This study has, however, identified persistent gaps in compliance as well as ROP recommendations to consider updates of the eight year old publication. Results of the current study will inform a CPQR/CARO Quality and Standards Committee joint initiative to maintain relevance, utility and uptake of CPQR-developed QA documents.

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LEARNING ONCOLOGY ONLINE: PATTERNS OF USE OF AN EXPANDING ONLINE RESOURCE FOR MEDICAL STUDENTS

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Purpose: Virtually all practicing physicians will encounter cancer patients, yet many physicians lack training in basic cancer prevention, detection, and management which has been in part attributed to deficits in training during medical school. We have developed a free online resource, learnoncology.ca, intended to improve the knowledge of medical students to provide competent, compassionate and interdisciplinary care to oncology patients. Presently the website is used as a resource in medical undergraduate curriculums globally. The objective of this study was to evaluate the usage patterns of the website to improve oncology education.

Materials and Methods: Google analytics of learnoncology.ca website, LearnOncology YouTube channel, and voluntary pop-up survey responses were collected and analyzed between July, 2017 and October, 2018. Data on page views, session details, browser statistics, user demographics, and traffic sources collected. Results were interpreted with descriptive statistics.

Results: Between 2017 and 2018, 7,337 unique users frequented learnoncology. The top viewed modules and videos were general topics such as "Basic Oncology Principles". Qualitative review of comments from videos reveal learners find the resource useful, unique and helpful to supplement their learning. We noted 8% increase in users using mobile phones to access the site between 2017 and 2019 reflecting increasing mobile use for accessing information at large. Mobile users spent much shorter amounts of time per view compared to laptop users which may reveal a primary function of mobile phones for quick fact-checks.

Demographic analysis revealed most viewers were medical students (47%), however, other health professional students including nursing, radiation therapy, and pharmacy also frequented the website. 52% of viewers were male and 48% were female with an age distribution mostly between 18-24 (48%) and 25-34 years old (45%).

Users spanned five different continents with most viewers coming from Canada (58%), followed by the US and the European countries. Only 49% of website and 37% of video viewers accessed the resource directly through a link, a previous saved visit, or from page-to-page, and a large fraction of views came from search engines including key words such as "basics of oncology", "dysplasia", and "radiotherapy".

Conclusions: Learnoncology.ca has a significant amount of traffic for an educational website and we demonstrate it is a useful resource for various healthcare professionals and students globally. Patterns of interests can be discerned with the data, including effectiveness of engagement, global demographics, popularity of topics, shifts to increasing mobile use, and access paths to resources. Additional studies are needed to evaluate the higher levels of learning to see if the site is impactful on knowledge, and ultimately contributes to improved cancer patient care.

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BUILDING CLINICAL CONSENSUS AND KNOWLEDGE TRANSLATION AND EXCHANGE TO DRIVE QUALITY OF CARE FOR PATIENTS THROUGH THE DEVELOPMENT OF A PROVINCIAL RADIATION TREATMENT FUNDING MODEL

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Purpose: Quality-based Procedures (QBP) are services across varying treatment domains that facilitate healthcare providers to share best practices to improve quality, system efficiencies, standardize care, and provide evidence-based care, while ensuring activity-based funding follows the patient. In 2018, the Ontario Ministry of Health and Long-Term Care approved the development of a QBP for radiation treatment services to address known high variability in cost, infrastructure, and practice variation. The objective of this work is to utilize multi-disciplinary clinical consensus and knowledge translation to inform a provincial funding model, adoption of best practices and ultimately improve the quality of care.

Materials and Methods: To date, the Radiation Treatment Program at Cancer Care Ontario is collaborating with over 100 radiation oncologists, therapists, medical physicists, nurses, and regional leadership across 14 cancer centres. Clinical consensus meetings of these experts employ the nominal group technique to develop radiation protocols and quality metrics using 29 Expert Panels, 11 Working Groups, and nine Advisory Committees. The aim is to determine a QBP that incorporates 15 disease-sites groups and 186 clinical practice sub-groups. In preparation, international literature and provincial data were analyzed in the patient pathway domains of pre-treatment, imaging and planning, quality assurance, treatment and follow-up.

Results: Preliminary results indicate that the nominal group technique has been successful in attaining clinical consensus of best practice radiation treatment protocols and quality metrics across five of the 15 disease sites. Emerging results of this technique include bringing attention to variation amongst regions, emerging technologies, and institutional guidelines. There were beneficial unintended results of the clinical consensus meetings, such as the ability to create a platform for regional knowledge translation and exchange in areas such as guidance documents and models of care.

Conclusions: Clinical consensus using the nominal group technique is driving high quality radiation treatment forward, while informing an activity-based provincial funding model. This approach may be helpful in driving quality improvement on a national level.

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EFFECTIVENESS OF PALLIATIVE HEMOSTATIC RADIOTHERAPY FOR HEMOPTYSIS; A PROSPECTIVE SINGLE ARM OBSERVATIONAL STUDY

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Purpose: Palliative external beam radiotherapy is commonly used for malignancy associated hemoptysis. Few studies have focused on the effectiveness of radiotherapy in a cohort of patients with uncontrolled bleeding. The purpose of this study is to determine radiotherapy control probability, durability and influencing factors.

Materials and Methods: This is a single institution prospective observational study that included patients ≥18 years with any lung malignancy and active hemoptysis at time of presentation. Hemoptysis severity was captured and monitored via an in-house developed patient reported outcome tool. The tool captures bleeding description, amount and frequency within one week prior to presentation and assigns a cumulative score ranging from 0-12. Patients were interviewed at enrollment, two weeks, three months and six months post-treatment. Definition of a complete response was a total score of 0, partial response was a decrease from baseline score but >0, and progression was an increase from baseline score. Descriptive statistics, Kaplan-Meier method, Wilcoxon signed-rank test and Cox regression models were used.

Results: From April 2016 to November 2018, 41 patients were enrolled. One patient withdrew consent and was excluded.

Median age was 68 years. Most patients were male (67%) with Stage 4 (87%), lung primary (85%) disease and ECOG performance status 2 (55%). Prior to enrollment, 15% of patients received a blood transfusion and 5% had a bleeding associated intervention. Median baseline bleeding score was 7 (IQR; 5-8). Most common fractionation scheme (72.5%) was 2000 cGy in 5 fractions. Median Planning Target Volume (PTV) was 364 cc. Median follow-up was 6.1 months (range 0.9-6.2). Forty patients had scores available at baseline versus 32, 19 and 10 scores at two weeks, three and six months respectively. Complete response was achieved in 17 (53%) of surviving patients at two weeks (z=-4.2, p<0.001), 15 (79%) at three months (z=-3.5, p<0.001) and eight (80%) at six months (z=-2.6, p=0.004). Of the patients with complete hemoptysis response, two (20%) recurred at three months and one (16%) at six months. The six-month OS was 26% (95% CI 0.13, 0.41). No patient received re-radiation for their hemoptysis. On univariate analysis, ECOG status (p=0.012) and prior radiation (p=0.006) were strongly associated with freedom from hemoptysis survival, while baseline hemoptysis score was borderline (p=0.072). Multivariate analysis was not performed due to small sample size.

Conclusions: Hemostatic radiotherapy is an effective modality for controlling hemoptysis in a poor prognosis population with acceptable durability and no re-treatments required. However, a larger sample size is required to assess the impact of influencing factors.

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EFFECT OF AN ELECTRONIC QUALITY CHECKLIST ON PRESCRIPTION PATTERNS OF PROPHYLACTIC ANTIEMETICS AND PAIN-FLARE MEDICATIONS IN THE CONTEXT OF PALLIATIVE RADIOTHERAPY FOR BONE METASTASES

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Purpose: International guidelines recommend prophylactic antiemetics and pain flare medications for subsets of patients receiving palliative radiotherapy for bone metastases. Anecdotally however, prescription rates seem variable. We hypothesized that a simple electronic quality checklist could increase the evidence-based use of these medications.

Materials and Methods: We implemented a single centre default force-function electronic quality checklist item for all patients planned to receive palliative radiotherapy for lumbar spine bone metastases. We reviewed prescription rates from six months pre- and post-intervention. Patients were stratified according to if they were treated within a dedicated rapid palliative (RPAL) radiotherapy program or not. Khi-square tests compared rates of prophylactic antiemetic and pain flare medications pre- and post-intervention and RPAL versus not.

Results: Two hundred and four patients were identified with 12% treated in the RPAL program. The proportion of the 204 patients prescribed prophylactic antiemetics and pain flare medications pre- and post-intervention were respectively 31% versus 71% (p<0.001) and 26% versus 48% (p=0.003). The corresponding proportions of the 24 patients from the RPAL program were 41% versus 81% (p=0.05) and 58% versus 100% (p=0.01).

Conclusions: Our data shows that a simple electronic quality checklist item can have a significant effect on the evidence-based use of prophylactic antiemetic and pain flare medications for patients treated with palliative radiotherapy for lumbar spine bone metastases. We believe such strategies should be routinely included in other clinical pathways to improve use of symptom control medications.

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STEREOTACTIC BODY RADIOTHERAPY FOR NON-SPINE BONE METASTASES: AN INTERNATIONAL SURVEY OF PRACTICE PATTERNS

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Purpose: Increasingly, stereotactic body radiotherapy (SBRT) is being delivered for non-spine bone metastases; however, the anatomical variability in tumour location and a lack of established guidelines create uncertainty in dose-fractionation selection and target delineation. To inform the development of consensus guidelines, we assessed practice patterns amongst international experts delivering non-spine bone (NSB) SBRT.

Materials and Methods: Nine international radiation oncologists were invited to participate based on demonstrated expertise with NSB SBRT. Experts were sent gross tumour volume (GTV) contours along with planning CT and MRI for 11 anonymized cases of NSB metastases. Cases were purposefully selected to represent a range of bony sites, including metastases to long bones (femur, humerus), pelvic bones (ilium, ischium, acetabulum, pubic symphysis) and thoracic bones (rib, sternum, scapula, clavicle). Experts completed an accompanying survey pertaining to the technical aspects of treatment planning (e.g. dose-fractionation schemes, clinical target volume [CTV] delineation) specific to the included cases and to their general practice. Descriptive analysis was conducted on the survey data.

Results: All experts participated and completed the survey. Most (78%) routinely fuse planning or diagnostic MR imaging (T1- and T2-weighted sequences) with planning CT images for target delineation. Dose-fractionation schemes varied considerably and included single-fraction (18-24 Gy/1), 2-fraction (24 Gy/2), 3-fraction (28-30 Gy/3), 5-fraction (30-50 Gy/5) and 10-fraction (42-50 Gy/10) schedules. Five-fraction schedules were most common, specifically 35 Gy/5 fractions with 56% opting for this dose-fractionation scheme in at least one case. Other dose-fractionation schemes used by ³ 2 different experts were 20 Gy/1, 24 Gy/2, 30 Gy/3, 30 Gy/5, 40 Gy/5 and 50 Gy/5. Three experts (33%) used a simultaneous integrated boost technique to target a high dose CTV within a lower dose CTV. In at least one case, all experts altered their dose selection based on a perceived risk of fracture or injury to nearby organs-at-risk. All experts routinely applied a CTV margin with intraosseous margins ranging from 2-10 mm (5mm most common) and extraosseous margins ranging from 4-5 mm (5 mm most common). Extraosseous margins were only applied in cases with soft tissue mass or cortical bone disruption. Nearly all experts (89%) manually reduce CTV volumes to spare joint spaces and respect barriers to spread including pleura, pericardium and peritoneal cavity.

Conclusions: Our findings highlight the heterogeneity worldwide in dose-fractionation selection and target delineation for NSB SBRT and supports the need for consensus guidelines. However, there is also strong international agreement on principles of CTV delineation specific to NSB metastases and the utility of MR imaging for treatment planning.

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CINE MRI-BASED ANALYSIS OF INTRAFRACTIONAL MOTION IN RADIATION TREATMENT PLANNING OF HEAD AND NECK CANCER PATIENTS

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Purpose: To investigate intrafractional motion of head and neck target volumes as it pertains to radiotherapy treatment planning including planning target volume (PTV) margins.

Materials and Methods: MR-cine imaging was performed as part of an institutional workflow for radiation treatment planning in 22 patients with head and neck cancer on 1.5T MRI between 2017-2019. Dynamic MRI scans (sagittal orientation, 2x2x7 mm^3 resolution), which ranged from 3-5 minutes and 900-1500 images, were acquired. Gross target volumes (GTV) were propagated on the T1 gadolinium-enhanced sagittal sequence using deformable image registration. For each tumour contour, the position of the maximum displacement along each direction in the anterior/posterior (A/P) and superior/inferior (S/I) position was recorded. Tumour displacement during deglutition and at rest was analyzed to determine average PTV margins that account for both setup error and motion.

Results: Tumour motion was quantified in 22 patients with head and neck cancer. Most common tumour sites were oropharynx (n=15), larynx (n=5) and hypopharynx (n=2). The mean duration for swallowing was 2.9 seconds (range 1.7-6.2s) with a frequency of 1.8 swallows per minute (range 0.2-6.3). The maximum range of displacements for A/P motion was 10.3mm/9.4mm and S/I was 12.5mm/20.1mm. The mean swallow had displacements A/P of 4.3mm/3.1mm and S/I of 4.3mm/6.6mm. At rest, the mean swallow displacement was A/P 2.0mm/1.5mm and S/I 2.1mm/2.9mm. Average PTV margins required for set-up error and tumour motion (swallowing included) for A/P/S/I positions were 4.2mm/3.9mm/5.7mm/7.6mm across all tumour sites, respectively. When accounting for non-swallowing motion, average PTV margins were 4.0mm/3.7mm/5.4mm/7.3mm (A/P/S/I), respectively.

Conclusions: The use of MR-cine in treatment planning allows for quantification of tumour motion during swallow and rest periods and should be accounted for during treatment planning. With motion considered, the derived margins exceed the commonly used 3-5 mm PTV margins employed for head and neck cancer patients. Quantification and analysis of tumour and patient-specific PTV margins is a step towards real-time adaptive planning.

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TREATMENT AND OUTCOMES IN PT4 WELL-DIFFERENTIATED THYROID CARCINOMA

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Purpose: Locally advanced, pT4 well differentiated thyroid carcinoma is a relatively rare entity and the benefit of external beam radiotherapy (EBRT) is unclear. The purpose of this study is to evaluate locoregional control (LRC) and cancer specific survival (CSS) of patients with pT4 well differentiated thyroid carcinoma in the largest retrospective cohort to date.

Materials and Methods: Electronic records of patients with pT4 well-differentiated thyroid carcinoma treated at our institution from 2001 to 2013 were reviewed. Log-rank test and multivariable Cox regression were used to establish factors impacting locoregional control and cancer specific survival.

Results: A total of 232 patients were treated during this time period. The most common histologies were papillary carcinoma (n=192) and follicular carcinoma (n=11). The median age was 58 and 61% were female. Median follow-up time was 11 years. The median tumour size was 3.1cm (interquartile range: 2.0-5.0cm), 60% had multifocal disease, 33% lymphovascular invasion, 9% perineural invasion and 64% had node positive disease. Local invasion into the strap muscles was seen in 51%, trachea 33%, larynx 4%, pharynx 3%, and recurrent laryngeal nerve 1%. 22% patients had an R0 resection, 55% R1 and 23% R2. Ninety-two percent of patients received adjuvant radioactive iodine therapy. A total of 88 patients received external beam radiotherapy with a median dose of 60Gy. There were 7 acute Grade 3 toxicities (three dysphagia, two nausea, and two pain) and seven late Grade 3 toxicities in the cohort (two dysphagia, three esophogeal stricture, one pain, one laryngeal stenosis). There were no Grade 4 toxicities observed.
Ten-year LRC was 65%, CSS was 85% and OS was 75%. On multivariate analysis, older age (p=0.02, HR 1.02, 95% CI 1.0-1.04), larynx invasion (p=0.05, HR 3.32, 95% CI 1.0-11.0) and larger tumour size (p=0.01, HR 1.17, 95% CI 1.04-1.32) were associated with worse LRC. Older age (p<0.001, HR 1.10, 95% 1.06-1.15), lymphovascular invasion (p=0.002, HR 3.3, 95% 1.5-7.2), perineural invasion (p=0.02, HR 2.9, 95% 1.19-7.48), and tracheal invasion (p=0.009, HR 2.7, 95% CI 1.3-5.5) were associated with worse CSS. Adjuvant RT was not associated with improved LRC and CSS when the entire cohort was assessed. However, for patients with microscopic or macroscopic residual disease (R1 and R2 resection), adjuvant radiotherapy was associated with improved LRC on multivariable analysis (p=0.02, HR 0.45, 95% CI 0.23-0.90).

Conclusions: Despite locally advanced disease; 10 year CSS was 85% in this cohort of patients with pT4 DTC. Adjuvant radiotherapy improved LRC for patients with R1 and R2 resections. There was a low rate of toxicity from EBRT for the cohort.

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PET SCAN ASSESSMENT OF RESPONSE 12 WEEKS POST RADICAL RADIOTHERAPY IN OROPHARYNX HEAD AND NECK CANCER: THE IMPACT OF P16 STATUS

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Purpose: This study evaluates the diagnostic performance and predictive value of FDG-PET/CT for detection of residual disease after radical radiotherapy for patients with squamous cell carcinoma (SCC) of the oropharynx, comparing p16 positive (+) versus p16 negative (-) disease.

Materials and Methods: A retrospective analysis of patients with SCC of the oropharynx at our institution treated with radical radiotherapy between 2012 to 2016 was performed (n=648). The primary and lymph node metabolic responses were evaluated on the post-treatment PET. The reference standard for sensitivity and specificity analysis was biopsy when available. Otherwise, subsequent post-treatment PET results or clinical follow-up was used. Any focal moderate or intense uptake was defined as residual disease whereas mild non-focal or no uptake was defined as complete metabolic response (CMR).

Results: Median follow-up was 28 (7-85) months. The cohort included 556 with p16+ disease and 92 with p16- disease. The median time of post-treatment PET was 96 (45-744) days after radiotherapy completion: 68% had CMR, 10% residual primary disease, 11% residual regional lymph node disease, 5% had residual primary and regional disease, and 6% had distant metastatic disease.

The local sensitivity was 100% regardless of p16 status and the regional sensitivity was 93% for p16+ versus 94% for p16- (p=1.0). The local specificity was 88% for p16+ versus 86% for p16- (p=0.59) and the regional specificity was 89% for p16+ versus 86% for p16- (p=0.32). The local positive predictive value (PPV) was 26% for p16+ versus 54% for p16- (p=0.01) and the regional PPV was 31% for p16+ versus 58% for p16- (p=0.01). The local negative predictive value (NPV) was 100% regardless of p16 status and the regional NPV was 100% for p16+ versus 99% for p16- (p=0.33).

For p16+ cases, local PPV was 0 versus 30% (p=0.06) and the regional PPV was 12% versus 35% (p=0.06) for PET scans performed at ≤12 weeks versus >12 weeks. For p16- cases, the local PPV was 67% versus 50% (p=0.65) and the regional PPV was 67% versus 55% (p=0.67) for PET scans performed at ≤12 weeks versus >12 weeks.

Five-year overall survival for those with CMR was 87% versus 51% without CMR (p=<0.001). On multivariate analysis, recurrence <12 months (HR 5.9-18.7, p=<0.001), SUV max of residual primary disease (HR 1.1-1.2, p=0.0003), and SUV max of residual lymph node disease (HR 1.0-1.1, p=0.015) were significantly predictive of inferior cancer-specific survival.

Conclusions: Metabolic response on post-treatment PET has an excellent NPV regardless of p16 status. The PPV is significantly lower in those with p16+ versus p16- disease, with a trend towards inferior predictive value if performed ≤12 weeks. CMR predicts for a significantly improved overall survival.

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BREAST TANGENT BEAM ENERGY AND LOCAL CONTROL AFTER BREAST-CONSERVING TREATMENT

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Purpose: High energy photons for adjuvant breast tangent radiotherapy beams lower skin dose and dose inhomogeneity, thereby reducing treatment-related acute and late toxicity. However, sparing of skin and superficial tissues may increase the risk of local recurrence, so some cancer centres use beam spoilers and bolus to increase the skin dose for higher energy beams. This study aimed to determine whether breast tangent beam energy affects the incidence of local recurrence after breast-conserving treatment.

Materials and Methods: This population-based study included newly diagnosed invasive breast cancers (pT1-4a, any-N, M0) treated with breast-conserving surgery and adjuvant whole breast radiotherapy without bolus or beam spoilers. Patients with skin involvement (cT4b, c, d or pT4b, c, d) and those with previous or synchronous breast cancers were excluded. The primary endpoint was the cumulative incidence of local recurrence using regional recurrence, distant recurrence and death as competing risks. A multivariable analysis was conducted with beam energy (6 versus >6 MV tangents), age, T-stage, nodal status, lymphovascular invasion, grade, margin status, extensive intraductal component, ER, PR, and HER2, as well as treatments: boost radiotherapy, hormone therapy and chemotherapy.

Results: The cohort consisted of 10,340 women diagnosed from 2002 to 2011, 7,374 treated with 6 MV tangents, 2,966 treated with >6 MV tangents and 1,319 treated with >10 MV tangents. The median follow-up by the reverse Kaplan-Meier method was 10.1 (95%CI: 9.9- 10.2) years. The 10-year cumulative incidence of local recurrence was 3.2% (95%CI: 2.7 – 3.7) with 6 MV tangents, 3.4% (95%CI: 2.7 – 4.2) with >6 MV tangents and 2.4% (95%CI: 1.7 – 3.4) with >10 MV tangents. The multivariable analysis demonstrated that a higher incidence of local recurrence was significantly related to higher grade histology, less use of hormone therapy, less use of chemotherapy and the presence of lymphovascular invasion, but not to age, ER, PR, HER2, T-stage, nodal status, margin status, boost usage, or beam energy.

Conclusions The use of beam energies >6 MV and >10 MV for breast tangent radiotherapy was not associated with an increased risk of local recurrence. Oncologists can be reassured that no special measures are required when high energy beams are used to reduce the toxicity of breast radiotherapy.

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MICROMETASTATIC (PN1MI) BREAST CANCER: TREATMENT AND OUTCOMES IN COMPARISON TO PN0, PN0(I+) AND PN1A IN THE MODERN ERA

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Purpose: To compare locoregional relapse-free survival (LRRFS) in breast cancer patients with nodal micrometastases (pN1mi) relative to node-negative (pN0), nodal disease ≤ 0.2mm (pN0(i+)) and macroscopic node-positive (pN1a) disease and to evaluate LRRFS according to locoregional treatment of pN1mi disease.

Materials and Methods: Data was prospectively collected in a population-based provincial database of patients referred between 2006 and 2011 with newly diagnosed Stage pT1-T2, pN0, pN0(i+), pN1mi, or pN1a, M0 breast cancer. Ten-year Kaplan-Meier (KM) LRRFS, distant relapse-free survival (DRFS), and breast cancer-specific survival (BCSS) were compared according to clinicopathologic and treatment characteristics using log-rank tests. Multivariable Cox regression analysis was performed to identify factors significantly associated with LRRFS in pN1mi patients.

Results: The median follow-up was 9.3 years for the 10,271 subjects with pN0 (n=7,496), pN0(i+) (n=302), pN1mi (n=622), or pN1a (n=1,851) disease. Sentinel node staging (alone or with axillary dissection) was used in 75%, 94%, 79%, and 58% (p<0.001); breast conserving surgery was used in 69%, 58%, 60% and 48% (p<0.001); regional nodal radiotherapy (RT) was used in 1%, 25%, 46% and 71% (p<0.001); chemotherapy was used in 26%, 41%, 50% and 66% (p<0.001); and hormone therapy was used in 72%, 78%, 86% and 80% (p<0.001), respectively.

Ten-year KM outcomes for the pN0, pN0(i+), pN1mi, and pN1a cohorts were: LRRFS 96%, 92%, 97%, and 96% (p<0.001), DRFS 94%, 91%, 90% and 84% (p<0.001), and BCSS 95%, 90%, 93%, and 87% (p<0.001), respectively.

In pN1mi patients treated with breast-conserving surgery, 10-year LRRFS were 94% for patients treated with surgery alone, 96% with surgery plus breast RT, and 100% with surgery plus locoregional RT (p=0.02). Amongst those treated with mastectomy, 10-year LRRFS were 95% with mastectomy alone and 99% with mastectomy plus RT (p=0.09).

On multivariable analysis of pN1mi patients, the only clinical, pathologic or treatment characteristics associated with improved LRRFS were nodal RT (p=0.04) and hormone therapy (p=0.03).

Conclusions: In the modern era of sentinel node staging and systemic therapy, regional nodal RT use was significantly higher in women with pN1mi breast cancer compared to pN0 and pN0

(i+) breast cancer, resulting in 10-year LRR risks <5% after BCS or mastectomy. Treatment factors associated with improved LRRFS were adjuvant nodal RT and hormone therapy.

54 WITHDRAWN

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THE ADVANTAGES OF TRUS WHEN COMPARED TO CT PLANNING FOR HDR PROSTATE TREATMENT

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Purpose: To compare the parameters that a centre needs to consider when transitioning from computed tomography (CT) imaging to trans-rectal ultrasound (TRUS) imaging for HDR prostate treatment, in terms of volumes, diameters and inter-observer variation.

Materials and Methods: A TRUS-based HDR procedure was introduced in 2016 in our centre. The first thirty patients to undergo the TRUS procedure were given a 15 Gy HDR boost. A CT on rails located in the brachytherapy suite was used to image the pelvis after the treatment. The treating radiation oncologist (RO); RO1, 2 or 3 in 2016, then contoured the prostate on both modalities. Two years later, four ROs (RO4 started in 2017) re-contoured the prostate on the CT and TRUS images for each patient. The RO's CT clinical experience was as follow, in terms of years: RO1=13, RO2= 18 RO3=7 and RO4= 1. A volume and diameters (at midplan) comparison between both modalities and between ROs was performed. A rigid registration between CT and TRUS images was completed for 20 patients using gold fiducials markers. The Jaccard Index (JI), which measured the overlap between contours, was computed to evaluate the inter-observer variability.

Results: The mean CT and TRUS volumes showed a significant correlation for the prostate of 0.95 ($p<0.001$). The volume ratio of TRUS/CT was 0.82 (95% interval 0.79-0.87), meaning the volume was 18% bigger on CT. The antero-posterior (AP) diameter was significantly different ($p<0,01$) between TRUS and CT for every RO but the left-right (LR) and cephalo-caudal (CC) diameters were not, meaning a prostate compression in the TRUS probe axis. CT planning led to significant variations for LR, AP and CC diameters when comparing each pair of RO, but the variation in TRUS diameters was only significant for LR. The mean JI for prostate contour was 87% for CT and 92% for TRUS when comparing all 4 ROs, with a significantly difference ($p<0.001$). The mean JI for the prostate on CT was significantly better ($p<0.001$) when comparing RO1, 2 and 3 together (RO1-2, RO1-3, RO2-3, mean=89%) than when comparing RO4 to the more experienced ROs (RO1-4, RO2-4, RO3-4, mean=85%). For TRUS planning, the mean JI was not significantly different ($p>0.05$) when comparing all ROs.

Conclusions: When transitioning from CT to TRUS planning for HDR, we must consider that the prostate volumes are 18% bigger on CT compared to TRUS, probably explained by the AP compression of the probe and the better soft tissue contrast. Interestingly, the inter-observer variation was significantly better with TRUS than with CT for diameters and contours' superposition, despite different clinical experiences. Therefore, the TRUS might lead to a more homogeneous planning technic in a RO team.

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NUTRITIONAL RISK INDEX IN PATIENTS UNDERGOING CHEMORADIATION THERAPY FOR ORAL CAVITY AND OROPHARYNX CANCER

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Purpose: Patients undergoing combined chemoradiotherapy (CRT) for oral cavity and oropharynx cancer are often malnourished before, during, and after treatment. Contributing factors include odynophagia, dysphagia, dysgeusia, and mucositis. A simple validated objective measure of malnutrition is the Nutritional Risk Index (NRI), calculated by: 1.519 x albumin + 0.417 x present weight/ideal body weight and patients are categorized as no malnourishment (>100), mild (97.5-100), moderate (97.4-83.5), and severe (<83.5) risk. While NRI has been validated in other cancers, it has not been assessed as a malnutrition screening tool for oral cavity and oropharynx cancer patients undergoing radiotherapy. The objectives of this study were to assess the NRI association with: 1) pre- and post-radiotherapy change in NRI; 2) risk factors; 3) complications and adverse outcomes.

Materials and Methods: A population-based review of British Columbia (BC) provincial database of oropharyngeal and oral cavity squamous cell carcinoma patients treated from 2013 to 2015 with curative intent CRT was performed. The provincial nutritional database prospectively collects basic anthropometric data, including initial weight, height, post-treatment weights and treatment complications. Basic demographic and oncologic staging and treatment information were collected retrospectively. Multivariate logistics regression analysis was used to assess the risks of greater NRI drop.

Results: One hundred and ninety-six patients were identified, of which 163 were males. The median age was 59 years. Tumour subsites were as follows: 85 tonsil, 75 base of tongue, 14 oral tongue, 14 oropharyngeal not otherwise specified, five floor of mouth and three soft palate. The average pre- and post-treatment NRI score difference was 10.5 and both clinically and statistically significant ($p<0.01$). Before radiotherapy, NRI scores were 82.4% no malnourishment, 6.6% mild, 10% moderate, and 1% severe malnourishment. In comparison, at the completion of RT, 49% had no malnourishment and 11% mild, 30% moderate and 8% severe malnourishment ($z=-8.00$, $p<0.01$). Elevent percent of patients had a prophylactic G-tube, 22% reactive G-tube and 9% reactive NG-tube. Twenty-five percent percent had a feeding tube complication. With the small sample size, on multivariable analysis, age, T-stage, N-stage, tumour site, prophylactic G-tube insertion were not predictive of greater NRI drop (all $p>0.05$). Having no surgery prior to RT was 2.6 times more likely to result in more NRI drop ($p=0.03$, 95% CI: 1.1-5.9).

Conclusions: NRI is a simple tool that can quantify the extent of malnutrition before and after CRT. There were significantly more people who had moderate to severe malnourishment after CRT (38%) compared to before CRT (11%). Surgery prior to RT was less likely to result in NRI drop. Further data analysis with more sites of head and neck cancer with NRI is planned. Validation of NRI with treatment complications will be conducted.

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LOCAL CONTROL FOLLOWING COMBINATION HYPOFRACTIONATED RADIOTHERAPY AND PEMBROLIZUMAB IN A PHASE II TRIAL OF RECURRENT OR METASTATIC ADENOID CYSTIC CARCINOMA PATIENTS

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Purpose: Adenoid cystic carcinoma (ACC) is a salivary gland malignancy that can require relatively high doses of radiation to achieve local control. Given distant recurrences are common and metastases can grow slowly, local treatments are often pursued. Here, we investigate the ability of hypofractionated radiotherapy (RT) to affect local responses when given in combination with the PD-1 inhibitor pembrolizumab (pembro) in a prospective phase II trial. We hypothesized the combination of pembro and RT would serve as effective local treatment, even at relatively modest radiation doses.

Materials and Methods: We enrolled patients with recurrent or metastatic ACC with evidence of progressive disease over the last year, >=1 measurable non-CNS lesion, and 1-5 lesions appropriate for RT prescribed to a dose of 30Gy/5. Twenty patients were randomized to receive pembro alone (200mg IV q3 weeks) or pembro with RT started within seven days of cycle 1, day 1 (10 patients each arm). The primary endpoint was objective response rate outside the RT field by RECIST 1.1. In this exploratory analysis, local responses of irradiated lesions were assessed using centralized imaging review. The product of the longest two perpendicular dimensions of all irradiated lesions were determined at each restaging scan on study as well as at two sequential time points >1 month apart prior to study treatment to confirm progression prior to study entry. We compared each time point to the baseline study scan to determine best overall responses (BOR).

Results: Nine of the 10 patients who received RT had measurable irradiated lesions. Among these nine patients, 11 lesions were treated: nine intrathoracic lesions and two liver lesions. All the lesions increased in size prior to study entry, with an average of 35.8% (range 2.9-84.1%) tumour growth. Following RT, all but one irradiated lesion decreased in size compared to baseline, although one patient experienced initial growth of an irradiated liver lesion (283%) before subsequent response. The mean BOR in the cohort was -47.4% (range: -3.9% to -85.7%) and five of nine patients had a BOR >50%. The median time to BOR was 4.9 months (range: 2.3-10.0 months). With a median follow-up of 5.5 months prior to withdrawal / censure (range: 2.8-12.9), eight of nine patients demonstrated an ongoing response of the irradiated lesion.

Conclusions: Preclinical studies suggest immune activation may enhance the local effects of RT. Here, we observed significant local responses within the RT field in growing ACC lesions treated with the combination of hypofractionated radiation to a dose of 30Gy and pembro administered on a phase II study. We also observed a potential case of pseudoprogression within the RT field, a phenomenon that has been previously linked to immune checkpoint inhibitors. Ongoing translational studies are investigating immunologic correlates associated with these responses. NCT03087019

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TARGETING AURORA KINASE TO ENHANCE THE CURATIVE POTENTIAL OF RADIOTHERAPY IN HPV RELATED CANCERS

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Purpose: Cervical cancer is caused by human papilloma virus (HPV), a sexually transmitted environmental agent. Approximately 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. Alisertib is a clinically approved, oral selective inhibitor of Aurora kinase A (AurkA,) which causes G2/M cell cycle arrest and apoptosis. High E7 oncogene expressing tumours and/or those carrying the *ARID1A* mutation are found in several disease sites, including cervix, and are more sensitive to AurkA inhibition. Our goal is to identify a clinically relevant treatment strategy, using AurkA as a therapeutic target in patients, to advance curative combination treatments with RTCT for HPVE7 related cancers. We hypothesize Alisertib influences the sensitivity to RT to improve primary tumour response and reduce lymph nodal disease compared to RT or drug alone. The aims are: 1) to determine the efficacy of fractionated RT combination with Alisertib in HPVE7/*ARID1A* expressing orthotopic cervical cancer PDXs on tumour growth delay response; and 2) to determine the effect on metastases development in response to AurkA inhibition with RT treatment.

Materials and Methods: HPVE7 expression profiles of the cervix PDX models were determined by qRT-PCR. An orthotopic patient derived cervix cancer xenograft was treated with RT (30Gy;2Gy/day) with or without Alisertib (30mg/kg/day) given concurrently with RT daily (3wks). Expression of anti-apoptotic and DNA damage response proteins was evaluated by western blot at the end of treatment. Tumour growth delay and lymph node metastasis was/will be assessed.

Results: The PDX HPV subtypes reflect the patient's clinical HPV status at diagnosis. In an E7 expressing PDX model, RT combined with Alisertib treatment shows prolonged tumour growth delay compared with RT alone. Reduced lymph node metastasis was observed with Alisertib alone compared to control. These studies are still in progress. Tumours analysed at end of treatment suggest that AurkA inhibition resulted in the loss of RT-induced anti-apoptotic expression and γ-H2AX phosphorylation was enhanced by the combined treatment relative to RT alone. This suggests that Alisertib may reduce repair of DNA damage induced by RT treatment, which is consistent with its expected action on AurkA. Further investigation is ongoing to assess mechanisms underlying the RT induced effects with Alisertib on tumour response.

Conclusions: Alisertib may enhance the curative potential of RT in patients with high E7 expressing cancers, and/or *ARID1A* mutations, which impacts on the sensitivity to treatment response. This study presents a promising approach to treating aggressive HPV cancers and may apply to other HPV-related cancers where RT plays a curative role and supports successful translation of new radiation-drug combinations to the clinic.

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EFFECT OF MAGNETIC FIELD DURING RADIOTHERAPY ON DOUBLE-STRAND DNA BREAKS AND CELL PROLIFERATION ON PROSTATE, CERVICAL, AND BREAST CANCER CELLS

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Introduction: MR-guided radiotherapy (RT) using MR-Linacs is an emerging technology. It allows for real-time tracking of targets and organs-at-risk to deliver RT with high precision. However, the biological effect of a strong magnetic field on cancer cells during RT is not well known, with conflicting data reported in literature. In this study, the effects of a magnetic field during RT on resulting DNA double-stand breaks (DSBs) and cell viability were investigated.

Materials and Methods: Human cancer cells from prostate (PC3), cervix (HeLa), and breast (MCF-7, MB 231, T47D) were cultured used DMEM media with 10% FBS. A Varian CLINAC (Palo Alto, CA, USA) 6 MV beam was used to deliver RT to a 96 well plate. The plate was mounted in a custom 0.21 T magnetic solenoid coil with the magnetic field oriented parallel to the RT beam. DSBs were assessed via γ- H2AX assay: cells were fixed 24-hours post-2Gy

of RT and immunostained with fluorescent *γ*- H2AX antibody probe, and the number of foci per cell was determined using a Molecular Imaging MetaXpress High Content Imaging Platform (San Jose, CA, USA). Cell viability was determined using Alamar Blue fluorescence assay at 72 hours post RT using calibrated dilution of cells per cell line at 2, 4, 6, and 8 Gy dose. Each RT experiment was done with and without the magnetic field turned on (RT and MRT, respectively).

Results: For PC3, fewer cells expressed >6 foci of DSBs under MRT than RT (58% versus 63%, p<0.01. In contrast, more cells demonstrated >6 DSB foci under MRT than RT for HeLa (18% versus 16%, p<0.01), MCF-7 (2.7% versus 0.1%, p<0.001), MB 231 (8.2% versus 1.5%, p<0.001), and T47D (2.3% versus 1.4%, p=0.027). Cell viability following 2 - 8 Gy of radiation for all cell lines demonstrated no significant difference between MRT or RT.

Conclusions: Preliminary results suggest differences in the quantity of DSBs were observed under MRT versus RT at 24 hours post-2Gy RT with a 0.21 T field, with a less proliferative cell line (PC3) demonstrating lower DSBs under MRT than RT, and the other highly proliferative cell lines showing the opposite trend. This did not manifest in altered cell viability under the doses of RT or magnetic field strength tested. Future studies aimed at exploring differing biological effects under different magnetic field strengths and cell lines should be explored.

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OPIOID CONSUMPTION AND PAIN IN GYNECOLOGICAL CANCER PATIENTS THAT UNDERWENT SPINAL ANESTHESIA FOR INTERSTITIAL BRACHYTHERAPY

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Purpose: Brachytherapy is an essential component of many gynecologic malignancies. Interstitial Brachytherapy (ISBT) is an effective option for delivering conformal high dose radiation to the target volume with better organ-at risk sparing. However, ISBT is associated with increased pain due to implantation of multiple needles and patients require anesthetic at the time of insertion. At our institution, anesthesia protocol was changed from general anesthesia (GA) to spinal in September 2017 due to workflow requirements. This study's objective was to look at pain levels and opioid consumption in the first cohort of patients who underwent spinal anesthesia for ISBT and compare with our previous cohort of patients that underwent GA.

Materials and Methods: The first 26 patients that underwent spinal anesthesia for ISBT from September 2017 to July 2018 were analyzed from a prospective institutional database. Mean age of the patients was 62. Primary diseases consisted of 15 cervical cancers, six recurrent endometrial, three vaginal and two others. Baseline patient characteristics, radiation treatment details, anesthesia records and inpatient charts were obtained. Opioid consumption was quantified as oral morphine equivalent per day (OMEq/day) from postimplant until template and needles removal. Pain score levels were collected by using an 11-point scoring system, numerical rating scales (NRS). Pain and opioid consumption were compared with a previously analyzed cohort of 48 patients in the same database who underwent ISBT with GA.

Results: Of the 26 patients, 17 patients underwent a second ISBT insertion with spinal anesthesia. Twelve patients required parenteral opioid analgesia post implant. No difference in OMEq/day or pain scores was seen between admissions (mean consumption 41.4mg and 48.6mg, p=0.64, median interquartile range pain scores 5 (2.75-7.75) versus 4 2-7, p=0.35). Patients who received IV opioids used larger amounts of opioids than patients with oral opioids (OMEq/day 69.7mg versus 17mg, p=0.04). Compared to a previous cohort of patients at our institution who underwent ISBT with GA, a significantly lower OMEq/day was noticed across all admission (44.1mg versus 65.2mg p=0.02) with spinal. There was no difference in intensity of the reported pain. Peak pain scores were seen in the evening with spinal compared to immediately following the insertion in the GA cohort.

Conclusions: In patients undergoing ISBT with spinal anesthetic, pain can be managed with oral analgesics in the majority of patients. Peak pain scores after the procedure are delayed in patients with spinal when compared to GA. Patients had similar levels of reported pain across cohorts however opioid use was lower in the spinal cohort as compared with GA cohort.

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TREATMENT OF LOCOREGIONALLY ADVANCED LARYNGEAL CANCER: INSTITUTIONAL OUTCOMES OF PRIMARY SURGERY COMPARED TO PRIMARY RADIATION

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Purpose: In the past, most locoregionally advanced laryngeal cancers were treated by surgery plus or minus adjuvant radiation. However, there has been a trend towards organ preservation with treating with primary concurrent chemoradiation (CRT). While locoregional control is thought to be improved with laryngectomy, overall survival has been shown to be similar between the two groups. Our objective was to retrospectively analyze our institutional outcomes for concurrent chemoradiation compared to laryngectomy in patients with locoregionally advanced larynx cancer.

Materials and Methods: An institutional database was used to identify patients treated for Stage III and IVa squamous cell carcinoma of the larynx between 2002 and 2014. Inclusion criteria were: Stage III or IVa disease and treatment with curative intent. Curative intent treatments included primary laryngectomy and neck dissection with or without adjuvant radiation or primary radiation (66-74Gy in 30-37 fractions) with concurrent systemic therapy. Exclusion criteria were: non-squamous cell pathology, cartilage invasion, failure to complete a minimum of 10 fractions of radiotherapy, treatment at another institution, previously treated head and neck malignancy, or simultaneous treatment for a synchronous primary. Kaplan-Meier estimates were used to compute time-to-event outcomes. Endpoints were three- and five-year overall survival (OS), locoregional control rates (LCR) and laryngectomy-free survival (LFS).

Results: One hundred and seventy-one patients were identified who received curative intent treatment for laryngeal cancer. Fifty-four patients were excluded from analysis for reasons identified above. One hundred and seventeen patients remained for analysis (surgery n=67, CRT n=50) with a median follow-up of 50 months (2 to 119 months). Primary disease site was supraglottic in 59% of patients (n=69), 37% glottic (n=43), 4% subglottic (n=5). Forty-one percent of patients were Stage III (n=48) and 59% Stage IVa (n=69). T-stage was T1, T2, T3, T4a in 1% (n=1), 0% (n=0), 24% (n=16) and 75% (n=50) for the surgery group and 0% (n=0), 12% (n=6), 78% (n=39) and 10% (n=5) for the CRT group, respectively. N-stage was N0, N1, N2a, N2b, N2c in 43% (n=29), 15% (n=10), 7%

(n=5), 10% (n=7) and 24% (n=16) for the surgery group and 52% (n=26), 16% (n=8), 4% (n=2), 16% (n=8) and 12% (n=6) for the CRT group, respectively.Three- and five-year OS was 64.0% and 50.6% for surgery and 77.7% and 60.2% for CRT, respectively (p=0.19). Three- and five-year LCR was 89.5% and 86.7% for surgery and 91% and 87.9% for CRT, respectively (p=0.82). Three- and five-year LFS for patients who underwent primary CRT was 67.7% and 52.3%.

Conclusions: Our study shows comparable OS and LCR rates for patients with locoregionally advanced laryngeal cancer who received surgery or CRT as their primary therapy. This suggests primary CRT for organ preservation may be offered to well-selected patients without compromising survival outcomes, understanding that many patients will require salvage laryngectomy.

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PRE-RADIOTHERAPY PROSTATE CANCER PATIENT EMPOWERMENT PROGRAM (PC-PEP) - RESULTS OF A FEASIBILITY STUDY

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Purpose: A 2018 Maritime-wide study of over 400 prostate cancer (PCa) survivors who completed a comprehensive on-line quality of life survey showed most men reported sexuality/intimacy issues, were suffering moderate to severe urinary symptoms, and reported problems sleeping, fatigue, emotional distress, and felt socially disconnected.[1] One in six men in this sample screened positive for clinical depression or anxiety and most were not on any medication for this. To address these issues directly we created a Patient Empowerment Program (PEP) to be delivered pre-surgery and/or radiotherapy to teach the men life skills/habits which are aimed to improve their fitness levels and quality of life including mental health during and after treatment, and to decrease treatment related side effects. Here we report the results of this 28-day feasibility study including compliance and evaluation.

Materials and Methods: The PEP program was created based on a review of the pre-habilitation literature, expert opinion and the experience of the lead investigators. Thirty men with a diagnosis of non-metastatic prostate cancer having received various treatment at different times participated in the program (mean age 69, range 56-83). The 28-day intervention consisted of: 1) information session about the science behind the PEP recommendations; 2) personalized strength and aerobic training; 3) pelvic floor training; 4) biofeedback stress reduction through meditation/mindfulness; 5) training on various forms of intimacy; 6) co-participants support; and 7) daily multi-media reminders on all the aspects of the intervention via text, emails, and video/webcasts provided by health professionals.

Results: All participants completed the program and compliance was high as measured by a weekly on-line survey. All pre- and post-intervention assessments were completed, and included a comprehensive 30 minutes quality of life on-line survey; fitness-level measurements (six minute walk, sit to stand, flexibility, balance); EEG and heart rate variability stress level assessments. After 28-days of intensive training, the group showed improved physical (urinary, bowel, sexual) and mental health (reduced anxiety) function as measured by validated self-report questionnaires. Physical assessments showed reduced overall stress levels as measured by heart rate variability and EEG, increased grip strength, endurance (sit to stand test), and hamstring flexibility. Overall evaluation of the program was 9.6/10.

Conclusions: A 28-day multi-dimensional program is feasible for men with non-metastatic PCa and appears to improve quality of life. The program is safe to be tested as a randomized trial for men undergoing surgery and/or radical radiotherapy +/- hormone treatment.

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PROSTATE AND CATHETER MOTION IN PROSTATE HDR BRACHYTHERAPY: FROM OPERATING ROOM TO SHIELDED DELIVERY VAULT

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Purpose: High dose-rate brachytherapy (HDR-BT) is increasingly being used to deliver conformal radiation in the treatment of prostate cancer. Delivery of HDR-BT typically requires a shielded OR, which is not available at many institutions. A viable alternative is to implant in a regular OR, and relocate the patient into a shielded vault for treatment delivery. However, this movement may introduce uncertainty in patient treatment due to anatomic shifts. We aim to characterize and quantify any motion in the prostate and catheters that may arise from such patient relocation.

Materials and Methods: We prospectively identified ten adult patients with prostate cancer treated with single-fraction HDR-BT boost at a single institution between October 2018 and January 2019. Patients were positioned on a movable OR table in the dorsal lithotomy position under spinal anesthesia, and catheters were implanted using real-time 3D transrectal ultrasound (TRUS) guidance. While maintaining the same position on the OR table, patients were then wheeled through two sets of doors and around a corner to reach the shielded delivery vault. TRUS images of the prostate were captured immediately before and after patient relocation. The prostate was then manually adjusted to correct for any misalignments from the initial planning scan before treatment was delivered, in accordance with our institutional quality assurance process. Contours of the prostate were independently drawn on the pre-movement and post-movement images using the Oncentra Treatment Planning System. The volume and centre of mass (CoM) of the prostate was compared for each patient on the pre- and post-movement TRUS scans. Catheters were identified on a reference plane 1/3 from the base to the apex, approximately corresponding to the maximum axial size of the prostate, and the radial distance was compared before and after movement.

Results: The distance and median duration of the move were 10 metres and 11 minutes (range: 9 to 14 minutes), respectively. Prostate volumes were consistent between pre- and post-move scans, with a median volume difference less than 0.2 cc. The median change in prostate CoM before and after movement was 0.6 m to the right (ranging from 1.4mm to the right to 0.2mm to the left), 0.8mm posterior (1.6mm anterior to 2.2mm posterior), and 0.6mm caudal (1.3mm caudal to 0.9mm cranial). The catheters displayed similarly small motion, with a median change of 0.9mm to the right (1.5mm to the right to 0.9mm to the left) and 1.0 mm posterior (1.7mm anterior to 1.8mm posterior). The catheter motion in the anterior-posterior direction was strongly correlated with the prostate CoM shift (R=0.83).

Conclusions: Our study shows that patient relocation from the OR to a shielded delivery vault resulted in minimal movement of the prostate and catheters, with less than 1mm shift in each direction. These findings support that this is a safe and reliable method for HDR-BT delivery in centres without shielded ORs.

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AUTOMATIC DEEP LEARNING BASED SEGMENTATION OF BRAIN METASTASIS ON MPRAGE MR IMAGES FOR STEREOTACTIC RADIOTHERAPY PLANNING

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Purpose: Stereotactic radiotherapy (SRT) for patients with brain metastasis requires precisely contoured gross tumour volumes (GTVs). We aimed to compare deep-learning-generated contours (DC) with expert contours (EC) on SRT treatment plans.

Materials and Methods: Dataset 1 (DS1) consisted of 78 brain metastasis SRT plans with fused MPRAGE MR scans from a single centre. Dataset 2 (DS2) consisted of 170 publicly available MR images with brain metastasis contoured by a CNS radiation oncologist. Convolutional neural networks were used to train separate models on DS1, DS2, and a combined model including DS1 and DS2 (DS-all). Two model variations were developed: DC-Axial, which relied solely on axial training slices, and DC-Multi, which used axial contours combined with multiplanar slices in order to reduce false-positive predictions. A validation dataset consisted of 28 MPRAGE MR scans with 46 individual brain metastasis GTVs from SRT treatment plans. The true-positive DCs were compared with ECs using the Dice Similarity Coefficient (DSC), 95% distance transform (DT-95%), and mean distance transform (DT-mean). Dosimetric analysis was performed by fusing the DCs to the SRT planning CT scans with MIM Maestro (version 6.7).

Results: The DC-Axial models identified 63%, 65%, 70% of metastasis for DS1, DS2, and DS-all respectively. The DC-Multi models identified 49%, 58%, 59% of metastasis for DS1, DS2, and DS-all respectively. The number of false positives for the DC-Axial models was 159, 138, 111 for DS1, DS2 and DS-all respectively. The number of false positives for the DC-Multi models was 12, nine, eight for DS1, DS2 and DS-all respectively. Comparing ECs to true-positive DS1, DS2 and DS-all models demonstrated a mean DSC of 0.68, 0.74, 0.77, a DT-mean of 0.77mm, 0.66mm, 0.57mm, and DT-95% of 1.71mm, 1.52 mm, 1.34mm respectively. The mean 80% isodose coverage was 100% for the ECs, 99.8% for DS1, 99.8% for DS2, and 99.9% for DS-all. The mean 90% isodose coverage was 100% for the ECs, 97% for DS1, 96% for DS2 and 97% for DS-all. There were no significant differences in the mean, max and minimum doses for DS1, DS2 and DS-all compared to the ECs.

Conclusions: We observed accurate delineation of true-positive DCs on MPRAGE MR images which demonstrates the feasibility of using deep learning models to aid in tumour delineation for SRT treatment planning. Similar isodose coverage, and mean, max and minimum dose for the models further demonstrates the spatial agreement between the DCs and ECs. Models trained with the largest combined dataset (DS-all) had the best volumetric and dosimetric agreement with ECs. Multiplanar models demonstrated a significantly lower false-positive rate and slightly higher false-negative rate for brain GTVs compared to models trained on axial slices alone. The true-positive detection rate can likely be improved in future studies that incorporate larger training datasets of MR images.

65 WITHDRAWN

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SALVAGE REIRRADIATION USING EXTERNAL BEAM RADIOTHERAPY FOR LOCAL FAILURE IN PROSTATE CANCER: A SYSTEMATIC REVIEW

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Purpose: Salvage therapies for localized prostate cancer failure after primary radiotherapy (RT) are underutilized. Salvage prostatectomy, high-intensity focused ultrasound, cryotherapy, brachytherapy and other investigational local ablative modalities have been described with variable success and toxicity. New technology has allowed salvage reirradiation (reRT) using external beam radiotherapy (EBRT) or stereotactic body radiotherapy (SBRT) to be implemented as a non-invasive alternative. We performed a systematic review to describe outcomes and toxicity for salvage EBRT/SBRT after primary RT for localized prostate cancer failures.

Materials and Methods: A systematic literature search was conducted using PRISMA guidelines. MEDLINE (Pubmed) and EMBASE were searched without language restrictions from inception through January 15, 2019. Reviews, case reports, and case series with fewer than 5 patients were excluded. Studies which utilized brachytherapy without EBRT, reRT for palliative intent, or reRT for a primary tumour other than prostate cancer were excluded. The most recently published data was utilized in duplicate patient cohorts. Outcome measures of interest included biochemical recurrence free survival (BRFS), genitourinary (GU) and gastrointestinal (GI) toxicity.

Results: From 2481 articles, 13 retrospective and one prospective studies were included (10 unique patient cohorts, 274 patients). Median follow-up ranged from 11.7–94 months. Median time between initial RT and salvage reRT ranged from 49.2–101 months. Median PSA at reRT ranged from 2.6–7.4 ng/mL. Robotic SBRT was the most commonly utilized EBRT platform in six of 10 cohorts. Dose and fractionation were diverse, with 240 patients treated using an ultra-hypofractionated approach of 2 - 6 fractions of 5 - 12 Gy per fraction. Equivalent dose in 2Gy fractions ranged from 38.6–98.6 Gy, $\alpha/\beta = 1.5$. Both whole and partial prostate reRT were utilized (152 and 122 patients respectively). BRFS was typically reported as 1- to 3-year rates ranging from 40% to 83.3%. Acute toxicity was predominately GU, with rare ≥ Grade 3 toxicity (range: 0–3.7%). Late ≥ Grade 3 GU/GI toxicity varied considerably (GU: 0% - 57%; GI: 0% - 61.9%). Most studies utilizing SBRT reported ≥ late Grade 3 GU/GI toxicity less than 5%, though with short follow-up. Severe toxicity (≥ Grade 3 GU/GI toxicity greater than 10%) was limited to two studies utilizing conventional fractionation and techniques for reRT.

Conclusions: Salvage reRT using EBRT/SBRT has been utilized for localized recurrence of prostate cancer, with early reported results comparable to other local salvage treatment options. The optimal dose, fractionation and technique remains to be identified. Based on available data, severe toxicity with SBRT is rare, though long-term follow-up of conventional fractionation reRT has demonstrated the potential for severe toxicity. Further research and longer follow-up are warranted to better characterize long-term outcomes.

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PATIENT ENGAGEMENT: A PAN-CANADIAN SURVEY OF RADIOTHERAPY CENTRES' CURRENT PRACTICES

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Purpose: Patient engagement has recently been encouraged and mandated in Canadian Radiotherapy (RT) centres. Various guidance documents have been developed: the 2014 Canadian Association of Radiation Oncology (CARO) Radiation Therapy Patient Charter, the 2016 Canadian Partnership for Quality Radiotherapy (CPQR) Patient Engagement Guidelines for Canadian Radiation Treatment Programs (PEG), and Accreditation Canada's 2017 refresh of Cancer Care Standards incorporating RT-specific measures.

As little is known regarding uptake of these guidelines, we conducted a survey of Canadian radiation oncology programs (ROP) to assess current patient engagement practices.

Materials and Methods: An e-survey was sent to all Canadian ROP (n=44), with one response per centre (reflecting multi-disciplinary input) requested. The survey focused on awareness and uptake of the Charter and CPQR PEG. Survey development was guided by these 2 documents, a literature review, and expert consensus, including membership of CARO's Quality and Standards Patient Education/Engagement working group.

Results: Almost half of the ROP completed the e-survey (n=21/44, 47%). Many responding ROP (71%) were familiar with the RT Patient Charter, while only 24% reported its use. Most ROP consider the Charter helpful to provide patients with expectations (75%) and to promote shared decision-making (55%).

More than half (53%) of responding ROP were aware of the CPQR Patient Engagement Guidelines, but only a third (37%) had previously completed a self-audit. As a component of this survey, ROP self-audit of the 12 guidelines revealed compliance was highest for informed consent (100%), documenting patient updates (100%), patient and family education (95%), and disclosure of medical errors (85%). Those reported as the most challenging included collection and use of patient satisfaction data (50%), patient feedback acknowledgement (53%), patient involvement in space and service review (58%), and patient input in quality assurance (71%). Patient and family education (50%) and patient reported outcomes (42%) were identified as highest priority amongst responding ROP. The majority of ROP (89%) reported willingness to share their best practices with others across the RT community.

Conclusions: Patient engagement is endorsed as highly important. However, gaps have been identified across ROP for awareness and use of patient engagement tools, as well as uptake of patient engagement activities considered critical to quality of care. Understanding current patterns of practice, including challenges, will inform a CPQR/CARO-supported pan-Canadian initiative to develop strategies for optimizing uptake of patient engagement activities.

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PROVINCIAL VARIATIONS IN RADIOTHERAPY UTILIZATION AS A MEASURE OF ACCESS: A PAN-CANADIAN STUDY

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Purpose: Access to radiotherapy (RT) is a key component of a cancer control strategy given its role in the curative and palliative management of Canadians diagnosed with cancer. However, RT utilization (RTU) rates fall short of desired benchmarks in certain provinces, meaning a proportion of residents do not receive RT that may benefit from it. The reporting of RTU is not mandated by province and it is presently unknown to what extent RTU varies across provinces. Our objective was to describe provincial variations in RTU across Canada, as a measure of access to RT.

Materials and Methods: We calculated RTU ratios for each of the ten provinces in Canada (RT case counts divided by incidence counts), by cancer type (all cancers, lung, breast, rectal, prostate) and treatment intent (curative, palliative) where data were available. This was done for the 2016 year, except for Quebec where data were from 2010. Data were extracted from each provincial RT data repository, cancer registry and/or RT department. We compared RTU ratios descriptively across provinces, and combined data from all provinces to calculate an estimated national RTU ratio. In provinces with capacity for data linkage, provincial RTU ratios were also compared to a linked method of calculating RTU, by linking each incident case count to whether RT was received within one year of diagnosis.

Results: Data have been collected and analyzed for five of the 10 provinces, with the remaining five provinces preparing data at this time. All-cancer RTU ratios varied by province: Alberta (0.34), Prince Edward Island (PEI) (0.38), Nova Scotia (NS) (0.39), New Brunswick (NB) (0.41), and Quebec (0.51). For both lung and breast cancers, RTU ratios were highest in PEI (0.55 and 0.79, respectively) and lowest in NS (0.36 and 0.59, respectively). For rectal cancers, RTU ratios were highest in Alberta (0.43) and lowest in PEI (0.38). For prostate cancers, RTU ratios were highest in NB (0.55) and lowest in Alberta (0.35). Estimated national all-cancer, lung, breast, rectal and prostate cancer RTU ratios are presently 0.45, 0.45, 0.64, 0.42 and 0.39, respectively.

Conclusions: This is the first study to describe RTU nationally, and a first step in developing strategies to improve access to RT. Data collection from the remaining provinces is in progress and will be presented at the meeting.

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OUTCOMES OF ORAL CAVITY SQUAMOUS CELL CARCINOMA PATIENTS UNDER THE AGE OF 40 YEARS: A PROPENSITY MATCHED ANALYSIS

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Purpose: Conflicting evidence exists regarding prognosis in younger patients with oral cavity squamous cell carcinoma (OSCC) compared to older counterparts. We compared the outcomes of OSCC patients <40-year-old to those between 40-70 years old treated at our institution.

Materials and Methods: All OSCC treated between 2005-2017 were reviewed. Clinical characteristics and outcomes of a younger cohort (age <40 years old) were compared to the all the older (40-70 years old) patients, and then to a 1:1 matched propensity score matched older cohort. The cohorts were matched including: gender, ECOG performance status (PS), pT- and pN-categories, primary tumour subsite (oral tongue versus other subsites), resection margin status, and presence of extranodal extension (ENE). The primary endpoint was five-year overall survival (OS, measured by Kaplan-Meier method), and secondary endpoints were five-year locoregional failure (LRF, analyzed by competing risk method), and disease-free survival (DFS, evaluated by Kaplan-Meier method).

Results: A total of 57 patients were identified in the younger (<40) cohort and 441 in the older (40-70) cohort. Among the younger (<40 years old) cohort: the median follow-up was five years, median age was 33, 24 (42%) females, 35 (61%) non-smokers, and 25 (44%) non-drinkers. Bilateral and ipsilateral neck dissection was performed in 12 (21%) and in 30 (53%), respectively. Post-operative radiation therapy was given in 23 (40%), and concurrent chemotherapy in 15 (26%).

Before applying the propensity score matching, a comparison of the younger cohort (n=57) and entire older cohort (n=441) showed that younger patients, had better ECOG PS (PS 0-1 98% versus 94%, p=0.02), had more oral tongue primary tumour site (81% versus 46%, p<0.001), fewer pT3-4 (18% versus 45%, p<0.001), less frequent pN+ (42% versus 65%, p<0.001), and less pENE+ (17% versus 34%, p=0.01). The young patients had better five-year OS (82% [95% CI 71%-93%] versus (66% [95% CI: 60-71%]) p=0.008, better five-year DFS (66% [95% CI: 54%-81%] versus 54% [95% CI 49%-60%]) p=0.031, and less LRF (26% [95% CI:16%-43%) versus 31% [95% CI: 27%-37%]) p=0.18.

Following propensity score matching (50 patients in each matched cohort); there was no significant difference between the younger and older cohort in five-year overall survival (81% [95% CI: 70%-94%] versus 71% [95% CI: 59%-85%], p=0.18), 5-yr DFS (63% [95% CI: 49%-80%] versus 64% [95% CI: 52%-79%], p=0.49), and five-year locoregional failure (28% [95% CI: 17%-47 %] versus 32% [95% CI: 21%-48%], p=0.29).

Conclusions: OSCC patients under 40 years old have better ECOG PS and pathologic features compared to the 40-70 year old counterparts. With propensity score matching, younger and older cohorts have comparable survival and tumour control. The clinical impression of poor outcomes for patients aged under 40 years may represent recall bias.

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QUANTIFYING TUMOUR DOSE USING INDIVIDUALIZED DOSIMETRY METHODOLOGY IN 177LU DOTATATE THERAPY

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Purpose: 177Lu DOTATATE (Lu) therapy can improve progression free and potentially overall survival in with progressive metastatic neuroendocrine tumours. The objective of this report is to quantify tumour absorbed doses and the impact of individualized dosimetry on the prescription of Lu.

Materials and Methods: A multi-institution prospective single arm study of Lu (four cycles) with individualized dosimetry, in patients with 68Ga DOTATATE positive, progressive metastatic disease is ongoing in Ontario (NCT02743741). Dosimetry calculations are based on quantitative SPECT/CT images acquired at 4, 24 and 72 hours post-Lu therapy. A 2cm spherical region of interest (ROI) is placed over normal kidneys and a vertebral body to estimate renal and bone marrow (BM) absorbed dose after each cycle. All patients received 7.4GBq for cycle (C) 1 (with modifications based on creatinine clearance and hematology for all cycles). Subsequent injected activities were varied based on renal absorbed dose (tolerance dose of 23Gy). Dose escalation was permitted to a max. of 11.1GBq/cycle. To quantify tumour absorbed dose, two methods was used. First a ROI was placed over representative (highest SUV uptake) intra and extrahepatic areas. Second, the liver was segmented and a threshold of >41%Max SUV was used to auto-segment liver tumours. To explore if tumour dose changed during treatment, we calculated the actual and normalized (using 7.4GBq) absorbed dose change.

Results: Between August 2016 and December 2018, 100 patients were accrued from the four consortium sites, 62 patients have completed the therapeutic phase, 53 patients have received all four cycles and were the basis of the current analysis. Using 29.6GBq (±10%) as the conventional total dose (when no Individualized dosimetry is used), 36 (68%) patients had dose escalation (>32.56GBq), nine (17%) patients no change, and eight (15%) patients had dose de-escalation (<26.64GBqi). The median (med) total renal dose absorbed was 18 (SD4, range 7 – 24) Gy. The med BM dose was 0.79 (SD1.3; range 0.15– 9.69) Gy. Using the threshold method, the med % liver containing tumour was 5 (SD 5; range 1- 31)%. The med liver tumour dose was 69 (SD 48; range 12 – 227) Gy. The med uninvolved liver dose was 10 (SD 8, range 5-33) Gy. Using the ROI method, the med liver tumour dose was 93Gy (SD64; range 20-291) Gy. The med extrahepatic tumour dose was (n = 23 with complete data across four cycles) 79 (SD 42; range 13-216) Gy. The C1 med liver tumour dose was 21 (SD19 range: 4 – 112) Gy. In contrast, the C4 dose was 16 (SD 16; range 2 – 67) Gy. The normalized med difference was -4 (SD 15; range -45 to 38) Gy.

Conclusions: Individualized dosimetry allowed dose escalation in 68% and de-escalation in 15% of patients while maintaining the renal dose within tolerance. Dose absorbed by tumour showed a >10-fold variation across patients. There is a trend for reduced dose absorption over time. The radiobiological effect of these absorbed doses on tumour control and normal tissue effect deserves further exploration.

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HUMANISM IN GLOBAL ONCOLOGY CURRICULA: AN EMERGING PRIORITY

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Purpose: Training in humanism provides the skills to achieve shared decision making with patients and their families, to navigate systems level challenges and to function positively within the healthcare team. However, there is potentially a lack of attention to humanistic competencies in global oncology curricula due to the dominance of the biomedical model in curriculum design, the challenge of assessing humanistic competencies and global cultural considerations. The aims of this study were to explore to what extent humanistic competencies are included in global oncology curricula and the nature of the humanistic competencies included.

Materials and Methods: Sixteen global oncology curricula identified in a prior systematic review were analysed. The curricula were coded using the Gold Foundation's I.E.C.A.R.E.S (Integrity, Excellence, Collaboration & compassion, Altruism, Respect & Resilience, Empathy and Service) humanistic competency framework and the CanMEDS framework. Descriptive statistics were used to describe the proportion of items attributed to each aspect of the framework

Results: 7733 curricular items were identified in the 16 curricula and 729 (9%) aligned with the I.E.C.A.R.E.S framework. The proportion of humanistic items in individual curricula ranged

from 2% to 26%. The proportion of humanistic items has been increasing from the curricula published in 1980-1989 (3%) to the curricula published in 2010-2017 with a mean of 11% (4 to 25%). There was a higher proportion of humanistic competencies in curricula from the European region (9%) than in other regions. Of the humanistic items 35% were under respect, 31% under compassion, 24% under empathy, 5% were under integrity, 2% under excellence, 1% under altruism, and 1% under service. The majority of humanistic items also aligned with the professional (35%), medical expert (31%) or communicator (26%) CanMEDS domains.

Conclusions: The proportion of humanistic competencies has been increasing in global oncology curricula over time however the overall proportion remains low. Humanism is largely represented by competencies of respect, compassion and empathy and there exists a conflation between humanism and professionalism. Future global curricular efforts may benefit from attention to incorporating all aspects of humanistic competencies.

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MEDICAL STUDENT EXPOSURE TO RADIATION ONCOLOGY THROUGH THE PRE-CLERKSHIP EXPLORATION PROGRAM (PREP): EFFECT ON CAREER INTEREST AND UNDERSTANDING OF RADIATION ONCOLOGY

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Purpose: Medical students receive little exposure to Radiation Oncology (RO) during pre-clinical training and clerkship. Pre-clerkship Residency Exploration Program (PREP) was developed by medical students at our institution to provide students with exposure to disciplines like RO with which they may not have had previous exposure, with the goal of helping with career decision making. The purpose of this study was to review how PREP affected self-reported interest in RO.

Materials and Methods: PREP is a two-week intensive elective developed by students at a Canadian medical school that provides exposure to 12 specialties, including RO. PREP includes five components: half day clinical rotations, skills sessions, simulations, specialty-specific workshops, and lunchtime panel discussions. PREP participants completed questionnaires pre- and post-participation to assess career interest and understanding of RO.

Results: Forty participants took part in PREP.Thirty-six responded to pre-PREP questionnaires and 37 to the post-PREP questionnaire. Participants reported increasing interest in RO (24 students, 64.8%) and an increase in the understanding of the role and responsibilities of a radiation oncologist such that they felt comfortable making a career decision about RO. Pre-PREP, 5 (13.8%) participants listed RO as a top three career choice. Post-program, this number increased to nine (25.0%) of the same surveyed participants.

Conclusions: PREP has demonstrated early exposure to RO can increase interest in RO as a career choice. Early clinical exposure experiences like we describe here may be useful for specialties such as RO which has an improving job forecast for trainees.

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AN INNOVATIVE LEARNING TOOL FOR RADIOTHERAPY TREATMENT PLAN EVALUATION: IMPLEMENTATION AND EVALUATION

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Purpose: Treatment plan (TP) evaluation is a core competency within radiation oncology (RO) and medical physics (MP). However, teaching and evaluating TP evaluation has been identified as a learning gap in these training progrmas. The objective of this study was to implement and evaluate an interactive TP evaluation learning tool for RO and MP residents.

Materials and Methods: Design of the TP evaluation learning tool has been previously described (CARO 2018). The tool, consisting of an interactive user module (case selection, learner response and feedback) and TP evaluation software (EVOQ), was pilot tested on current RO (n=20) and MP (n=4) residents over two sessions. Residents were provided with an in-person overview and a set of instructions describing tool navigation. This included how to select a clinical case, enter information regarding their TP evaluation, access the corresponding answer key and, if relevant, the modified acceptable plan. During the pilot, three cases were reviewed, representing different clinical sites, levels of difficulty and TP errors. Residents were then asked to complete an evaluation pertaining to tool design, content and perceived impact on learning, using a 4-point Likert-scale (strongly disagree to strongly agree). Suggestions for improvement were also solicited. Descriptive analyses were performed.

Results: To date, 67 cases covering various clinical sites, levels of difficulty and classification errors have been curated. A total of 16 RO (80%) and 4 MP (100%) residents attended, and 90% completed the evaluation form. The TP evaluation learning tool was positively endorsed with respect to design, content and perceived impact on learning. Residents strongly agreed that the user module and TP evaluation software was easy to navigate and use (94%), answer keys were clear and direct (94%) and adequate instruction was received (100%). Regarding case content, all agreed that the tool reinforced key concepts in TP evaluation. Furthermore, 88% strongly agreed that its interactivity (3D navigation and immediate feedback) provided increased educational value compared to other current learning methods and 100% recommended its use to other residents. A common suggestion for improvement was providing more detailed answer keys.

Conclusions: RO and MP residents were enthusiastic about the TP evaluation learning tool that we developed and its ability to help attain TP evaluation competencies. Its interactivity was highlighted as its major strength and advantage over other learning methods. Future directions will include increasing details and key learning points in the answer keys, expanding the number of cases and assessing feasibility for expansion to other programs.

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A NEW PREDICTIVE MODEL OF FUTURE NEED FOR EXTERNAL BEAM RADIATION THERAPY REFLECTING THE LOCAL ENVIRONEMENT TO INFORM CANCER CARE SERVICE PLANNING

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Purpose: The lifetime indication for RT quoted in the literature varies between 40.6% and 52.4%. Statistical methods to predict RT use include epidemiologic evidence-based estimation (EBEST) and criterion-based benchmarking (CBB). Despite universal availability and publically funded cancer care, there is variation in access to care. It is essential for cancer service planning to estimate future needs for RT, both in the initial treatment period, as well as along the trajectory of the disease in a changing environment.

Objective: Establish utilization ratios of radiotherapy services across tumour sites in Nova Scotia (NS) and compare to established evidence-based benchmarks. Present a statistical model which estimates future demands for radiotherapy services based on

current environment and utilization.

Materials and Methods: The Provincial Cancer Registry and the cancer centre-based data system provide information on cancer diagnosis and RT utilization between 1996 and 2015 in NS. The cumulative RT utilization ratio (CRUR) was used to describe the long-term use of RT. It is the ratio of the number of distinct RT courses delivered to a cohort of newly diagnosed cancer patients over time. To capture the impact of current treatment protocols, a period based-time-to-event analysis was used. These findings have been compared to established benchmark rates for the utilization of RT in Canada and Australia.

Results: The CRUR one, five, 10 and 15 years post diagnosis is 39.5%, 47.4%, 49.5% and 50.4% respectively. The total usage and time of usage of RT varies by cancer site. The highest ratios at 15 years were seen in head and neck cancer (79.3%), esophageal cancer (77.4%), NSCLC (72.9%), breast cancer (71.5%) and brain cancer (70.8). Comparing 15 years Nova Scotia (NS) utilization ratios with published evidence based Canadian rates (C-EBEST) and Australian rates (A-EBEST): Breast 71.5%/66%/87%, Lung 72.9%/61%/77%, Prostate 56.1%/61.2%/58%, Rectum 60.4%/72.3%/60%, Cervix 69.1%/65.4%/71%, All Cancers 50.4%/-/48.3%.

Conclusions: Based on current practice, the NS CRUR 15 years of diagnosis is 50.4%. Comparison to C-EBEST and A-EBEST rates is problematic as these estimates produce widely different results and do not include all aspects of RT utilization. EBEST and CBB alone may not be sufficient for benchmarking, but are still of value, in particular when combined with CRUR, reflecting the current local environment in NS including current indications to treat, historical referral patterns, aspects of access to care, age, stage at initial diagnosis etc. For future planning, advancements in new technology and treatment protocols favoring ultra-hypo-fractionated radiotherapy, current and future debatable indications for RT and new indications such as SBRT for oligometastatic disease as well as predicted incidence and prevalence of cancer (+4%/year) in NS need to be considered.

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PERMANENT BREAST SEED IMPLANT FOR PARTIAL BREAST RADIOTHERAPY FOLLOWING PARTIAL MASTECTOMY FOR FAVORABLE BREAST CANCER: RESULTS FOR 67 PATIENTS

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Purpose: Adjuvant partial breast radiotherapy (PBRT) is an accepted standard of care for early stage favorable breast cancer according to GEC-ESTRO, ASTRO and ABS Guidelines. Modalities include external radiotherapy and brachytherapy. We report dosimetry, acute and late tolerance for 67 LDR brachytherapy permanent breast seed implants (PBSI).

Materials and Methods: From July 2012 to October 2019, 67 postmenopausal women with unifocal T1N0 invasive ductal breast cancer or DCIS, ER positive, negative margins, Grade 1 or 2, and no LVI received PBRT using permanent implantation of stranded Pd-103 seeds on a REB approved Phase 2 trial. Following breast conserving surgery, PBSI delivered 90Gy to the seroma + margin (1.25 to 1.5cm: max PTV 125 cc). Implants were planned with CT simulation and performed as an outpatient procedure under light anesthesia, guided by live ultrasound (US). Visualization of the seroma on both CT and US is essential. Post-implant CT dosimetry used fusion with the original planning scan for seroma delineation. Evaluations were at one, two, six and 12 months and then annually.

Results: More than 95% of women suitable by oncologic criteria would consent to PBSI. Only about 40% are technically suitable due to seroma volume, location, or lack of visibility on CT or US. For 67 patients, median seroma volume was 6.6 cc (1.7-20.4), PTV 61 cc (31-117), # of needles 18 (10-30) and seeds 75 (42-134). In Day 0 dosimetry, median seroma D90 was 132 Gy (V100:97%), seroma+ 5mm 106Gy (V100:93%) and seroma+10mm 80Gy (V100:85%). Seroma location was 58% lateral, 31% central, 9% inframammary fold and one lower inner quadrant. The local reaction peaks at six weeks and is limited to the skin overlying the implant: 51% had Grade 1 erythema, 12% superficial desquamation. Needle puncture marks are not visible at four weeks. Late reactions (>2 years) are generally minimal: 35% no sequellae, 43% localized palpable asymptomatic fibrosis, 20% minimally apparent telangiectasia (6% more significant but asymptomatic), 22% slight lateral contour change or skin dimpling. All cases with more pronounced breast contour change (n=6) followed deforming surgery (nipple excision, marked post-operative nipple deviation, etc). With a minimum of 6 months follow-up, 94% of respondents were "very satisfied" or "totally satisfied". At a median follow-up of 3.3 years (6-75 months), there has been one in-breast recurrence (different quadrant) detected at 12 months and treated with mastectomy at the patient's request. Three patients have had biopsies of palpable fibrosis, all negative for malignancy. Two patients have had contralateral breast cancers, one of whom had partial mastectomy followed by a second PBSI, while the other opted for bilateral mastectomy for reasons of cancer anxiety despite satisfaction with the first procedure.

Conclusions: Our experience with PBSI for PBRT is favorable with a high patient acceptance and satisfaction, excellent early efficacy and very satisfactory cosmesis.

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SURVIVAL OUTCOMES AND TOXICITY OF BRACHYTHERAPY VERSUS EXTERNAL BEAM BOOST IN THE TREATMENT OF LOCALIZED PROSTATE CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Purpose: To conduct a systematic review and meta-analysis of randomized controlled trials (RCTs) to assess survival and toxicity outcomes in men with localized prostate cancer treated with external-beam radiotherapy (EBRT) versus low (LDR)- or high dose-rate (HDR) brachytherapy (BT) boost.

Materials and Methods: A librarian and two reviewers conducted a systematic review of the literature. Five electronic databases were searched for RCTs. The primary endpoint was bDFS at five years and secondary endpoints were OS at five years, acute genitourinary (GU) and gastrointestinal (GI) toxicity and late GU and GI toxicity. Eligible RCTs reported one of our endpoints in patients with localized prostate cancer treated with EBRT versus BT boost. Mantel-Haenszel with random-effect models and Peto methods were used as appropriate to pool estimates for odds ratios (ORs) with 95% confidence intervals (CIs). Subgroup analyses were performed to compare outcomes for LDR versus HDR boost.

Results: Of 6,577 distinct records identified, six RCTs met criteria for inclusion. One was excluded due to insufficient data. Two trials (40%) used LDR for the boost. At five years, BT boost was associated with 58% reduction in the odds of developing a

biochemical recurrence (OR 0.42; 95%CI 0.3-0.6). On subgroup analysis, both LDR (OR 0.37; 95%CI 0.24-0.58) and HDR boost (OR 0.52; 95%CI 0.29-0.94) were associated with better bDFS compared to EBRT with no statistically significant subgroup difference (p=0.36). There was no difference in five-year OS between EBRT and BT boost (OR 0.83; 95%CI 0.54-1.27). There was no difference in acute GU/GI toxicity by study arm (OR 1.88; 95%CI 0.65-5.42) or dose-rate (test for subgroup differences, p=0.32). Late GU toxicity was worse in the BT boost arm (OR 1.87; 95%CI 1.23-2.85). There was increased late GU toxicity in patients treated with LDR boost versus EBRT (OR 3.31; 95%CI 1,84-5.94) but not in patients treated with HDR boost versus EBRT (OR 1.01; 95%CI 0.55-1.86) (test for subgroup differences, p=0.006). Late GI toxicity was not statistically different in the BT boost arm (OR 1.85; 95%CI 0.94-3.61). BT boost was not associated with increased late GI toxicity compared to EBRT (test for subgroup differences p=0.34). Urethral stricture was more prevalent with BT boost (OR 4.36; 95%CI 1.99-9.57). LDR was associated with increased odds of urethral strictures (OR 5.3; 95%CI 2.06-13.63) while there was no difference between patients treated with HDR boost versus EBRT (OR 2.84; 95%CI 0.69-11.62).

Conclusions: Patients treated with either LDR or HDR boost had better bDFS compared to those treated with EBRT. Late GU toxicity and urethral stricture were increased in the BT boost arm particularly with LDR boost. Despite pooled data analysis, there was no significant difference in five-year OS between the two arms. However, five years is likely insufficient to detect an OS difference in this population. Longer follow-up and more events are needed to improve the data quality.

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COMPARISON OF HRCTV AND ORGANS AT RISK CONTOURS BETWEEN TRUS AND MR IMAGES IN IB CERVICAL CANCERS: A PROOF OF CONCEPT STUDY

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Purpose: Magnetic resonance (MR) image-guided brachytherapy (IGBT) has become the gold-standard for patients with locally advanced cervical cancer. However, this treatment is time and resource intensive. Transrectal ultrasound (TRUS) IGBT is potentially faster and a more cost-effective alternative. The aim of this study is to compare volume and dimensions of the high-risk clinical tumour volume (HRCTV) seen in TRUS and in MR and also analyse contour inter-variability agreement between these two image modalities.

Materials and Methods: In this prospective, observational study, five patients with FIGO Stage IB cervical cancer treated with MR-IGBT using a ring and tandem technique were analysed. All patients underwent MR-scan prior to BT and these images were used as a gold-standard reference for comparison with 1mm thick, axial TRUS images acquired intra-operatively, immediately before ring and tandem insertion. TRUS and MR images were analysed and contoured at dedicated MIM planning station at two different time points (TP); by five radiation oncologists (RO) at TP 1 and four RO at TP 2, respectively. HRCTV was defined as per GEC-ESTRO recommendations. HRCTV dimensions and volume were compared between imaging modalities. MR and TRUS-based HRCTV and organs at risk (OARs) contours were transferred to MATLAB and Kappa indexes (K) were calculated. Median (range) K values were used to describe the data. Descriptive statistics was performed in Stata v13.0 software.

Results: TRUS HRCTV was smaller than the analogous MR contoured volumes. The average volume difference between TRUS and MR HRCTV reduced from TP 1 to TP 2 (10 to 6cc, respectively). TRUS HRCTV thickness (antero-posterior direction) was found to be consistently smaller than MR contours in all patients. There was no observable trend in the difference of the reported width and height between the two different imaging modalities. Both TRUS and MR HRCTV inter-rater agreement was graded as "substantial", with a slight superiority seen in MR contours (K 0.66 [0.56-0.77]) than TRUS-based contours (K 0.64 [0.47-0.77]). Organs at risk inter-rater volumetric agreement was also investigated. For bladder, median K were 0.81 (0.69-0.89) and 0.80 (0.62-0.85) for MR and TRUS contours, respectively. For the rectum contours, median K were 0.85 (0.78-0.91), and 0.78 (0.67-0.89) for MR and TRUS images, respectively.

Conclusions: For Stage IB cervical tumours, use of TRUS imaging alone leads to consistent and accurate HRCTV and OAR contours. Median HRCTV inter-contour variability was "substantial" in both imaging modalities. OARs had "substantial" to "almost perfect" inter-contour agreements in both MR and TRUS. Small differences in HRCTV volumes were seen between contours in TRUS and MR and this is likely due to the consistently smaller HRCTV thickness seen in TRUS images.

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ACUTE AND LATE GENITOURINARY TOXICITY AMONG PATIENTS RECEIVING VAGINAL HIGH DOSE RATE INTERSTITIAL BRACHYTHERAPY

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Purpose: High dose rate (HDR) interstitial brachytherapy (ISBT) is an effective modality to deliver highly conformal doses of radiation for treatment of malignancies centred within the vagina. The aim of this study was to evaluate urethral dose and its correlation to the incidence of genitourinary complications among patients undergoing vaginal ISBT.

Materials and Methods: Thirty-nine patients treated with ISBT between January 2017 and April 2018 were retrospectively reviewed after REB approval. Clinical characteristics were collected from the electronic medical records and CTCAE version 5.0 was used to grade toxicity. ISBT dosimetric information was collected through review of individual treatment plans as generated in Oncentra Brachy(R). Urethral contours were retrospectively added to the structure sets using a 1cm diameter brush and dose to 0.1cc (D0.1cc), D0.2cc and D0.5cc of the urethra were obtained. Then, the total (ISBT +/- EBRT) equivalent dose in 2 Gy fractions (EQD2) received by HRCTV (Gy10) and OARs (Gy3) were calculated. Numerical counts (%) and medians (Inter-Quartile-Range) were used to characterize the data. Fisher's exact and the Mann-Whitney-Wilcox tests were used as appropriate to determine statistical significance.

Results: Median age for the cohort was 66 years (57-73). Median follow-up was 9.3 months (6.4-15.3). 21 (54%) patients had endometrial, 13 (33%) had vaginal, four (10%) had vulvar primaries. One (3%) patient had a metastasis from a rectal primary. Thirty (77%) patients received external beam radiation prior to ISBT. 17 (44%) underwent a single brachytherapy insertion and 22 (56%) received two. A median of 4 (3-6) ISBT fractions were delivered to each patient and a median of 15 needles (13-17) were used. Median total EQD2 were 55.4Gy (46.4-72.5), 52.3Gy (46.0-67.1), 50.9Gy (45.6-62.5) for urethral D0.1cc, D0.2cc and D0.5cc respectively. Median bladder D2cc was 65.5cc (46.2-75.1). Sixteen of 39 (41%) patients experienced any acute and eight of 30 (27%) experienced any late urinary toxicity (nine patients did not have follow-up >6 months). Four (10%) had Grade 2 and 0 (0%) had Grade 3+ acute GU toxicity. 1 (3%) patient had Grade 2 and 1 (3%) had Grade 3 late GU toxicity. Median urethral D0.1cc, D0.2cc and D0.5cc were

73 Gy (51.7-93.8) and 50.5 Gy (45.2-63.7; p=0.009), 69.2Gy (48.9-87.4) and 49.6Gy (42.7-58.4; p=0.011) and 62.9Gy (47.9-79.6) and 48.6 Gy (39.2-55.7; p=0.015), respectively in patients with and without any CTCAE GU toxicity. Additionally, seven (44%) patients and one (4%) without GU toxicity had bladder intrusion (p=0.004). There was no significant difference in urethral dosimetry between patients experiencing and not experiencing late toxicity.

Conclusions: Urethral dose appears to predict for acute genitourinary toxicity in ISBT of vaginal tumours. Further study with an expanded cohort and longer follow-up is warranted.

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DEGREE OF LVSI IS NOT A RISK FACTOR FOR RECURRENCE IN ENDOMETRIAL CANCER PATIENTS TREATED WITH VAGINAL BRACHYTHERAPY ALONE

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Purpose: Lymph-vascular space invasion (LVSI) is an important adverse prognostic factor in endometrial cancer. A three-tiered scoring system (none, focal, substantial) from the pooled analysis of PORTEC-1 and 2 data found substantial LVSI (versus focal or none) the strongest independent risk factor for recurrence. The purpose of this study was to review our outcomes of Stage I-II endometrial cancer patients treated with adjuvant vaginal brachytherapy (VB) alone, stratified by the degree of LVSI.

Materials and Methods: Retrospective chart review identified patients with Stage I-II endometrial cancer treated with VB alone from 2011-2015. Patient and disease characteristics were collected. Pathology reports were reviewed for description on degree of LVSI, and these were categorized into the three-tiered system. Patients where no descriptor was found were excluded from analysis. In comparing between groups for variables the Kruskal-Wallace or Fisher's exact test was used. For outcome analysis Kaplan-Meier method was employed for all estimates and the Log-Rank test was used to determine significance between variables. For multivariate analyses the cox proportional hazards model was used. Variables included age, Grade (1 or 2 versus 3 or serous or clear cell or MMMT), depth of myometrial invasion, and cervical involvement.

Results: We identified 235 patients treated with VB alone over the study period. LVSI status was none (181), focal (36), and substantial (18). Median FU was 40 (25-51) months. Overall, 25 (11%) patients developed recurrent disease. Kaplan-Meier estimated DFS was 90 (86-94)% at 36 months. On cox proportional hazards modelling, no significant difference was seen between the subgroups of substantial versus focal LVSI, however we maybe underpowered to detect a difference if one existed. We found high grade [HR: 3.9 (1.5-10.4); p=0.006] and LVSI [HR No versus substantial: 3.6 (1.3-10.0); p<0.001] predicted for overall disease recurrence. While no factors were predictive of local or pelvic failure, high grade [HR: 6.7 (2.0-22.2); p=0.002] and LVSI [HR No versus substantial: 6.0 (1.9-19.0); p=0.002] predicted for distant failure. High grade tumour [HR: 4.6 (1.0-21.4); p=0.048] and presence of LVSI [HR No versus substantial: 14.5 (3.0-77.9); p=0.002] also predicted for worse overall survival.

Conclusions: Patients with substantial versus focal LVSI as interpreted at our institution did not appear to have higher rates of pelvic failure or lower survival when undergoing VB alone. Differentiating between the presence and absence of LVSI may be sufficient in guiding adjuvant therapy in intermediate risk endometrial cancer patients.

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TOXICITY AND QUALITY OF LIFE RESULTS FROM A RANDOMIZED PHASE II TRIAL OF HDR MONOTHERAPY FOR LOW AND INTERMEDIATE-RISK PROSTATE CANCER

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Purpose: To report health-related quality of life (HRQOL) and toxicity outcomes at 4-years in prostate cancer patients treated with high-dose rate (HDR) brachytherapy as monotherapy using single-fraction of 19 Gy or 2 fractions of 13.5 Gy (27 Gy/2 fractions one week apart).

Materials and Methods: Patients with low or intermediate-risk prostate cancer were accrued to a randomised phase II clinical trial of HDR brachytherapy as monotherapy, randomised to either 19 Gy/1 or 27 Gy/2. HRQOL (Expanded Prostate Cancer Index Composite [EPIC]), urinary symptoms (International Prostate Symptom Score [IPSS]), and toxicity (Common Terminology Criteria for Adverse Events [CTCAE], v4.0) were assessed prospectively. Comparison between the two arms was analysed using Fisher exact test. Univariate linear and logistic regression analysis was used to investigate association between HRQOL/toxicity and baseline covariates.

Results: Median follow-up is 51 months. 170 patients were treated (87 with single 19 Gy, 83 with 27 Gy/2). Late (>6 months) GI toxicity was minimal in both arms, with G-2 toxicity <1%, and no difference between the arms. Late G-2 urinary toxicity was low and <2%, except for urinary frequency and incontinence. G-2 urinary frequency was similar between arms (19% for 19Gy/1 and 10% 27Gy/2; p=0.27). There was significantly more late G-2 urinary incontinence with 19Gy/1, and none with 27Gy/2 (6% versus 0%, p=0.0318). G 2-3 urinary tract obstruction was only observed in four patients, all of whom were treated with 19Gy/1. No change in the median EPIC scores at four years (follow-up - baseline score) was observed with 27Gy/2 for urinary, bowel or hormonal domains, but a decline in sexual function by 16 points. In the single fraction arm, there was no change in the bowel or hormonal domains too, but a drop in sexual domain by 9 points, comparable to 27Gy/2 (p=0.53). There was a significantly greater drop in urinary domain, function, and bother with 19Gy/1 (-3.5 versus 0.0, p=0.003; -5.0 versus 0.0, p=0.004; and -3.57 versus 0.0, p=0.006, respectively). Urinary QOL was slightly worse with 19Gy/1 compared to 27 Gy/2, with greater clinically significant decrement (defined as a decrease in EPIC score >0.5 SD) in urinary domain (46.15% versus 16.67%, p=0.007), function (52.5% versus 15.38%, p=0.0008) and bother (43.59% versus 16.67%, p=0.0136). Treatment with 19Gy/1 (OR 4.286, p=0.0082) and higher PTV V100 (OR 1.6, p=0.02) were the only factors predictive of clinically significant decrement in urinary QOL. There was no difference in clinically significant decrement between arms in other QOL domains (bowel, sexual, or hormonal).

Conclusions: Both single 19Gy and 13.5Gy x 2 are well tolerated with low toxicity and good HRQOL at four years. Single fraction 19Gy is associated with higher rates of G-2 urinary toxicity, worse urinary function and bother, and greater decline in urinary QOL at four years. Treatment with 19Gy/1 and having higher PTV V100 are predictive of decrement in urinary QOL.

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DOSE RECONSTRUCTION OF CERVICAL CANCER ADAPTIVE RADIOTHERAPY DELIVERED WITH HYBRID CBCT-MRI GUIDANCE

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Purpose: Women receiving radiotherapy for intact cervix cancers can exhibit unpredictable organ deformation and tumour response that is challenging to visualize with cone-beam CT (CBCT). In an effort to spare normal tissues and maintain treatment precision, highly conformal plans were recently implemented in a novel platform combining a linear accelerator and 1.5 T MR-on-rails for daily guidance. The aim was to develop a dose reconstruction workflow to evaluate the dosimetric impact of organ deformation and adaptive re-planning interventions using cervix cancer as a proof-of-concept.

Materials and Methods: Patients received 45Gy/25 fractions using volumetric modulated arc therapy (VMAT) consistent with EMBRACE II, plus margins accounting for bladder filling and daily pre-treatment CBCT. Daily post treatment axial T2w MRI acquired in the same patient position, was reviewed offline for geometric-only assessment of tumour motion. To reconstruct the actual delivered doses, scripts were developed to automatically retrieve, apply density corrections and perform dose calculations on all CBCTs in the treatment planning system. Daily MRIs were rigidly registered to CBCT. The primary target CTV and normal tissues were delineated by an expert clinician first on all CBCTs, then MRIs. The CBCT contours were used to guide hybrid deformable image registration in order to map and accumulate the daily CBCT doses on the planning CT. Deviations in dose-volume metrics ≥5% versus planning were considered to be clinically significant and reported.

Results: Two cervix patients have been treated to date. The daily MR-defined CTVs were 16.6 cc (26%) smaller on average than corresponding CBCTs (P<0.01). Patient 1 had no remarkable organ motion on daily CBCT or MRI (acquired for 8/25 fractions) that warranted adaptive re-planning. Post-treatment dose reconstruction using CBCT confirmed no significant dose deviations >5%. Patient 2 had substantial bladder and rectum deformations causing displacement of the uterine fundus on daily CBCT. On review of MRI (acquired for 17/25 fractions), geometric miss of CTV and potentially the GTV was presumed and adaptive re-plan was initiated on fraction 19. Post-treatment dose reconstruction using CBCT resulted in a 5% decrease in minimum CTV dose (in the uterine fundus, but not GTV) and 13% increase in rectum V40 relative to the initial plan. There were no dose deviations >5% relative to the re-plan or overall composite plan, confirming the adaptation strategy.

Conclusions: A dose reconstruction workflow was developed for cervix patients treated on a hybrid CBCT-MRI guided protocol. Integrating this dosimetric information into clinical practice will aid clinicians in adaptive re-planning decisions. Owing to the improved soft-tissue visualization, MRI-only workflows are being developed for more precise guidance and dose reconstruction, permitting further normal tissue sparing and integration with adaptive MR-guided brachytherapy.

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PAW PATROL TO THE RESCUE! MINIMIZING ANAESTHESIA USE IN PAEDIATRIC RADIATION THERAPY

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Purpose: Although generally safe, daily anaesthesia exerts both an emotional and physical toll on children receiving radiation therapy. Since radiation treatments cannot be delivered all at once and must be fractionated over 5 to 30 treatments, creating a positive daily experience for these patients is a priority. Our centre has developed a multifaceted approach to reduce anaesthesia utilization. The goal of this study was to evaluate the effectiveness of our approach by measuring general anaesthesia (GA) rates across all age categories and to compare with published GA rates in the literature.

Materials and Methods: Paediatric patients aged ≤18 treated with RT from 2014-2018 were retrospectively reviewed. GA use was defined as need for conscious sedation or GA for at least one CT simulation or treatment session. The following methods were used to reduce GA utilization: presence of a dedicated paediatric nurse for procedural preparation, radiation therapists specialized in paediatric treatment, comfort objects (stuffed animal and blanket), and audio-visual distraction (television and large collection of DVDs). Comparison of GA rates across age categories was done using the chi-square trend test. Multivariable logistic regression was used to identify clinical or disease factors associated with GA use.

Results: There were 377 unique patients who received RT over 6 411 fractions of radiation. 939 sessions of GA were administered. The median age of patients was 9.8 years (range, 0-18). Among all patients, 68 (18%) required some or all RT fractions under GA. GA utilization was 100% in those under age 3, 37.5% in those age 3-6, 1% in those age 7-12, and 1% in those ≥12 years of age (p<0.0001). The GA rate between age 5-13 was 2%. No child between age 6-9 required GA. Age was the sole predictor of GA use, with each year increase in age resulting in 2.9-fold decreased odds of requiring any GA (odds ratio 0.344, 95% confidence interval 0.25-0.47, p < 0.0001). Body site, diagnosis, treatment technique (including IMRT, VMAT, 3DCRT or total body irradiation), use of craniospinal irradiation, year of treatment, and method of immobilization were not predictive of GA use.

Conclusions: Our institutional rates of GA use are low in the age 3-6 category (37.5% versus 79-95% in the literature) and age 5-12 category (2% versus 47% in the literature). The data shows that our current methods in reducing anaesthesia use have been successful. Other cancer centres may consider adopting our methods, allowing for a more positive experience for paediatric patients and their families.

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PALLIATIVE CARE OUTREACH: IMPROVING PALLIATIVE RADIATION THERAPY UTILIZATION IN THE COMMUNITY

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Purpose: Palliative radiation therapy (PRT) has an essential role in cancer symptom control but is under-utilized in Ontario. This initiative aimed to develop and implement an educational outreach intervention to improve knowledge of and access to PRT among inter-professional palliative healthcare teams across the Central Local Health Integration Network (LHIN) in Ontario.

Materials and Methods: A needs assessment was completed from June to September 2018, with inter-professional palliative healthcare teams in the Central LHIN. Facilitated discussions were completed to understand perceived opportunities, barriers, and enablers to recommending or referring patients for PRT. All

participants completed a survey and results were analyzed using thematic analysis to develop the educational outreach intervention. The educational outreach intervention was completed from October 2018 to January 2019 with inter-professional palliative healthcare teams. All participants completed a survey and results were analyzed using descriptive statistics to evaluate the impact of the educational outreach intervention.

Results: A total of 78 survey responses were analyzed for the needs assessment. Thematic analysis informed content of the educational outreach intervention and included: how to access rapid response PRT, common indications for PRT, case studies, and management of side effects after completion of radiotherapy. A total of 131 survey responses were analyzed following the educational outreach intervention. Although only 22.9% of participants had previously recommended or referred patients for PRT, 96.2% of participants agree or strongly agree that they are likely to recommend or refer patients for PRT in the future.

Conclusions: The educational outreach intervention improved knowledge and the likelihood of inter-
professional palliative healthcare teams accessing PRT for patients in the community. As a future direction, ongoing monitoring of radiotherapy referrals from the community could provide insight regarding the impact of the educational outreach intervention on local PRT utilization rates.

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A NEW APPROACH FOR WEEKLY REVIEW ASSESSMENTS

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Purpose: The weekly review assessment (WRA) of breast radiotherapy patients have traditionally been performed by nurses (RNs) and radiation oncologists (ROs) in weeks 1, 2, and 3. To decrease the number of patient visits to the weekly review clinic and to improve efficiency for breast cancer patients and staff, radiation therapists (RTTs) in our centre began performing the week 2 WRAs. This study was performed to ensure assessment of skin reactions were similar between RTTs and ROs.

Materials and Methods: Photographs of skin reactions Grades 1-4 as defined by the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0 (NCI CTCAE v4) were obtained via internet and local patients consenting to photography. An RO specializing in breast cancer radiotherapy treatment scored the test cases and these scores served as the gold standard. These photos were embedded in a mandatory self-guided learning module containing a skin anatomy review, and radiation skin reaction principles. At the end of the module participants were required to assess and score nine different test cases with photos of skin reactions.

Results: Forty-eight RTTs (100%) completed the learning module and had their scores compared to the gold standard. The test cases contained photos of skin reaction Grades 1-3. Agreement between RTTs and RO was 100% for four cases, 95.8% for one case and 87.5% for another. Overall, 42/48 of RTTs had either all cases correct or had one case incorrect.

Conclusions: RTTs are accurately assessing skin reactions of breast cancer patients saving the patient a visit to the review clinic. This initiative saved 483 review clinic visits for breast patients last year. We also have RTT doing WRA on weeks 2, 3, 5, and 6 for prostate cancer patients saving 730 review clinic visits last year. The next expansion is skin cancer patients treated on the superficial treatment unit. RTTs will do WRA on weeks 1 and 2 which can save an additional 130 review clinic visits.

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FACULTY DEVELOPMENT NEEDS AND WANTS IN RADIATION MEDICINE

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Purpose: The rapid change in radiation medicine (RM) principles of practice and technology application place an increasing demand and expectations upon busy practising RM professionals (RM-P) as expert teachers. The learning needs and tools that have the greatest appeal to engage RM-P is not well described. The objective of our study is to explore the faculty development (FD) needs for RM-P within a single institution.

Materials and Methods: Guided by a literature review of medical FD strategies, we designed a two-part survey (21 items). First, respondents were asked to rate themselves on their level of expertise in 13 teaching competencies using a five-point scale (1: novice, 2: competent, 3: proficient, 4: expert, 5: all-star). Second, respondents were asked to identify their preferred learning conditions in five categories. Three open-ended questions probed respondents regarding other factors to be considered related to FD and asked for additional suggestions for incorporation into a FD program designed for them. The survey was sent by email to all staff (n=247) across the three disciplines (therapy, oncology, and physics) regardless of whether they had university faculty appointments (n=81). Two reminders were sent to maximize response.

Results: Fifty-eight responses (23.4% response rate) were received. Self-assessment results fell into three categories – "most confident" (weighted average (WA) > 2.5): setting objectives, providing clear/simple presentations, presentation skills); "less confident" (WA = 2 – 2.5): differentiating between scientific and educational presentations, engaging learners, knowledge of various educational formats/technologies, evaluating own performance, and influencing practice change; and "least confident" (WA < 2): promoting oneself, talking to media, tracking accomplishments, and edu-tainment. Faculty preferred real-time learning (85%) over asynchronous education; face to face (79%) over online formats; and learning inside of work hours (88%) instead of outside. There was a slight preference for group (61%) over individual learning, and approximately equal preference for learning in frequent small chunks (54%) versus longer, less frequent segments (46%).

Conclusions: Our results suggest a spectrum of learning styles and needs among our respondents. There was a preference for real time, face to face group learning offered during work hours. A portfolio of topics requiring faculty development were identified as well as a suggestion on which are easiest to obtain and those that might be developed further into an academic career. We anticipate developing a FD "Hub", an online portal that will serve as an access point for resources, track personal achievements, as well as encourage busy RM-P to develop increasing educational competence.

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A COLLABORATIVE APPROACH TO CARE: MULTIDISCIPLINARY HEAD AND NECK CANCER CLINIC PILOT REVIEW

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Purpose: In 2017, head and neck cancer patients in Nova Scotia experienced excessive wait times from initial diagnosis to start of

treatment. Studies show that wait time correlates with decreased loco-reginal control and overall survivial, up to 5% per month. Delays are compounded by the need to see multiple disciplines before a final treatment decision is made. The Provinical Head and Neck Cancer Site Team recognized the need for improved collaboration and coordination of care in order to expedite the evidence-based treatment decision making process. A proposal was made for the implementation of a multidisciplinary clinic for this patient population supported by the Nova Scotia Cancer Care leadership. The scope of the project included a feasibility study to assess the clinic space and the creation of a vision for future multidisciplinary clinics in a newly designed cancer centre.

Materials and Methods: In June of 2017, the Head and Neck Cancer Site Team, in colloaboration with a project manager, presented a proposal which included the project structure, priorities, and anticipated outcomes at at interprofessional stakeholder engagement meeting. This session solidified support for the project and futher refined the project structure and goals. A steering committee was formed to oversee the project and subcommittees were formed to delegate work to be completed. An industrial engineer was engaged to aid in planning the new clinic work flow. A second stakeholder meeting in March 2018 finalized the project plan. From July 2018 to Jaunuary 2019, six multidisciplinary clinics were completed. Staff and patient satisfaction surveys were sent out at the end of each clinic. For staff, the Assessment of Interprofessional Team Collaboration Scale (AITCS) was implemented. For patient reported outcomes, a survey was developed to determine baseline satisfaction for the current treatment process and was repeated after each multidisciplinary clinic.

Results: Implementation of the multidisciplinary clinic resulted in the development and use of a new comprehensive interprofessional assessment and documentation tool, an optimized model for patient flow, and multidisciplinary rapid rounds to solidify the care plan. Survey results showed improvement in staff satisfaction with each subsequent clinic and improved patient satisfaction over baseline. Initial analysis showed a decrease in the number of days from ready to treat to start of treatment.

Conclusions: With support from the provincial leadership team, a vision for a new integrated multidisciplinary care model was developed. This process assessed feasibility of the model in the current space and aided in the development of a future model of collaborative care to be implemented within other cancer site teams and within the design of a new cancer centre. This new model piloted by the Head and Neck Cancer Site Team has formed the basis of a new approach to care within the centre.

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HIGH DOSE-RATE BRACHYTHERAPY AS MONOTHERAPY FOR PROSTATE CANCER: ONE FRACTION MAY NOT BE ENOUGH

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Purpose: Low dose-rate brachytherapy is associated with excellent long-term control rates for men with low and intermediate risk prostate cancer. Similar control rates are reported for fractionated high dose-rate brachytherapy (HDR). Single fraction 19 Gy HDR may be equivalent to fractionated HDR regimens. We report PSA kinetics, disease-free survival (bDFS) and local control after either 19 Gy x 1 or 13.5 Gy x 2 in a randomized clinical trial.

Materials and Methods: Eligible patients had NCCN low or intermediate risk disease, a prostate volume < 60 cc, International Prostate Symptom Score (IPSS) of 18 or less and no use of androgen deprivation therapy. Patients were randomized to receive either 19Gy HDR as a single fraction (1F), or 27Gy in 2 fractions one week apart (2F). Treatment was delivered using an out-patient ultrasound-based technique. Relative dosimetry was similar between arms with median prostate V100, V150, V200 and D90 of 97%, 35%, 11.4% and 110%, respectively. Follow-up with toxicity assessment, physical examination and serum prostate specific-antigen (PSA) level occurred at week 6, week 12, every 3 months for the first year, every six months until year 5, and annually thereafter. Biochemical failure was defined as nadir + 2 ng/ml. Rising PSA was investigated with CT, MRI, bone scan and in some cases PSMA PET. Local recurrence was confirmed by biopsy.

Results: A total of 170 patients were randomized between June 2013 and April 2015: 87 to 1F and 83 to 2F arms. Median age was 65 years, median PSA was 6.3 ng/ml and 72% had Gleason 7 cancer. NCCN low, favourable intermediate and unfavourable intermediate was present in 28%, 49% and 23%, respectively, with similar distribution between arms. Median follow-up was 51 months (range 24-68 months). PSA decreased more rapidly in the 2F arm: median PSA at one, two, three, four and five years was 1.60, 1.20, 1.25, 0.89 and 0.75 ng/ml in the 1F arm and 1.20, 0.63, 0.39, 0.29 and 0.21ng/ml, respectively in the 2F arm. Biochemical failure occurred in 20 patients – 18 in the 1F arm and 2 in the 2F arm, with a five-year bDFS of 74.5% and 97.3%, respectively (p=0.002). Most recurrences were local (16/18) in the 1F arm, almost all at the site of initial disease, while only one of the two failures in the 2F arm had a component of local failure. Distant metastases-free survival was 98% at five years.

Conclusions: Despite linear quadratic considerations, single fraction 19Gy is inferior to two fractions of 13.5Gy, which provides control rates similar to that in most LDR series. Single fraction 19Gy is associated with a significantly higher nadir PSA value, and a 9-fold higher risk of local failure. As recurrence is predominantly at the site of initial bulk disease, local dose escalation to the initial dominant disease, or dose escalation to the whole prostate, may provide better cancer control. The former strategy is being evaluated in the ongoing CCTG PR19 clinical trial.

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RADIOTHERAPY VERSUS TRANS-ORAL ROBOTIC SURGERY FOR OROPHARYNGEAL SQUAMOUS CELL CARCINOMA: RESULTS OF A RANDOMIZED TRIAL

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Purpose: The incidence of oropharyngeal squamous cell carcinoma (OPSCC) has risen rapidly, due to an epidemic of human papillomavirus (HPV) infection. Radiation therapy (RT) has historically been the standard treatment, but transoral robotic surgery (TORS) has surpassed RT in the US as the most common approach, based on assumptions of reduced toxicity or improved quality of life (QOL). No randomized trials have previously compared these treatments.

Materials and Methods: The ORATOR trial (NCT01590355) enrolled patients with T1-T2 N0-2(≤4 cm) OPSCC amenable to TORS. We randomly assigned patients, stratified by p16 status, to RT (70 Gy/35 fractions, or as chemoradiotherapy [CRT] if N1-2) versus. TORS (± adjuvant RT or CRT based on pathology). The primary endpoint was a definitive comparison of swallowing QOL at one-year using the MD Anderson Dysphagia Inventory (MDADI), powered to detect a 10-point improvement (a clinically-meaningful change [CMC]) in the TORS arm. Secondary endpoints included adverse events (AEs), other QOL outcomes [including EORTC Head and Neck-35 (H&N-35) scale and other scales], overall and progression-free survival (OS, PFS). Herein we report pre-specified primary and secondary outcomes with a post-hoc analysis of outcomes by treatment intensity.

Results: Between 2012 and 2017, 68 patients were randomized (n=34 in each arm), at six centres in Canada and Australia. Median age was 59 years; 87% were male. Primary tumours sites were palatine tonsil (74%) or base of tongue (26%). Arms were well-balanced for baseline factors, including p16 status (88% in each arm). Median follow-up was 27 months. MDADI scores at one-year were statistically superior in the RT arm (mean ± SD: 86.9 ± 11.4 versus 80.1 ± 13.0 in the TORS arm; p=0.042), but not meeting the definition of a CMC. For other QOL metrics, outcomes were similar at 1-year. Percutaneous feeding tube rates at one-year were 3% (n=1) versus 0% respectively. Rates of treatment-related Grade ≥ 2 AEs were similar (91% versus. 100%, p=0.24), with more neutropenia, hearing loss, constipation and tinnitus in the RT arm and more trismus in the TORS arm (all p<0.05). There was one TORS bleeding-related death. Longitudinal QOL analysis over time confirmed the statistical superiority of RT in the MDADI scores (p<0.001), with average differences below the threshold of a CMC. In the RT Arm, one-year MDADI scores based on treatment intensity were as follows: RT alone 89.5 ± 6.2; CRT alone 88.0 ± 11.5 RT; CRT with salvage surgery 68.0 ± 7 (ANOVA p=0.044). In the TORS arm, the one-year MDADI scores by treatment intensity were: TORS alone 82.8 ± 10.5; TORS with RT 78.5 ± 11.0; TORS with CRT 80.4 ± 19.6 (ANOVA p=0.760). OS and PFS were similar in the two arms.

Conclusions: RT had superior swallowing QOL scores at one-year compared to TORS, but the difference was not a CMC. Toxicities differed between the arms. This study provides the first level 1 evidence to inform patients of the QOL impact of RT and TORS.

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A BIOCHEMICAL DEFINITION OF CURE FOLLOWING BRACHYTHERAPY OF PROSTATE CANCER

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Purpose: Retrospective outcome data for 13,299 patients with localized prostate cancer from five participating institutions treated with brachytherapy were analyzed. Based on PSA measured four years (range 3.5-4.5, n=7,603) or five years (range 4.5-5.5, n=6,545) post-treatment in patients who have not experienced clinical failure, a population is sought that is cured at long-term follow-up at 10 or 15 years.

Materials and Methods: Eligible patients were treated with either brachytherapy alone, or in combination with external beam radiotherapy (EBRT) and/or androgen deprivation (ADT). PSA measurements prior to the two intervals of interest were excluded, and patients who failed clinically prior to the intervals were excluded from the analysis. KM analysis was carried out using clinical failure (local, distant, or regional) as endpoint for each of four PSA categories: PSA≤0.2 ng/ml, PSA >0.2 to ≤ 0.5 ng/ml, PSA > 0.5 to ≤ 1.0 ng/ml, and PSA>1.0 ng/ml.

Results: The patients were distributed by risk category as 37% low, 55% intermediate, and 8% high-risk. The results of KM analysis show that 79.3% of patients had a PSA ≤ 0.2 ng/ml at four and five years and had a > 99% chance of being free of recurrence at 10 years (95% CI: 98.9-99.5) and >98.5% at 15 years (CI: 97.9-99.1). Eleven percent had a PSA >0.2 to ≤0.5 ng/ml at five years. This was associated with 89% being disease-free at 15 years (CI 81.5-93.4). Only 4% had a PSA >0.5 to ≤1.0ng/ml and although the chance of being disease-free at 10 years was still 88.8% (CI: 80.4-93.7) by 15 years this had fallen to 60.8% (CI 35.9-78.5). For those with a PSA >1.0 at five years (5.7%), only 62.8% were disease free at 10 years (CI 55-69.7) and 38.9% at 15 years (CI: 27.1-50.5). The association of treatment success with PSA range was highly significant (p<0.0005) for both PSA at four years and at five years. Over 2000 patients remain in follow-up beyond 10 years and >300 beyond 15 years.

Conclusions: Patients with a PSA < 0.2ng/ml at four to five years post-treatment have >98% chance of remaining disease-free beyond 15 years. As this applies to almost 80% of patients, we suggest that this be adopted as the biochemical definition of cure for patients with ≥4 years' follow-up.

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ULTRA-HYPO (UHF) COMPARED TO MODERATE-HYPO (MHF) FRACTIONATED PROSTATE IGRT WITH HDR BRACHYTHERAPY BOOST: LONG TERM TOXICITY, ACCEPTABILITY AND EFFICIENCY OF DELIVERY

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Purpose: To compare and report long-term toxicities between an UHF and two MHF IGRT regimens, plus an HDR brachytherapy boost (BB), with or without a short-term androgen deprivation therapy (STADT). Our aim is to reduce the social, and economic burden of treatment for patients, and increase efficiency of health care facilities with acceptably low toxicities.

Materials and Methods: Four hundred and ninety-seven D'Amico's intermediate risk prostate cancer patients were grouped according to the treatment fractionation approach. Cancer risk grouping and demography were compared. An IGRT technique using fiducial gold markers for daily match on prostate and 1st cm of seminal vesicles was used adding a single 15Gy BB. The 3 groups received the following treatment regimens expressed with Dose (Gy)/Fractions as follow: 37.5/15 (MHF2.5); 36/12 (MHF3) and 25/5 (UHF5). The BED equivalent are respectively: 265, 273 and 273.3 Gy (a/b=1.5). STADT (4-6 months) was administered per physician's preference. Patients were followed prospectively with IPSS, GU, GI, sexual toxicity and quality of life questionnaires. Follow-up results are reported after brachytherapy at 1, 3, 6, 12, 18 and 24 months. Chi-square test was used to test proportion between categorical variables. Difference between numeric variables were tested by one-way analysis of variance.

Results: Patient's median age was 68 years old with Gleason scores of 7 (99.4%). The stage distribution was: T1C (54.6 %) - T2A

(31.5%) - T2B (13.7 %), and PSA at diagnosis being average 6.40 (± 3.41). All three variables being non-statistically significant (NS) different between groups. The groups differ in median follow-up (FU) being respectively 33.5; 21 and 24 months for MHF2.5, MHF3 and UHF5. Evaluated at one, three, six, 12, 18 and 24 months, the IPSS scores show NS differences between groups through the two years FU. There was no difference between groups in occurrence of nocturia, dysuria, urgency, nor with GI side effects (diarrhea, irritation, rectorragia and tenesmus). No G3-4 GI side effects were reported. Patient reported toxicity did not show a statistical difference with STADT use. The sexual function and quality of life tools did not show a statistically significant differences between groups throughout the two years FU. The median treatment course span over the full course treatment were given respectively in: 21/35; 16/32.5 and 6/20 days for the MHF2.5, MHF3 and UHF5.

Conclusions: UHF5 + BB reduced the number of fractions and the span of treatment time significantly without increasing side effects. Though a longer FU is needed, UHF5 will contribute to reduce the social and economic burden of treatment for the patients and increase health care facility's efficiency.

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QUALITY OF LIFE OUTCOMES AFTER STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR) VERSUS STANDARD OF CARE PALLIATIVE TREATMENTS: A SECONDARY ANALYSIS OF THE SABR-COMET RANDOMIZED TRIAL

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Purpose: The use of SABR in patients with oligometastases has been associated with improvements in progression-free survival and overall survival. Quality of life (QoL) is of substantial importance in the metastatic setting, since treatments have historically been considered palliative-intent. However, randomized data assessing the longitudinal QoL impact of SABR in the oligometastatic setting are lacking. Herein we report longitudinal QoL outcomes from the SABR-COMET randomized trial.

Materials and Methods: We enrolled patients who had a controlled primary malignancy with 1-5 metastatic lesions, all of which were amenable to SABR, with good performance status and life expectancy >6 months. We stratified by the number of metastases (1-3 versus 4-5) then randomized in a 1:2 ratio between standard of care (SOC) treatment [SOC Arm] versus SOC plus SABR to all metastatic lesions [SABR Arm]. Due to the wide variety of tumour sites and treatment targets included, QoL was measured using a general tool, the Functional Assessment of Cancer Therapy – General (FACT-G), which includes 4 subscales: Physical Well Being, Social/Family Well Being, Emotional Well Being, and Functional Well Being. A 5-point decline in the total FACT-G scale, or a two-point decline on a subscale, is generally considered a clinically meaningful change (CMC). QoL changes over time and between groups was assessed with linear mixed modeling.

Results: Ninety-nine patients were randomized (33 in Arm 1, 66 in Arm 2). Median age was 68 (range: 43-89) and 60% were male. The most common primary tumour types were breast (n=18), lung (n=18), colorectal (n=18) and prostate (n=16). Most patients (n=92) had 1-3 metastases. Median follow-up was 26 months. Because of the inferior survival of the SOC arm, as previously reported, the time for attrition in QOL respondents to <10% of subjects was shorter in the SOC versus SABR arm (30 versus 42 months). In the whole cohort, QoL declined over time after randomization: there were significant declines in total FACT-G score over time compared to baseline ($p<0.001$), due to declines in physical and functional subscales (both $p<0.001$), with no declines in social and emotional subscales. However, the magnitude of declines were small, and CMCs were not seen at most time points. Comparison between arms showed no differences in QoL between the SABR and SOC arms in total score ($p=0.42$), or in the physical ($p=0.98$), functional ($p=0.59$), emotional ($p=0.82$) or social ($p=0.17$) subscales.

Conclusions: For patients with oligometastases, average QoL declines slowly over time regardless of treatment approach, although the changes are small in magnitude. The use of SABR, compared to SOC, was not associated with a QoL detriment. This suggests that QoL changes are due to underlying disease processes over time. (NCT01446744)

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IS SABR COST-EFFECTIVE IN OLIGOMETASTATIC CANCER? AN ECONOMIC ANALYSIS OF SABR-COMET

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Purpose: The phase II randomized study SABR-COMET demonstrated that in patients with a controlled primary tumour and 1-5 oligometastatic lesions, SABR was associated with an improvement in both progression-free survival and overall survival compared to standard of care. SABR is associated with higher costs and treatment-related toxicity. The aim of this study was to assess the cost-effectiveness of SABR versus standard of care in patients with oligometastatic disease.

Materials and Methods: A Markov model was constructed to perform a cost-effectiveness analysis from the Canadian health care system perspective comparing SABR to standard of care. The model included the following health states: 1) pre-progression; 2) post-progression; 3) death from cancer; 4) death from adverse event; and 5) non-cancer death. Utility values and transition probabilities were derived from individual-level data from the SABR-COMET trial. Overall survival and progression outcomes were internally and externally validated. Costs were obtained from the published literature and adjusted to 2018 Canadian dollars. Deterministic sensitivity analyses were performed to obtain thresholds at which each strategy would be preferred. Probabilistic sensitivity analysis was performed to assess the robustness of model. A lifetime horizon was used with a cycle

length of 3 months. A willingness-to-pay threshold of $100,000/QALY was used. Quality adjusted life years (QALYs) and costs were discounted at a rate of 1.5%, as recommended in the Guidelines for the Economic Evaluation of Health Technologies: Canada.

Results: In the base case scenario, the SABR strategy provided 2.77 QALYs at a cost of $169,697 in comparison to 1.85 QALYs at a cost of $135,452 with the standard of care. SABR was therefore cost-effective in the base case, at an incremental cost-effectiveness ratio (ICER) of $37,250 / QALY. This finding was most sensitive to the number of metastatic lesions treated with SABR (ICER $28,137-64,587/QALY), the chemotherapy regimen (ICER $27,242-53,870/QALY), and hazard ratio of progression free survival between strategies (ICER $31,763-53,908/QALY). Probabilistic sensitivity analysis revealed that SABR was a cost-effective strategy in 97% of the iterations.

Conclusions: Based on this decision-analytic model created from a combination of literature and individual-patient clinical trial data, administering SABR is cost-effective for patients with 1-5 oligometastatic lesions compared to the standard of care.

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DON'T BE FAZED BY PHASE II: THE USE OF RANDOMIZED PHASE II TRIALS IN RADIATION ONCOLOGY

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Purpose: Phase II (PII) trials test efficacy and side effects of interventions in advance of costly Phase III (PIII) trials. Traditionally deployed as single arm studies, the use of randomized phase II (RPII) trials has increased in an effort to reduce bias while achieving adequate power with modest sample size. In radiation oncology, randomized trials fail at a high rate, with poor accrual the most frequent cause. Innovative trial designs, including novel PII 'screening' designs which compare experimental and standard interventions with less stringent type I/II error, may improve success rates. We sought to review and characterize the use of RPII trials in Radiation Oncology over the past 12 years.

Materials and Methods: To identify radiotherapy (RT) RPII trials**,** clinicaltrials.gov was queried between 2007 and 2018. Inclusion criteria included interventional RPII designs involving RT for cancer that had completed, finished accrual, or been stopped. Included trials had variations in radiation treatment (use, dose, fractionation, target, etc) between arms. Trials with identical RT prescriptions between arms and those categorized as "unknown status" were excluded. Two independent reviewers screened titles and trial records. Multiple factors were abstracted including design (selection, screening, phase II/III, parallel non-comparative), type of investigation (RT versus no RT, RT technique), endpoints, etc. For completed trials with results, clinicaltrials.gov and PubMed were queried to identify associated studies. Publications resulting from screened trials were reviewed and abstracted.

Results: Of 378 search results, 82 trials met inclusion criteria. Screening-type trials were most common (50), followed by selection (26) and phase II/III (six). From 2007-2018 inclusive, 18 studies published abstracts or manuscripts including 9 (18%) screening, six selection (23%) and three phase II/III (50%). Of published studies, 12 recommended PIII, and five referenced ongoing PIII trials on the topic. Three PIII trials directly linked to successful RPII were identified. Accrual was the most common cause of failure (16). Most common sites included lung (19), prostate (12), and head and neck (10), with a mix between early (27), locally advanced (28) and metastatic (27) stage. Oligometastatic disease was investigated in 12 trials, with four trials investigating stereotactic RT with immunotherapy. Most commonly, studies compared RT with an alternate treatment (42) while the remainder examined treatment technique. Most common endpoints included toxicity (22%), progression-free survival (22%), and response rate (16%).

Conclusions: Over the past 12 years there have been several successfully completed, positive RPII trials, but most have not clearly led to randomized PIII trials. Further investigation is warranted on the relationship between RPII trial design and success, the link between successful RPII trials and PIII trials, and differences between RPII and non-randomized PII designs.

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CAREGIVER BURDEN FOR INFORMAL CARERS OF PATIENTS UNDERGOING RADIOTHERAPY FOR MALIGNANCY: A SYSTEMATIC REVIEW

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Purpose: Outpatient radiotherapy (RT) can require a significant amount of care from caregivers (CG) of oncology patients. Informal or family CGs of this population have been shown to experience high levels of distress and caregiver burden (CGB), including low quality of life (QOL), psychological distress, poor sleep, and altered social or financial dynamics. We performed a systematic review to summarize existing data on CGB in carers of patients receiving RT for malignancy.

Materials and Methods: EMBASE and PubMed were queried to identify published English language studies examining CG QOL or CGB of patients undergoing RT. Inclusion criteria included studies with an outcome of CGB, QOL or a proxy measure in a population of informal, unpaid carers for cancer patients recently receiving RT. Abstracts, reviews, small studies (<10 CGs) or those without a quantitative measurement tool were excluded. Titles, abstracts and full texts were screened and abstracted by two reviewers.

Results: Five hundred and thirty-three studies were initially screened and 18 met all inclusion criteria for analysis. Extracted study dates ranged from 1989 to 2018 and included a total of 1549 unique CGs. Two studies were randomized control trials, eight were longitudinal cohort studies, and eight were cross sectional studies. The most commonly utilized CGB scales included the Distress Thermometer (three), Caregiver Reaction Assessment (three) and Caregiver Quality of Life Index (three). Proxy metrics were assessed by nine studies including sleep, stress, psychological factors. In 12 publications, CGB, or proxy measures were found to be moderate to high for CGs of patients undergoing RT when compared to tool thresholds or population controls. In studies evaluating burden pre- and post-RT four showed worsening scores during treatment, and four showed no change; No studies showed improvement during RT. After completion of RT, reporting studies showed either stability (six) or improvement (two) in scores up to one year post. Factors negatively correlated with CGB included worse patient QOL, young patient age, low CG confidence, CG depression, and CGs that were female, spouses, or with low education/income. Receiving RT (versus not) was the largest predictor of CG hopelessness, while longer RT increased CGB. Counselling interventions did not result in a change in CGB over time. Level of distress may be underreported with some CGs declining enrollment due to high levels of distress.

Conclusions: This systematic review found consistently elevated CGB for patients receiving RT. CGB appears to be correlated to patient symptom burden and QOL, and several caregiver factors. Further investigation is required to identify interventions and practices to improve QOL in the CGs of patients undergoing RT.

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DOSIMETRIC COMPARISON OF HDR BRACHYTHERAPY AND VMAT FOR ACCELERATED PARTIAL BREAST IRRADIATION (APBI)

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Purpose: Accelerated partial breast irradiation (APBI) is an option for some early stage breast cancer patients. The rationale of APBI consists of irradiating only the lumpectomy cavity and a margin that defines a volume where about 95% of the recurrence occurs after surgery. A smaller treated volume means a higher achievable dose per fraction and fewer fractions for a treatment with similar tumour control and toxicity rates. Its utilisation is increasing and a variety of technics can be used. The objective of this study is to compare the dosimetry of APBI plans delivered by high dose rate (HDR) brachytherapy and volumetric modulated arc therapy (VMAT).

Materials and Method: Twelve patients treated with brachytherapy were retrieved from our database. Eight patients were treated by APBI and received a BID regimen of 33 Gy in 9 fractions (prescribed at V95≥5 %). Four patients received a boost as part of their WBI treatment and their plans were adjusted to match the APBI prescription. All patients had a pre-implantation CT scan which was used to create VMAT plans following the OPAR protocol. The 30 Gy in 5 fractions prescription dose (prescribed at D100≥95%) was used to yield a biological equivalent dose similar to the HDR prescription. Then, the t-test was used to compare HDR and VMAT dose distributions in terms of D_{max}, D_{min}, D_{mean}, and V_{dose} to targets and organs at risk.

Results: First, the cavity's volumes were similar (V_{mean}^{VMAT}=*17.38*±23.95 cc; V_{mean}^{HDR}=*18.40*±20.13 cc) but not the CTV (V_{mean}^{VMAT}=*74.45*±71.04 cc; V_{mean}^{HDR}=*18.40*±20.13 cc). The HDR offers a higher cavity D_{mean} (D_{mean}^{VMAT}=*30.2*±0.4 Gy; D_{mean}^{HDR}=*44.6*±3.5 Gy). Small differences (p<0.001) were observed to the conformity index (CI_{VMAT}=*1.19*±0.07 ; CI^{HDR}=*1.12*±0.12), the ipsilateral lung V_{30} (V_{30}^{VMAT}=*5.3*±3.5 %; V_{30}^{HDR}=*1.2*±1.5 %) the contralateral breast D_{max} (D_{max}^{VMAT}=*0.622*±0.236 Gy; D_{max}^{HDR}=*0.246*±0.163 Gy), and the heart D_{mean} (D_{mean}^{VMAT}=*0.433*±0.193 Gy; D_{mean}^{HDR}=*0.624*±0.355 Gy). No statistical difference were found in the dose to the contralateral lung, the contralateral breast D_{mean} (D_{mean}^{VMAT}=*0.141*±0.063 Gy; D_{mean}^{HDR}=*0.047*±0.029 Gy), the ipsilateral lung V_{10} (V_{10}^{VMAT}=*12.8*±5.6 %; V_{10}^{HDR}=*12.7*±9.3 %) and the heart D_{max} (D_{max}^{VMAT}=*0.472*±0.633 Gy; D_{max}^{HDR}=*0.324*±0.280 Gy).

Conclusions: Comparing VMAT and HDR APBI plans is complex due to their intrinsic differences, such as the prescription of the dose. That and the small number of patients included limit the conclusions that can be draw from our data. With that in mind, in this study, HDR brachytherapy allowed a higher dose at the cavity while effectively sparing OAR. However, both techniques offer a safe treatment, an adequate dose to the cavity and doses to the organs at risk well below the constraints, with minor dosimetric differences. Yet, those nuances can guide the choice of a method to use for an individual patient considering some characteristics such as the tumour location, the patient's comorbidities, previous irradiation and the preference of the patient.

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DOES FREE NICOTINE REPLACEMENT THERAPY LEAD TO IMPROVED SMOKING CESSATION RATES IN CANCER PATIENTS? RESULTS OF A PILOT STUDY

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Purpose: Cigarette smoking is carcinogenic and has been linked with inferior treatment outcomes and complication rates in cancer patients. Herein, we report the results of an 18-month pilot smoking cessation program that provided free nicotine replacement therapy (NRT).

Materials and Methods: The smoking cessation program began offering free NRT for actively cigarette smoking cancer patients in January 2017. Newly referred patients were screened for cigarette use, and those identified as active smokers were referred to a smoking cessation champion who offered additional counselling. Health care professionals were provided a process map that facilitated physicians prescribing NRT for patients motivated to quit smoking. The cost of four weeks of NRT was covered by the program, and follow-up was provided by the smoking cessation champions. Institutional health research ethics approval was obtained to collect baseline patient characteristics and follow-up smoking-related data. Two investigators contacted patients to determine cigarette use. Univariable logistic regression was used to determine factors predictive of smoking cessation and reduction.

Results: From January 2017 to June 2018, 8,095 cancer patients were screened for cigarette use, of which 1,135 (14.0%) self-identified as current or recent smokers. All were offered a referral to the smoking cessation program, and 313 (27.6%) attended a referral appointment. Of these, 117 patients (37.4%) accepted an NRT prescription. The rates of patient referrals and patients attending a referral appointment were significantly higher compared to 2015-2016 (100% versus 89%, p<0.0001; 27.6% versus 11%, p<0.0001). Median follow-up was 9.0 months (IQR 5.7-11.6 months). In patients who accepted NRT, the median decrease in numbers of cigarettes used was 58.3% (IQR 16.7-100%). Twenty-five patients (35.2%) reported complete smoking cessation, while 32 patients (45.1%) only reported decreased cigarette smoking. On univariable analysis, no factors were significantly predictive of smoking cessation whereas reporting >10 (versus ≤10) initial cigarettes was significantly predictive of smoking reduction (OR 5.04; 95% CI: 1.46-17.45; p=0.011).

Conclusions: This pilot study of free NRT demonstrated improved rates of referral and acceptance of NRT, and that a majority of patients had either decreased cigarette use or quit entirely. Further work is needed to improve rates of referral appointment attendance, and to assess and optimize long-term cessation rates.

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LUNG STEREOTACTIC ABLATIVE RADIOTHERAPY FOLLOWING PNEUMONECTOMY: A SYSTEMATIC REVIEW OF CLINICAL AND TOXICITY OUTCOMES

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Purpose: Survivors of lung cancer are at risk of second primary lung cancers, which are often curable. However, in patients who have previously undergone pneumonectomy, treatment options are limited. The aim of this study is to perform a systematic review of publications examining treatment planning considerations, clinical outcomes, and toxicity rates of stereotactic ablative radiotherapy (SABR) following pneumonectomy.

Materials and Methods: A systematic review of the literature was conducted in accordance with PRISMA guidelines using PubMed and EMBASE from inception to July 2018. A total of 220 entries were identified. Articles were limited to those published in the English language. One hundred and fourteen unique articles were assessed for eligibility. Inclusion criteria consisted of non-review articles with at least two patients who received exclusively

lung SABR post-pneumonectomy. Two reviewers independently performed abstract and full-text review, with discrepancies settled by a third reviewer.

Results: Of the 114 articles identified by the initial search, five articles comprising 51 patients who received lung SABR post-pneumonectomy met inclusion criteria. Median age was 69 (range 69-74), and most patients were male (median 77.8%, 76.9-100%, n=3). The weighted average incidence of Grade 3 or higher toxicity was 13.6% (0-33.3%, n=5). There was one treatment-related death from one case report that was infectious in nature, but the attributable effects of radiation could not be ruled out. The median 1-year rate of logoregional control was 90.5% (range 84.0-100%, n=4), which is consistent with previously published SABR data. Median BED_{10} was 105.6 Gy (87.5-151 Gy, n=5), and the most common dose fractionation schemes were 54Gy in 3 fractions (n=3), 48Gy in 4 fractions (n=3), and 60Gy in 3 fractions (n=2). All of the studies used 4DCT image acquisition, a technique that captures a 3DCT volume over a period of time thereby describing the motion of a desired target. Respiratory gating was only employed in a single study.

Conclusions: SABR appears to be a safe and effective option for solitary pulmonary nodules in survivors of lung cancer with prior pneumonectomy. Multi-institutional and/or prospective studies would be helpful to determine the true risk and appropriateness of SABR in this high-risk patient population.

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A REVIEW OF CURRENT STEREOTACTIC ABLATIVE RADIOTHERAPY CLINICAL TRIALS FOR OLIGOMETASTATIC CANCERS

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Purpose: The oligometastatic state is a proposed entity between localized cancer and widely metastatic disease, comprising an intermediate subset of metastatic cancer patients. Most data to support locally directed treatment, such as stereotactic ablative radiotherapy (SABR), for oligometastases are from retrospective institutional reports. Given the paucity of prospective data evaluating SABR in oligometastatic cancers, herein we review the current landscape of ongoing clinical trials in this context.

Materials and Methods: A review of current registered clinical trials was performed using the ClinicalTrials.gov database from inception to February 2019. A search of actively recruiting trials, using the key words oligometastases, SABR, and various related terms was performed. Search results were independently reviewed by two investigators, with discrepancies settled by a third. Data abstracted from identified studies included study type, primary disease site, oncologic endpoints, and inclusion/exclusion criteria.

Results: Of the initial 216 entries identified, 64 met our review eligibility criteria after full-text review. The most common study type was a Phase II clinical trial (n=35, 55%) with other study designs ranging from observational registry trials to Phase III randomized controlled trials. A minority of trials were randomized in design (n=17, 27%). While most studies allowed for metastases from multiple primary disease sites (n=22, 34%), the most common was prostate (n=13, 15%), followed by breast, gastrointestinal, non-small cell lung cancer and renal (n=6, 9% each). In studies with a solitary target site, the most common was liver (n=6, 9%) followed by lung (n=3, 5%). The most common primary endpoints were progression-free survival (n=20, 31%) and toxicity (n=10, 16%). A combined strategy of systemic therapy and SABR was an emerging theme (n=23, 36%), with more recent studies specifically evaluating SABR and immunotherapy (n=9, 14%).

Conclusions: The safety and efficacy of SABR as oligometastasis-directed treatment is increasingly being evaluated within prospective clinical trials. These data are awaited to compliment the abundance of existing observational studies to guide clinical decision-making.

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SERUM CYTOKINE PROFILING AS A POTENTIAL BIOMARKER IN INTERMEDIATE RISK PROSTATE CANCER: AN EXPLORATORY STUDY

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Purpose: To identify a profile of serum cytokines that may predict for biochemical failure or radiation toxicity for further study in a population of men with intermediate risk prostate cancer treated with brachytherapy.

Materials and Methods: Study population consisted of 25 men with intermediate risk prostate cancer treated with curative intent using brachytherapy plus or minus external beam radiotherapy at Sunnybrook Health Sciences Centre. Serial blood samples were collected pre-treatment, at 1 month, 6 months and 12 months post-treatment. Samples were submitted for cytokine profiling using a Bio-Plex-based human cytokine screening assay of 65 cytokines (Eve Technologies; Calgary, AB, Canada). Prostatic specific antigen (PSA) values were also recorded serially. A decrease of PSA to a value below 1.00 at one year has been previously suggested as an early predictor of biochemical failure, and thus, was chosen as a surrogate of biochemical response for our study (response time). Any toxicity attributable to radiotherapy was recorded. A univariate general linear mixed model was performed to detect any associations between response time or radiation toxicity and cytokine kinetics.

Results: IL17A and CXCL10 profiles differed between patients whose PSA values declined to a value of <1.00 over less than one year compared to those whose response time was greater than one year. Similarly, IL12p40 and IL20 profiles were different between patients with documented toxicity versus those without.

Conclusions: This study identifies a number of candidate serum cytokines which show promise for further study towards establishing possible serum-based biomarkers for radiation toxicity or PSA response.

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REAL WORLD UTILIZATION OF INTERMITTENT ANDROGEN DEPRIVATION THERAPY (IADT) FOR CASTRATION SENSITIVE METASTATIC PROSTATE CANCER IN MANITOBA

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Purpose: Androgen depravation therapy (ADT) is the primary treatment for men with castration sensitive, metastatic prostate cancer (CS-MPC). Recently reported randomized trials have found intermittent ADT (iADT) to be non-inferior to continuous ADT (cADT) for MPC outcomes. Furthermore, iADT is associated with superior quality of life and is more economical compared to cADT. This study aimed to determine the utilization rate of iADT for patients with CS-MPC in a Canadian province and identify risk factors associated with the receipt of cADT.

Materials and Methods: The provincial cancer registry was utilized to identify all patients with newly diagnosed or recurrent MPC from 2012 to 2016 and was linked to provincial pharmacare data in order to identify patients who received ADT. Baseline patient, disease, and treatment variables were extracted via the electronic medical record including type of ADT received and PSA values during follow-up. Univariable and multivariable logistic regression analysis was conducted in order to identify risk factors associated with the receipt of cADT.

Results: Four hundred and three men with CS-MPC were included with a median age of 71 (range 48-97), a pre-treatment median PSA doubling time (PSADT) of 25.2 months, and mean BMI of 28.5. 71.0% had bone metastases and 46.2% had visceral metastases prior to starting ADT. 57% of the cohort received iADT. Factors significantly associated with receipt of cADT on univariable analysis included advanced age, higher Gleason score, higher baseline PSA and, slower PSADT. Multivariable regression analysis found older age category (OR 0.22, 95%CI 0.06 to 0.84), slower PSA doubling time (OR 5.14, 95%CI 1.62 to 16.3), and lack of antecedent radiotherapy or surgical intervention (OR 0.22, 95%CI 0.08 to 0.61) associated with receipt of cADT.

Conclusions: Utilization of iADT for patients with CS-MPC was suboptimal during the study period and knowledge translation efforts to increase its utilization are warranted.

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RE-IRRADIATION FOR CHILDREN WITH RECURRENT SUPRATENTORIAL HIGH-GRADE GLIOMA

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Purpose: Long-term disease control among children with supratentorial high-grade glioma (HGG) is poor. Only a few studies have addressed the role of re-irradiation (RT2) for children with recurrent supratentorial HGG. The aim of this study was to report effectiveness and safety of RT2 in this population, and to compare the results to patients who did not receive repeat irradiation.

Materials and Methods: Forty-one children (≤18 years) with recurrent supratentorial HGG and at least one course of RT between 2001 and 2018 were identified and included in a retrospective cohort study. In-field re-irradiation volumes included focal or whole brain RT, with doses ranging from 30-54 Gy delivered at least six months after first RT (RT1). Clinicopathologic variables were recorded. Suspected mutations were confirmed with germline sequencing. The primary outcome of interest was overall survival (OS). Survival times were counted from the first day of RT2. Institutional research ethics board approval was obtained.

Results: Fourteen of the 41 patients received RT2. Li-Fraumeni syndrome, Lynch syndrome, and constitutional mismatch repair deficiency was identified in two patients each. Median survival of all re-irradiated patients from the first day of RT2 was 6.5 months. Patients with ≥12 months between RT1 and RT2 experienced longer OS than patients with <12 months (p=0.009). There was no difference in OS between patients with or without germline mutations (p=0.20). Ten patients received RT2 overlapping with RT1 volumes for locally-recurrent disease. Of these, 80% experienced clinical benefit from in-field RT2, defined as clinical/radiologic response or stable disease. Ninety-three percent of all patients completed the prescribed course of RT2. One patient developed Grade 3 radiation necrosis four months after RT2. When compared to 27 patients without re-irradiation, those with RT2 had improved median survival from time of first disease progression (9.4 versus 3.9 months, p=0.005).

Conclusions: Re-irradiation for children with recurrent supratentorial HGG is a safe and effective treatment that provides short-term disease control, even for patients with germline genetic mutations.

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THE ONCOLOGY RESEARCH INTERNSHIP (ORION): A MUTUALLY BENEFICIAL PILOT PROGRAM FOR MEDICAL STUDENTS FACILITATED BY RESIDENT RESEARCH SUPERVISORS

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Purpose: Research supervision, mentorship of students, and academic inquiry are recognized as core to the fundamental competency of developing physicians as scholars; however, there are few opportunities to develop these skills during residency. Medical students interested in research require access to suitable supervisors and projects: a needs assessment of our medical student (MS) Oncology Mentorship Group identified research opportunities as a major priority for students. To address these deficiencies concurrently, we developed a quality improvement initiative pairing residents with MS to write and publish a case report. We report the results of this program: the Oncology Research Internship (ORIoN).

Materials and Methods: ORIoN application details were published online and emailed to MS. Successful MS applicants were paired with resident supervisors; each pair was supervised by an oncologist. Pairs were assigned a case and independently established project timelines. The MS assumed leadership in project execution. At the program's conclusion, each MS delivered an oral presentation of their completed case report. Resident and MS participants then received a questionnaire exploring pre-/post-program experiences. Responses were collected on a 5-Point Likert scale in combination with open-ended free text responses.

Results: Of 32 applicants, nine MS (two, first year; seven, second year) were accepted. Seven residents volunteered to participate. To date, eight manuscripts have been completed with six submitted for publication (three published, three under review). Survey response rates were 86% and 89% for residents and MS, respectively. All MS respondents reported feeling more comfortable contributing to a research project (25% strongly agree [SA], 75% agree [A]) and writing a case report (75% SA, 25% A). MS participants unanimously agreed that ORIoN was a beneficial experience and 88% felt the program contributed towards their career goals. Residents felt comfortable as a supervisor (33% SA, 67% A), reviewing manuscripts (33% SA, 50% A), and providing written and oral feedback to trainees (17% SA, 67% A). Residents unanimously agreed that developing supervision skills is an important aspect of residency training and 83% agreed ORIoN was beneficial to developing these skills.

Conclusions: The implementation of a novel resident-supervised research internship for medical students was perceived very favourably by participants as mutually beneficial in developing critical scholarly competencies and successful in creating opportunities for academic output. ORIoN could serve as a template for other programs to address a current gap in postgraduate and undergraduate medical curricula.

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PATTERNS OF RECURRENCE AND PREDICTORS OF SURVIVAL IN BREAST CANCER PATIENTS TREATED WITH NEOADJUVANT CHEMOTHERAPY, SURGERY AND RADIATION

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Purpose: Neoadjuvant chemotherapy (NAC) is standard of care for locally-advanced breast cancer and is increasingly used for early-stage high-risk disease. Previous studies have shown wide variation in radiation (RT) practice and limited data on locoregional relapse (LRR) following NAC. We hypothesized a low LRR risk after treatment with modern NAC, surgery and RT, and aimed to elucidate patterns of LRR and predictors of disease-free survival (DFS) and overall survival (OS) in these patients.

Materials and Methods: Data from 416 Stage II/III breast cancer patients treated with NAC, surgery and adjuvant RT at our institution between 2008 and 2015 were retrospectively reviewed. Hormone receptor (HR) and HER2 status defined molecular subtype: HR+HER2- (45%), HR-HER2+ (11%), HR+HER2+ (22%), and HR-HER2- (22%). DFS and OS rates were calculated using the Kaplan-Meier method. LRR rate was estimated using the cumulative incidence function, treating death as a competing risk. Multivariable survival analysis was performed using Cox regression.

Results: Median follow-up was 4.7 years (range 0.5-10.7). Median age was 48 years (range 24-79). Most patients had cT2/3 (75%) cN1 (62%) disease and underwent mastectomy (76%) and axillary dissection (84%). pCR was achieved in 23% of patients: 8% of HR+HER2-, 53% of HR-HER2+, 19% of HR+HER2+ and 41% of HR-HER2- subtype. All patients received adjuvant RT, most (99%) with 50Gy in 25 fractions. Nodal RT was given to 96% of the patients: 83% axilla and supraclavicular fossa (SCF); 8.5% SCF alone; 8% axilla, SCF and internal mammary nodes (IMN); and 0.5% SCF and IMN.There were 27 LRR (12 HR+HER2-, 0 HR-HER2+, 6 HR+HER2+, 9 HR-HER2-) and 88 distant failures (DM). Of the 27 patients with LRR, all but four developed distant metastases (DM), 13 synchronously. Two developed LRR two months after surgery, prior to adjuvant RT. LRR could be mapped in 22 patients: most (19) recurred in the RT field (in-field); one in- and out-of-field; and two out-of-field (one isolated IMC recurrence; one IMC with DM). The five-year LRR, DFS and OS were 6.4%, 77% and 90% for the entire cohort, respectively. On multivariable analysis, HR-HER2- subtype, Stage III disease and non-pCR were associated with poor DFS (HR 2.2, 95% CI 1.3-3.6, p=0.002; HR 1.8, 95% CI 1.1-2.8, p=0.01; HR 4.2, 95% CI 1.9-9.1, p<0.001, respectively) and OS (HR 3.9, 95% CI 1.9-8.0, p=<0.001; HR 1.7, 95% CI 0.9-3.4, p=0.095; HR 2.6, 95% CI 1.04-6.7, p <0.001, respectively).

Conclusions: Breast cancer patients treated with NAC, surgery and RT have low 5-year LRR risk. Most LRR occur in-field. HR-HER2- subtype, Stage III disease and non-pCR are associated with poor DFS and OS.

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RETROSECTIVE ANALYSIS OF OUTCOMES OF CYBERKNIFE RADIATION THERAPY TO LIVER

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Purpose: Cyberknife stereotactic body radiotherapy is a treatment method being used for metastatic and primary cancers in the liver. We carried out a single institution retrospective review of patients treated with liver cyberknife between January 2011 and November 2017.

Materials and Methods: Patients treated with cyberknife radiotherapy to liver primaries and metastases from various primary cancers at the Ottawa Hospital were identified. A retrospective chart review of treatment outcomes including local control, overall survival, and time to new liver metastases was carried out.

Results: We identified 100 consecutive patients at the Ottawa hospital with 131 liver tumours treated with liver cyberknife. There were 32 patients with colorectal cancer and 25 patients with hepatocellular carcinoma with these being the most common types of cancer primaries. Other tumour types included breast, lung, renal, esophageal, GIST and melanoma. The BED_{10} that was used to treat the patients ranged between 37.5 to $200Gy_{10}$, with the median BED_{10} being $86Gy_{10}$. The median radiation dose was 48 Gy (range 25Gy to 54Gy), and median number of fractions delivered was 3 (range 3-8).
The median follow-up time was 14 months, the longest being 56 months. The overall survival following treatment during the follow-up period was 61%. Local control in 12 patients was indeterminate. A total of 17 local failures occurred in 15 patients. Among these, the median time to local failure was 9.4 months (range 21 days to 18.4 months).
A total of 43 patients developed new liver metastases during the follow-up period. The median time to development of new liver lesions in these patients was 8.1 months (range 1.3 to 35 months).

Conclusions: The majority of patients treated with liver cyberknife radiotherapy didn't experience local failure during the follow-up period. Cyberknife radiotherapy for hepatocellular carcinoma and liver metastases offers useful local control.

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CYBERKNIFE STEREOTACTIC RADIOSURGERY FOR TREATMENT OF BENIGN INTRACRANIAL MENINGIOMA: LONG-TERM SAFETY AND EFFICACY

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Purpose: Radiotherapy (RT) is an effective treatment modality for benign intracranial meningioma (ICM), particularly for non-surgical candidates and when emergent decompression is not required. Stereotactic radiosurgery (SRS) has been emerging as a viable alternative to conventional fractionation, and with single and hypofractionated schedules, SRS allows for increased patient convenience using a more localized approach. However, there still is a need for modern data showing long-term efficacy and complication rates, especially given the higher ablative dose administered to cranial tissue.

Materials and Methods: A retrospective cohort review was conducted on adult patients with Grade I ICM treated at the Juravinski Cancer Centre in Hamilton, Ontario. Eligible patients were treated with SRS using the CyberKnife platform for primary or recurrent disease and had a planned treatment course of 1-5 fractions from 2011-2018. Patients were required to have at least one surveillance MRI and follow-up visit ≥ 3 months post-treatment. Clinical and treatment data were summarized including lesion size, location, RT dose-fractionation, PTV volume, prescription isodose line, and conformity index. Local control was assessed based on radiographic stability (RANO criteria), and late toxicity/radionecrosis rates were recorded (CTCAE v5.0). Overall survival (OS) and progression-free survival (PFS) was estimated using the Kaplan-Meier method.

Results: A total of 73 patients (age range 26-87) with 81 treated tumours were included in this study. Primary RT was delivered in 66.7% of cases, and RT following recurrence was delivered in

33.3%. The most common tumour locations were the convexity of the brain (39.5%) and base of skull (30.9%). Tumour size ranged from 0.1 to 51.8 cc (median = 4.3 cc). The median PTV volume was 5.9 cm^3 and median prescription isodose line was 75%. Total dose ranged from 14 to 25 Gy in 1 to 5 fractions, with the most common schedule being 18 Gy in 3 fractions (35.8%). Treatment was completed as planned in 98.6% of patients. After a median follow-up of 50 months, crude local control rate was 97.5%. Five-year OS and PFS were 93.9% and 90.7%, respectively. Overall, the late Grade III/IV toxicity rate was 2.7%. Radionecrosis rate was 6.2%, with 60% of cases being symptomatic necrosis. One patient had a surgical resection and the others were managed conservatively with corticosteroids. The median time from treatment completion to radionecrosis presentation was seven months. There were no deaths attributable to ICM or treatment-related complications.

Conclusions: Based on the data from our centre, SRS remains a safe modality to treat low-grade ICM with acceptable long-term toxicity and radionecrosis rates. Efficacy is similar to conventional fractionation and even larger lesions may be treated with a hypofractionated course. SRS should be offered to patients who are not ideal surgical candidates, for recurrent disease, and for those who wish to avoid an invasive operation.

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"RESILIENCE BY DESIGN" - DESCRIPTION OF A PILOT RADIATION ONCOLOGY WELLNESS PROGRAM

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Purpose: A recent national survey of Canadian Oncology residents found a burnout rate of 42% in respondents[1]. Low resiliency has been associated with higher burnout, and therefore strategies to improve resident resiliency may decrease burnout rates. Prior research has shown that strategies such as group discussions, mentorship and teaching communication and stress management skills have promoted resiliency and wellness in oncology residents. A pilot wellness program was developed at our centre for Radiation Oncology residents.

Materials and Methods: The structure of the pilot program included an initial two-hour resident wellness seminar with a pre-, post- and three-month post-survey. The seminar, led by a local Radiation Oncologist, covered topics such as mindfulness, healthy habits and reframing stress with an interactive focus on experiential learning and group discussion. A follow-up resident and staff session was a one-hour informal group discussion session focused on sharing personal experiences of dealing with difficult cases and discussing stress-management and self-care strategies.

Results: The resident group (n=8) had a burnout rate of 50% and an average Connor-Davidson Resiliency score of 68, which was comparable to the national population[1]. Overall rating of the initial resident seminar was 8.3/10. Individual topics were rated from 7.0-8.9/10 in terms of usefulness to participants as residents. Overall rating of the resident and staff session (nine attendees) was 8.4/10 with individual activities rated from 8.3-8.8/10. Many comments indicated an interest in participating in these sessions more frequently.

Conclusions: The pilot Radiation Oncology resident program had excellent initial feedback with strong interest from many participants for more sessions focused on fostering resiliency and wellness in the future. These results suggest that resilience education is an essential part of Radiation Oncology residency curriculum and is valued highly by both residents and faculty.

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AN ESCAPE ROOM AS A NOVEL MULTIPLE MINI INTERVIEW (MMI) STATION FOR RADIATION ONCOLOGY RESIDENT SELECTION

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Purpose: Selection of residency candidates in a fair and effective way is a critical task for residency programs. Our program has employed a Multiple Mini Interview (MMI) format for selecting Radiation Oncology residents which abides by published guidelines[1]. A novel Escape Room (ER) – style station was developed to assess critical thinking, problem-solving and time management skills.

Materials and Methods: Our selection process assesses candidates based on objective scoring of the online CaRMS application as well as an MMI interview. The MMI included four stations, each designed to assess a quality relevant to Radiation Oncology training. The ER station included five linked puzzles and a self-assessment component with prompts from evaluators. An evaluation rubric was created using existing critical thinking assessment tools and an evidence-based rubric design approach to assess problem-solving, implementation of potential solutions, time management, organization and self-assessment[2-4]. Successful "escape" was not included in the evaluation. Correlations between individual station rank lists, total interview rank list and overall rank list, were examined using Pearson correlation coefficient (r).

Results: The ER ranking was similarly correlated with the total interview rank list (r=0.70) and overall rank list (r=0.67) when compared to the other three stations (r=0.70 - 0.76 for total interview rank list correlation and r=0.50 - 0.79 for overall rank list). All correlations were statistically significant except for the Station 1 correlation with overall rank list (r=0.50, p=0.39). There was not a significant correlation between the ER rank list and any other station rank list, indicating the ER assessed different characteristics and was not redundant.

Conclusions: A novel ER style MMI station produced a rank list that was correlated with the overall rank list, and was not strongly correlated with another station, implying it provided valuable non-redundant assessment information.

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INDIVIDUALIZED DOSE-ESCALATION OF HDR PROSTATE BRACHYTHERAPY IMPLANT TO DECREASE REQUIRED EXTERNAL BEAM RADIATION DOSE: A RETROSPECTIVE FEASIBILITY STUDY

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Purpose: High dose rate brachytherapy (HDR-BT) is commonly combined with external beam radiation therapy (EBRT) for the treatment of localized prostate cancer. Escalating the HDR-BT dose as far as organ at risk (OAR) constraints allow, on a personalized basis, would allow for a reduction in EBRT dose, while achieving similar total biological equivalence. The primary objective of this study was to determine the dosimetric feasibility of escalating the HDR-BT dose from 15Gy to 16Gy or 17Gy, while continuing to meet OAR constraints from the original 15Gy plan, on an individualized basis.

Materials and Methods: Fifty-three consecutive HDR-BT plans were retrospectively assessed to determine what percentage of plans could be re-optimized to deliver a dose of 16Gy or 17Gy, while meeting defined 15Gy OAR constraints. Factors independently associated with successful dose escalation were examined.

Results: Thirty-nine plans (74%) and two plans (4%) were successfully escalated to a dose of 16Gy and 17Gy, respectively. Rectum V80 and urethra Dmax were independently predictive of ability to dose escalate to 16Gy.

Conclusions: Individualized HDR-BT dose-escalation beyond 15Gy, without compromising the OAR constraints, is dosimetrically feasible. Such an approach could allow a corresponding reduction of EBRT dose and would be beneficial in terms of resource-savings for a department, convenience for the patient, and potentially better tolerance of treatment, noting the expected reduction in biologically equivalent dose to OARs. A clinical trial is being developed investigating personalized HDR-BT/EBRT dose-fractionation for localized intracapsular prostate cancer.

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ATTITUDES TOWARDS RESEARCH DURING RADIATION ONCOLOGY RESIDENCY TRAINING: A SURVEY OF CANADIAN RADIATION ONCOLOGY RESIDENTS AND PROGRAM DIRECTORS

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Purpose: It is essential that Radiation Oncologists develop a working knowledge of clinical appraisal and how research is done, even if they are not directly involved in investigator-led studies. A deeper understanding of the barriers to performing research during residency, what factors promote resident interest in research, and what factors are supportive to residents completing high quality projects will be helpful to programs as they restructure research participation with Competence-by-Design (CBD) implementation.

Materials and Methods: Following local ethics approval, anonymous, voluntary, online surveys were circulated to all Canadian Radiation Oncology Program Directors and residents. Information collected included unidentifiable demographics, prior research experience and description of current research environment and barriers to engaging in research and scholarly activities.

Results: The response rate was 32% (34/105) for residents and 71% (10/14) for program directors. 97% of residents, and 90% of program directors, felt research/scholarly activity was an important part of residency training but 47% did not think that it was adequately protected from other activities. 60% of programs allowed one month or less of protected research/scholarly activity time. Seventy-four percent of residents would engage in research/scholarly activity even if it wasn't a required curriculum aspect. The highest barriers to completing research/scholarly activity projects were lack of protected time (for both residents and faculty), high resident clinical workload and lack of experience in developing a proposal or manuscript writing. With CBD implementation, 50% of programs intend to integrate research longitudinally at various phases of training.

Conclusions: Residents expressed strong enthusiasm to participate in research/scholarly activity, yet lack of protected time and competing demands are identified as major barriers. Re-structuring of research/scholarly activity with the transition to CBD as well as provision of more formal training in research methodology may be worthwhile to improve the resident research/scholarly activity experience.

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WELL-MED: A MULTIDISCIPLINARY APPROACH TO SUPPORTING RADIATION ONCOLOGY WELLNESS

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Purpose: Wellness has emerged as an important area within post-graduate medical education. Our objective was to identify the wellness needs of radiation oncology residents in our program, and to develop a multifaceted curriculum to develop and support wellness.

Materials and Methods: Curriculum development was mapped using Kern's six-step approach. A literature review was conducted to assess the wellness landscape in postgraduate medical education, in general, and radiation oncology, specifically, and to identify gaps. Targeted needs assessments of radiation oncology residents were done in the areas of general wellness, mentorship and leadership. The results of the literature review and needs assessments were used to inform the design, development and implementation of a wellness curriculum, including goals/objectives and educational sessions.

Results: The literature review and needs assessments identified reflection, mentorship and leadership as wellness program pillars, and were combined under the name "Well-Med." For each component, educational design was undertaken and included a syllabus, lesson plan or guideline development. For the Reflection component, a narrative medicine workshop series (n=4) was developed exploring themes of identity, work-life balance, uncertainty and creativity in oncology. The Mentorship component includes implementation of a formal mentorship program with tool development to facilitate faculty-trainee matching, mentor bios, suggested guidelines for mentorship relationships and a template for individualized career plan discussion. The Leadership component comprises key topics including interpersonal and leadership styles, teamwork, negotiation and conflict management. A leadership speaker series was initiated on some of these topics, and tailored workshops will address the remainder. Well-Med was introduced to residents in February 2019 and will be implemented in a step-wise roll-out during protected academic time.

Conclusions: We present a strategy for developing a formalized, multi-faceted program supporting radiation oncology trainee wellness. This may serve as a framework for other post-graduate training programs. Further research will include an evaluation of the curriculum and consideration for expansion to other programs.

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ROBUSTNESS OF THE PHOENIX BIOCHEMICAL FAILURE DEFINITION 10 YEARS AFTER COMPLETING DOSE ESCALATED RADIOTHERAPY IN A COHORT OF INTERMEDIATE RISK PROSTATE CANCER PATIENTS

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Purpose: Biochemical recurrence (BCR) following radiotherapy for prostate cancer is accepted as treatment failure and is used to guide clinical management. The Phoenix definition is most commonly used to establish BCR, however, not all patients that meet the definition progress to clinical recurrence. The purpose of this study is to analyze the performance of the Phoenix definition in a cohort of patients with intermediate-risk prostate cancer, treated with external beam radiotherapy (EBRT) with or without hormones.

Materials and Methods: We conducted a retrospective review of all intermediate risk prostate cancer patients treated curatively

at our institution. Patient demographics, cancer, treatment and clinical course details were obtained from the electronic medical record. Descriptive statistics, Kaplan-Meier (KM) survival estimates and Cox proportional hazards were used to analyze risk factors for clinical recurrence in patients with BCR.

Results: Between 2002 and 2007, 542 men were treated with EBRT to a median dose of 76Gy (70 - 85 Gy). Median age was 70 years (40 - 83 years), median PSA was ng/mL (1.3 – 20 ng/mL). Seventy-three percent had Gleason 7 and 54.3% had Stage T1. Median follow-up was nine years (three months- 16 years). Ninety-three patients (17.15%) had BCR (median follow-up of 10.5 years, range two-16 years). Demographics and tumour characteristics for these patients were similar to those in the main cohort. Treatment at BCR included: hormonal treatment for 74%, local treatment for 7.5%, while 18.5% were observed. The actuarial probability of having BCR at 10 years was 24.9%. PSA at diagnosis (HR=1.4, p=0.02) and Gleason 7 (HR=2.07, p=0.01), were statistically significant risk factors for BCR. Forty-nine (52.7%) patients with BCR developed clinical recurrence at a median of 13.5 months (0-132 months), for an actuarial probability of clinical recurrence of 40% at five years and 71% at 10 years. One patient developed clinical recurrence without having BCR. There were no statistically significant risk factors for clinical recurrence identified. Patients with Stage T2 (HR=1.7, p=0.07) and with PSA at time of BCR >5 showed trends towards increased clinical recurrence risk (HR=1.7, p=0.08).

Conclusions: In a large cohort of intermediate risk prostate cancer patients, treated with high dose radiation with or without hormones, the risk of biochemical recurrence is modest at 10 years and 70% develop clinical recurrence ten years after biochemical recurrence. The Phoenix definition of BCR does a reasonable job of predicting long term outcomes.

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WHEN BIOCHEMICAL FAILURE DOES NOT MEAN CANCER RECURRENCE IN MEN TREATED BY EXTERNAL BEAM RADIOTHERAPY AND ADJUVANT HORMONES FOR INTERMEDIATE RISK PROSTATE CANCER

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Purpose: Biochemical recurrence following prostate cancer radiotherapy is the accepted barometer of treatment failure and is used to guide clinical management in a given patient as well as to compare the relative efficacy of different treatments. As normal prostatic acini recover from radiotherapy, they secrete PSA even though all the cancer in the prostate may have been eradicated. Knowledge about when such PSA increases that meet the definition of biochemical failure but do not indicate cancer recurrence is important. To determine this rate, we studied our mature institutional experience treating intermediate risk prostate cancer with external beam radiotherapy (EBRT).

Materials and Methods: A retrospective review of our experience with intermediate risk prostate cancer (PSA 10-20 and/or Gleason score 7 and/or T Stage< T3), treated for cure with EBRT (with or without adjuvant hormones) and a minimum of 10 years since completion of the radiation was performed. Patient demographic, cancer, treatment and subsequent clinical course details were abstracted from the electronic medical record. Biochemical failure status as per the Phoenix definition was determined. Among the patients with biochemical failure, clinical cancer recurrence was defined as the occurrence of any of the following:1) PSA >5; 2) initiation of hormonal treatment; 3) utilization of any salvage locoregional treatment; 4) clinical/imaging determination of local, regional or metastatic recurrence; and 5) unknown status.

Results: Between 2002 and 2007 542 men were treated by a 3D CRT or IMRT EBRT technique to a median dose of 76Gy in 38 fractions. Age ranged from 40 to 83 years (median 70) Median follow-up was 76 months (range 3 to 191), 82.9% (449 patients) remain in remission and 17.1% (93 patients) have developed biochemical failure. Among the patients with biochemical failure 15% (14 patients) have had no clinical cancer recurrence for a calculated actuarial probability of patients with biochemical failure actually NOT having clinical cancer of 19% at five years. Serum testosterone levels are available in 11 of these 14 patients. Nine out of 11 had normal testosterone and two out of 11 are hypogonadal.

Conclusions: An appreciable proportion of patients with biochemical failure following EBRT for intermediate risk prostate cancer do not have clinical cancer recurrence. This 19% (an underestimate as a proportion of patients who had hormones initiated as soon as biochemical failure was diagnosed likely did not have cancer) presumably reflects recuperating benign prostatic epithelium and should be considered both when comparing the treatment efficacy of EBRT with other modalities and when contemplating initiation of hormones or local salvage treatments.

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OUTCOME COMPARISON BETWEEN EARLY STAGE ADENOCARCINOMA AND SQUAMOUS CELL CARCINOMA LUNG CANCERS TREATED WITH STEREOTACTIC BODY RADIATION THERAPY

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Purpose: Stereotactic body radiation therapy (SBRT) has become one of the main treatment options for early stage lung cancer. Recent studies demonstrate a potential role of tumour histology on SBRT outcomes but current highly standardized treatment techniques do not take this into account. This study aims to characterize the SBRT outcomes of early stage Adenocarcinomas versus Squamous Cell Carcinomas (SCC) along with associated patient and treatment factors.

Materials and Methods: Three hundred and thirty-six consecutive patients treated between 2008 and 2015 at The Ottawa Hospital Cancer Centre were reviewed from an ethics-approved database of Stage I NSCLC patients. All selected patients had biopsy confirmed adenocarcinoma or SCC treated with SBRT for curative intent. Survival analyses were conducted using Kaplan Meier Estimate with comparison made through Log-Rank Test. Univariate and multivariate analyses were computed through Cox Regression.

Results: The study population consisted of 229 adenocarcinoma and 107 SCC patients with a median follow-up time of 36 months. SCC patients had worse overall survival (OS) than adenocarcinomas with median survival of 45 versus 55 months (p=0.04). Their respective three-year OS rates were 56% versus 69% and at five years were 33% and 41%. Progression free survival (PFS) of SCC was also worse with median survival of 41 versus 51 months (p=0.05). There was a trend in greater risk of recurrence regionally for SCC (HR (95% CI): 1.91 (0.92-3.96), p=0.08). No significant differences were found between local (HR (95% CI): 1.36 (0.67-3), p= 0.44) and distant recurrences (HR (95% CI): 0.64 (0.34-1.22), p=0.18). On univariate analysis, SCC histology was associated with worsening OS (HR (95% CI): 1.38 (1.01-1.88), p=0.04) along with right sided tumours, increased age, PET SUV and tumour size. Different histology was not associated with survival differences on multivariate analysis.

Conclusions: While worse OS and PFS were found in the SCC population, this did not translate into statistically significant

differences in rates of local and distant progressions. There was a trend of increased regional recurrence in the SCC population but this failed to reach statistical significance. These finds suggest a more complex interplay than just histology driving the survival differences and lead to avenues for further research.

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STEREOTACTIC BODY RADIOTHERAPY THERAPY FOR RECURRENT HEAD AND NECK CANCERS: DOSIMETRIC STUDY BETWEEN 3 DIFFERENT RADIATION MODALITIES

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Purpose: Despite effective treatment for head and neck cancers, a portion of patients recur locally or regionally. Re-irradiation has demonstrated feasibility in inoperable recurrences but is challenging due to toxicity from high cumulative doses and sensitivity of regional organs at risk (OARs). Toxicity can be mitigated with precise dose delivery through stereotactic body radiation therapy (SBRT). This was demonstrated in recent Phase II studies using a dose fractionation of 36Gy in 6 fractions. This study aims to compare dosimetric outcomes in such retreatment scenarios with 3 difference SBRT techniques: Volumetric Modulated Arc Therapy (VMAT), Helical Tomotherapy (HT) and Cyberknife Robotic Radiosurgery (CK).

Materials and Methods: This single centre study analyzed 10 patients previously underwent radiation therapy for head and neck cancer and subsequently re-irradiated for local or regional recurrence. Re-irradiation plans were re-targeted consisting of a GTV encompassing the gross recurrent tumour and a 5mm PTV expansion. OARs were standardized for all plans. These were planned by specialized VMAT, HT and CK planners. In the initial phase, plans were optimized for coverage and conformality. A subset of plans with significant OAR cumulative doses from their initial treatment and the SBRT retreatment was then re-planned in a second phase to dose-spare OARs.

Results: The 10 cases consisted of five that recurred in the neck, two at the base of the skull (BOS), and single cases in the maxilla, vestibule and nose. In the first phase of the study, aiming for coverage and conformality, all three techniques were able to achieve targeted dose coverage with D95 for HT, CK and VMAT being 35.98Gy (CI 95%: 35.86-36.1Gy), 36.2Gy (CI 95%: 36.15-36.24Gy), and 36.09Gy (CI 95%: 35.99-36.18Gy) respectively. Plans from all 3 techniques were highly conformal with conformality index respectively in HT, CK and VMAT of 1.06 (CI 95%: 1.01-1.11), 1.03 (CI 95%: 1.02-1.05) and 1.05 (CI 95%: 1-1.09). CK plans were significantly more heterogeneous than VMAT and HT.
In the second phase, four plans were re-targeted to spare adjacent OARs. This led to drop in PTV coverage with lowest D95 in HT, CK and VMAT plans being 30.89Gy, 33.04Gy, 32.11Gy respectively. Coverage for GTV were maintained with D95 at or above 36Gy for all three techniques. Decreased homogeneity was seen in HT and VMAT while it was maintained in CK. OAR constraints were unable to be met for the optic nerves and brain for tumours in close proximity for all three techniques. No clear advantage in OAR sparing was seen between the three modalities.

Conclusions: All three SBRT techniques were able to deliver highly conformal plans that provided adequate dose coverage with CK plans being more heterogeneous. However, when attempting to spare adjacent OARs, the heterogeneity of both HT and VMAT increased, mitigating their homogeneity advantage. Sparing the adjacent brain and optic nerves provided the most challenge in recurrences near these OARs.

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OPTIMAL HYPOFRACTIONATED RECTAL DOSE-VOLUME CONSTRAINT FROM THE PROSTATE CANCER PATIENTS OF THE PCS V TRIAL

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Purpose: Hypofractionated radiotherapy (HF RT) is now a standard of care management option for prostate cancer (PCa). However, existing recommendations on dose volume constraints from phase III trials have not been correlated with toxicity. There is a need to better understand how HF RT to the prostate could be planned to minimize gastrointestinal (GI) toxicity. Through a retrospective analysis of a phase III trial that implemented HF RT, we sought to elucidate accurate rectal dose-volume constraints.

Materials and Methods: Dose volume histogram (DVH) data was collected for patients enrolled in PCS V, a randomized Phase III trial that compared conventional fractionation (CF; 76Gy in 38 fractions) and HF (68Gy in 25 fractions) RT regimens in PCa patients. PCS V's prospective reports of GI toxicity, defined as per Common Terminology Criteria for Adverse Events (CTCAE) version 4, were classified as either acute or late; acute if they arose between zero to six months or late if six to 24 months after RT's start. We extracted the V50, V60, V65 V70, V75, Dmax, and Dmean values for the rectal wall and the whole rectum from both CF and HF RT plans. Receiver operating characteristic (ROC) analysis was conducted to identify the optimal dose constraint thresholds that would predict toxicity. Only the ROC curves with an area under the curve (AUC) of ≥0.6 were reported.

Results: Of the 155 patients for which full dosimetric data was obtained, 24 acute and eight late Grade 2+ GI toxicity events were prospectively reported. For CF, the threshold dose constraints for acute GI toxicity obtained with the rectal wall V50, V60, V65, V70, V75, and Dmean were 41%, 26%, 23%, 19%, 14%, and 47Gy, respectively. Using the whole rectum, the V60, V65, V70, and Dmean thresholds were 26%, 21%, 16%, and 50 Gy respectively. For late toxicity, only the ROC analysis with Dmax yielded an AUC of over 0.6, and the threshold was 78Gy for both the rectal wall and the whole organ. For HF regimen, the threshold dose constraints for acute GI toxicity obtained with the rectal wall and the whole organ were both a Dmean of 44Gy. Late GI toxicity for the rectal wall V50, V60, V65, and Dmean were 38%, 18%, 13% and 44Gy, respectively. Using the whole rectum, the V50, V60, and Dmean points were 38%, 24%, and 45Gy, respectively.

Conclusions: ROC analyses of PCS V's DVH and toxicity data for CF were similar to the dose constraints reported by QUANTEC, supporting this study's methodology. Application of the same methods to the HF RT toxicity data generated several threshold dose constraints that can guide the production of even more

tolerable PCa treatments with HF. The proposed HF dose constraints for the rectal wall and whole are V50=38%, V60=18%, V65=13%, Dmean=44Gy.

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RADIOTHERAPY AND CARDIOVASCULAR IMPLANTABLE ELECTRONIC DEVICES - AN EVIDENCE-BASED GUIDELINE AT MCGILL UNIVERSITY

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Purpose: Patients with cardiovascular implantable electronic devices (CIEDs) requiring radiation therapy (RT) are becoming increasingly common. Existing guidelines are based on recommendations from over two decades ago and focus on limiting the total dose to CIEDs to below a certain threshold. Since then, CIED and RT technologies have evolved. Thus, there is a need to revisit the monitoring and management policies of patients with CIEDs undergoing RT.

Materials and Methods: A retrospective review of patients with CIEDs who were treated with RT at the McGill University Health Centre between February 2008 and July 2017 was conducted. Oncologic and cardiovascular data were collected from each patient's medical record. Dosimetry data from each plan were reviewed. The incidence of CIED malfunction was recorded.

Results: We identified 362 treatment plans in 223 patients, 169 (75.8%) and 54 (24.2%) of whom had pacemaker and defibrillators, respectively. Most patients were treated with 6MV beams (79.3%). The most common treatment site was the thorax (43.6%). The most common treatment technique was intensity-modulated RT (IMRT; 32.9%). For 10 plans, the device was either directly in the beam path or immediately adjacent to the field edge, resulting in an average mean dose of 6.34Gy (SD 7.98) and maximum dose of 20.47Gy (SD 13.78) to the CIEDs. For another 20 plans, the device was <2.5cm from the beam path, and the average mean and maximum dose to the device was 0.58Gy (SD 0.36) and 2.22Gy (SD 1.07), respectively. In total, only two (0.9%) patients with device events were identified. Both patients had pacemakers and were non-dependent. One patient developed atrial high rate during the beginning of the first treatment session. Another patient's device was reset to backup mode after completing a course of palliative radiotherapy to the pelvis. Both were malfunctions that occurred at estimated doses that were below the historical 2Gy threshold.

Conclusions: Our findings highlight the rarity and stochastic nature of CIED malfunction during RT. The rare events were seen at doses below historical thresholds, while some devices tolerated a much greater dose without incident. Given these findings and following review of the literature, we propose an algorithm for risk stratification that is based on risk factors other than dose threshold. We stratify patients as high-risk if any of the following criteria are met: beam energy ≥10 MV, device located ≤2.5cm to treatment field, device capable of defibrillation, and device-dependent. All high-risk patients are monitored with an electrocardiogram during each treatment and their device is interrogated weekly. All patients are assessed prior to and at completion of RT by a cardiologist trained in electrophysiology, at which time, their devices are interrogated. This algorithm can guide clinicians in the management and monitoring of CIED patients undergoing RT.

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HOW EFFECTIVE IS ADJUVANT RADIOTHERAPY IN THE MANAGEMENT OF STAGE I HIGH-RISK ENDOMETRIAL CANCER?

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Purpose: A recent randomized controlled trial PORTEC-3 has demonstrated that in endometrial cancer patients with high-risk features, addition of chemotherapy to radiotherapy results in a significant improvement on failure-free survival. However, in the study, the statistical significance was limited to Stage III patients, while the benefit was less pronounced in Stage I and II patients and remains to be elucidated. In this study, we present the result of the 18 years of retrospective data on the pattern of practice and clinical outcomes in Stage I high-risk endometrial cancer patients at our institution.

Materials and Methods: A single-centre retrospective study was conducted on women with high-risk endometrioid-type endometrial cancer according to PORTEC-3 inclusion criteria (FIGO 2009 Stage I, endometrioid-type Grade 3 with deep myometrial invasion and/or lymph-vascular space invasion), who have undergone hysterectomy at our institution between 1998 and 2015. Data on surgical and radiation treatments, as well as patient and tumour characteristics were collected and correlated with clinical outcomes. Statistical analysis was carried out using Kaplan-Meier method to compare clinical outcomes to previously reported studies.

Results: A total of 46 Stage I high-risk endometrioid-type endometrial cancer patients were identified. Median age at diagnosis was 63 years (range 49-86 years) and median follow-up was 4.2 years. All patients underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO). Surgical staging was performed with pelvic lymph node dissection on 38 (82.6%) patients. The majority (80.4%) of patients underwent adjuvant radiotherapy alone (73.3% EBRT and 7.1% vaginal brachytherapy), two (4.3%) patients underwent combined chemoradiotherapy, and nine (19.6%) patients received no adjuvant treatment. Five-year disease-free survival and overall survival rates were 74.2% and 80.2%, respectively. Five-year disease-specific mortality rate was 14.1%. Among nine patients with recurrent disease, most disease (88.9%) relapsed outside pelvis and only one (12.5%) patient had regional recurrence in perirectal lymph node six months after completion of treatment (she remains clinically disease free two years after SBRT).

Conclusions: Clinical outcomes for Stage I high-risk endometrial cancer in our study are comparable to that of PORTEC-3. Adjuvant radiotherapy results in excellent locoregional disease control. However, the use of systemic therapy remains very low, while distant relapse rate remains significant. Addition of systemic therapy to adjuvant radiotherapy may be indicated in not only Stage III high-risk endometrial cancer, but also in Stage I and II high-risk patients to further reduce distant relapse rate and improve disease-free survival.

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DOSE-SPARING EFFECT OF DEEP INSPIRATION BREATH HOLD TECHNIQUE ON CORONARY ARTERY AND LEFT VENTRICLE SEGMENTS

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Purpose: Survival benefit from adjuvant radiotherapy after breast-conserving surgery is offset by 1% increase in non-breast cancer

mortality at 15 years, 90% of which is cardiovascular in origin. Certain cardiac segments of coronary artery (distal left anterior descending [LAD] coronary artery) and left ventricle (LV; apical and septal walls) are more prone to radiation-induced injury than other segments. Deep inspiration breath hold (DIBH) technique has the potential to reduce radiation dose to the heart and coronary arteries. We present dosimetric analysis on potential dose reduction in the heart and individual cardiac segments of LV and LAD in patients treated with DIBH technique, compared to free breathing (FB) technique.

Materials and Methods: Since the introduction of DIBH at our institution in 2017, all patients with left-sided breast cancer post-breast-conserving surgery, who could tolerate DIBH underwent both DIBH and FB scans. They were treated with two tangential fields at 40.05-42.56Gy in 15-16 fractions. In addition to the left breast, heart and lungs, cardiac segments, including coronary artery (proximal/middle/distal LAD, left main coronary artery [LMCA], left circumflex artery [LCX] and right coronary artery [RCA]) and LV were contoured by a single observer (JS) on both DIBH and FB scans. Fusing both scans using the breast/chest wall as the registration point, the same beam arrangements were applied on DIBH and FB scans and dose volume histograms for each structure of interest were compared. Statistical analysis was carried out using paired sample t-test.

Results: A total of 75 consecutive patients were identified. Significant reduction in Dmax to LAD was observed in DIBH (19.91.6Gy) compared to FB (31.91.2Gy) (meanSEM). In addition, DIBH reduced Dmax in all individual segments of LAD (DIBH versus FB): proximal (3.2Gy versus 7.9Gy), middle (16.1Gy versus 27.4Gy) and distal (18.7Gy versus 31.3Gy). The absolute dose reduction in DIBH compared to FB was greater in distal LAD (-12.6Gy) than middle (-11.3Gy) and proximal (-4.6Gy) LAD. Similarly, DIBH reduced doses in other structures (DIBH versus FB): whole heart (Dmean; 1.3Gy versus 2.8Gy), LV (Dmean; 1.8Gy versus 5.2Gy) and left lung (V20Gy; 9.86% versus 11.17%). Dmax to LMCA, LCX and RCA was negligible (<2Gy) in both DIBH and FB. Structure volume was larger (lungs), smaller (whole heart and LV) and similar (LAD) between DIBH and FB. All dose reductions in DIBH compared to FB were statistically significant (p<0.001).

Conclusions: Our study is one of the largest series demonstrating dose-sparing effect of DIBH in all cardiac segments, with the greatest dose sparing in distal LAD. This potentially translates into the largest reduction in major coronary events, as distal LAD has been previously shown to be the most vulnerable site for radiation-induced injury.

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AGE AS AN INDEPENDENT PREDICTIVE FACTOR FOR SURVIVAL OUTCOMES IN PRIMARY CNS LYMPHOMA: A REVIEW FROM TERTIARY INSTITUTION

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Purpose: Primary central nervous system lymphoma (PCNSL) is a rare malignancy with a poor median survival. Multimodality treatments with high-dose methotrexate (HD-MTX)-based systemic therapy and/or whole brain irradiation for consolidation or salvage constitutes the most commonly used treatment approach. Due to severe treatment toxicity and aggressive course of the disease, not all patients benefit from this treatment approach. In this retrospective study, we aimed to identify various clinical parameters that predicted outcomes on survival, and response to various treatments in patients with PCNSL.

Materials and Methods: Patients diagnosed with PCNSL between 2002 and 2017 were selected for analysis. Data on patient demographics, tumour characteristics and treatment were collected and analyzed for correlation with clinical outcomes. Survival curves were generated with the Kaplan-Meier method and compared using log-rank test. Multivariate analysis was performed where prognostic variables and patient outcome were correlated with Cox proportional hazard model.

Results: A total of 82 patients were identified and selected for analysis. Median age at diagnosis was 68 years (range 30-89 years) and median follow-up was 3.7 years. Among the 82 patients, 10 (12.2%) patients received systemic therapy (CT) only, 31 (37.8%) patients received radiotherapy (RT) only, and 23 (28.0%) patients received systemic therapy followed by salvage radiotherapy (CRT). Eighteen (22.0%) patients received supportive care (SC) only. Median overall survival (OS) of the entire cohort was 11.1 months (95% CI 6.1-15.5 months). Median OS was 8.8 months (95% CI 4.5-11.3 months) for RT group, 30.1 months (95% CI 19.3-41.0 months) for CRT group and 3.3 months (95% CI 0.8-5.8 months) SC group. Median OS for CT group was not reached. Multivariate analysis demonstrated that both the use of systemic therapy (hazard ratio [HR] 0.23, 95% CI 0.11-0.49, p<0.001) and radiotherapy (HR 0.54, 95% CI 0.32-0.92, p=0.022) were associated with improved survival in the total population. Systemic therapy in patients younger than 70 years of age was associated with improved OS (HR 0.13, 95% CI 0.05-0.32, p<0.001), whereas in elderly patient population (70 years of age or older), addition of radiotherapy was associated with improved OS (HR 0.45, 95% CI 0.21-0.96, p=0.039).

Conclusions: Our results concur with the published literature demonstrating the survival benefit with the use of systemic therapy in younger patient population. Radiotherapy was independently associated with an improved overall survival in patients older than 70 years and therefore should be considered as palliative treatment of choice in the elderly population who may not be candidates for systemic therapy. Further prospective studies are required to validate our findings as well as optimization of radiotherapy in this population.

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AN UPDATE ON TREATMENT OF INTERMEDIATE-RISK ENDOMETRIAL CANCER USING MINIMALLY INVASIVE SURGERY AND ADJUVANT RADIOTHERAPY

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Purpose: Modern series of technical skills in minimally invasive surgery (MIS) for hysterectomy have resulted in improvement in patient outcome compared to that of traditional laparotomy in patients with endometrial cancer. MIS has been increasingly used since its introduction in 2010 at our institution. In addition, prospective randomized trials have shown that adjuvant radiotherapy (RT) following surgical staging significantly improves locoregional control among the intermediate-risk patients. Our study aims to investigate efficacy and safety of combined treatment using MIS and adjuvant RT among these patients at our institution.

Materials and Methods: A single-centre retrospective study was conducted on patients with FIGO Stage I endometrioid-type endometrial cancer with intermediate risk factors as defined by PORTEC-1 (<50% myometrial involvement and Grade 2-3, or >50% myometrial involvement Grade 1-2), who have undergone surgical staging and adjuvant RT at our institution between 2010 and 2015. Data on surgical and radiation treatments, as well as patient and tumour characteristics were collected and correlated with clinical outcomes. Statistical analysis was carried out using

Kaplan-Meier method to compare clinical outcomes to previously reported studies.

Results: A total of 179 intermediate-risk endometrial cancer patients were identified and 135 (75.4%) patients who received adjuvant RT were selected for study. Median age at diagnosis was 63 years (range 40-89 years) and median follow-up was 4.4 years. Lymphovascular space invasion (LVSI) was identified in 31 (23.0%) patients. Sixty-one (45.2%) patients were identified as high-intermediate risk (HIR) and 74 (54.8%) patients as low-intermediate risk (LIR), according to PORTEC-1 criteria. Surgical staging was performed with pelvic lymph node dissection on 107 (79.3%) patients, while 94 (69.6%) and 41 (30.4%) patients underwent MIS and laparotomy, respectively. Twenty-eight (20.7%) patients received external beam radiotherapy and 107 (79.3%) patients received vaginal brachytherapy. Five-year disease-free survival and overall survival rates were 92.8% and 94.8%, respectively. Only 3 (2.2%) locoregional and 3 (2.2%) distant recurrences were observed within the five-year follow-up period. No significant postoperative complication was reported.

Conclusions: Clinical outcomes for intermediate-risk endometrial cancer at our institution remain excellent with few locoregional recurrences, and are comparable to that of previously published randomized studies. Our results confirm that MIS combined with adjuvant RT, especially vaginal brachytherapy, should be offered for patients with intermediate-risk endometrial cancer.

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PALLIATIVE CRANIAL IRRADIATION IMPROVES SURVIVAL IN PRIMARY CNS LYMPHOMA PATIENTS INELIGIBLE FOR SYSTEMIC THERAPY

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Purpose: Primary central nervous system lymphoma (PCNSL) is a very rare type of cancer representing only 3% of all CNS malignancies and 1% of non-Hodgkin lymphomas (NHL). Prognosis is generally poor with a median survival of less than 3 months if untreated. Standard of care for PCNSL is upfront high-dose methotrexate-based chemotherapy and/or whole brain radiotherapy (WBRT). However, in recent years, the role of WBRT in a primary management has been questioned due to its toxicity and lack of convincing data for survival benefit. Even its role in a palliative setting remains to be clearly elucidated. In this retrospective study, data on WBRT for patients who are ineligible for systemic therapy were analyzed and correlated to patient outcomes, compared to the supportive care only.

Materials and Methods: Patients diagnosed with PCNSL between 2002 and 2017 were selected. Patients were excluded if they received systemic therapy or focal radiation only. Data on patient demographics and WBRT (total dose, fractionation, tumour biologically effective dose [/=10, BED10]) were collected and correlated with clinical outcomes. Survival curves were generated with the Kaplan-Meier method and compared using the log-rank test. Multivariate analysis was performed where prognostic variables and patient outcomes were correlated with the Cox proportional hazard model.

Results: A total of 48 patients were selected for analysis. Median age at diagnosis was 74 years (range 30-89 years) and median follow-up among survivors was 4.4 years. The majority (85.4%) of tumours were identified as diffuse large B-cell lymphoma (DLBCL) on histology. Among all patients, 29 (60.4%) patients completed WBRT, two (4.2%) patients did not complete WBRT and 17 (35.4%) patients received no treatment. Median time interval between diagnosis and WBRT was 34 days (range 7-359 days). Median overall survival (OS) was 4.4 months. Patients who received WBRT had significantly better OS (8.81.8 months) compared to those with no WBRT (3.31.0 months) (p=0.003). In multivariate analyses, the addition of WBRT was associated with improved OS (hazard ratio [HR] 0.37, 95% CI 0.18-0.76, p=0.006). Among patients who received WBRT, whole brain dose higher than 30Gy was not associated with survival outcomes (p=0.43). However, higher dose to the whole brain (35Gy, p=0.051) and BED10 of 45Gy to gross tumour (p=0.017) were associated with improved OS.

Conclusions: PCNSL patients who are ineligible for systemic therapy may still benefit from WBRT with a significant improvement in survival outcomes, compared to the best supportive care. Dose escalation through the addition of a gross tumour boost in these patients was associated with an improved overall survival. Future prospective studies are necessary to test the validity and confirm the significance of our study results.

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A COMPARISON OF RADIATION TECHNIQUES IN PATIENTS TREATED WITH CONCURRENT CHEMORADIATION FOR STAGE III NON-SMALL CELL LUNG CANCER

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Purpose: The standard of care in the management of Stage III non-small cell lung cancer (NSCLC) is concurrent chemoradiation. Recently, newer more conformal techniques with intensity modulated radiation therapy (IMRT) and volumetric arc therapy (VMAT) are being used. It is unclear whether a more conformal technique ultimately improves survival in patients with Stage III lung cancer. We looked at population-based data to examine this question.

Materials and Methods: A retrospective cohort of Stage III NSCLC patients treated with concurrent chemoradiation with curative intent between 2009-2014 in Ontario were identified from the ICES (Institute of Clinical Evaluative Sciences) database. Patients were excluded if they had surgery, sequential chemoradiation or radiation alone. Outcomes were compared for patients treated with 3D conformal radiation (3D-CRT), IMRT and VMAT. The primary endpoint was overall survival (OS), calculated using the Kaplan-Meier method and compared using log-rank test. Cox regression was used to investigate effect of radiation type on OS. A minimal clinically important difference (MCID) was set at ≥15%.

Results: Between 2009-2014, a total of 2507 patients were treated with 3D-CRT (n=925), IMRT (n=1227) or VMAT (n=355). The rate of 3D-CRT use declined (from 65% in 2009 to 14% in 2014) while the rates of IMRT (35% to 53%) and VMAT (0% to 33%) use concurrently increased. Median survival in months was 22.7 [95% CI 21.0-24.4] for 3D-CRT, 20.8 [95% CI 19.6-22.2] for IMRT and 24.3 [95% CI 20.6-27.9] for VMAT (p=0.041 for all three groups, and p=0.046 for 3D CRT versus IMRT alone). The five-year overall survival was 22.1% [95% CI 19.2-25.1] for 3D-CRT versus 18.1% [95% CI 15.4-20.9] for IMRT (p=0.046). Prognostic factors for survival on multivariable analysis included male sex [HR 1.29, 95% CI 1.18-1.42, p<0.001], income quintile [HR 0.95, 95% CI 0.92-0.99, p=0.004], age [HR 1.03, 95% CI 1.00-1.06, p=0.04], and radiation type [IMRT HR=1.12, 95% CI 1.01-1.24; VMAT HR=0.91, 95% CI 0.76-1.09, p=0.012].

Conclusions: There is increased uptake of more conformal techniques over time amongst Stage III NSCLC patients. Although a statistically significant difference in OS was observed, this was likely driven by unmeasured patient selection effects. Absolute differences were modest and did not meet clinical significance.

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VALIDATION OF DEEP LEARNING-BASED AUTO-SEGMENTATION FOR ORGANS AT RISK AND GROSS TUMOUR VOLUMES IN LUNG STEREOTACTIC BODY RADIOTHERAPY

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Purpose: Accurate contouring of organs at risk (OAR) and gross tumour volumes (GTV) is particularly important in stereotactic body radiotherapy (SBRT) where smaller margins are used. Manual segmentation is labour intensive and can suffer from significant inter-observer variability. Here we evaluate the performance of deep learning auto-segmentation models trained from retrospective manually drawn contours from a single centre and assess whether these models can accurately segment patient planning CT scans from a different cancer centre with acceptable results.

Materials and Methods: Auto-segmentation models were trained using a deep convolutional neural network based on a U-net architecture using 210 planning CT scans, which included 160 publicly available planning CT scans with ground truth contours reviewed by a radiation oncologist and 50 lung SBRT CT scans from a single centre (centre A). Deep learning models were then used to segment 100 planning CT scans, which consisted of 50 additional scans from centre A and 50 planning CT scans from a separate cancer centre (centre B). The original clinical contours (CC) were compared with the deep learning-based contours (DC) using the Dice Similarity Coefficient (DSC) and 95% Hausdorff distance transform (DT).

Results: Comparing DCs to CCs for all 100 contoured planning CT scans, the mean DSC and 95% DT were 0.93 and 2.8 mm for aorta (n=81), 0.81 and 3.3 mm for esophagus (n=99), 0.95 and 5.1 mm for heart (n=100), 0.98 and 3.1 mm for lung (n=190), 0.56 and 6.6 mm for brachial plexus (n=101), 0.82 and 4.2 mm for proximal bronchial tree (n=100), 0.90 and 1.6 mm for spinal cord (n=87), 0.91 and 2.3 mm for trachea (n=100), and 0.71 and 5.2 mm for lung GTVs (n=85). The DSC and 95% DT were not significantly different for centre A and centre B for aorta, lung GTV, heart, lung, brachial plexus, spinal cord, and trachea. Structures with significantly different DSC or 95% DT between the two centres included the esophagus DSC (0.80 versus 0.83, p=0.02) and proximal bronchial tree 95% DT (3.6 versus 4.8 mm, p=0.001).

Conclusions: Deep-learning auto-segmentation models can provide accurate segmentation for OARs used in lung SBRT. Models trained with a single institution's data were accurate when validated on a separate institution's planning CT scans, despite variations in scan quality and contouring practices. Deep learning lung GTV segmentation models reliably located the target lesions but generally were less accurate than the organs at risk models due to the variable location and size of lung tumours. Deep learning auto-segmentation can provide an accurate starting point for review and manual adjustment and should improve efficiency in lung SBRT planning.

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COMPARING DEEP LEARNING-BASED AUTO-SEGMENTATION OF ORGANS AT RISK AND CLINICAL TARGET VOLUMES TO EXPERT INTER-OBSERVER VARIABILITY IN RADIOTHERAPY PLANNING

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Purpose: Automatic segmentation methods aim to alleviate labour intensive contouring of organs at risk (OAR) and clinical target volumes (CTV). Although deep learning-based contouring (DC) has shown improvement over manual and atlas-based auto-segmentation, the majority of previous studies were limited to one expert observer per scan. We aim to determine if DC models trained by a single Radiation Oncologist are comparable to multiple expert Radiation Oncologists manual contours (EC).

Materials and Methods: Multiple Radiation Oncologists at a single centre were asked to contour central nervous system (CNS), head and neck (H&N), and prostate RT OARs and CTVs on radiotherapy planning computed tomography (CT) scans. DCs were generated using deep learning auto-segmentation software based on a U-net architecture and trained using contours from a single Radiation Oncologist on publicly available datasets. DC and ECs were compared using the Dice Similarity Coefficient (DSC) and 95% Hausdorff distance transform (DT). Radiation oncologists recorded manual contouring time for each scan.

Results: We compared DCs to 129 expert contoured structure sets on 43 CT scans. Each scan had 2-4 ECs, for a total of 60 CNS, 39 H&N, and 30 prostate EC structure sets. The mean DC and EC contouring times were 1.1 versus 8.0 minutes for CNS, 2.7 versus 27.8 minutes for H&N, and 1.4 versus 17.8 minutes for prostate structures. Differences in contouring duration were significant ($p<0.005$). For CNS structures, the DC to EC DSC and 95% DT were not significantly different from the EC to EC comparisons for brainstem and optic chiasm. The EC to EC comparisons were more similar for the optic globe DSC (0.88 versus 0.89; p=0.009) and optic chiasm 95% DT (6.2 versus 4.2 mm; $p<0.005$). For H&N structures, the DSC and 95% DT were not significantly different for the parotid gland and submandibular gland, and were different for the neck CTV DSC (0.75 versus 0.80; $p<0.005$), neck CTV 95% DT (9.3 versus 6.4 mm; $p<0.005$), and spinal cord 95% DT (4.5 versus 2.6 mm; $p<0.005$). For prostate structures, there was no difference for seminal vesicles DSC and 95% DT. There was more similarity in the DC to EC comparisons for bladder DSC (0.97 versus 0.96; p=0.03), bladder 95% DT (2.9 versus 3.1 mm; p=0.02), femoral head DSC (0.92 versus 0.89; $p<0.005$), femoral head 95% DT (5.4 versus 8.4 mm, p=0.006), rectum DSC (0.84 versus 0.81; p=0.02), and rectum 95% DT (6.9 versus 10.0 mm; p=0.01). The EC to EC comparison was more similar for the prostate DSC (0.81 versus 0.84; p=0.01).

Conclusions: We observed minimal differences in DSC and 95% DT from ECs to other ECs compared to those from ECs to DCs. These findings demonstrate that the accuracy of well-trained deep learning-based auto-segmentation models trained using a single Radiation Oncologist contours is similar to expert inter-observer variability for CNS, H&N, and prostate RT structures.

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RECTAL WALL VERSUS WHOLE RECTUM DOSE: WHICH VOLUME BETTER PREDICTS GASTROINTESTINAL TOXICITY FROM PROSTATE EXTERNAL BEAM RADIOTHERAPY?

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Purpose: Radiation-induced gastrointestinal (GI) toxicity is an important complication of prostate cancer (PCa) radiotherapy (RT) that radiation oncologists seek to minimize by respecting dose constraints for the rectum. It remains unclear whether dose to the rectal wall or whole rectum better predicts GI toxicity. This study used prospectively collected toxicity data from a registered phase III randomized trial to address this question.

Materials and Methods: Dose-volume histogram (DVH) data was extracted from patients enrolled in PCS V, a multi-institutional phase III trial that compared conventionally fractionated (76Gy in 38 fractions) to hypofractionated RT (68Gy in 25 fractions) in PCa patients. Acute and late GI toxicity was assessed at 0-6 months and 6-24 months, respectively, using the Common Terminology Criteria for Adverse Events (CTCAE v.4). Rectal wall and whole volumes were collected prospectively. Dosimetric values evaluated were the whole rectum and rectal wall V50, V60, V60, V65, V70, V75, Dmax and Dmean. Spearman's rho (*r*) was used to correlate each DVH point of both rectum contours to acute and late GI toxicity. A Fisher's z-transformation was then performed to test the significance of the difference between the rectal wall and whole rectum *r*'s for individual DVH points. Wilcoxon signed rank test was used to determine whether paired differences of the GI toxicity grade associated with rectal wall versus whole rectum were significant.

Results: In total, DVH data was obtained from 155 patients, with 83 patients having been treated conventionally and 72 with hypofractionation. Spearman's *r* correlation test revealed a strong association between the whole rectum DVH points and acute GI toxicity, namely for V60 (p=0.04), V65 (p=0.01), V70 (p=0.01) and Dmax (p=0.04). When the same analysis was conducted for late toxicity, only the V50 and Dmean points yielded a marginally significant correlation (p=0.049 and 0.042, respectively). These findings were not observed in the hypofractionated arm. There was no significant association between the rectal wall's DVH points with either acute nor late GI toxicity in both arms. While the Fisher's z-transformation analysis did not reveal any significant differences between the correlations of individual DVH points obtained from the rectal wall and whole rectum with acute or late GI toxicity, the distribution of Spearman's *r* was significantly higher for the whole rectum, compared to its wall for acute toxicity (p=0.047) in the conventional arm.

Conclusions: Our data suggests that the whole rectum DVH profile better correlates with acute GI toxicity than that of the rectal wall. Furthermore, the whole rectum's DVH distribution rather than individual DVH points correlated more reliably with acute GI toxicity. Set-up protocols aiming to minimize rectal wall inter- and intra-fractional movement to improve the accuracy of rectal wall dosimetric values to predict toxicity are thus worthy of future study.

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ENGAGING INTER-PROFESSIONAL COLLABORATION TO IMPROVE RESIDENT TREATMENT PLANNING KNOWLEDGE AND SKILLS

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Purpose: As of July 1, 2019, Canadian Radiation Oncology residency programs will transition to a Competency by Design (CBD) model of training. Within CBD, residents are expected to prescribe, plan and supervise radiotherapy (competencies 3.5 & 3.6), and are required to observe radiation planning and delivery in both the Transition to Discipline and Core Stages. Within our centre, a dedicated rotation focusing on radiotherapy planning and delivery has been established to ensure residents gain high yield practical experiences to meet these objectives. As part of a needs assessment for this curriculum, we conducted a survey of our radiation therapy staff to solicit opinions on both key content as well as perceived gaps in knowledge and skills.

Materials and Methods: A short anonymous electronic survey was sent to 102 radiation therapists, planners, mould room and simulation staff at our centre. Respondents were asked to indicate all clinical areas in which they worked (multiple selections were permitted). They were also asked to identify 3-5 basic skills or knowledge they feel residents should gain during their training and any perceived gaps in knowledge or skills among residents rotating through their area. Answers were organized into themes and reviewed with the existing Royal College Radiation Oncology Competencies and required training experiences documents. These were collated to create a log book and self-assessment guide for resident learners on a dedicated treatment planning and delivery rotation.

Results: Twenty-one responses were collected (21/102 = 20.5%). Thirty nine percent of respondents identified that they spent most of their clinical time working on radiotherapy LINACS (11/28); 25% within treatment planning (7/28) and the remainder within mould room, CT/MR simulators, brachytherapy, Quality Assurance, orthovoltage machine, and management. Seventy-five key learning points were generated in addition to 14 perceived gaps, organized into the following five themes: 1) recognition of patient factors that affect treatment plan execution; 2) lack of experience watching set-up on treatment machines and troubleshooting; 3) complex techniques and the resources required to execute them; 4) plan evaluation; and 5) emergency treatments. From this, a 58 item Log book of required experiences, many of which require interaction with therapy and physics staff and encompass these themes, and a 50 question self-assessment have been created and will be piloted with future rotating residents.

Conclusions: Our radiation therapy colleagues are important inter-professional educators and their insights into residents' knowledge and skills gaps should be solicited and incorporated into training objectives. It is our hope that this curriculum will help guide self-directed learning on a dedicated treatment planning and delivery rotation and will address perceived resident knowledge gaps, especially as we move forward with a CBD curriculum.

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SMALL CELL CARCINOMA OF THE BLADDER: RETROSPECTIVE LONG TERM OUTCOMES OF CHEMORADIATION

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Purpose: There is paucity of literature regarding the optimal management of Small Cell urothelial cancer (SCUC), especially with chemoradiation (CRT). Our centre published a small (n=14)

case series of patients treated with CRT between 1985 and 1996, demonstrating a 44% five-year overall survival (OS). Other series for limited stage SCUC have demonstrated wide ranging five-year OS, from 8% to 36%. This study reports the long-term outcomes of patients treated at BC Cancer (BCC) who had curative intent CRT. Objectives of the study were to: 1) describe the epidemiology of SCUC, 2) assess oncologic outcomes after CRT for SCUC.

Materials and Methods: All SCUC patients treated with curative intent CRT in the province from 1999 to 2018 were identified. Patients treated with palliative intent therapy or cystectomy were excluded. Demographic and staging information were collected retrospectively. Type of chemotherapy, radiation dose to bladder, and frequency of prophylactic cranial irradiation were recorded. Overall survival and cancer specific survival (CSS) were assessed using Kaplan Meier and competing risk methods respectively.

Results: Thirty-two patients had curative intent CRT. Of these 22 (69%) were males, 10 (31%) females. The median age was 72.5 (range: 50-92), 48% had ECOG performance status 0/1. All patients had a transurethral bladder resection prior to CRT. AJCC 8th edition stages were 6.3% T1 N0, 34.4% T2 N0, 46.9% T3-4 N0/Tany N1, and 12.5% T any N1-3 disease. The median dose of RT was 51Gy (EQD2) and16% had prophylactic cranial irradiation. Nine percent of patients received neoadjuvant chemotherapy and 91% had concurrent chemotherapy. The most common chemotherapy protocol used was cisplatin and etoposide, followed by carboplatin and etoposide. Five-year OS was 22% [median survival= 26.5 months (95% CI: 16.4-36.8)], and the five-year CSS was 47%. One patient received salvage radical cystectomy after CRT. Among the surviving patients, bladder preservation rate was 100%.

Conclusions: This population-based provincial retrospective study of SCUC demonstrates that CRT is a reasonable approach for the treatment of limited stage SCUC and is associated with a long term survival for a meaningful proportion of patients. Multivariate analysis of the survival outcomes and surgery cohort matched analysis are planned.

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3D PRINTER TECHNOLOGY FOR CUSTOM BOLUS AND IMMOBILIZATION DEVICE FABRICATION IN THE MANAGEMENT OF PALMAR OR PLANTAR FIBROMATOSIS WITH RADIOTHERAPY: TECHNICAL AND DOSIMETRY ASPECTS

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Purpose: Palmar or plantar fibromatosis is a benign fibro-proliferative disorder affecting the fascia of the hands or feet. Management involves surgery, typically reserved for cases where progression limits function. Retrospective series demonstrate that radiation (RT) can stabilize the disease course in a large proportion of patients and improve symptoms in some cases. RT techniques vary between use of electrons, superficial or orthovoltage photons and often require lead cut outs or custom boluses. We present a new approach demonstrating the implementation and effectiveness of 3D printed bolus material in patients receiving RT for fibromatosis.

Materials and Methods: A total of 3 patients, one with plantar and two with palmar fibromatosis were treated with radiation using 3D printed boluses over the past year. Bolus design was based on CT imaging data. Palmar patients were treated with a single en-face electron field, with a two-part accessory which acted both as a bolus and an immobilization device encasing the hand. The plantar case required 6MV photons delivered with a VMAT technique to adequately cover the deeper target volume. Dose and fractionation were based on guidelines from the Royal College of Radiologists in the UK. CT was used to assess printed shape and density accuracy.

Results: Mean deviations in shape between the printed bolus pieces and their designs were all less than 0.4 mm. The differences in mean HU between the printed boluses and their expected values were between 7 and 44 HU. No significant issues were encountered when applying the bolus to patients. TLDs used demonstrated dose accuracy to within TLD precision (5%).

Conclusions: 3D printing bolus technology represents a novel approach to treating fibromatosis with radiation. It offers potential benefits in terms of generating a custom bolus and simultaneous immobilization device with a high degree of accuracy. It also saves setup time on the treatment unit.

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FEATURES OF PATIENTS LIVING LESS THAN 3 MONTHS FOLLOWING SPINE STEREOTACTIC BODY RADIOTHERAPY

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Purpose: Stereotactic body radiotherapy (SBRT) to the spine offers superior local control and potentially pain relief compared to conventional radiotherapy. Patients with longer survival realize these benefits most, and physician prognostication is historically poor. The purpose of this study was to report factors associated with < 3-month survival after spine SBRT.

Materials and Methods: A prospective database of consecutive patients treated with spine SBRT between 2009 and 2017 was reviewed. Dates of death were obtained through institutional records and obituaries.

Results: A total of 21 of 230 patients (9.1%) passed away within three months of starting treatment representing 48 total spinal segments treated. There were three deaths (14.3%) related to progression of spinal disease. The median survival and age were 56 days (range: 14-79 days) and 61 years (range: 29-85 years), respectively. The most common indications for SBRT were retreatment (n=8, 38.1%) and de novo metastases (n=8, 38.1%), followed by post-operative SBRT (n=5, 23.8%). Median time from cancer diagnosis to spine SBRT was 20 months (range: 0.9-116 months). Most patients were ECOG 0 or 1 (n=14, 66.7%) and had no neurologic deficits (n=17; 81.0%). Lung (n=7, 33.3%) and renal cell carcinoma (n=6, 28.6%) were most common primary cancers and seven patients (33.3%) had oligometastatic disease. Most patients had other sites of visceral metastases to sites such as the liver, lung or brain (n=17, 81.0%). Many had epidural (n=10, 47.6%) and/or paraspinal extension of spinal disease (n=12, 57.1%). Thirteen patients (61.9%) had SINS potentially unstable or unstable lesions. In 27 segments evaluable with follow-up imaging, four (14.8%) had radiologically progressed prior to death.

Conclusions: We report excellent patient selection in those who receive spine SBRT. Patients who passed away <3 months after SBRT were heavily pretreated, with 62% of patients having had surgery or prior radiotherapy to the same spinal segments. A relatively large proportion of patients with visceral disease burden and paraspinal and epidural spinal disease died <3 months after treatment. Further work to elucidate factors associated with poor survival are needed to further identify patients who will benefit most from spine SBRT.

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DOSIMETRIC STUDY OF HIPPOCAMPAL SPARING IN PATIENTS TREATED WITH CYBERKNIFE FOR BRAIN METASTASES

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Purpose: Cranial irradiation is associated with significant neurocognitive sequelae and can reduce quality of life. This neurotoxicity may be linked to damage to neural progenitor cells within the hippocampus, which has led to the hypothesis that reducing hippocampal dose may improve neurocognitive function. Preliminary results of NRG-CC001 trial indicate that hippocampal sparing leads to a modest benefit in neurocognitive function in patients with brain metastases. Despite intensity modulated radiotherapy (IMRT)-based hippocampal sparing, though, 58% of patients continued to experience a decline in neurocognitive function at six months.

Objectives: Given potential benefits to neurocognitive function that have been demonstrated with hippocampal sparing using IMRT, we hypothesized that similar benefits may be seen using hippocampal avoidance in patients treated with stereotactic radiation. Our study evaluated whether the hippocampal dose could be significantly reduced in the treatment of brain metastases using CyberKnife, while maintaining target coverage.

Materials and Methods: Dose received by the hippocampus was evaluated in 24 patients treated with CyberKnife in 2018. CyberKnife plans were re-optimized to minimize dose to the hippocampus while maintaining target coverage and tolerance of organs at risk. Mean and maximum doses to the hippocampus were compared between the baseline and re-optimized plan. A two-tailed p-value below 0.05 was considered significant.

Results: Median age was 64.5 years. Mean number of metastases was 5.9 (range 1 to 16 mets). Primary cancers included lung, melanoma and breast. Baseline Cyberknife plans showed the following: average Dmax to the hippocampus was 666cGy (range 86 – 2020 cGy) and average Dmean to the hippocampus was 310cGy (range 32 to 1340 cGy). Dmax to the hippocampus was reduced on average by 400cGy ($p<0.0001$; range 61 to 1520cGy), with an average reduction of 63%. Dmean to the hippocampus was reduced on average by 164cGy ($p=0.002$), with an average reduction of 46%.

Conclusions: Our study demonstrates that significant dose reduction to the hippocampus is possible in the treatment of brain metastases with CyberKnife using dose optimization. We propose a prospective trial evaluating the clinical benefit of hippocampal sparing with optimized radiosurgery techniques.

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PROGNOSTIC INDEX FOR LOCALIZED LIVER RADIATION - HEPATOCELLULAR CARCINOMA (PILLIR-HCC): DEVELOPMENT AND ANALYSIS OF A CLINICAL PROGNOSTIC TOOL TO IMPROVE PATIENT SELECTION FOR LIVER DIRECTED RADIOTHERAPY IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Purpose: External beam radiotherapy (EBRT) is an increasingly utilized treatment for patients with hepatocellular carcinoma (HCC) who are not eligible for curative intent treatments such as resection or transplantation. Liver EBRT is associated with toxicities such as nausea and fatigue, with quality of life measures tending to return to baseline by three months. Many patients with HCC, however, may not live long enough to benefit from this treatment. The aim of this study was to develop a prognostication tool to aid in patient selection for liver directed EBRT for patients with HCC.

Materials and Methods: A prospectively collected liver radiotherapy database was used to identify patients who had been treated with EBRT to the liver with local control intent. Exclusion criteria: single fraction EBRT, primary disease other than HCC, lost to follow-up <4 months. Pre-treatment patient and tumour characteristics associated with early death (<4 months) were identified using univariate analysis. Variables found to be significant were entered into a multiple logistic regression model using forward selection to identify those factors which independently predicted early death. Three-fold cross validation and bootstrapping using 500 random samples was performed. The PILLiR-HCC was created using the variables determined most significant in the multiple logistic regression model.

Results: Two hundred and twelve patients were identified as having received liver EBRT. One hundred forty-nine patients were excluded (single fraction EBRT n=17, non-HCC primary n=126, follow-up <4 months n=6). Sixty-three patients remained for analysis with a four-month mortality rate of 23.8%. Elevated bilirubin, low serum albumin, Child-Pugh score, ECOG performance status and gross tumour volume (GTV) were found to be significant predictors of early death on univariate analysis and were included in the multiple logistic regression model. Using forward selection to maximize the area under the curve, elevated bilirubin, ECOG performance status and GTV were found to best predict patients unlikely to live longer than four months.A prognostic index (PILLiR-HCC) was created, with 1 point for bilirubin>17μmol/L, 1 point for 75mL<GTV≤175mL or 2 points for GTV>175mL and 2 points for ECOG≥2 (AUC 0.853). Four month mortality was 0%, 0%, 9.1%, 33.3%, 55.6% and 75.0% for patients with 0 (n=7), 1 (n=8), 2 (n=22), 3 (n=12), 4 (n=9) and 5 (n=4) points, respectively.

Conclusions: Elevated bilirubin, large GTV and poor performance status were found to be risk factors for mortality less than four months in patients being considered for liver EBRT for HCC. We created the PILLiR-HCC to aid clinicians in determining which patients are unlikely to live long enough to benefit from liver EBRT. Future work includes validating the PILLiR-HCC with an independent dataset.

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PROGNOSTIC INDEX FOR LOCALIZED LIVER RADIATION - METASTATIC (PILLIR-M): DEVELOPMENT AND ANALYSIS OF A CLINICAL PROGNOSTIC TOOL TO IMPROVE PATIENT SELECTION FOR LIVER DIRECTED RADIOTHERAPY FOR LIVER METASTASES

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Purpose: Liver metastases are common and associated with a high mortality rate. With improved treatment planning and delivery techniques, external beam radiotherapy (EBRT) is increasingly utilized for treating liver metastases. Many of these patients, however, are unlikely to live long enough to reap the benefits. The aim of this study was to develop a prognostication tool to aid in patient selection for liver directed EBRT in patients with liver metastases.

Materials and Methods: A prospectively collected liver radiotherapy database was used to identify patients who had been treated with EBRT to the liver with local control intent. Exclusion criteria: single fraction EBRT, primary HCC or cholangiocarcinoma, benign pathology, lost to follow-up <4 months. Pre-treatment patient and tumour characteristics associated with early death (<4 months) were identified using univariate analysis. Variables found to be significant were entered into a multiple logistic

regression model using forward selection to identify factors independently predicting early death. Three-fold cross validation and bootstrapping using 500 random samples was performed. The PILLiR-M was created based on this model.

Results: Two hundred and twelve patients who had received liver EBRT were identified. One hundred and nine patients were excluded (single fraction EBRT n=17, HCC n=63, cholangiocarcinoma n=22, benign pathology n=1, follow-up <4 months n=6). One hundred and three patients remained for analysis with a four-month mortality rate of 27.2%.Ascites, elevated bilirubin, low serum albumin, Child-Pugh score, ECOG performance status, non-colorectal primary, presence of extrahepatic disease and previous liver directed therapy were found to be significant predictors for early death on univariate analysis and were included in the multiple logistic regression model. Using forward selection to maximize the area under the curve, non-colorectal primary, ECOG, presence of extrahepatic disease and serum albumin were found to best predict patients unlikely to live longer than four months.A prognostic index (PILLiR-M) was created with 1 point for each of the following: non-colorectal primary, presence of extrahepatic disease, ECOG ≥2 and serum albumin<35g/L (AUC 0.852). Four month mortality was 0%, 3.1%, 43.6%, 66.7% and 100% for patients with 0 (n=16), 1 (n=32), 2 (n=39), 3 (n=9) and 4 (n=3) points, respectively.

Conclusions: Non-colorectal primary, presence of extrahepatic disease, poor performance status and decreased serum albumin were found to be risk factors for mortality less than four months in patients being considered for liver directed EBRT for metastatic disease. We successfully created the PILLiR-M to aid clinicians in determining which patients are unlikely to live long enough to benefit from liver EBRT. Future work includes validating the PILLiR-M with an independent dataset.

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DOES "5+5" EQUAL BETTER RADIATION TREATMENT PLANS IN HEAD AND NECK CANCERS?

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Purpose: Accurate contouring in head and neck cancers (HNC) is critical. International consensus guidelines for contouring primary tumours in HNC recommend the "5+5mm" rule wherein both high-dose and low-dose clinical target volumes (CTV-P1 and CTV-P2 respectively) are created using successive 5mm expansions on the gross tumour volume (GTV). Histopathological surgical series demonstrate the majority of microscopic extension in HNC can be encompassed within 5mm of the GTV, and the physical properties of modern photon-based HNC radiotherapy plans may result in adequate coverage of the low-dose CTV-P2 merely due to dose fall-off. To our knowledge, the necessity of contouring a low-dose CTV-P2 has never been assessed, therefore we evaluated the dosimetric impact of adding a CTV-P2 expansion using the "5+5mm" rule compared to contouring with a high-dose CTV-P1 alone.

Materials and Methods: A retrospective study of clinically-delivered (chemo)radiotherapy HNC treatment plans was conducted. All patients were treated with 70Gy in 35 fractions using volumetric modulated arc therapy (VMAT). Original treatment plans were generally created using a 5mm expansion from GTV to CTV-P1, and a CTV-P2 was retrospectively contoured using international consensus guidelines (5mm expansion on CTV-P1, carving off specified barriers to spread). Our institutional standard was a 5mm planning target volume (PTV) expansion. The primary outcome was whether 95% of the volume of the PTV for the CTV-P2 contour (i.e. PTV-P2) received at least 56 Gy. To assess dose fall-off, the coverage of a PTV-RING structure (created by subtracting PTV-P1 from PTV-P2) by at least 56 Gy was evaluated as a secondary outcome.

Results: Twenty-seven patients from four HNC subsites (base of tongue, tonsil, hypopharynx and supraglottic larynx) were included. In all 108 treatment plans, at least 95% of the PTV-P2 structure received at least 56Gy (inadequate coverage rate: 0%, 95% confidence interval: 0-3.4%). The mean volume of the PTV-P2 structure receiving at least 56Gy was 97.4%. Eight of 108 treatment plans had borderline coverage of the PTV-RING substructure alone, where 90-95% of PTV-RING received at least 56Gy, with the minimum coverage by at least 56Gy being 90.6%.

Conclusions: In the setting of 5mm PTV expansions, the addition of a low-dose CTV-P2 structure using the "5+5mm" rule would have had no dosimetric impact and appears redundant. The "5+5mm" rule adds additional contouring time, treatment planning complexity, and potentially could introduce errors. The "5+5mm" rule may have value in other settings, such as when smaller PTV margins are used or in proton radiotherapy, and warrants further evaluation with prospective or randomized studies addressing the optimal target volumes in HNC.

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PROFESSIONAL CONDUCT IN CLINICAL RADIATION ONCOLOGY RESEARCH

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Purpose: Our study aim was to better understand the research experiences of Canadian physicians in radiation oncology pertaining to possible areas of interpersonal conflict in clinical research.

Materials and Methods: Between August 20 2018 and November 12 2018, 62 respondents completed an online anonymous survey open to radiation oncology residents, fellows, and staff physicians across Canada. There were 29 questions in total inquiring about possible areas of research conflict including: theft of intellectual property, refusal to acknowledge contributions, authorship inclusion and order, conflict relating to the use of a research database, as well as institutional research demands.

Results: Sixty percent of respondents were male and 84% were staff physicians. Institutional expectations for first or last-authored publications each year were 0 for 36% of respondents, one for 8%, two for 7%, and three or more for 11% of respondents (38% unsure). This led to moderate-significant pressure to publish in 24%. The most common occurrences of research conflict included theft of intellectual property (21%), wrongful authorship (writing the manuscript but not credited as first author, 18%; senior authorship position taken by someone minimally involved, 30%; and overall gift authorship, 43%), and uncredited contributions (abstraction of original data, 25%; writing the research proposal, 14%; data analysis, 14%; writing sections of the manuscript, 7%). These instances resulted in either a permanently damaged relationship with a colleague or longstanding resentment in 24%. When respondents were invited to provide guidance on how to avoid these conflicts in the future, the most common recommendations were discussing and establishing authorship order prior to starting the study and having clear institutional policies for resolving research conflicts.

Conclusions: In our small survey of Canadian physicians in radiation oncology, we found that interpersonal research conflict resulted in almost a quarter of respondents having either a damaged relationship with a colleague or longstanding resentment. Proposed measures to reduce conflict include establishing authorship order upfront and clear institutional policies.

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LOW Z TARGET BEAM ENHANCES GOLD/GADOLINIUM NANOPARTICLE MEDIATED CELL KILL IN ZEBRAFISH XENOGRAFT MODEL

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Purpose: Nanoparticles (NPs) 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 secondary 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. *In silica*, replacing the standard Cu/W linac target with a low Z (sintered diamond) material predicted a 7.7 fold dose 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 setup: 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.
In vitro assays: Panc1 (pancreas), FaDu (hypopharynx), HSC3 (tongue) 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 assay. CellROX probe was used to measure reactive oxygen species (ROS) production via flow cytometry.
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 1 dpi (days post injection) with 8Gy. Tumour viability was measured by a standard *ex vivo* proliferation assay at 3 dpi.

Results: NP trafficking within the cell was found to be cell line dependent. NP mediated cell kill was enhanced in FaDu cells when combined with low Z beam and correlated with increased production of reactive oxygen species. Results were consistent in NP-labeled xenografts irradiated with the low Z beam.

Conclusions: In a proof of principle experiment, we have shown enhanced radiologic cell kill in low-Z target irradiation in xenografted NP labeled cells. We are in the process of testing the model in additional cells with plans to examine tumour response in adult fish model.

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OUTCOMES OF STEREOTACTIC RADIOSURGERY FOR BRAIN ARTERIOVENOUS MALFORMATIONS: A SINGLE CENTRE EXPERIENCE

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Purpose: Brain Arteriovenous Malformations (BAVM) are high flow, high pressure vascular lesions that have a 2-4% annual risk of hemorrhage. BAVMs can be treated with Stereotactic Radiosurgery (SRS) depending on its size, depth of its venous drainage, and location near eloquent brain with a high success rate. We conducted a retrospective chart review to assess clinical outcomes in patients with BAVMs treated with SRS at our centre.

Materials and Methods: Eligible patients were those with BAVMs treated with SRS. Minimum follow-up of 36 months was required. The primary outcome of this study was nidus obliteration on either Magnetic Resonance Imaging (MRI) or Angiography. Secondary outcomes of this study were short-term complications including re-hemorrhage, seizure, or focal neurological deficits, and long-term complications including late structural changes, radiation necrosis, radiation induced tumours, brain edema, and residual neurological deficits. Statistical analyses of these end-points were performed.

Results: Twenty-five eligible patients with BAVMs were treated with SRS between 2004 and 2018. Median follow-up was 55 months. The median size of BAVMs treated was 22mm, and the median Spetzler-Martin Score for BAVMs was 3. All treatments were delivered in a single fraction with a median dose of 18Gy (16-22.5 Gy). In total, Nidus Closure was observed in 72% of patients (18/25). Eight percent of patients (2/25) required re-treatment with SRS for failure of nidus obliteration, and 12% of patients (3/25) underwent a secondary treatment with either surgical resection or embolization for nidus obliteration, or for late structural changes associated with SRS. Twelve percent of patients (3/25) had long-term complications associated with SRS, including radiation necrosis, cyst formation and chronic brain edema.

Conclusions: Preliminary data analysis shows modest rates of nidus obliteration with SRS alone, with 20% of patients (5/25) requiring repeated treatments to achieve nidus obliteration. There were relatively low rates of long-term complications associated with SRS for BAVM. Further analysis will be conducted on short-term and long-term complication prior to presentation.

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INTRACRANIAL CONTROL AND RADIONECROSIS IN MELANOMA PATIENTS WITH BRAIN METASTASES TREATED WITH STEREOTACTIC RADIOSURGERY

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Purpose: Melanoma commonly metastasizes to the brain and is radioresistant. Stereotactic radiosurgery (SRS) confers durable local control of brain metastases (BM) while maintaining neurocognitive function. These advantages are increasingly important as survival among these patients improves secondary to advances in systemic therapies. This study investigated the local control (LC), intracranial PFS (iPFS), freedom from radionecrosis (FFRN), and overall survival (OS) among melanoma patients receiving SRS for BM.

Materials and Methods: We retrospectively reviewed clinical outcomes of melanoma patients with brain metastases treated with SRS between October 2008 to January 2017 in a large academic centre. Post-SRS, patients were followed in a multidisciplinary clinic with clinical examination and brain MRI every three months. Survival outcomes were estimated using the Kaplan-Meier method.

Results: In total, 97 patients with 283 brain metastases (including 12 surgical cavities) treated with SRS were identified. Median age was 60.5 (24.4-90.7). Median follow-up was 9.6 (2.2-74.7) months after first SRS. Median prescription dose was 21 (10-24) Gy delivered in a single fraction. Thirty (30.9%) patients had WBRT post-SRS, 36 (37.1%) patients had BRAF-positive disease. Per lesion (n=283), one-year LC and FFRN were 84.4%, and 90.1%,

respectively; medians were not achieved for either LC and FFRN. Radionecrosis (RN) occurred in 20 (7.1%) lesions. Per patient (n=97), median OS and iPFS were 16.0 and 5.3 months, respectively; one-year OS and iPFS rates were 62.0%, and 30.1%, respectively.

Conclusions: SRS resulted in excellent rates of LC, with a low risk of RN. However, most patients developed intracranial progression within one year. Further analyses to establish correlates (lesion size, SRS dose, and molecular status) to LC, FFRN, OS, and iPFS will be performed prior to the final presentation.

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STEREOTACTIC ABLATIVE RADIOTHERAPY FOR MEDIASTINAL AND HILAR LYMPHADENOPATHY: A SYSTEMATIC REVIEW

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Purpose: Stereotactic ablative radiotherapy (SABR) is a form of high dose hypofractionated radiotherapy typically delivered ≤ 5 fractions and a desired $BED_{10} \geq 100Gy_{10}$. While established for parenchymal lung tumours, its safety and effectiveness for mediastinal and hilar lymphadenopathy (MHL), is not well established, given the potential for toxicity due to proximity of nearby organs at risk. Therefore, the objective of this study was to summarize reported outcomes following SABR for MHL.

Materials and Methods: A systematic review, based on the PRISMA guidelines, was performed using MEDLINE® (PubMed®), EMBASE and Cochrane Library databases from inception until December 2018. Studies reporting outcomes from SABR specifically for MHL from all primary malignancies were included. Studies were not excluded based on SABR dosage and fractionation prescribed. Non-English studies, guidelines, reviews, non-peer reviewed correspondences, and studies with fewer than 5 patients were excluded. If multiple publications were found from the same institution, only the most recent publication and/or largest cohort were included for data abstraction.

Results: From the 223 studies initially identified, four studies totaling 196 unique patients met all inclusion criteria. All studies were retrospective in design, and from single institutions. The majority (65%) of patients (n=127) had a diagnosis of non-small cell lung cancer, and breast was the second most common with 16 patients (8%). Median follow-up periods ranged between 12.0-32.2 months. SABR dose and fractionation ranged from 21Gy to 60Gy in 3-11 fractions, which corresponded to a median BED_{10} ranging from 46-106 Gy_{10}. Planning tumour volume (PTV) margins employed ranged from 3 to 5 mm. Three studies reported local control (LC) rates, which were: study I) 97% (one-year) and 77% (five-year); study II) 66% (16-month) and study III) 88% (two-year). Overall survival (OS) was calculated from time of treatment in three studies, with a weighted median OS of 24.3 (18.0-27.2) months. Weighted progression-free survival (PFS) calculated from two studies were 11.4 (9.0-13.1) months. Overall, SABR was well tolerated; with a weighted Grade 3-5 toxicity rate of 6% (n=11). The weighted treatment-related mortality (i.e. Grade 5 toxicity) rate was 2% (n=4).

Conclusions: Despite the potential for serious toxicity, SABR for MHL appears to be feasible and effective. Considering the inconsistency of reported patients, SABR prescriptions, treatments, and outcome variables, both multi-institutional and/or prospective data would be helpful to determine the relative therapeutic benefit of SABR in this high-risk treatment scenario.

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EXTERNAL VALIDATION OF 7TH AND 8TH EDITIONS OF THE AJCC TNM STAGING CLASSIFICATION SYSTEM FOR ANAL CANAL CANCER: A MULTI-INSTITUTIONAL QUALITY ASSURANCE STUDY

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Purpose: Accurate cancer staging is essential to determine extent of disease, to implement a treatment plan, and to inform prognosis. Recently, the American Joint Committee on Cancer (AJCC) 8th edition (AJCC 8) has updated its anal cancer staging system to reflect changes in definitions of N stage, and consequently changes in definitions of overall stage groupings. The present study aims to validate the new AJCC 8 prognostic staging system using a provincial, multi-institutional cohort of anal cancer patients, and to compare its performance with the previous AJCC 7 staging system.

Materials and Methods: Patients with anal carcinoma treated with curative intent chemoradiotherapy in Alberta, Canada from 2000 to 2017 were identified from a prospectively maintained database. Demographic, disease and treatment-related data were abstracted. Patients were reclassified as per AJCC 8, and descriptive statistics were calculated. Kaplan-Meier curves of progression free survival (PFS) and overall survival (OS) were evaluated for statistical difference using the log-rank method. Cox proportional hazards regression was used to evaluate the predictive performance of both AJCC 7 and 8 staging systems. Akaike information criterion (AIC) was applied to correct for potential bias in comparing prognostic systems with a different number of stage groupings. A smaller AIC value indicates a superior model for predicting outcomes. Each model's ability to distinguish overall stage groupings and N stage definitions were considered significant at a value of $p<0.05$.

Results: For the 285 eligible patients, median age was 58.0 years, 73.0% were female, 89.1% had squamous cell carcinoma histology, 36.8% were clinically lymph node positive, and 26.3% had clinical T Stage ≥T3. After a median follow-up of 5.7 years, 11.9% had distant progression only, 4.4% had local progression only, and 3.9% progressed locally and distantly. Compared with the previous edition, AJCC 8 upstaged 27.0% of patients, and downstaged 8.1%. AJCC 8's overall stage groupings had modestly better predictive performance for PFS (AIC 656.2, $p=0.001$) and OS (AIC 956.2, $p<0.001$), compared to AJCC 7 (PFS: AIC 656.5, $p<0.001$; and OS: AIC 956.7, $p<0.001$). However, AJCC 8's new N stage definitions provided more accurate stratification for PFS (AIC 651.2, $p<0.001$) and OS (AIC 977.9, $p=0.010$), compared to AJCC 7's previous N stage definitions (PFS: AIC 661.2, $p=0.012$; and OS: AIC 978.9, $p=0.059$).

Conclusions: This is the largest cohort study to validate both AJCC 7 and 8 staging systems for anal cancer. Overall stage groupings in AJCC 8 showed modest improvements in predictive ability compared to AJCC 7. Although both staging systems performed well, the new definitions of N stage introduced in AJCC 8 more accurately predict survival outcomes for anal cancer patients, and thereby supports its use in clinical practice.

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RE-DEFINING VENTRICULAR TARGET VOLUME IN GERMINOMA: IS INCLUSION OF TEMPORAL HORNS NECESSARY?

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Purpose: Current treatment efforts for intracranial germinomas aim to reduce late effects while maintaining excellent clinical outcomes. Exclusion of the temporal ventricular horns (TVHs) from the clinical target volume (CTV) may reduce dose to the hippocampi and lead to fewer neurocognitive toxicities. We reviewed the outcomes of a retrospective germinoma cohort and analyzed radiotherapy plans to determine dosimetric differences to critical structures depending on whether TVHs were included or excluded.

Materials and Methods: Clinical data from 26 pediatric patients treated for intracranial germinoma with photon radiation were analyzed. Critical structures of interest (temporal ventricular horns, hippocampi, and temporal lobes) were contoured on patients with available radiotherapy plans. Dose differences to these structures were compared based on inclusion or exclusion of the TVHs using two-sided t-tests. A SIMPLE consensus contour was generated for TVH-sparing ventricular CTVs via deformable image registration.

Results: Twenty-two patients had available radiotherapy plans for analysis. Twelve patients were treated with ventricular RT that included their TVHs, while ten patients had their TVHs excluded from their ventricular CTVersusAll patients received chemotherapy with at least partial response prior to radiotherapy. Median follow-up for all patients was 83 months. All 26 patients were living at the time of analysis. One patient relapsed 16 months post-radiotherapy in the fourth ventricle, which had been omitted from the radiotherapy field. No patient recurred in the TVH. Mean dose was significantly lower to the hippocampi (Δ = -578 cGy, p = 0.0016) and temporal lobes (Δ=-599 cGy, p=0.0007) in the TVH-excluded cohort compared to those with TVH inclusion within the treatment field. Significant dosimetric differences persisted even after dose normalization to account for differential treatment dose prescriptions.

Conclusions: Exclusion of the TVHs from the photon ventricular CTV results in significant dose sparing to the hippocampi and temporal lobes. Clinical outcomes remain excellent with no deaths and no TVH failures. Exclusion of TVHs from the ventricular CTV in germinoma requires prospective study in order to validate its non-inferiority and potential benefits to neurocognitive outcomes.

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LEARNING FROM MISTAKES - EVENT REPORTING AND ORGANIZATIONAL LEARNING IN THE RADIATION ONCOLOGY PROGRAM

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Purpose: Medical errors are happening at an alarming rate in the health system. Event learning refers to the feedback loop of event reporting, review and analysis in order to prevent medical errors. One of the major contributing factors to events in radiotherapy (RT) is the introduction of new technologies and the increased level of computerization. Recognizing that events occur regardless of whether or not they are reported, event learning provides opportunities to improve quality and prevent adverse outcomes through a formal management system.

Objectives: This study looked at outcomes of the event learning system at our centre implemented to promote organizational learning for safer RT delivery.

Materials and Methods: The management system for event learning at our centre utilizes reporting software, customized to reflect the unique processes in the delivery of RT. It was set up according to definitions and guidelines in the "Consensus recommendations for incident learning database structures in radiation oncology" (Med. Phys. Volume 39 (12), December 2012). We looked at event reporting of external beam RT treatment related incidents from 2014-2018.

Results: There was an increase in RT incident reporting from 2014 to 2018 fiscal years with 44 reported events in 2014/2015, 55 events in 2015/2016, 62 events in 2016/2017 & 67 events in 2017/2018. For these dates, most reported events occurred during treatment delivery (144 events) followed by imaging for RT planning (38 events) and pre-treatment review and verification (30 events).In the 2018 calendar year, there were a total of 75 RT events categorized by error type as follows: not applicable (other) – 31, incorrect geographical area – 13, imaging – 10, incorrect dose - eight, carepath/task – seven, collision – four, incorrect modality/energy – two. Most of the RT incidents (64) did not result in any dosimetric outcome (prescribed dose delivered), while 11 events had minor dosimetric variation (defined as <5% from prescribed dose).

Conclusions: Event learning plays a key role in improving the quality and safety of RT delivery. At our centre, the Radiation Oncology Program has increasingly adapted strategies and methods to prevent medical errors. Our goal is to foster a culture of organizational learning rather than blaming and increase event reporting. We are also working on implementing the National System for Incident Reporting –Radiation Therapy (NSIR-RT) program into our system.

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DOES A ROCKY TREATMENT COURSE IN HEAD & NECK CANCER PATIENTS PREDICT ONCOLOGIC OUTCOMES?

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Purpose: A Rocky Treatment Course (RTC) is a previously defined intermediate-term composite outcome in head and neck cancer (HNC) patients receiving radiotherapy (RT). It is a composite of six variables: patient-driven interruptions in RT ≥1-day, incomplete RT, incomplete chemotherapy(c) (<2 cycles), >5 visits to a walk-in nursing clinic, gastrostomy tube (G-tube) dwell time ≥90 days, and unplanned G-tube insertion (≥21 days after RT start). Previous work in an earlier cohort of patients showed that components of the RTC were predictive of oncologic outcomes and late toxicities. Our objective was to investigate if having a RTC predicts oncologic outcomes and late toxicities in a more recent, independent cohort of HNC patients.

Materials and Methods: A retrospective review of HNC patients receiving RT as part of curative intent treatment from September 2013 to December 2017 was conducted. A random sample of 300 patients was drawn, of whom half attended, and the other half did not attend, a pre-treatment educational class. RTC component variables, as well as detailed treatment and toxicity data, were abstracted from chart review and merged with our prospectively collected Anthology of Outcomes quality assurance tool. Univariable analyses was conducted with individual components of, and the composite RTC; and dependent variables

of overall survival (OS), locoregional recurrence (LRR), locoregional recurrence-free survival (LRFS), and unexpected Grade 3 toxicity. Multivariable analysis was performed for OS and LRFS.

Results: Overall, 123/300 (41%) patients experienced a RTC. Among those with RTC, 2-year results were: OS 74%, LRR 4.2%, LRFS 73%, and unexpected Grade ≥3 toxicity 5.7%. Among those without RTC, analogous figures were: 84%, 1.7%, 84%, and 3.9%, respectively. The differences were statistically significant for OS (p=0.033) and LRFS (p=0.015), but not for LRR (p=0.22) or toxicity (p=0.48). Among RTC components, only RT interruption was associated with worse OS (OR 1.82, CI 95% 1.04 – 3.17, p=0.035) and LRFS (OR 1.95, CI 95% 1.13 – 3.37, p=0.017) on univariable analysis. On multivariable analysis, variables (HR, 95% CI, p-value) associated with worse OS were: RTC (2.08, 1.11-3.91, 0.023), ECOG performance status ≥1 (5.11, 2.55-10.26, <0.001), N2/3 disease (2.83, 1.38-5.8, 0.0044) and treatment modality other than cRT: RT alone (3.2, 1.39 - 7.38, 0.0064), surgery with postoperative cRT (20.41 , 6.99 - 59.6, <0.001), and surgery with postoperative RT (4.28, 1.72 - 10.68, 0.0018). Similar results were seen for LRFS.

Conclusions: The association of a rocky treatment course with worse oncologic outcomes in HNC has been independently validated and could be used as an intermediate outcome variable in future prospective studies.

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A COMPARISON OF THE TUMOUR RESPONSE IN ESOPHAGEAL CANCER PATIENTS TREATED WITH TRI-MODALITY APPROACH USING EITHER CISPLATIN/5-FU OR CARBOPLATIN/PACLITAXEL AND CONCOMITANT RADIATION THERAPY

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Purpose: We know that a major pathologic tumour response following neoadjuvant therapy is associated with an increased overall survival. In recent years standard of care chemotherapy regimen in neoadjuvant management of esophageal cancer has changed from cisplatin/5-FU (CIF) to carboplatin/paclitaxel (CAP). We compared treatment responses among patients who received neoadjuvant therapy using CIF or CAP with concomitant radiation therapy (RT).

Materials and Methods: Retrospective chart review of all patients who received neoadjuvant therapy followed by surgery for esophageal cancer diagnosed between 2008- 2018 at a single academic centre was completed. Descriptive statistics and bivariate analyses (Chi-square, t-tests) were utilized to analyze the data.

Results: Of the 80 eligible patients, 84% were male with a median age was 62.5 years, most (85%) had lower esophageal lesions and the most common histology was adenocarcinoma (86.3%), followed by squamous cell carcinoma (12.5%). Most patients received 50Gy radiation dose (92.5%) with fewer receiving 41.4Gy (7.5%). All recent patients (57.5%) received CAP in comparison with historical controls (42.5%) who received CIF. Median time between completion of neoadjuvant therapy and surgery was 65.5 days. Following neoadjuvant therapy, (63.2%) had a tumour regression grade (TRG) of 0 or 1. There was no significant difference in tumour regression grade of (0 and 1) or (2 and 3) between groups receiving CAP or CIF (p=0.686), or in tumour down staging (ypT) (p=1.0). There was no change in TRG after excluding patients receiving 41.4 Gy. Most resection specimens (74%) were negative for lymph node metastasis (ypN0). Pathologic ypT stages (AJCC 8th e.) were 0 (37.5%), 1A (3.8%), 1B (8.8%), 2 (12.5%) and 3(37.5%). Five patients (6.3%) had positive resection margins; of these, three died of metastatic disease and two are well with no evidence of local recurrence or metastatic disease.

Conclusions: Most esophageal cancer patients had a major pathologic response (TRG score 0 or 1) to neoadjuvant chemo-radiation therapy and were ypN0. There was no significant difference in tumour regression grade or tumour down-staging between the two chemotherapy regimens.

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USE OF COMBINED HORMONE THERAPY WITH POST-OPERATIVE RADIATION TREATMENT FOR PROSTATE CANCER: IMPACT OF RANDOMIZED TRIALS ON CLINICAL PRACTICE

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Purpose: Approximately one third of men who undergo radical prostatectomy (RP) for localized prostate cancer (PC) will experience biochemical relapse (BCR). A proportion of these patients benefit from post-operative (post-op) radiotherapy (PORT) in the adjuvant (ART) or salvage (SRT) settings. Additionally, two randomized phase III studies (GETUG-AFU 16 and RTOG 9601) showed improved outcomes with the addition of combining hormone therapy (HT) to PORT. We sought to assess the impact of these trials on clinical practice patterns, and to determine the rates and characteristics of patients receiving PORT-HT.

Materials and Methods: After obtaining Institutional approval, patients diagnosed with localized PC treated with RP who received PORT from January 1, 2006- June 30, 2007 (period 1); July 1, 2011- December 31, 2012 (period 2); and January 1, 2017- June 30, 2018 (period 3) were included. Patient demographics, tumour characteristics, PSA kinetics, and treatment details were collected. ART was defined as PORT within one year of RP with undetectable PSA. Early SRT (eSRT) was defined as PORT delivered >1 year after RP with undetectable PSA, or with PSA levels >0.05ng/mL and <0.5ng/mL. SRT was defined as PORT delivered with PSA >0.5 ng/mL. HT included LHRH-agonists or antagonists, and anti-androgens. Clinicopathologic and treatment characteristic variables were analyzed descriptively and compared using parametric or non-parametric tests where appropriate. All statistical tests were two-sided and a p value <0.05 was considered significant.

Results: Five hundred and two patients were included: 152 (period 1), 185 (period 2), and 165 (period 3). Mean age was 61, and median PSA at diagnosis ranged from 7.3-8ng/mL between periods. The most frequent post-op profile was pT3aN0, ISUP Grade 2, and undetectable post-op PSA. PORT was delivered as ART and eSRT respectively in 12.5% and 62.5% of cases (period 1), 14.1% and 55.7% (period 2), and 9.1% and 68.5% (period 3) (p=0.44). The proportion of patients with extraprostatic extension (pT3a) and PSA at time of PORT ≤0.5ng/mL respectively increased from period 1 (49% and 73%) to period 3 (62% and 89%) (p=0.03 and p<0.001) The use of combined HT increased through the study periods from 14.5% to 32% to 42% (p<0.001). Conversely, the proportion of patients that met eligibility criteria for either GETUG or RTOG trials decreased over time from 49% to 33% to 36% (p=0.04).

Conclusions: In contrast to evidence showing steady underutilization of PORT, the use of combined HT with PORT increased through the study periods. In addition, we found that only a third of contemporary patients undergoing PORT are represented in the GETUG and RTOG trials, highlighting the need for further characterizing the utilization of PORT-HT, and modern studies assessing the clinical benefits of the combined approach.

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LOCALIZED PROSTATE CANCER PATIENTS' PREFERENCES FOR HYPOFRACTIONATED RADIOTHERAPY: A DISCRETE CHOICE EXPERIMENT PILOT STUDY

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Purpose: Several fractionation schedules exist to treat localized prostate cancer. Some clinicians are hesitant to prescribe moderate hypofractionation while waiting for clinical trial data to mature due to late toxicity concerns, and no phase III trials comparing stereotactic ablative radiotherapy (RT) to conventionally fractionated RT have been published. If the trade-off men are willing to make for treatment convenience at the expense of toxicity was quantified, then when the trial data are available clinicians will be better able to counsel localized prostate cancer patients regarding their external beam radiotherapy (EBRT) options. The purpose of this study was to pilot a Discrete Choice Experiment (DCE), a type of hypothetical conjoint analysis, as a method to elicit how patients weigh these different attributes of treatment choice. A pilot study was completed to determine; 1) the feasibility of conducting a DCE in this patient population; 2) test if the attributes and levels are appropriate; and 3) calculate parameter estimates and the minimum sample size required to design an efficient DCE.

Materials and Methods: After review of the literature the attributes 'treatment length', 'fiducial markers, 'risk of PSA rising within five-years', 'risk of acute gastrointestinal (GI) and genitourinary (GU) toxicity', and 'risk of late GI and GU toxicity' were selected. In each choice set respondents chose between two EBRT scenarios described by the five attributes and 2-3 possible levels that were systematically varied. There were 12 scenarios from the experimental design and six to test reliability and validity, and a semi-structured interview. With a multinomial logit model the attribute parameters, where larger magnitude indicates higher importance, were estimated. The minimum sample size for 80% power and significance level of 0.05 was calculated.

Results: The six pilot study participants ranged in age from 68-80 years, three were currently undergoing and three had completed EBRT. The efficacy attribute 'risk of PSA rising within five-years' that was believed a priori to be most important had the second largest parameter value of -0.25 and was ranked second overall in the interviews. Patients gave an unexpectedly high weighting to avoid 'fiducial markers' with the largest parameter estimate of -0.31. The attribute 'risk of late GI and GU toxicity' was ranked as most important by four participants and had the third largest parameter estimate (-0.18). 'Treatment length' was deemed most important by one participant and estimated at -0.13, and the attribute 'risk of acute GI and GU toxicity' was least important overall (estimate -0.04). The minimum required sample size to design an efficient DCE was 55.

Conclusions: A DCE with the selected attributes and levels is feasible and appropriate in this patient population, and these results will be used to plan a full study to determine if participants are willing to trade off some efficacy and toxicity for shorter treatment time.

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A COMPARISON OF STEREOTACTIC BODY RADIOTHERAPY MODALITIES: VOLUMETRIC MODULATED ARC THERAPY VERSUS INTENSITY MODULATED RADIATION THERAPY IN TREATMENT OF KIDNEY CANCER

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Purpose: The effect of treatment technique on reducing kidney dose is not fully understood. Several treatment techniques exist to treat kidney cancers with SBRT (stereotactic body radiation therapy). The most commonly used technique is VMAT (volumetric modulated arc therapy) which provides a continuously moving and shifting arc beam around the patient during treatment. The advantage of this technique is fast treatment time, however VMAT may allow for spillage of radiation dose across the abdomen which may affect distant nephrons in the treated and contralateral kidney. IMRT (intensity modulated radiation therapy) is similar to VMAT, but is delivered using fixed beam paths. The advantage of IMRT is fixed field apertures reducing spillage of radiation across the abdomen but may lead to higher doses within the treated kidney, where it is theorized the majority of renal dysfunction occurs post SBRT. The purpose of this study is to compare these techniques to provide a comparative analysis of effect on target coverage, treated kidney dose, untreated kidney dose, and dose to other organs at risk (OARs).

Materials and Methods: Design of this study is a retrospective cohort single institution study. Study population includes 15 patients with primary renal cell carcinoma treated with kidney IMRT or SBRT at the Juravinski Cancer Centre (JCC). Patients were at least 18 years of age. Anatomic and dosimetric parameters were collected on this cohort. Primary endpoints were amount of radiation to the gross tumour volume, clinical target volume, planning treatment volume, and organs at risk (adrenal glands, stomach, duodenum, small bowel, large bowel, liver, heart, chest wall, skin, spinal cord, esophagus, and normal kidneys) for each patient with each treatment technique.

Results: All IMRT and VMAT plans satisfied the dose constraints set for OARs. In all subjects, coverage of 95% of the PTV was greater than 95% of the prescription dose and similar between techniques (p=0.20). No statistically significant dose differences between planning techniques for the treated kidney, contralateral kidney, duodenum, or adrenal glands were found.There was a trend toward statistical significance for less maximum point dose using VMAT technique in small bowel, large bowel, skin, and stomach (p=0.06-0.07). The chest wall, heart, esophagus, liver, and spinal cord received negligible amounts of radiation in all cases, with no difference between techniques (p>0.1).

Conclusions: VMAT and IMRT deliver similar target coverage while meeting OAR dose constraints. There was no statistical difference in dose to OARs between IMRT and VMAT techniques for treating kidney cancers in this patient group; however, individual patient differences may favour one technique over the other; for example, when treating patients where bowel toxicity may be important (e.g. inflammatory bowel disease), a VMAT technique may be preferable to limit the maximum point dose.

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ARE FEMALE RADIATION ONCOLOGISTS STILL UNDERREPRESENTED IN THE PUBLISHED LITERATURE? AN ANALYSIS OF AUTHORSHIP TRENDS OVER THE PAST DECADE

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Purpose: Female researchers have historically been underrepresented in authorship lists. We examined whether female representation has improved in the radiation oncology (RO) literature over the past decade, and whether the introduction of double-blind peer review (where reviewers are blinded to author names and vice-versa) impacts female authorship rates.

Materials and Methods: We analyzed authorship lists over a ten-year period (January 1, 2007 to December 31, 2016) from the

two highest impact factor RO journals: The International Journal of Radiation Oncology, Biology, Physics (IJROBP) and Radiotherapy and Oncology (R&O). From each journal, 20 articles per year were chosen at random. Data abstracted included the total number of authors, percent female authors, and gender of the first, second, and last authors. 'Collaborating authors' were defined as those not in the first, second, or last position. We created the Female Author Impact Ratio (FAIR), a new metric representing the average percentage of female first and last authors. [FAIR = (% female first authors + % female last authors)/2*100]. FAIR values range as a percentage from 0-100, with higher numbers reflecting a higher proportion of females in the first and last authorship positions. Time trend analyses were performed by year, journal, and five-year time period (2007-2011; 2012-2016). Chi-square, Fisher's Exact, two-sample T-test or Wilcoxon rank sum tests were used as appropriate.

Results: Across 400 articles, the mean percentage of female authors was 30.9% (SD ± 22.0). 34.8% of first, 36.7% of second, and 25.4% of last authors were female. The median number of authors per article was seven (interquartile range (IQR): 5, 10) with a median of two female authors per article (IQR: 1, 4). The percentage of female authors per year increased from 2007 to 2016 (p=0.005), but there were no significant increases in the percentage of first (p=0.25), second (p=0.06), or last (p=0.21) female authors. However, the percentage of female collaborating authors increased significantly (p<0.001). The mean FAIR score across all 10 years was 30%, with no significant increase in FAIR scores over time (p=0.09). After the introduction of double-blind peer review in the IJROBP, an increase in the mean percentage of female authors was observed (2012-2016: 34.0%; versus 2007-2011: 27.4%; p=0.012), corresponding to a rise in the proportion of female second (p=0.018) and collaborating (p=0.02) authors only.

Conclusions: Although the percentage of female authors in RO has increased over the past decade, this did not correspond to a higher representation of women in high-profile authorship positions. The FAIR score, measuring the proportion of female first and last authors, did not increase over time. Introduction of double-blind peer review was associated with a rise in female authorship, suggesting that all journals should establish this practice to help mitigate gender bias throughout the publication process.

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DOES VERTEBRAL BODY SPARING VMAT CSI CONFER SIGNIFICANT ORGAN-AT-RISK SPARING? A DOSIMETRIC STUDY

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Purpose: Cranial Spinal Irradiation (CSI) is an integral component in the treatment of pediatric central nervous system tumours, including medulloblastoma. For young patients who has not achieved their full growth potential, the entire vertebral body is typically included in the target volume to reduce the risk of asymmetrical growth. Published work focusing on vertebral body sparing proton therapy CSI has demonstrated lower incidence of scoliosis than initially predicted. It is unknown whether Vertebral Body Sparing (VBS) Volumetric Modulated Arc Therapy (VMAT) photon technique confers Organ-at-Risk (OAR) sparing compared to Vertebral Body Covering (VBC) VMAT technique.

Materials and Methods: CT simulation datasets from five pediatric patients, age 2-14, were used in this analysis. Organs at risk were contoured and independently verified by separate investigators. VBS and VBC VMAT CSI, with the prescribed dose of 3600 cGy/20 (as used in high-risk medulloblastoma), were planned on each patient's CT simulation dataset. The dose to OARs were compared between the two plans for each patient.

Results: The Planning Target Volume of VBC CSI were on average 234cc (SD 141cc) larger compared to VBS CSI. Dosimetric outcome for all OARs were higher for VBC compared to VBS. The mean dose to the bilateral kidneys was 259cGy (SD 133cGy) higher, mean heart dose was 242cGy (SD 163cGy) higher, and mean liver dose was 254cGy (SD 71cGy) higher. The V20Gy for bilateral lungs was 6% higher (SD 1%). The maximal dose to the stomach was 1205 cGy (SD 342cGy) higher. The V15Gy for bowel bag was 212cc (SD 216cc) greater.

Conclusions: The OAR doses with VBS CSI using photon VMAT is lower than that seen for VBC CSI VMAT. The benefit may be clinically significant for pediatric patients receiving high dose CSI. Further research utilizing modelling is planned to predict risk of OAR toxicity using VBC and VBS techniques. Prospective research is also needed to determine the rate of scoliosis for pediatric patients receiving photon VBS VMAT CSI.

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SUCCESSFUL INCREMENTAL IMPLEMENTATION OF DEEP INSPIRATION BREATH HOLD FOR ADJUVANT RADIATION IN LEFT-SIDED BREAST CANCER

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Purpose: Deep inspiration breath hold (DIBH) is a well-established technique used to minimize the radiation dose delivered to the heart during adjuvant radiotherapy for left-sided breast cancer patients. Comparative planning studies have shown that DIBH yields superior heart dosimetry compared to free breathing (FB). However, there remain limitations to widespread clinical DIBH use, including patients' varying ability to reliably breath-hold, and the potential resource burden (*e.g*. longer planning visits).

Materials and Methods: During implementation of DIBH at our institution, cardiac-dose directed DIBH usage (in two 3-month sample periods from January to March in 2016 and 2017, n=84 and 115 patients, respectively) was compared to routine DIBH usage (in a subsequent 3-month sample period from January to March 2018, n=94 patients). A retrospective chart review of electronic records was conducted to examine: clinic-demographic characteristics, radiotherapy techniques, and dosimetric outcomes of patients receiving curative-intent adjuvant breast radiotherapy for left-sided breast cancers during these time periods.

Results: With routine implementation of breath hold simulation (2018), 85% of patients with left-sided breast cancer were able to complete a DIBH simulation. Simulation appointments for DIBH also included routine FB simulation, and the appointment times were reduced from 40 minutes for the inaugural time periods, to 30 minutes at the time of routine implementation. Non-DIBH simulation appointments were reduced from 20 minutes to 15 minutes during the same time. The proportion of patients treated with DIBH increased from 25.6% (2016) to 31.3% (2017) to 58.5% (2018). For the DIBH versus FB groups, there were no significant differences in the mean age of patients, 56.2±11.5 years (SD) versus 62.55±11.1 years (SD) respectively, nor in the mean prescribed radiation dose, 43.3±3.8 Gy (SD) versus 43.3±.2Gy (SD). The average mean heart dose in the radiation treatment delivered was reduced in each time period, from 182.3cGy (2016) to 177.9cGy (2017) to 139.3cGy (2018).

Conclusions: Incremental implementation of DIBH was successful in achieving routine use of DIBH, and also in reducing mean heart

dose in planning dosimetry proportional to use of DIBH. Future directions would be to further examine DIBH exclusion reasons, and evaluate the late toxicity profile, particularly with respect to cardiac events. Overall, the results suggest that the clinical implementation of DIBH improved the quality of the radiotherapy delivered, particularly with respect to reducing cardiac doses, with a limited increase in resource utilization.

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CLINICAL AND RADIOGRAPHIC TRIGGERS FOR ON-TREATMENT IMAGE-GUIDED ADAPTIVE RADIOTHERAPY REPLANNING: A LITERATURE REVIEW

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Purpose: Interfraction changes in patient weight and contour, along with size and location of target volumes, have a significant impact on the effectiveness of radical radiotherapy (RT). Image-guided adaptive radiotherapy (IGART) utilizing repeat simulation and treatment planning on-treatment addresses these variations, with previous studies suggesting improved volume coverage and decreased organ at risk (OAR) dose. However, reflex re-planning of every patient would be prohibitively resource-intensive. Identification of clinical or radiological indicators predictive of improved clinical outcomes after replanning would support optimal utilization of resources and personalized medicine objectives.

Materials and Methods: A Medline literature search examining English publications (2007-2019) revealed 85 related articles, supplemented by hand searches of reference lists (44 further articles). The following keywords were used: radiotherapy; radiation; adaptive; replanning. After excluding case reports and conference abstracts, as well as those which did not describe specific indicators, 18 studies remained.

Results: Primary sites represented were head and neck (13/18), breast (two of 18), and pancreas, lung and prostate (one each). Reported triggers for replanning were related to the patient; tumour; treatment; or dosimetry. Four studies suggested the use of automatic replanning at set time intervals. Patient factors included: age; density assignment method calculated density changes; baseline body mass index; absolute weight loss; contour depth variation; and rate of weight loss. Baseline tumour factors included: stage; location; and presence of atelectasis. Treatment factors included: concurrent chemotherapy; radical intent; and post-operative seroma. Dosimetric factors included: baseline OAR volume; planned OAR dose; and absolute distance between target volume and OAR. Few studies reported specific non-dosimetric recommendations for replanning consideration; examples included any breast seroma >30cm^3 which is completely or partly associated with an initial TBV >=35cm^3, or a body contour depth decrease by >1.5cm.

Conclusions: With increasing utilization of IGART, there is a need to identify markers predictive for the need for replanning on-treatment. No clear consensus on optimal triggers exists for any tumour site. The paucity and heterogeneity of robust published studies suggests significant uncertainty exists surrounding indications for IGART.

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FEASIBILITY OF USING NATURAL LANGUAGE PROCESSING TO EXTRACT CANCER PAIN SCORE FROM CLINICAL NOTES

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Introduction: Research has shown that pain is a significant problem for up to half of all cancer patients [1]. Pain is recognized to be the sixth vital sign by Canadian Partnership Against Cancer [2]. Various reports have shown that patients who have indicated their pain outcomes in real-time and have them acted upon have a better chance of survival compared to patients who did not [3]. While distress screening can help facilitate immediate improvements in current clinical care, new and emerging Artificial Intelligence (AI) technologies are starting to show promise for predicting in advance patient outcomes such as pain, allowing the outcomes to be treated prophylactically. Natural Language Processing (NLP) techniques, which extract measurable information from clinical texts, is showing promising results to predict outcomes and improve treatment techniques [4].

Materials and Methods: We developed and tested a NLP pipeline (Figure 1) to extract and evaluate pain scores from clinical notes. For this study we used a publicly-available deidentified clinical notes dataset provided by the i2b2 National Centre for Biomedical Computing [5]. Our NLP algorithm was developed in Python using the NLTK and Spacy NLP toolkits. Biomedical concepts are extracted from the text of consultation notes using Unified Medical Language System (UMLS) Metamap toolkit. A set of 42 unique pain-related terms was identified in the UMLS concepts and extracted from consultation notes using rule-based algorithms. Associated pain scores were obtained using a negation detection algorithm.

Results: Our NLP software was tested on 1240 consultation notes from the i2b2 database. 4488 unique indications of pain were detected. Pain was found in 91% of the consultation notes. Based on an audit of 400 of these records, our NLP algorithm showed over 95% accuracy in identifying and quantifying pain documented in patients' consultation notes. Pain score was detected with 89% accuracy.

Discussion and Conclusions: Acurate pain assessment is very important for successful pain management. Our NLP toolkit successfully detected and quantified pain in i2b2 consultation notes. The goal is to implement our model to extract pain from the consultation notes of cancer patients. If successful, when applied to radiation oncology data, the findings of this study will be used to help predict cancer distress and thereby potentially improve the quality of life of cancer patients. Our ultimate goal is to combine our NLP algorithm with image processing techniques (radiomics) to quantify and predict pain from consultation notes and radiographic images of cancer patients.

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DOSE ESCALATION IN 5-FRACTION PALLIATIVE THORACIC RADIOTHERAPY: A FEASIBILITY AND SAFETY PLANNING STUDY

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Purpose: Short course palliative radiotherapy is an effective and convenient treatment in patients with incurable advanced lung cancer to manage symptoms. Standard 5-fraction regimens often deliver a lower overall dose, limiting durable local control. We performed a planning study to evaluate the feasibility and safety of 5-fraction dose escalation.

Materials and Methods: In this research ethics board approved study, 10 patients with advanced lung cancer who received palliative thoracic radiotherapy between 2015-2016 were identified from our institutional database. Four 5-fraction plans were generated for each patient: 20Gy using a parallel opposed pair (POP) beam arrangement, as compared with 25 Gy, 30Gy and 35Gy using volumetric modulated arc therapy (VMAT). The gross target volume (GTV) was expanded volumetrically by 1cm to obtain the planning

target volume (PTV). The fields for POP plans were defined by extending 8mm from the PTV. VMAT plans were optimized by prioritizing organs at risk (OARs) allowing compromise of PTV coverage (PTV-eval =PTV - overlapping OARs, with an aim for D95≥95%). Conservative dose constraints were selected from literature, with OARs including spinal cord, esophagus, trachea, proximal bronchial tree and brachial plexus. For Lung-eval (lung-GTV), a V20 of ≤10% was targeted, with ≤15% accepted if required. Published radiobiological models were employed to evaluate the likelihood for toxicity to OARs, with a specifc focus on esophageal toxicity.

Results: The median PTV was 316cc (range 165 -551cc). In the reference 20Gy POP plans, the median lung-eval V20 were 6% (range 1%-22%) and D95≥95% coverage was achieved in 30% cases. For 25Gy VMAT plans, the pre-specified OARs tolerance were met in all cases. For 30-35Gy VMAT plans, the pre-specified OARs tolerance were met in all except 1 case, which had a lung-eval V20 of 15.5% and 19.5% with the 30 Gy and 35Gy plans respectively. The D95≥95% coverage was achieved in 90% cases for 25Gy, 20% for 30Gy, and 0% for 35Gy. The coverage evaluated by D90 were as following: 25Gy median 97% (range 97%-100%), 30Gy median 96% (92%-98%), and 35Gy median 88% (range 83-96%). The predicted probability of ≥Grade 2 esophagitis for 20Gy, 25Gy, 30Gy and 35 Gy plans were 1.7%, 3.3%, 5.0% and 5.0% respectively, based on the Belderbos normal tissue complication probability model.

Conclusions: In this planning study of 5-fraction palliative thoracic radiotherapy, dose escalation from 25 to 35 Gy in 5 fractions appeared feasible using VMAT techniques without significant predicted toxicity. While dose escalation to 25Gy without PTV compromise was feasible in most cases, significant compromise of PTV was required for 30- and 35Gy to minimize predicted toxicity. Based on these data, a dose-escalation clinical trial is planned under the auspices of the Canadian Pulmonary Radiotherapy Investigators (CAPRI) Group.

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THE IMPACT OF ADVANCED IMAGE REGISTRATION AND 3-D EQD2 DOSE CONVERSION ON PTV AND CTV COVERAGE IN THE RETREATMENT OF NASOPHARYNGEAL CANCER: A CASE STUDY

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Purpose: Retreatment of nasopharyngeal cancer (NPC) can pose a challenge for clinicians. Previous treatment with high dose of radiation (60-70 Gy) limits the dose deliverable to the targets and the organs-at-risk (OAR). There is uncertainty in estimating previous radiation dose distributions on new CT scans due to geographical and/or anatomical differences between planning CT scans. There is also uncertainty associated with estimating the biological effect of adding together different treatment regimens. Commercial software such as MIMS Maestro (MIM Software Inc.) offering more advanced image registration and 3-D radiobiological dose conversion options may aid in the optimization of target volume(s) coverage while limiting dose to the OAR. The objective of this study is to assess the impact of advanced image registration and EQD2 dose conversion on Planning Target Volume (PTV) and Clinical Target Volume (CTV) coverage in the retreatment of patients with NPC.

Materials and Methods: Maximum cumulative EQD2 dose to the brainstem, spinal cord and brain were based on Quantec and preset at 59Gy, 54Gy and 72Gy respectively. All plans were generated using Varian Eclipse v.11 AAA algorithm. The remaining allowable EQD2 dose was then converted to absolute dose and used for the replan. Re-treatment plan was first generated based solely on maximum allowable doses to the brain stem, spinal cord and brain defined as: [Preset Max EQD2 – delivered $EQD2_{(first\ course)}$]. The same re-treatment case was alternatively planned using advanced image registration and 3-D EQD2 dose conversion and summation tools offered by MIM. PTV and CTV coverage were then compared.

Results: The mean dose, V90, V95 and D99 for the PTV were 47Gy, 84%, 81% and 16Gy versus 39Gy, 49%, 31% and 7Gy with and without advanced image registration and EQD2 3-D dose conversion respectively. The corresponding mean dose, V95, V100 and D99 for the CTV were 50Gy, 94%, 91% and 34Gy versus 44Gy, 49%, 8% and 18Gy respectively.

Conclusions: This case illustrates how advanced image registration and 3-D EQD2 radiobiological dose conversion can significantly enhances PTV and CTV coverage in the retreatment of NPC. We plan to expand our study to include a total of 10 cases. Factors such as overlap and proximity to OAR, overlap with previous treatment and application of repair factors are likely to influence coverage and will be examined in the next phase of this study.

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COMPARATIVE PLAN ANALYSIS FOR A COMPLICATED SUPRAORBITAL SQUAMOUS CELL CARCINOMA USING 3D PRINTED MODULATED ELECTRON BOLUS

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Purpose: To determine if the use of electron therapy dosimetry using a novel modulated electron bolus (MEB) leads to comparable or improved plan metrics, when compared with status-quo treatment techniques for a complicated supraorbital squamous cell carcinoma.

Materials and Methods: Retrospectively six plans were generated from initial planning CT simulation images with no mask or bolus. Evaluated plans included: volumetric modulated arc therapy (VMAT) with 0.5cm bolus, tangential photons with 0.5cm bolus, appositional electron therapy with 0.5cm bolus, direct electron with block bolus, and MEB without and with the use of a hotspot correction feature. All boluses were generated by the Eclipse planning system, except for MEB which were created by the 3DBolus 2.0 software (Adaptiiv Medical Systems). Plans were normalized to achieve 90% dose covering 98% of the planning target volume (PTV). Evaluation metrics included: maximum dose (Dmax to 0.1cc) to the brain, right/left lenses and globes, volume of brain receiving 80%, 50% and 20% of the prescription dose (V80, V50, V20), and a homogeneity index (HI).

Results: For the ipsilateral lens, which overlapped the PTV, the VMAT plan yielded the lowest Dmax (78.4%), and the appositional electron the highest (103.9%). Between the MEB plans, using the hotspot correction provided a reduction in Dmax of the ipsilateral lens from 98.45% to 94.35%. The lowest Dmax for normal brain was given by MEB plans without and with hotspot correction (75.9%/77.8%), and Dmax was greatest for the direct electron plan with appositional bolus (112.9%). MEB plan with no hotspot correction yielded the lowest V80 (0.02cc) and V50 (4.26cc). The tangential plan resulted in the lowest V20 to normal brain (8.86 cc), followed by MEB without/with hotspot correction (15.84/20.27cc), with VMAT the highest (93.44cc). The VMAT plan produced the most optimal HI (0.09), with appositional electron plan giving the worst HI (0.35). For the MEB plans, use of the hotspot correction improved the HI slightly (0.31 versus 0.33).

Conclusions: Among all plans and metrics evaluated, the tangential plan was felt to be the most optimal, due to the combination of low

V80, V50 and V20 of normal brain, comparably low homogeneity index, and acceptable ipsilateral lens dose. The VMAT plan provided the best dose homogeneity within the target volume and ipsilateral lens sparing, at the expense of increased volume of brain receiving low and moderate doses. The MEB plans provided an improvement in the DVH for the normal brain distal to the PTV and were associated with acceptable ipsilateral lens dose and homogeneity. Use of the hotspot correction feature allowed for an improvement in the dose to the ipsilateral lens and dose homogeneity among the MEB electron plans. Thus, MEB can provide benefits to complicated skin cancer cases, and should be considered against other standard options.

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SUCCESSES AND BARRIERS TO THE INTEGRATION OF THE NATIONAL SYSTEM FOR INCIDENT REPORTING-RADIATION TREATMENT (NSIR-RT) TAXONOMY INTO A PROVINCIAL INCIDENT REPORTING AND LEARNING SYSTEM

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Purpose: At the provincial level, the need had been identified to standardize data collection for incident reporting across services and facilities, in order to facilitate trending and analysis, and share learning opportunities. Concurrently, the National System for Incident Reporting-Radiation Treatment (NSIR-RT) minimum data set (MDS) had been developed, validated, piloted, and released. While standardization of reporting across services was desired, the organization understood the value of a validated taxonomy, and contributing towards a national repository for radiation treatment events (RT). It was also recognized that dual data entry is a barrier for incident reporting. As such, the decision was made to integrate the NSIR-RT MDS into the provincial reporting system. Here we describe the process, barriers, and experience integrating the NSIR-RT MDS into the provincial reporting system.

Materials and Methods: RL Solutions was chosen as the reporting platform for the province. Following approval by senior leadership, an RT standalone form was built using the 2017 NSIR-RT MDS. To facilitate provincial standardization, data fields were aligned wherever possible, and new fields were created for RT elements. Conditional formatting was used based on the MDS, and hover-over definitions were provided. The unique RT form was created in the test environment, followed by production, education and go-live for all RT departments within the province.

Results: Successes factors included: mandated provincial alignment, sustained and consistent local/national engagement, optimizing existing technology, and the use of a validated taxonomy (NSIR-RT). Challenges of the project included: provincial re-structuring, buy-in of senior leadership not familiar with RT, time/resources to build the system, aligning practices in different centers, areas of MDS overlap or disparity, and legal agreements.

Conclusions: Successful integration of the NSIR-RT MDS, has allowed for the appropriate and unique classification of RT related events within the provincial framework, while allowing for provincial standardization and future batch uploading into the national repository.

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VALIDATION AND INTER-RATER RELIABILITY OF TWO METRICS USED AS PREDICTORS OF HEART DOSE IN PATIENTS TREATED WITH ADJUVANT RADIOTHERAPY TO THE LEFT BREAST

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Purpose and Objectives: Patients undergoing radiotherapy (RT) for left-sided breast cancer may receive radiation dose to the heart which may increase the risk of cardiac events and possibly mortality. To mitigate these cardiac dose and associated risk, breath-hold RT techniques are often utilized. The Contact Heart and fourth arch predictive models have been useful in gauging the need for breath-hold by pre-determining how much heart may be in the initiated field. This study aimed to validate these metrics and assess their inter-rater reliability using an independent cohort of patients.

Materials and Methods: A total of 117 patients treated with two-field whole breast irradiation to the left breast between 2014 and 2018 at one institution were randomly selected for retrospective review. Using CT imaging, the Contact Heart and fourth arch measurements were calculated for each individual patient. Dosimetric endpoints were Mean heart dose (MHD) ≥1.7Gy and V25 Gy≥ 10cc. Univariate logistic regression analysis and receiver operating characteristic curves were used to validate the previous model, its associated cut-off, and to revise the existing predictive cut-off value. Intra-class correlation coefficient (ICC), Cronbach's alpha, and Cohen's Kappa statistic were used to assess reliability.

Results: Both fourth arch and Contact Heart were found to be significantly predictive of both MHD ≥1.7Gy and V25Gy≥10cc. More optimal fourth arch cut-offs of 13mm for MHD ≥1.7 Gy and 10mm for V25Gy ≥10cc, and Contact Heart cut-offs of 56 mm for MHD ≥1.7Gy and 71 mm for V25 Gy≥ 10cc were found to have greater predictive ability. Both Contact Heart and 4th arch models showed excellent inter-rater reliability as continuous variables, with fourth arch demonstrating slightly increased reliability (Cronbach's alpha: 0.993, ICC: 0.994). The fourth arch cut-offs were found to be more consistent than Contact Heart cut-offs.

Conclusions: We have validated both the fourth arch and Contact Heart models for predicting heart dose and have identified more optimal cut-off points. The metrics of 4th arch and Contact Heart demonstrate excellent test characteristics to guide the selection of patients requiring breath-hold RT. However, the fourth arch model showed slightly better inter-rater reliability, especially when examining clinically-meaningful cut-off parameters.

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MARGIN ASSESSMENT AND DOSIMETRIC IMPACT AS PART OF IMPLEMENTATION OF PROSTATE SBRT

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Purpose: As part of implementation of prostate stereotactic body radiation therapy (SBRT), our institution assessed: 1) the potential for planning target volume (PTV) margin reduction associated with the proposed SBRT imaging workflow; and 2) the associated dosimetric impact. The assessment utilized existing cone beam computed tomography (CBCT) data of prostate patients with implanted fiducial markers (FM).

Materials and Methods: The imaging workflow involves an initial orthogonal kV FM match followed by adjustments on CBCT. Retrospective data closely reflecting this was available for five patients: kV FM matches followed by CBCT for anatomy review. A best-fit FM match was performed on CBCT. PTV contours of varying margins were created. Two oncologists evaluated the images and selected the smallest PTV that covers the prostate and seminal vesicles (SV). Patients were re-planned for 3625cGy in 5 fractions comparing our standard margins with the proposed

reduced margin. OAR tolerances from the NRG-GU005 trial were used.

Results: A 5mm margin was sufficient to cover the prostate and SV in 98% and 88% of the cases. Where a larger margin was required, significant deformation was noticeable due to bladder and rectum filling. Minor intrafraction motion was observed. A PTV margin of 5.2mm was calculated using the Van Herk formalism, excluding contouring uncertainty. A 5mm uniform margin is proposed. Using standard margins (0.7cm uniform, 0.5cm post), three patients showed acceptable variation for rectum and bladder dosimetry. One unacceptable bladder variation was reported. Using the proposed 5 mm margin, all patients were within tolerance.

Conclusions: Based on an imaging workflow utilizing initial FM match and final soft tissue adjustment, our institution adopted a 5mm uniform PTV margin. This would enable us to meet the dosimetric constraints necessary for prostate SBRT.

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IMPACT OF PELVIC INTENSITY-MODULATED RADIOTHERAPY (IMRT) ON LYMPH NODE COVERAGE AND DOSE TO CRITICAL ORGANS, COMPARE TO THREE-DIMENSIONAL CONFORMAL RADIATION THERAPY (3D-CRT), IN LOCALIZED HIGH-RISK PROSTATE CANCER

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Purpose: Men with high-risk prostate cancer (HR-PrCa) are typically treated with combined androgen deprivation therapy and curative radiotherapy (RT) consisting of pelvic nodal and prostate/seminal vesicle (PrSV) irradiation followed by PrSV boost RT. 3D-CRT or IMRT are used for the treatment of pelvic nodes. A phase II randomized study examining the effect of RT technique on patient Quality of Life (QofL) was completed in our institution. Here, we report an early analysis of the dosimetric impact of 3D-CRT versus IMRT in patients participating in this study.

Materials and Methods: A total of 105 men with HR-PrCa were randomized at 1:1 ratio to receive either pelvic 3D-CRT (standard 4-field conformal technique) or multi-beam IMRT, consisting of 4500cGy in 25 fractions to planning target volume (PTV) 1, followed by boost RT to PTV2 of 2496cGy in 13 fractions. The latter was delivered using a 7-field IMRT in all patients. Organs-at-risk (OAR) and clinical target volumes (CTV) were delineated on CT simulation images. The lymph node target included the common, internal, external iliac, obturator and pre-sacral lymph nodes in accordance with RTOG guidelines. CTV1 consisted of nodal CTV plus PrSV. CTV2 was minimized to PrSV. The PTV consisted of an expansion of 7 mm beyond CTV. For consistency, in comparison between the two techniques, IMRT fields were modified to results to similar superior border coverage as 3D-CRT, at the level of L5-S1. Bladder and rectum were contoured as solid organs. To take inter-fractional bowel motion into account, bowel was delineated as whole pelvic and abdominal cavity exclud¬ing bones, muscle, and other OAR.

Results: Pelvic RT with 3DCRT missed significant percentage of pelvic nodal volume. PTV1 D95% showed mean difference of -4.96, 95% CI (-6.41, -1.74); p=0.0013 and D99% showed mean difference of -11.56, 95% CI (-14.96, -8.17); p< 0.00001 in favour of IMRT. There was significant difference in PTV1 heterogeneity index (D2%-D95%/D50%) (mean diff =0.22, 95%CI (0.14, 0.29); p<0.00001). IMRT decreased dose to OAR. Rectum V30 was 97% in 3DCRT compare to 93.41% in IMRT arm with absolute difference of 3.81% (95% CI (1.52, 6.11); p=0.0014). Bladder V40 and V50 were significantly reduced (V40: 84 % versus 62% for 3DCRT versus IMRT, absolute difference of 22% (95%, CI (15.55, 28.2); P<0.0001); V50 absolute reduction of 18% with IMRT (95%, CI (11.53, 24.48); P<0.0001). Similarly, IMRT reduced total body/bone irradiation significantly.

Conclusions: This randomized study of 3D-CRT versus pelvic IMRT is an appropriate setting to investigate the dosimetric impact of pelvic IMRT and help define its potential benefits on patient QofL. This early analysis suggests that utilization of IMRT for pelvic RT could offer dosimetric advantages by improve lymph node coverage and reducing RT dose to OAR. The results are in agreement with an improved bowel-related QoL observed in this study. On-going analysis examines correlations between dosimetric and patient QofL data.

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PERIPHERAL DOSE MEASUREMENTS IN THE PRESENCE OF CARDIOVASCULAR IMPLANTABLE ELECTRONIC DEVICES IN MEGA-VOLTAGE RADIOTHERAPY

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Purpose: Cardiovascular implantable electronic devices (CIEDs) are known to potentially malfunction in the presence of mega-voltage radiation. Since it is not uncommon for patients with CIEDs to receive radiotherapy, there is a need to adopt an approach to manage these patients.

Objectives: Perform measurements with varying bolus, field sizes, energies and distances to characterize each peripheral dose and determine the procedure that should be taken to reduce it.

Materials and Methods: Peripheral dose measurements were performed near an implantable cardioverter defibrillator (ICD) under various conditions including beam modalities, energies, field sizes, beam orientations, and the application of bolus. Comparisons between the treatment planning software (TPS) Eclipse and our measured values were performed for each condition.

Results: Measurements 4cm from the field edge were determined to be 20-40% less than 2cm. Using a smaller field size reduces peripheral dose by 10-20% for photon beams but has no effect on electron beams. Adding a 3cm bolus reduces the peripheral dose by 45% for an anterior-posterior (AP) photon beam but has no effect on the peripheral dose with volumetric modulated arc therapy (VMAT) plans or AP electron beams. Using 6 instead of 18 MV reduces peripheral dose by 43%. Eclipse underestimated the peripheral dose for all AP beams.

Conclusions: The best way to reduce peripheral dose to a CIED with an AP beam would be to use a lower energy, use a smaller field size, place a 2cm bolus on the patient where the device is implanted and irradiate as far as possible from the device. Peripheral dose 2cm from the field edge for 6 MV and electron beams appears to be low enough that it should not cause a problem to a CIED.

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CAPACITIVE MONITORING TECHNIQUES FOR INTRA-FRACTION PATIENT MOTION DETECTION

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Purpose: To present an innovative technology for continuous patient position monitoring during precision radiation therapy treatment. The system can detect intra-fraction patient motion with sub-millimeter accuracy in 3D during SRS treatment. It can also be used to detect respiratory motion during lung, breast, or liver treatment. The system provides real-time motion monitoring with no direct contact with the patient and without the use of ionizing radiation or relying on surrogates such as skin.

Materials and Methods: This technology relies on continuous capacitance measurements for motion detection. The system is sensitive to position of the body (cranium, chest, etc.) and insensitive to the position of the surrounding immobilization devices, fabric, etc. Due to the conductivity of the human body, placing a conductive sensor near the body forms a capacitor and monitoring the resulting capacitance provides real-time information regarding the distance between the sensor and region of interest (ROI) of the body. A cranial array of four conductive sensors (4 by 6 inch) placed around the cranium was used to detect 3D motion of the cranium within the thermoplastic mask in real time with the help of a volunteer.
A respiratory array comprised of three sensors (2 by 4 inch) was used to detect the respiratory motion for different regions of interest for chest and abdominal breathing with the help of a volunteer.

Results: Our cranial prototype can detect 0.5mm motion with 0.1mm accuracy in three dimensions. The respiratory prototype can detect chest and abdominal motion in agreement with the RPM system. The system is not sensitive to the thermoplastic mask, fabrics, etc. and does not require an unobstructed view of the region of interest.

Conclusions: This new technology provides a non-contact, real time, and non-ionizing motion monitoring system that is not dependent on deformable surrogates i.e. skin and does not require unobstructed view of the body.

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PSMA-PET GUIDED INTENSIFICATION OF RADIOTHERAPY FOR PROSTATE CANCER: PRELIMINARY DETECTION RATE AND IMPACT ON RADIOTHERAPEUTIC MANAGEMENT

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Purpose: PSMA-PET/CT is more sensitive in detecting prostate cancer than current imaging standard of care, and commonly changes patient management despite lack of evidence of impact on patient outcomes.

Objectives: To determine if preliminary rates of new lesion detection and RT intensification in a randomized trial align with those reported in the literature.

Materials and Methods: Patients enrolled in a prospective standard-care registry (PERa NCT03378856) were randomly selected (1:1) to be offered participation in a study of PSMA-PET/CT-guided radiotherapy (PSMAgRT) if they were planned for definitive radiotherapy, Charlson ≤4, and considered at high risk of harbouring undetected oligometastatic disease prior to initiating hormonal therapy (strata: post-prostatectomy salvage, high-risk localized with CAPRA ≥6, oligometastatic disease, or focal brachytherapy salvage post RT). All randomly selected patients subsequently consented to study (NCT03525288) and underwent injection of [18F]DCFPyL (Progenics Pharmaceuticals) prior to imaging. New lesion detection rate was reported by nuclear medicine, and images with visible disease were registered for radiotherapy planning. Physicians were instructed to intensify their radiotherapy plans based on PSMA-PET/CT findings, and to report changes in treated volumes and/or dose.

Results: Twenty-five patients were randomly selected and all underwent PSMA-PET/CT prior to RT. Most patients were planned for salvage RT after prostatectomy (36%), followed by high-risk disease (28%), oligometastatic disease (20%), and salvage focal brachytherapy (16%). Overall PSMA-PET/CT new lesion detection rate was 40%, more common in patient with known oligometastatic disease (80%) versus other cohorts (25-33%). The rate of intensification of RT was 54%, primarily due to an expansion in treated volume (84%) versusescalation of dose (31%).

Conclusions: PSMA-PET/CT results in intensification of RT in approximately half of randomly selected patients considered at high risk of harbouring undetected disease, in line with published reports. The impact of such change in RT management on failure-free survival outcomes remain to be determined with continued randomized trial enrolment and follow-up.

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CLINICAL IMPLEMENTATION OF AN INTEGRATED MR-GUIDED LINEAR ACCELERATOR FOR OFFLINE ADAPTIVE RADIOTHERAPY FOR CERVICAL CANCER

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Purpose: The superior soft-tissue visualization enabled with online MRI provides an opportunity for high-precision image guidance, response assessment and novel adaptive radiotherapy (ART) processes. At our institution, we have developed a novel platform integrating a 1.5 T MR scanner-on-rails with a 6 MV linear accelerator capable of daily in-room MRI. The aim of this work was to develop a hybrid CBCT-MRI image-guided radiotherapy (IGRT) workflow and describe our preliminary experience with implementing in-room MRI for offline ART for intact-cervix cancer.

Materials and Methods: Process mapping, hazard analysis and mock procedures were used to design a hybrid IGRT workflow consisting of CBCT-guided treatment delivery, immediately followed by post-delivery in-room MRI. Patients were transferred to the MR in the treated position via an air-cushion hover-board and then coils were placed for imaging. Treatment planning using VMAT was performed as per EMBRACE II (45 Gy/25 fractions). The primary CT was acquired with full-bladder, and simulation MRI with both full and empty-bladder were included to define the internal target volume (ITV). Daily CBCT guidance used the primary CT as the reference and in-room MRI consisted of a fast T2w axial scan covering the pelvis and primary target. All images were imported to the planning system, co-registered to the plan via the treatment position alignment and reviewed offline by a multi-disciplinary team for geometric assessment of organ motion and target coverage.

Results: Two patients with intact-cervix cancer were treated to date with the CBCT-MRI workflow. In-room MRI were acquired for 17/25 and 8/25 fractions. Facility down-time for servicing was the primary reason for missed MRI. The mean time between CBCT and MRI was 16 mins (range = 10–27 mins). The mean time between treatment delivery completion and MRI was 10 mins (6–18 mins). During offline review, large inter-fraction variations in bladder, bowel and target positioning were noted for the first patient. Systematic motion of the uterine fundus beyond the PTV was noted on CBCT, but complete visualization of the GTV, vagina and uterus required MRI. An adaptive replan with modified ITV was created for the final 7 fractions for this patient, which effectively maintained target coverage within the PTV. Comparing the CBCT and MRI, large intra-fraction variations in the bladder and primary target were observed. The mean change in bladder volume was 60 cc (1–161 cc) for the first patient and 29 cc (1–83 cc) for the second.

Conclusions: We have successfully demonstrated a hybrid IGRT workflow with in-room MRI for offline ART for cervical cancer. Monitoring daily variations with MRI empowers a comprehensive adaptive paradigm that will become our new standard-of-care for intact-cervix cancer treated with VMAT. Further efforts are underway to optimize IGRT workflows with pre-delivery MRI, as well as to develop state-of-the-art dose accumulation and online ART processes.

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APPLICATION OF NOVEL RADIOTHERAPY AND IMAGING FEATURES FOR HEAD AND NECK PATIENT LOCOREGIONAL FAILURE PREDICTIONS

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Purpose: Quantification of patient images for predictive and prognostic model building, also known as radiomics, has seen increased interest in recent years. In this work, we augment the traditional radiomics pipelines to include quantified interventional features extracted from radiation therapy (RT) plans (RTx-omic features), where RTx-omic features are designed to quantify a patient's unique RT dose pattern as determined by their disease and surrounding intrinsic anatomy. We built a fully automated pipeline for automatic extraction and analysis of clinical imaging and interventional information. As a proof of concept, we tested the ability of RTx-omic and radiomic features derived from oropharyngeal cancer patients' planning CT and RT dose volume, in combination with standard clinical features, including age, sub-site, HPV status, etc., to predict locoregional failures (LRF).

Materials and Methods: CT images and RT dose volumes from 64 oropharyngeal cancer patients without dental artifacts were quantified using a custom Pyradiomics module. Radiomic, RTx-omic and clinical features were used to predict LRF at three years with Random Forests (RF), Logistic Regression with Recursive Feature Elimination (LOG) and Isolation Forests (IF). Training and validation was repeated 100 times using stratified subsampled portions of the data, 75 and 25% respectively, without replacement. Dimensionality reduction was performed using Spearman rank analysis prior to model fitting. The mode prediction for each patient across the 100 subsampled fittings were used to calculate the Area under the curve (AUC), and confidence intervals (CI) were calculated with bootstrapping.

Results and Discussion: Clinical features with LOG modelling had the highest AUC of 0.80 (0.65-0.96). Radiomic and RTx-omic features both performed best with clinical features and LOG with AUC=0.80 (0.64-0.95) and AUC=0.75 (0.58-0.92), respectively. Large CIs indicated too few LRF events are present in our dataset, hence prevented us from making a definite conclusion on the performance of either model. In this initial study, we used uniform data from a single institution where we did not observe any LRF causing variations; however, this lack of variability may have negatively affected the prediction capability of the model, which suggests that more diverse training data is needed.

Conclusions: LOG modeling with clinical features had the non-significantly higher AUC for LRF prediction at three years compared to other models. In future studies we will include datasets from multiple institutions to increase the diversity of training data, as well as re-plan data sets. Even though our current results do not provide immediate evidence that RTx-omic and radiomic features provide complementary information to clinical features for prediction of LRF in this cohort, they do demonstrate the potential of applying automated information generation and Big Data methods to data not previously used in prognosis generation before.

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ARE POST ONCOPLASTY SURGICAL CLIPS A RELIABLE RADIOGRAPHIC SURROGATE OF TUMOUR BED LOCATIONS? A PHANTOM BASED STUDY

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Purpose: Oncoplastic breast surgery (OBS) combines the advantages of breast conserving surgery with improved cosmesis for early stage breast cancer. Radiation oncologists routinely use surgical clips to aid tumour bed delineation for post-op breast boost and ablative cases. However, due to the variability of their final position post OBS, they may not provide a reliable radiographic surrogate of the tumour bed location.The goal of this study is to develop a method to prospectively determine surgical clip reliability in tumour bed delineation post-OBS.

Materials and Methods: Using an in-house method, a realistic silicon-based breast phantom prototype (815.8cc) was constructed. It contained materials simulating the breast parenchyma, epidermis, areola & nipple, chest wall, and a tumour (9.7cc, 10 o'clock position, 1.7cm depth). The phantom's posterior surface was adhered to an acrylic plate. A racquet incisional approach was used to excise the tumour with 1cm gross margins including the overlying skin to the chest wall level. Titanium surgical clips (8) were placed at the level of the excised tumour on the surrounding cavity walls (4) and at the level of the chest wall (4) to mark the excision volume. Additional surgical staples (24) were used to map the cavity walls. OBS closure was then performed. CT scans were acquired: 1) after initial clip placements (pre-CTV); and 2) post-OBS closure (post-CTV), showing clip displacements. An in-house built localization system that affixes to the phantom's plate allowed CT acquisition with the same imaging isocentre. The CTs were imported to the Monaco Treatment Planning System. The tumour bed walls were mapped based on the clips and staples. A 0.5mm expansion margin was added to wall interfaces to create a CTV-like margin on each CT. Based solely on the surgical clips, a clinical CTV volume was also contoured by a radiation oncologist. Expansion margin volumes were compared in terms of volume differences and the dice similarity coefficient (DSC), with the post-CTV taken as the reference.

Results: Our phantom provides a customizable, cost-efficient (<$60) research & educational tool. While it can be used for various radiation physics applications as well, we adopted it to

communicate OBS information relevant to radiation oncology practices. The consistency and components of the phantom were suitable for emulating surgical practice. Based on the CTs, the excision volume was 136.9 cc. The DSC and volume differences were found to be 0.5 & 0.4, and 39.1% & 66.0%, for the pre-CTV and clinical CTV, respectively.

Conclusions: Preliminary results suggest that relying solely on the surgical clips to determine relevant CTVs may not be sufficient, especially with post OBS techniques where substantial tissue displacement can occur. Our technique allows us to precisely extract tumour bed displacements. Future work includes studying various OBS techniques and determining their contribution in tumour bed delineation uncertainties.

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AUTOMATED VMAT/IMRT BREAST PLANNING: A WORKABLE MODEL GEARED FOR IMPLEMENTATION IN THE MODERN HIGH VOLUME RADIATION CENTRE

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Purpose: Adjuvant breast radiotherapy constitutes a significant proportion of the total workload in most Canadian radiotherapy departments. Modern inverse IMRT or VMAT planning techniques improve target coverage and dose homogeneity but are labor intensive and require experienced staff for patient dosimetry. The dilemma is more problematic when nodal sites have to be covered together with the breast or chest wall. In a busy department this increased workload leads to increase waiting times from simulation to treatment start. We developed an integrated template based technique utilizing VMAT for the nodes and IMRT for the breast (AVA) for clinical use and to see if an automatic planning template would reduce workload by increasing the plan optimization process and produce plans of similar or better clinical quality compared to the existing technique using field-in-field tangents junctioned to a 3D conformal nodal plan (STANDARD4F).

Materials and Methods: AVA was developed using a training dataset of 10 breast cancer patients of varying body habitus who required breast/chest wall and nodal radiation. The nodal Clinical Target Volume (CTV) and Planning Target Volume (PTV) were contoured based on departmental consensus contouring guidelines. The 10 cases were then used to create and "train" a template to deliver the prescribed dose to the PTV with VMAT. The template was developed with a standard body size patient and then tested with different body sizes. The template was then tuned whenever the template did not suit a test patient. This VMAT nodal technique was junctioned onto a breast IMRT template currently in use for breast only radiotherapy. Fifteen patients scheduled for breast and nodal radiotherapy were then planned using both AVA and STANDARD4F. Radiation oncologist contouring time, dosimetry resource time, target coverage and dose to OAR were compared between the two techniques.

Results: Dosimetry resource times for AVA and STANDARD4F were 40 versus 240 minutes (p=0.001). Coverage of the PTV (V90) was significantly improved with AVA versus the STANDRAD4F (95.0% versus 78.0%, p=0.003). The dose constraints to the OARs were all met for each plan using both techniques .The mean dose to OARs were not statistically significant between the techniques. Features of AVA and methodology of its development will be presented.

Conclusions: The integrated AVA technique is a practical solution for a breast nodal template for clinical use in a large volume centre. AVA significantly improved PTV nodal coverage whilst providing a reduction in planning (and re-planning) time for nodal breast irradiation. The simplification of the planning process by the use of a template allows junior dosimetry staff to be template "trained" allowing minimal workload to be used for VMAT/IMRT plan production.

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BIO-MARKERS IN BREAST CANCER: QUANTIFYING DISCORDANCE WITH BEST PRACTICE WHEN RECEPTOR STATUS IS AN EXTRAVAGANCE

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Purpose: Molecular profiling has evolved breast cancer management. In Zimbabwe, patients in public institutions struggle to raise USD 150 to finance profiling before management and many are treated without. The study objectives were first, to describe the therapeutic approaches of hormone undefined breast cancer patients managed at a Zimbabwean institution, and second to ascertain level of discordance with the ideal treatment strategy (based on NCCN guidelines) if hormone receptor status is known.

Materials and Methods: A retrospective chart review of actual treatments recommended and received by breast cancer patients January 1 2014 - December 31 2016 with unknown receptor status at diagnosis was undertaken. Molecular subtyping analysis was conducted for the purpose of our study where technically feasible. The level of agreement between treatments received and NCCN recommended treatments had the receptor status been known were tested using a weighted kappa statistic to establish any discordance.

Results: Of the 295 patients identified, 197 (67%) had no receptor status at time of treatment decision. Receptor status was subsequently established in 80/197 (41%) patients enabling eligibility for analysis. Stage at presentation was SI-III in 40 (50%) and SIV in 38 (47%) patients, unknown in two of 80. Luminal A was the most common occurring in 24/40 (60%) SI-III and 22/38 (58%) of SIV patients. The treatment approaches of 40/80 (50%) patients with SI-III diseases were in substantial agreement with NCCN guidelines (kappa 0.73). Endocrine therapy was received by 37 from the eligible 58 (64%, kappa=0.267) though initiation was delayed (median eight months) in 34/37 (92%) due to untimely availability of receptor status. Chemotherapy was recommended to 72/80 (89%) patients of which 35/72 (49%) had SIV disease. Treatment received was incongruent with NCCN recommendations since 22/35 (63%) SIV patients could have avoided chemotherapy had hormone receptor results been available at initial presentation (kappa=0.0625).

Conclusions: Treatment approaches were largely in agreement with best practice for SI-III patients with reference to NCCN guidelines. Discordance was noted in SIV patients with inappropriate use of chemotherapy over hormone therapy when receptor status is unknown. Considering the relative cost alone of chemotherapy (averaged USD 300/month), and tamoxifen (average USD 20/month), cost savings alone by avoiding inappropriate use of chemotherapy will fund receptor testing at time of diagnosis for all SIV patients.

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CARO SANOFI

THE NEW DIABETES DRUG CANAGLIFLOZIN ENHANCES THE RESPONSE OF PROSTATE CANCER TO RADIOTHERAPY

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Purpose: Radiotherapy (RT) is standard therapy for prostate cancer (PrCa). However, PrCa is highly resistant to RT, requiring high doses to enhance local control, which lead to increased pelvic toxicity. There is need to develop radio-sensitizing agents in PrCa. We reported that, the FDA and Health Canada approved anti-diabetic drug, Canagliflozin (CANA) has anti-proliferative effects in PrCa through the activation of the molecular energy stress sensor AMP activated kinase (AMPK). Here, we examined CANA's ability to sensitize PrCa cell-line and xenograft models to RT.

Materials and Methods: Proliferation, clonogenic, and immunoblotting assays were used to analyze hormone resistant (PC3, DU145) and sensitive (22RV1, LNCap) PrCa cell lines. Cells were treated with a combination of increased doses of CANA (0-30 *m*M) and RT (0-16 Gy). Immunosuppressed nude mice, grafted with 22RV1 cells, were subjected to treatment with CANA with or without RT (10Gy). Tumours were crushed and homogenized for protein extraction and immunoblotting analysis.

Results: CANA inhibits the proliferation and clonogenic survival of both hormone resistant (PC3/DU145) and sensitive (22RV1/LNCap) PrCa cells and blocks complex I supported respiration. This is associated with activation of AMPK, inhibition of the mammalian Target Of Rapamycin (mTOR) pathway, suppression of Acetyl-CoA Carboxylate and de novo lipogenesis. Tumour lysates are being analyzed to examine signaling pathways regulating tumour survival and mechanisms of cell death.

Conclusions: Clinically achievable doses of CANA, suppress survival and enhance the response of PrCa to RT. Its mechanism of action includes suppression of mitochondrial respiration and inhibition of key signaling pathway involved in protein and lipid synthesis. Being an approved and well-tolerated agent, CANA can be rapidly investigated in PrCa clinical trials in combination with RT.

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POLYMORPHISM OF FORMYL PEPTIDE RECEPTOR 1 (FPR1) REDUCES THE THERAPEUTIC EFFICIENCY AFTER NEOADJUVANT CHEMORADIOTHERAPY (NEOCRT) TREATMENT IN LOCALLY ADVANCED RECTAL CANCER (LARC)

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Purpose: Loss of function single-nucleotide polymorohism in formyl peptide receptor 1 (FPR1) [rs867228: c. 1037A>C, p. Glu346Ala] was reported which has a negative impact on anthracycline or oxaliplatin treatment patients with breast cancer and colorectal cancer. In this study, we investigated the role of FPR1 for therapeutic efficacy in LARC patients treated with neoCRT.

Materials and Methods: Two hundred and eleven patients with LARC were treated at CMUH hospital from 2006 to 2014. Among these patients, 130 received neoCRT followed by surgery. Genomic DNA from non-tumour tissues of rectal cancer patients was extracted from FFPE using a QuickExtract™ FFPE DNA Extraction Kit. Genotyping of *FRP1* SNP was performed using the iPLEX® HS panel on the MassARRAY® System and interpreted using SpectroTYPER v4.0 software.

Results: Annexin A1 (ANXA1) is a danger-associated molecular patterns which release from cancer cells to induce immunogenic cell death and then initial the immune response. FPR1 is a receptor for ANXA1 and play a key regulator in innate immunity. We found that the polymorphism of FPR1was associated with the status of tumour regression grade (TRG), disease-free survival (DFS) and overall survival (OS). In 10-year analysis, LARC patients who received with neoCRT treatment carrying the FPR1-E346A variant had a significantly shorter DFS and OS than patients with wild-type FPR1 (35% versus 57% and 41% versus 61%, respectively). Age, pT Stage, pN Stage, TRG, and polymorphism of FPR1 were identified as independent risk factors for 10-year OS by multivariate analysis (HR = 2.68, 5.45, 2.47, 3.07 and 2.34; 95% CI: 1.25-5.24, 1.70-19.26, 1.67-5.39, 1.43-6.80 and 1.15-5.08, respectively). Our data revealed that FPR1 polymorphism (E346A/ rs867228) is associated with the therapeutic efficacy of neoCRT and the survival outcome of LARC patients.

Conclusions: FPR1 polymorphism is prognostic biomarkers for therapeutic efficacy and the survival of LARC patients treated with neoCRT.

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UTILITY OF MRI BASED ADC IMAGE SETS IN DELINEATING GTVRES VOLUMES IN CERVICAL BRACHYTHERAPY: A MULTICENTRE STUDY

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Purpose: With the emergence of MRI-based brachytherapy, perineal interstitial brachytherapy (P-ISBT) has become increasingly common to deliver highly conformal doses to bulky locally advanced cervix cancers. Previous studies have shown variability between observers in delineation of gross tumour volume (GTV_{res}) for MRI-guided brachytherapy, with conformity index (CI) of 0.58. This difference may be more pronounced when interstitial catheters are present potentially causing needle distortion and edema. Functional imaging such as apparent diffusion coefficient (ADC) map derived from diffusion weighted MRI may help increase agreement in GTV_{res} delineation. This study aimed to determine if the use of ADC map would reduce interobserver variability in GTV_{res} delineation in cervical cancers treated with P-ISBT.

Materials and Methods: Four cervical cancer cases treated with P-ISBT were retrospectively selected for inclusion in this study. In all cases, MR image sets including ADC maps were obtained using a single Philips scanner. For each patient, two sets of images were anonymized: one after completion of external beam radiotherapy but pre-brachytherapy (pre-BT) with a vaginal cylinder in situ and one obtained at the time of the first brachytherapy insertion (BT). Clinical stems including radiologist interpretation of the pre-external beam radiotherapy MRI scans and physical examination at the time of brachytherapy were created to guide contouring. Four radiation oncologists from three centres with expertise in gynecologic brachytherapy contoured on four scans for each case: Pre-BT and BT T2 image sets alone, and Pre-BT and BT brachytherapy T2 image sets with ADC available to guide contouring. Kappa (K) and CI values were calculated between observers.

Results: The mean GTV_{res} volume was 31cc. For BT contours, the mean K (0.664) and CI (0.610) showed a substantial level of inter-observer agreement. The mean pre-BT K was slightly higher (0.684), indicating increased agreement without interstitial catheters (and accompanying MRI compatible stylets) in-situ. With the addition of ADC map, the overall mean K increased from 0.668 to 0.680. However, on more detailed review, in two of the four BT cases K did not improve with the addition of ADC. These were the case with smallest mean non-ADC GTV_{res} volume (8.5cc) and lowest K (0.491) and the case with the largest mean non-ADC GTV_{res} volume (77.4cc) and highest K (0.777).

Conclusions: In centres with specialized expertise in P-ISBT, there is consistency between GTV_{res} contours. However, in presence of interstitial needles, there is an increase in contour variability between observers. ADC images may help decrease this variability. Further study is warranted.

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HIGH-DOSE-RATE BRACHYTHERAPY AS MONOTHERAPY FOR THE TREATMENT OF INTERMEDIATE RISK PROSTATE CANCER: TOXICITY RESULTS
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Purpose: High conformality of delivered dose and the high susceptibility of prostate cancer (PrCa) to high dose radiation therapy has warranted a closer look at high dose-rate (HDR) brachytherapy as monotherapy in recent years.

Objectives: We present the acute and late genitourinary (GU) and gastrointestinal (GI) toxicities among a cohort of medium risk PrCa patients who received HDR monotherapy.

Materials and Methods: Between January 1, 2016 and November 30, 2017, 42 patients were treated using CT-planned HDR brachytherapy as a single, 21Gy fraction. Dose was prescribed as per GEC-ESTRO guidelines, except for the urethra D0.1cc = ⩽110Gy EQD2. The Common Toxicity Criteria for Adverse Event, Version 4.0 (CTAE v4.03) was used to report toxicity. In addition to the one-week post-treatment interval, toxicity assessments were grouped at the 1, 3, 6, 12, and 24 months non-overlapping intervals.

Results: With a median follow-up of 13.5 months, (range 1-28.5), and median age of 69 years, 59% of our patients developed acute GU toxicity (Grade 1), 7% of our patients developed late GU toxicity (Grade 2). Most frequent GU toxicity was hematuria (52%) within the first week, followed by dysuria (17%) in the first 3 months. GI toxicity was observed in 9% (all Grade 1). There was one patient developed Grade 3 urethral stricture at 18 months. Pre-treatment PSA was 7.5 ug/L (range 2.1-18.0). Patients reached an average nadir of 1.7ug/L (range 0.1-9.0) at 10.6 months.

Conclusions: HDR monotherapy resulted in very low late GU toxicity (7%, G2; 2.3% G3) and no G2 or above late GI toxicity. These results are favorable compare to published data. In light of the advantages associated with this treatment modality, HDR brachytherapy is the ultimate extreme hypofractionation we can offer our patients.

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3D PRINTED, INDIVIDUALLY CUSTOMIZED HIGH-DOSE-RATE BRACHYTHERAPY APPLICATOR FOR TREATMENT OF CHRONIC DIGITAL PSORIASIS
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Purpose: Treatment of refractory psoriasis of the nails and nail beds can be challenging. Contact brachytherapy is an attractive approach to deliver radiation to the distal fingers and nail beds, given the complextopology of the region. In this abstract, we discuss the development and commissioning of novel3D-printed surface applicators for high-dose-rate brachytherapy treatment.

Materials and Methods: A young woman with distalfinger and nail bed psoriasis, refractory to traditional and biologic therapies received high-dose-rate brachytherapy at our institution. The process of manufacturing the applicator included the following: a dentalalginate impression of distal digits of her right hand was created. A stone mouldreplica of the digits was then formedwhich was laser scanned and imported into a computer drafting software. The catheter pathways were designedwith a distance of 3mm from the surface. Eight individual catheters were equally distributedaround each finger for a total of 40 catheters. Five distinct applicators were printed using a Clearview photopolymer (3D Systems Inc., USA). Each applicator was CT scanned with line markers in place. The dimensions and integrity of each applicator was validated. Subsequently, the images imported into Oncentra Brachy treatment planning system. Distal 3-4 cm (from the tip to the proximal interphalangeal joints) of all five digits were treatedto a totaldose of 2160cGy in 12 fractions. A treatmentdose of 180cGy per fraction was prescribedto the surface; extracare was taken in the region of the nail bed to avoid hot spots. Separate plans were developed for each digit and delivered on a phantom with an optically stimulated luminescent dosimeter (OSLD) that was normalizedfor Ir-192 energy response. Custom lead shielding, which surrounded the patient'shandwas designed and fabricated to limit the whole body doseto less than 5mSv.

Results: Five optimized plans were developedthat delivered a dose of 160cG to a depth of 2mm, such that 180cGy per fraction to the surface was achieved. OSLD measurements corresponded to the treatment plan within 2.7% (range -1.7% - 7.1%). The plan for the third digit had the highest dose discrepancy (7.1%) secondary to contribution from the surrounding digits. The discrepancyis likely due to the TG-43 calculationinadequatelyaccounting for the lack of attenuation from the air between each of the applicators. The whole body dose measured by an OSLD placed at the proximal arm was confirmed to be less than 0.25mSv from the entire treatment.

Conclusions: Customized 3D printed brachytherapy applicators for treatment of skin conditions in topologically difficultsurfaces are feasible. Optimized treatment plans to deliver uniformdose to the surface while limiting dose to wholebody andother organs areachievable.

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IMAGE-GUIDED BRACHYTHERAPY FOR PRIMARY VAGINAL CANCER: CLINICAL AND TOXICITY OUTCOMES
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Purpose: In 2010, Ultrasound-based catheter guidance was introduced at our institution in vaginal interstitial brachytherapy in an effort to improve local control and reduce toxicities. This retrospective study reports our experience on a cohort of 26 patients treated for primary vaginal cancer between 2010 and 2018.

Materials and Methods: Twenty-six patients were treated for vaginal cancer with brachytherapy between 2010 and 2018 with a median dose of 25 Gy in 5 fractions. Twenty-three of 26 patients underwent interstitial brachytherapy, mostly using Transrectal Ultrasound (TRUS) guidance for catheter insertion. Endocavitary brachytherapy only was used on 3/26 patients with Stage I disease. EBRT (median dose 45Gy) was added in 25/26 patients. Sixteen of 25 patients had concomitant chemotherapy. Inverse planning was used for dose optimisation with an effort to reduce high-dose points in the vaginal mucosa. Acute and late genitourinary (GU), gastrointestinal (GI), and vaginal toxicities were reported using the Common Terminology Criteria for Adverse Events version 5 (CTCAE v5). Local control (LC), metastatic disease-free survival (mDFS) and overall survival (OS) were evaluated using Kaplan-Meier survival curves.

Results: Mean age was 69.7. Median follow-up was 35.5 months (range 0-85months). Nineteen of 26 patients had Squamous Cell Carcinoma (SCC), five of 26 (19%) Adenocarcinoma, one of 26 (4%) Clear Cell Carcinoma and one of 26 (4%) Melanoma. Thirteen percent, 71%, 8%, and 8% of patients had FIGO Stages I, II, III, and IV. Local control of 83% and 83%, mDFS of 91 % and 91%, and OS of 80% and 66 %, were respectively achieved at 3 and five years. When limited to SCC only, local control of 88% and 88%, mDFS of 94 % and 94%, and OS of 87% and 70%, were respectively achieved at three and five years. There were no late G3-4 GU/GI toxicity. Acute and late G3 vaginal toxicity occured in 19% and 42% of patients, respectively. Three cases of vaginal necrosis and one suspicion of fistula were reported, all associated with a local progression of the disease. No patient needed Hyperbaric Oxygen Therapy (HBOT).

Conclusions: Excellent local control can be achieved with the use of TRUS-guided vaginal brachytherapy in primary vaginal cancer, especially for squamous cell carcinoma, with a favorable toxicity profile. GU and GI toxicities are mild but there is a significant number of G3 vaginal stenosis in this cohort of older patients.

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INTRAOPERATIVE RADIOTHERAPY OUTCOMES IN EARLY BREAST CANCER

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Purpose: Breast-conserving therapy with external beam radiotherapy (EBRT) is currently the standard of care for women with early breast cancer. Our aim was to determine if early-stage breast cancers treated with lumpectomy and intraoperative radiotherapy (IORT) have comparable local recurrence rates to standard breast-conservation therapy with EBRT.

Materials and Methods: Patients who underwent breast-conserving therapy with IORT from 2007-2017 were identified retrospectively. The primary outcome was ipsilateral breast cancer recurrence (IBTR). Secondary outcomes included wound complications. A time to event analysis was performed, Kaplan-Meier estimates (KM) report the fraction of patients living free of recurrence. Patients were followed for up to 10 years, censoring on death or date of last follow-up.

Results: One-hundred and six patients with a median age of 70 (IQR 65-75 yrs) were identified. Median follow-up time was 33 months (IQR 14-60 months). The majority of patients had screen-detected (94.3%), unifocal (88.7%), T1 (98.1%), estrogen-receptor positive (96.2%), HER2neu negative (93.4%), invasive ductal carcinomas (92.5%).

Thirteen (12.9%) required adjuvant EBRT for either close margins (n=5), nodal positivity (n=6), both close margin and nodal positivity (n=1) or an unexpected finding of lobular histology on final pathology (n=1). Forty-nine (46.2%) were prescribed adjuvant endocrine blockade. Ipsilateral breast cancer recurrence occurred in 5 patients, 3 in the previous lumpectomy site and 2 in another quadrant (five-year local recurrence rate 5.4%, 95% CI 1.4, 9.3%). All recurrences occurred five years or later and only in the 93 patients treated with IORT alone without EBRT. There were no regional or distant recurrences or deaths.

Five-year estimate of patients alive and local recurrence-free was 95% (95% CI 90.7, 98.6%). Symptomatic seromas occurred in 23 (21.7%), while only 10 (9.4%) persisted chronically. The wound infection rate was 9.4%.

Conclusions: In this cohort of post-menopausal women with early breast cancer treated with breast-conserving surgery and IORT, the overall IBTR rate at five years was 5.4%. Despite the selection of low-risk patients, the local recurrence rate was higher than reported in the literature with EBRT and external-beam partial-breast radiotherapy (PBI). Although this might be in part due to the lower rate of endocrine therapy usage, long-term results beyond five years in existing trials of breast IORT will be important to compare.

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ACUTE URINARY SYMPTOM COMPARISON BETWEEN PROSTATE BRACHYTHERAPY TREATMENT APPROACHES

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Purpose: Brachytherapy is a key radiotherapy option for the treatment of prostate cancer. Depending on patient characteristics, disease status, and operational infrastructure, brachytherapy can be delivered via low-dose-rate (LDR) or high-dose-rate (HDR), potentially in combination with external beam radiotherapy (EBRT). In this study, we compare acute urinary symptoms between three treatment options offered to prostate cancer patients at our centre: LDR monotherapy, EBRT combined with LDR boost, and EBRT combined with HDR boost.

Materials and Methods: We retrospectively reviewed prostate brachytherapy patients treated at our centre since January 2018, when HDR brachytherapy was introduced as a treatment option. One hundred and thirteen patients were identified; 15 were excluded due to incomplete data, leaving 98 patients for analysis. Of this patient cohort, 52 received LDR monotherapy (144Gy using ^{125}I seeds), 27 received an LDR boost (110Gy using ^{125}I seeds), and 18 received an HDR boost (15Gy in one fraction). American Urological Association (AUA) symptom scores were assessed via questionnaire at baseline and at one and three months subsequent to brachytherapy.

Results: The initial PSA was higher for those receiving combined modality therapy compared to monotherapy, with a mean ± standard deviation of 8±3 ng/mL, 14±11 ng/mL, and 14±10 ng/mL for LDR monotherapy, LDR boost, and HDR boost, respectively ($p<0.001$; ANOVA). Baseline AUA scores were balanced between the groups: 6±5, 6±5, 9±8 for LDR monotherapy, LDR boost, and HDR boost, respectively ($p=0.17$; ANOVA). 92% of LDR patients experienced an increase in their AUA scores in the first month; 10±8 and 7±8 increase for monotherapy and boost respectively. In comparison, only 60% of HDR boost patients experienced worsening AUA scores over this time period, with a smaller increase of 2.6±0.4. In the subsequent two months, approximately half of all patients saw some improvement in their AUA scores; however, three months post-brachytherapy, 25%, 15%, and 6% of LDR monotherapy, LDR boost, and HDR boost patients, respectively, had AUA scores categorized as severe (20-35). At our centre, brachytherapy boost is preferentially delivered after EBRT; however, this may be altered depending on patient preference and available resources. In this cohort, five of 45 patients received brachytherapy prior to EBRT; with a median gap of 27 days (range 19-56 days) from brachytherapy to the first EBRT fraction. None of these patients experienced severe AUA scores at either time point.

Conclusions: Brachytherapy, either as monotherapy or in combination with EBRT, can be a key component in the treatment of prostate cancer. It is important to consider urinary side effects; these have been reported to be at their worst in the short-term follow-up to brachytherapy (particularly LDR), and subside over the subsequent months. Continued follow-up of these patients will allow assessment of acute and late urinary toxicities, in combination with local control.

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BRACHYTHERAPY FOR PROSTATE CANCER A VALUED TECHNIQUE BY RADIATION ONCOLOGIST BUT WITH VERY LITTLE AVAILABILITY IN CHILE

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Purpose: The purpose of this work is to present the opinion of chilean radiation oncologist about the usefulness indications and availabillity of brachytherapy for prostate cancer in Chile.

Materials and Methods: The Chilean radiotherapy society (SOCHIRA) called on its members to participate in two face-to-face meetings and two online surveys on the appropriate treatment of prostate cancer. All members that treated prostate cancer where requested to complete a online survey about apropiate treatment for prostate cancer questions regarding the role of brachytherapy where the focus of this work.

Results: Of the 78 Radiation oncologist of the country, 38 participated on the consensus meetings and surveys (48.7%). For very low risk patients 94.7% agreed and only 2.6% would offer brachytherapy. For low risk 51% would recommend active surveillance (AS), 24,3% would recommend external beam radiotherapy (EBRT) and 18.9% would recommend brachytherapy (BT). For an intermediate favorable patient 65.8% would prescribe moderate hypofractionated EBRT, and 10.5% BT. For a high-risk prostate cancer 57.8% would recommend dose escalated EBRT and 39.5% would recommend EBRT plus BT boost. When asked about BT for low risk and intermediate favorable patients. 55.2% consider this technique equivalent to EBRT and could suggest it case by case approach. 23.7% consider this technique as the best approach and feel should be offered to every patient and refer to a centre with BT unit case this is not available locally. 18.4% mention that this procedure is not available in local context and should be implemented in the future. When asked about dose escalation with BT for high-risk patients 39.5% consider that it has advantage over EBRT alone and that should be offered for every suitable patient but 39.5% mention that they won´t recommend it because this treatment is not available in the current practice. 5.26% mention they won't recommend this procedure because it hasn't proved an OS over EBRT.

Conclusions: Prostate Brachytherapy is a valued treatment technique by Chilean radiation oncologist, however its availability is very low which hinders access to this treatment in national environment.

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DOES POINT A PREDICT LATE TOXICITY IN CERVICAL CANCER PATIENTS TREATED WITH CT GUIDED INTERSTITIAL BRACHYTHERAPY?

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Purpose: To evaluate the usefulness of reporting Point A doses and its relation with long term toxicity for patients with locally advanced carcinoma of the cervix, who are treated with external beam radiation therapy (EBRT) along with CT-guided intracavitary+interstitial brachytherapy.

Methods and Materials: Dosimetric data for patients who had been treated for FIGO Stages IB1 to IVA cervical cancer at the Jewish General Hospital Montreal, were analysed retrospectively, in relation to their rates of late GU, GI and vaginal toxicity. All doses were converted to 2Gy fraction equivalents using the A/B value of 10Gy. The EBRT was given as 45Gy in 25 fractions. The high-dose-rate CT-guided brachytherapy followed the McGill University recommended dose of 24Gy in 3 fractions prescribed to the GTV and included interstitial needles along with an intracavitary applicator in all three implantations. Doses to the rectal point and the left and right points A were recorded as per ICRU 38. Also, D2cc of rectum aand bladder along with D90 GTV were reported as per the GEC-ESTRO criteria. Toxicities were assessed using the Common Toxicity Criteria for Adverse Events (CTCAEv4.0). Pearson correlations were used to investigate the relationship between the different dosimetric criteria themselves. Ordinal logistic regression compared the predictive power of different dosage criteria for vaginal toxicity.

Results: Thirty-eight patients were included with a median follow-up of 28.45 months. Vaginal toxicities consisted of 36.8% Grade 15.8% Grade 2, 13.2% Grade 3 and no Grade 4. There was no GU toxicity. There was one rectovaginal fistula, repaired (Grade 3 GI). The mean dose (standard deviation, SD) in Gy to the right and left point A and D90 GTV were 105.38 (39.98), 96.19 (28.29), and 83.97 (1.09) respectively. The mean (SD) D2cc of rectum and ICRU rectal point were 60.15 (6.23) and 65.18 (8.13) Gy respectively. The left and right points A did not significantly predict the D90 GTV. Point A doses also failed to predict the probability of developing late vaginal stenosis while the ICRU rectal point, D2cc of rectum and the D90 GTV did predict that (p=.037, .006, .047 respectively). The Grade 3 GI toxicity occurred in the patient who had posterior tumour extension with possible recto-vaginal septum invasion.

Conclusions: Point A dose does not appear to be predictive of late vaginal toxicity, even in much higher than standard doses, in interstitial brachytherapy for carcinoma of the cervix. Therefore, in spite of being a long standing routine practice, reporting Point A doses not find justification in our results. Comparable toxicity rates in our study with MRI-based series confirms the utility and safety of using the more accessible CT scans for this type of treatment as well.

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A PILOT STUDY TO COMPARE TEACHING PATIENTS IN A GROUP SETTING VERSUS ONE-ON-ONE, FOR PATIENTS WHO WILL BE UNDERGOING PROSTATE BRACHYTHERAPY

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Purpose: To assess a change to the method used to educate patients in preparation for a prostate brachytherapy procedure and assess the feasibility and acceptability for the purpose of designing a future study.

Materials and Methods: Previously at our institution, all patient appointments for prostate brachytherapy ultrasound simulation (PBUS) were booked with an individual patient education afterwards. In order to improve efficiency for RTTs and RO, a new booking template was created compatible to group teaching. Three patients are now scheduled for PBUS back to back. Afterwards one RTT can run a group education session for the patients and families. The RO will return to consent and answer questions one-to-one. From July to November 2018, patients undergoing PBUS were asked to consider participating in this group education format. Patients were given the participant information and consent form to read whilst they were waiting. After the group education session, each patient was asked to complete a short patient satisfaction questionnaire. Once the patient data was collected the 5 brachytherapy RTTs completed a questionnaire regarding their own experience with the group education sessions.

Results: Eleven patients completed the questionnaire. All five Radiation Therapists completed their questionnaire. Overall, the patients were satisfied (8; 73%) or found that the group education session exceeded their expectations (3; 23%). Examples of patient comments relate to wait times and being in a supportive group. Four out of five of the RTTs wanted to go back to one-to-one education citing difficulties with patient personalities, concern that patients weren't properly comprehending what was being said and too many differing treatment combinations/trials.

Conclusions: The questionnaires were easy to use and analyze, so could be used for a future larger study. The patients were satisfied with the group education session but the majority of RTTs wished to revert back to one-to-one patient teaching.

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THE EFFECT OF BOLUS ON LOCAL CONTROL AFTER POST-MASTECTOMY RADIOTHERAPY

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Purpose: The routine use of bolus, a tissue equivalent material applied to the chest wall to increase radiation dose to the skin and superficial tissues, in breast cancer patients undergoing mastectomy is controversial. While the relationship between the use of bolus and skin/chest wall toxicities is well established, whether bolus use improves local control is unclear. At our institution, bolus has been used in patients receiving chest wall radiotherapy (RT) without reconstruction and omitted in patients undergoing reconstruction. This practice created an opportunity to evaluate local control outcomes in two cohorts treated with and without bolus.

Materials and Methods: The study included newly diagnosed invasive breast cancers (pT1-4a, any-N, M0) treated with mastectomy and adjuvant RT. Patients with skin involvement (T-stage cT4b,c,d or pT4b,c,d) or recurrent disease were excluded. The two comparative cohorts were patients treated with chest wall RT with bolus and patients undergoing reconstruction treated with RT without bolus. The primary endpoint was the cumulative incidence of local recurrence using regional recurrence, distant recurrence and death as competing risks. A multivariable analysis was conducted with use of bolus, T-stage, N-stage, lymphovascular invasion (LVI), margin status, triple negative receptor status, as well as systemic therapies received: hormone therapy and chemotherapy.

Results: The entire cohort consisted of 1891 women diagnosed from 2007 to 2011, 789 with bolus and 1102 without bolus. The median follow-up was 8.7 years. The two cohorts were similar in the distribution of tumour characteristics (T-stage, N-stage, LVI, margin status) and treatment characteristics (hormone therapy, chemotherapy). The median age in the bolus cohort was higher (56 versus 54 years, p=0.03, median test). The five-year cumulative incidence of local recurrence was 1.8% (95%CI: 1.1 – 2.9) with bolus and 1.6% (95%CI: 0.9 – 2.8) without bolus. The multivariable analysis demonstrated that local recurrence was not significantly related to use of bolus, T-stage, N-stage, LVI, margin status, triple negative receptor status, hormone therapy or chemotherapy.

Conclusions: In this large population-based analysis, the use of bolus did not appear to impact local control in breast cancer patients who underwent mastectomy. Longer follow-up and further prospective studies are required to validate the routine omission of bolus in this setting.

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PATTERNS OF PROSTATE CANCER RECURRENCE AFTER BRACHYTHERAPY IMAGED WITH PSMA-TARGETING 18F-DCFPYL PET/CT

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Introduction: Brachytherapy is a highly effective treatment in localized prostate cancer. A previous study from our institution indicated a low rate of local failure after prostate brachytherapy (Lo, IJROBP 2015). However, the study was limited by the absence of post-implant prostate biopsy and by utilization of conventional imaging to document local, regional and distant recurrence. In this study, we evaluate patterns of recurrence after brachytherapy utilizing positron emission tomography (PET) tracers that target the prostate specific membrane antigen (PSMA).

Materials and Methods: The study included patients enrolled in our ongoing institutional prospective trial, "PSMA PET/CT for Assessment of Recurrent Prostate Cancer" (NCT02899312). Patients with recurrent prostate cancer were eligible if they were candidates for salvage local therapy and there was no recurrent disease visualized on conventional cross-sectional imaging and bone scans. Biochemical and PSMA PET/CT recurrence were defined according to PHOENIX (Roach, IJROBP 2006) and PROMISE (Eiber, JNM 2018) criteria respectively.

Results: Between July 20, 1998 and August, 2018, 6380 patients have been treated with brachytherapy at our institution. Between March 2017 and August 2018, 208 patients were enrolled in the PSMA PET/CT trial, open for 13 months during this time. During the same time period, 1349 brachytherapy patients had follow-up PSA recorded and 81 experienced biochemical recurrence. In these patients with biochemical recurrence, median follow-up was approximately seven years and median time to biochemical recurrence was 50 months. Thirty-five out of 208 study patients were identified as receiving brachytherapy as part of initial curative treatment. In these brachytherapy patients, 68.6% had local recurrence in the prostate, 37.1% had seminal vesicle involvement, 34.3% had nodal recurrence and 28.6% had distant metastases. The basal segments of prostate were involved in 80.0% of local recurrences, which was significantly different than involvement of the mid (31.4%) and apical (11.4%) segments; p<0.001.

Conclusions: Contrary to previous evidence, our study showed that local failure is a common pattern of recurrence in patients who experience biochemical relapse after prostate brachytherapy. Further study is underway to correlate implant dosimetry with the location of intra-prostatic recurrence.

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IS ADJUVANT RADIOTHERAPY ALONE (WITHOUT HORMONE THERAPY) A TREATMENT OPTION FOR WOMEN 70 YEARS OR OLDER WITH EARLY STAGE BREAST CANCER?

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Purpose: Adjuvant breast radiotherapy (RT) following breast conserving surgery (BCS) is the standard of care for women

with early stage breast cancer (BC). NCCN guidelines V. 3.2018 recommends omitting RT after BCS in Stage I, estrogen-receptor positive (ER+ve) BC patients ≥70 years of age who receive adjuvant endocrine therapy (ET). Since RT alone is a treatment option for this group of patients in our health region, we conducted a population-based study to determine the outcomes of women treated with RT alone.

Materials and Methods: Data was collected from women aged ≥70 with ER+ve, early Stage BC treated with BCS followed by adjuvant treatment from 2005 to 2015. Survival endpoints for progression free survival (PFS), overall survival (OS), and cause specific survival (CSS) were calculated.

Results: A total of 1618 patients were identified. Median follow-up was 75 months. Adjuvant treatments received were: No adjuvant therapy (NAT): 194 (12.0%), RT alone: 587 (36.5%), ET alone: 190 (11.5%), and RT+ET: 647 (40.0%). Ten-year PFS rates were: NAT: 83.9%, RT alone: 94.0%, ET alone: 98.2%, and RT+ET: 92.2% (p=0.0001). On multivariate analysis, BCS+RT, BCS+ET and BCS+ET+RT led to significant reduction in recurrences compared to BCS alone with estimated risks of 0.26, 0.06, and 0.14 respectively. 10-year OS rates were 29.2%, 69.1%, 30.1% and 66.3% and 10-year CSS rates were 75.8%, 93.1%, 87.1% and 91.5% for NAT, RT alone, ET alone, and RT+ET respectively. In multivariate analysis, breast cancer death risk was 0.27 (RT alone), 0.51 (ET alone) and 0.19 (RT + ET), compared to NAT after BCS.

Conclusions: Our study shows that elderly women with Stage I, ER+ve BC had high-risk of local recurrence (LR) after BCS if managed with NAT. The risk of LR and the risk of breast cancer deaths were reduced to a similar extent by either RT alone or ET alone. Therefore, RT alone may be an appropriate treatment option for this group of BC patients.

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A BREAST SKIN ASSESSMENT PILOT (POSI B-SKIP) COMPARING PATIENT REPORTED OUTCOMES AND THERAPIST ASSESSMENT OF MOIST DESQUAMATION IN BREAST RADIOTHERAPY

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Purpose: Radiation dermatitis generally peaks after the completion of RT, during the time period when patients are not routinely assessed. A reliable patient reported outcome (PRO) tool to monitor skin toxicity during and after radiotherapy (RT) would be useful for implementing skin care interventions and to monitor the incidence of moist desquamation. We present a pilot study assessing the reliability of a PRO tool for acute skin toxicity for patients undergoing breast RT compared to skin assessments performed by radiation therapists.

Materials and Methods: Patients were grouped into five categories based on body mass index, bra size, skin fold size, and mastectomy. A twelve point PRO questionnaire was designed to focus on skin reactions, with open skin indicating moist desquamation. Size and location of open skin was monitored. Electronic tablets were used in the clinic to collect PRO at baseline, one week prior to completion of RT, last day of RT and one and two weeks post-RT. Skin assessments were performed at the time of PRO. For patients unable to return post RT, surveys could be completed on-line or by mail. Therapists used a 7-point scale derived from the NCI CTCAE V4 radiation dermatitis scale to score areas of moist desquamation.

Results: Eighty patients enrolled in the study have completed treatment; 35/80 (44%) returned to the clinic for both post-RT assessments, 42/80 (52%) completed the PRO on-line only and three of 80 (4%) did not complete the PRO assessments. For the 35 assessments completed by both PRO and radiation therapist, PRO positive predictive value was 0.75, negative predictive value was 0.89, sensitivity was 0.86, and specificity was 0.81 for moist desquamation in the infra-mammary fold.

Conclusions: This PRO questionnaire offers patients a tool to self- report skin reactions during and following RT, allowing closer monitoring of skin care by therapy staff. Accrual, data collection and analysis are ongoing in order to determine the suitability of this PRO to capture true rates of moist desquamation.

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REVIEW OF THE MANAGEMENT OF PATIENTS WITH ADVANCED ESOPHAGEAL CANCER AT RADIOTHERAPY CENTRE, PARIRENYATWA GROUP OF HOSPITALS, HARARE, ZIMBABWE

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Purpose: Esophageal cancer is rising in the third world with the highest rates in sub-Saharan Africa. We aim to describe the patterns of care for locally advanced esophageal cancer at a single referral radiotherapy centre in Zimbabwe.

Materials and Methods: A retrospective chart review was conducted. Patients with histologically confirmed epithelial esophageal cancer (SIIB and III) between January 1 2012 – December 31 2016 were included. Staging consisted of CT chest abdomen and endoscopy.

Results: One hundred and nine patients were eligible for analysis. The median age was 68 (range 20-85) years M:F ratio was 1.2: 1. Histology was SCC in 99 and adenocarcinoma in 10. Tumour was located in the lower third in 29, (mid 17 and upper one). KPS was 80-100 in 33 patients, 60-70 in 65 and <50 in 11 patients. Clinical stage was IIB in eight and III in 101 patients. HIV status was positive in 23 patients (negative 62, unknown 24) (CD4 count was ≥200 18; <200 in four). Treatment intent was curative in 20 (CRT in five, CRTS one, RT 14). Severe toxicities were described in eight patients (six GI, one hematological, one both). Clinical complete response was observed in 10/12, three out of four, three out of three patients who attended follow-up at six weeks, three months and six months. Treatment was palliative in intent in 89 patients (82%), consisting of RT in 28 patients (30Gy in 10 fr in 23, and other in five), CT in 10 and best supportive care in 51 patients. Partial symptom response was observed in five of 21, four of 10 and one of 1patient available for follow-up at six weeks, three and eight months post-RT.

Conclusions: Only 5% of patients presenting with local regional disease were suitable for curative therapy at our centre. Strategies to restore nutrition and general condition is needed to improve the proportion of patients who are candidates for curative therapies.

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ANALYSIS OF RADIATION DOSIMETRY PREDICTIVE FOR TOXICITY IN RECTAL CANCER PATIENTS TREATED WITH LONG COURSE CHEMO-RADIATION

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Purpose: Rectal cancers are one of the most commonly diagnosed cancers in the Canadian population. Patients who have locally advanced disease, receive chemo-radiation either in the neo-adjuvant or adjuvant setting which involves concurrent treatment with a fluoro-pyrimidine and long-course radiation (≥45Gy in 1.8Gy/fraction). Current predictors of toxicity after long course chemo-radiation are based on small cohorts that analyzed dosimetric parameters correlated with toxicity. Our objective was to identify the toxicity associated with long-course chemo-radiation in rectal cancer patients in terms of small bowel obstructions and bone fractures, as well as identify correlations of these events with radiation dosimetry.

Materials and Methods: Rectal cancer patients treated at our institution between 2010 and 2016 were included in the study. All patients who received long course chemo-radiation were identified. Organs at risk were contoured in all the study sets and complete dosimetry data from all the treatment plans were retrieved. Follow-up data for all these patients were also obtained and the radiation related toxicity data was analyzed. The correlation of toxicity with radiation dosimetry was evaluated and reported.

Results: Two hundred and twenty-six patients with rectal cancer were treated with radiation of which 717 patients received long course chemo-radiation in both the neo-adjuvant and adjuvant setting. Five hundred and ten patients were included in this analysis and there were 26 (5%) events of small bowel obstruction (≥ Grade 2), as well as five (0.9%) events of left sided hip fractures and two sacral fractures (0.3%). There was a trend of increasing incidence of small bowel obstructions with increasing dose and volume of small bowel irradiated (particularly V30Gy, V45Gy), but the correlation did not reach statistical significance. No significant correlation could be identified between the incidence of fractures and the dose of radiation to the pelvic bones. Analysis is ongoing with updated results to be reported at the meeting.

Conclusions: Our study reports on the toxicity associated with long course chemo-radiation in a large cohort of rectal cancer patients. The events of toxicity reported at our institution are low, substantiating the safety of our planning constraints, which are consistent with the current radiation dose tolerances followed for treatment planning of rectal cancers.

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LONG TERM SURVIVAL OF PATIENTS WITH GASTRIC CANCER TREATED WITH ADJUVANT RADIOCHEMOTHERAPY: PROPOSAL OF A PROGNOSTIC INDEX WITH IMPLICATION FOR TREATMENT MODIFICATION

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Purpose: Definitive surgery followed by adjuvant radiochemotherapy has been the standard of care for patients with gastric cancer since the publication of INT0116 study in 2001. This study is to analyze the outcomes of patients with gastric cancer treated with adjuvant radiochemotherapy.

Materials and Methods: After definitive surgical resection, patients with Stage IB to IVM0 gastric cancer were treated with fluorouracil (5-FU) and leucovorin. Radiotherapy with concomitant 5-FU was initiated in the second month of the treatment. Radiotherapy, 4500 cGy in 25 fractions, five days per week, was delivered to the tumour bed, the regional nodes, anastomosis, and the residual stomach. All patients were regularly followed. All the sites of recurrent disease were verified by image or biopsy.

Results: Between 2002 to 2013, 81 patients, male 61, female 20, aged 38 to 79 years old, who finished a full course of adjuvant radiochemotherapy were identified. The median post-radiotherapy follow-up was 57 months (10-196 months). Forty-eight (59.3%) patients survived ≥3 years. Fifteen patients (18.5%) survived ≥5 years, and nineteen patients (23.5%) survived ≥10 years. Eighteen out of 81 (22.2%) patients are still alive with a median survival of 142 months (57-196 months). The tumour and nodal staging, margin status, and lymphovascular invasion are all related to prognosis, but nodal status and lymphovascular invasion in particular were significantly related to prognosis for survival. A prognostic index based on pathologic features has been established to correlate with patient survival with implication for treatment selection.

Conclusions: Long- term survival of patients with gastric cancer who received adjuvant radiochemotherapy is possible for a significant portion of patients. A prognostic index has been established to be used for possible risk-based treatment modification.

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INVESTIGATION OF STRATEGIES TO IMPROVE PATIENT SUCCESS IN PREPARATION FOR CT SIMULATION FOR PROSTATE RADIOTHERAPY

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The requirement for patients undergoing prostate radiotherapy to meet particular standards in bladder and bowel preparation for simulation and daily treatments can be challenging to patients and treatment units, and this has become even more significant with the use of reduced margins and hypofractionated regimes. While there may be slightly more flexibility in these parameters for daily treatment, it is crucial that the standards are met for treatment planning purposes and patients are required to prepare for simulation by achieving an empty rectum (< 6 cm) and a comfortably full bladder.

Patients who cannot achieve these standards may need to have multiple simulation scans, occasionally returning on a different day, and may need to spend considerably more time at the cancer centre than expected. This is inconvenient for the patient and also very disruptive to CT simulator workflow, leading to delays for other patients. A retrospective audit of patients simulated from September to December 2018 showed that problems occurred in 24 of 116 patients (20.7%), and this included patients requiring multiple scans or patients who had to wait considerably past their appointment in order to fill their bladder. 4 patients had to return for scanning on separate days. Of these 24 patients, 41.7% had issues with bladder filling, 20.8% had issues with bowels, and 37.5% had issues with both.

More detailed tracking was implemented in January 2019 we saw that 27/65 patients (41.5%) experienced issues with bowel or bladder preparation. For 63% of these patients, the challenge was bladder-filling and 18.5% each did not have adequate bowel preparation or both bowel and bladder issues. One patient had to be scanned on a subsequent day.

We then began a program of having a radiation therapist telephone patients three days prior to their simulation appointment to ensure that they had received their preparation instructions and understood what was required of them. Early results indicate that this is having little impact on the success rate of preparation and that bladder-filling continues to be the greatest challenge. Despite knowing what preparation is required, many patients do not understand what a comfortably-full bladder feels like or are too dehydrated for the recommended water volume to fill their bladder. In addition, patients are not required to use a laxative

if they have regular bowel movements, but they often still have excess stool or gas in their rectum even though they have had a bowel movement prior to their simulation appointment.

Phase III of this project will continue with telephoning patients but also add a requirement for patients to be booked to arrive one hour ahead of their scan time in order for bladder filling and bowel preparation to occur at the cancer centre. This project will allow us to evaluate which strategy leads to the most improvement in prostate simulation success and will determine future department policies.

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THE RISK OF INFECTION AFTER PROSTATIC FIDUCIAL GOLD MARKERS INSERTION FOR IMAGE GUIDED RADIATION THERAPY

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Purpose: To report the infection rate and severity associated with the use of trans-rectal implanted fiducial gold markers for prostate image guided radiotherapy (IGRT).

Materials and Methods: Between November 2017 and January 2019, 121 prostate cancer patients (two cohorts) who had intraprostatic fiducial marker inplantation under transrectal ultrasound guidance answered a symptoms questionnaire at the time of the CT Planning. All had oral prophylactic quinolone 60 minutes before implantation and the next day. Seven days after, the patients were asked about infective symptoms and the treatment received including antibiotics or hospital admission. After the CT planning, patients were followed weekly during IGRT. Infective events were confirmed through urine or blood culture. Infection was related to the procedure if it occurs in the seven days that follows the fiducial markers insertion.

Results: The procedure was well tolerated. There was no interruption of implantation with regards to pain or hemorrhage. All patients completed the questionnaire. Twenty-one patients (17.35 %) experienced increased urinary frequency and dysuria. At seven days post-insertion, no patients reported infection. Meanwhile, later on, two patients developed a urinary tract infection that could be related to other causes than the marker insertion. The first had coagulase-negative staphylococci urinary infection. He was hospitalized and died from urosepsis. The second presented an escherichia coli infection that occurs 30 days after the procedure and recovered after two weeks of antibiotic treatment.

Conclusions: Transrectal fiducial marker implantation for image guided radiotherapy in prostate cancer is a well-tolerated procedure and the rate of infection is lower than the 3.5% rate of infection after transrectal prostate biopsies. These results need to be validated in a larger cohort of patients.

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DNA REPAIR GENES POLYMORPHISMS, TUMOUR CONTROL AND TREATMENT TOXICITY IN PROSTATE CANCER PATIENTS TREATED WITH PERMANENT IMPLANT PROSTATE BRACHYTHERAPY

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Purpose: To evaluate the association of inherited germline variations in DNA repair associated genes with tumour control and treatment toxicity in patients treated with permanent implant prostate brachytherapy (PIPB).

Materials and Methods: The cohort consists of 478 I-125 PIPB patients with a median follow-up of 51 months after seeds implantation. Upon consent of patients, DNA was prepared from mononuclear cells and genotyped for 215 haplotype tagging single nucleotide variations (htSNPs) in genes of DNA damage response and repair pathways. Their association with biochemical recurrence (BCR) was assessed using Cox regression models and Kaplan-Meier survival curves with log-rank tests. Linear regressions and analysis of covariance (ANCOVA) between early and late International Prostate Symptom Score (IPSS) with htSNPs were used to evaluate the association with urinary toxicity.

Results: After adjustment for the established risk factors including age, PSA at diagnostic, Gleason score and androgen-deprivation therapy use; 17 htSNPs in eight different genes were initially found to be associated with an altered risk of BCR, with adjusted hazard ratios (HRadj.) ranging between 0.27 - 12.39 ($p \leq 0.05$). Upon adjustment for multiple testing, one marker remained significant ($q<0.001$). Compared to carriers of the ERCC3 rs4150499 T allele, patients homozygous for C allele (n= 23) had a significant higher risk of BCR with a HR of 12.39 (IC95% 4.22-36.39; $p<0.0001$; $q<0.001$). The Kaplan-Meier survival curve revealed a median BCR-free survival time reduced from 213 ± 7 to 99 ± 12 months (log-rank $p<0.00001$) for homozygous carriers of the ERCC3 rs4150499 C allele compare to non-carriers. The regression models included pre-treatment IPSS, age, hormone-therapy status, Gleason score, PSA level and htSNPs as potential predictors of post-treatment IPSS. For early IPSS (one to six months post-treatment), no htSNPs were found to have predictive value. For late IPSS (more than six months post-treatment), htSNP rs6544990 from MSH2 showed a statistically significant b-coefficient of 1.848±0.518 ($p<0.001$; $q<0.1$). Homozygous carriers of the MSH2 rs6544990 C allele (n=62) had a mean late IPSS 3.6 points higher than patients homozygous for the A allele (n=132). This difference was significant when tested by ANCOVA using pre-treatment IPSS as a covariate ($p<0.01$).

Conclusions: This study suggests an association of the intronic variants of ERCC3 and MSH2 with elevated risk of BCR and late urinary toxicity, respectively, after PIPB. An independent validation is required whereas the underlying biological mechanisms remained to be assessed.

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BONE SCANS IN THE MANAGEMENT OF METASTATIC CASTRATE-RESISTANT PROSTATE CANCER: SURVEY OF PATTERNS OF PRACTICE IN CANADIAN RADIATION ONCOLOGISTS, MEDICAL ONCOLOGISTS AND UROLOGISTS

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Purpose: Assessing response to systemic treatment in metastatic castrate-resistant prostate cancer (mCRPC) is an evolving paradigm, particularly in the era of access to advanced imaging tools. Tc-99m methylene diphosphonate bone scans are a sensitive test to detect skeletal metastases in men with mCRPC; however, their use to assess mCRPC patients in routine clinical practice (outside of clinical trial protocols) remains a topic of debate.

Objective: This study aims to clarify the current patterns of practice on the utilization of bone scans to assess response to systemic therapy in the management of mCRPC patients.

Materials and Methods: We surveyed practicing radiation oncologists, medical oncologists and urologists in Canada via an online survey tool designed to obtain background information including experience in treating mCRPC patients with systemic therapy, and patterns of use of bone scans in the management of mCRPC patients. Responses were analyzed using descriptive statistics.

Results: Ninety-one physicians participated in our survey: 41 (45%) radiation oncologists, 34 (37.4%) medical oncologists and 16 (17.6%) urologists. 51.2% of the participants indicated they do not schedule bone scans in asymptomatic mCRPC patients. Of those who would schedule a bone scan in an asymptomatic patient, the frequency of the scans ranged from every three months to every 12 months. 18.4% of physicians order bone scans in mCRPC patients and a rising PSA. Suspected progression on bone scan was considered the least important marker of treatment response (weighted average 2.7/5.0), whereas symptomatic progression was considered the most important (weighted average 4.0/5.0). The majority of physicians (80.7%) used the wording of the bone scan report to determine disease progression. 23.9% applied PCWG3 criteria, while 53.6% confirm suspected progression on a bone scan with a CT.

Conclusions: Wide variation exists among practicing physicians in the use of bone scans for the management of mCRPC patients. Most physicians do not routinely order bone scans in asymptomatic real-world patients, in contrast to those physicians who use the PCWG3 clinical trial recommendations. The role of bone scans as a parameter of treatment response in mCRPC in routine clinical practice needs to be further explored, notably also in the context of rapidly emerging molecular imaging techniques such as PSMA PET/CT.

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PATTERNS OF RECURRENCE IN STAGE III NON-SMALL CELL LUNG CANCER TREATED WITH DEFINITIVE IMRT: EXPERIENCE AT AN ACADEMIC CANCER CENTRE

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Purpose: Advances in staging and treatment have improved outcomes of patients with locally advanced non-small cell lung cancer (NSCLC), but relapses remain a challenge. In order to improve outcomes further, it is important to identify patterns of recurrence. Thus, we examined the pattern of recurrences in locally advanced NSCLC patients treated with IMRT at a large academic centre.

Materials and Methods: A REB approved retrospective review of Stage IIIA and IIIB NSCLC patients treated with definitive IMRT between 2011-2016 was conducted. Patients were identified through a prospective institutional cancer database. Demographics, disease, treatment and follow-up data were recorded. Surveillance imaging scans were reviewed to categorize the number and sites of first recurrence.

Results: One hundred and thirty-six patients were identified. Ninety-six patients were treated with definitive chemoradiotherapy, and 40 patients were treated with definitive radiotherapy alone. Median age was 67, 65% were men. 85 patients had Stage IIIA and 51 had IIIB NSCLC. Adenocarcinoma comprised 69% of the cases. Median radiation dose was 66Gy in 33 fractions. Median follow-up was 21.3 months. Crude survival rate at one year was 72%, and 49% at two years. Ninety-two patients had recurrences, at a median time of 8.6 months. Most common first site of recurrence was distant only in 62 patients, and in combination with locoregional recurrence in 13 patients. The most common sites of distant recurrence were lung (32.8%) and brain (21%). Eleven of those patients had a solitary metastasis (seven brain, four lung) at the time of initial recurrence. Local recurrences as the first site were seen in 22 patients, and regional in 16 patients.

Conclusions: Early distant relapse was most commonly seen in this PET staged, modern cohort of patients. Patients with solitary brain or lung metastases could be potential candidates for metastasis-directed salvage ablative therapy. It remains to be seen whether the addition of consolidative immunotherapy changes the pattern of recurrence in Stage III NSCLC patients.

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CLINICAL OUTCOMES OF SURGICALLY UNRESECTABLE ENDOMETRIAL CANCERS

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Purpose: Up-front surgery is standard of care for endometrial cancer but can be challenging in locally advanced cases. There is a paucity of literature on clinical outcomes for locally advanced unresectable, but medically resectable, endometrial cancers managed with neo-adjuvant or definitive radiation and/or chemotherapy.

Objectives: To determine outcomes of patients with unresectable endometrial cancer managed with definitive or neo-adjuvant radiation (RT) and/or chemotherapy.

Materials and Methods: Patients with unresectable Stages II-IVA endometrial cancer who were treated with curative intent between January 2000 and March 2018 were identified. Overall survival (OS) and disease-free survival (DFS) were analyzed using the Kaplan-Meier method and compared using the log rank test. Multivariate logistic regression analysis was performed to identify factors associated with receipt of surgery. Multivariate Cox regression analysis was performed to identify factors associated with OS and DFS.

Results: Of the 59 patients identified, the median age was 63 years (range: 37-88) and histology was endometrioid in 59%. Median follow-up was 2.2 years (range: 0.3-9.8). Seventeen patients (29%) received neo-adjuvant chemotherapy, 28 (47%) neo-adjuvant RT, and 14 (24%) definitive RT; 39 (66%) underwent surgery. Patients who received surgery had higher three-year OS and DFS than those who did not (84% versus41%; p=<0.001 and 56% versus11%; p=<0.001, respectively). Factors associated with higher odds of surgical resection included: younger age, endometrioid histology and earlier stage. Younger age, endometrioid histology and surgical resection were significantly associated with higher OS. Surgical resection was also associated with higher DFS.

Conclusions: Surgical resection following RT and/or chemotherapy for locally advanced, unresectable endometrial cancer is associated with higher DFS and OS and more likely to be achieved in endometrioid subtypes.

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PATIENT REPORTED OUTCOME MEASURES IN PATIENTS UNDERGOING RADIOTHERAPY FOR HEAD AND NECK CANCER

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Purpose: Head and neck cancer patients experience a significant burden of acute side effects during treatment. This study evaluates patient reported outcomes (PROs) in head and neck patients undergoing radical radiotherapy.

Materials and Methods: Head and neck cancer patients undergoing radical radiotherapy at our multi-centre institution completed the 50-item Vanderbilt Head & Neck Symptom Survey 2.0 prior to radiotherapy. Each question ranks symptom severity on a ten-point scale. Three questions were added to evaluate chemotherapy related side effects. A twelve item partial survey was completed weekly during radiotherapy. The questions were selected to include symptoms that could be potentially managed by physician or allied health professional intervention. Between October 2016 and October 2018, 318 patients completed a baseline survey and at least one weekly survey.

Results: The mean age was 62 years (range: 12-88 years), 80% were male and 20% female. A third (34%) were former smokers, 28% current smokers and 37% lifetime non-smokers. Alcohol was consumed by 29%. The majority (87%) were ECOG performance status 0-1. The most common tumour sites were oropharynx (37%), larynx (18%) and oral cavity (11%). Sixty-three percent had T1/T2 tumours and 37% had T3/T4 tumours; 69% had nodal involvement. Almost half (46%) received concurrent chemotherapy and 32% had prior surgery. The mean radiotherapy dose was 66Gy (range 50-71 Gy).
The average number of weekly questionnaires completed was five (range: 1-8). The median maximum weekly scores were highest for the following questions: dysgeusia (seven of 10), pain level (six of 10), and mouth sores causing pain (five of 10) and these scores increased over time (Spearman rank order correlation coefficient all $p<0.05$). The median maximum scores were lower for weight loss due to difficulty swallowing food (four of 10), mucus causing choking/gagging (four of 10), pain causing sleeping difficulties (three of 10), and choking on solids (three of 10). Multivariate analysis showed that nasopharynx, paranasal sinus, oral cavity and oropharynx tumour sites were associated with worse mucositis relative to larynx, thyroid and salivary gland tumour sites (all $p<0.05$). Patients who were younger, female, current smokers, had oropharynx cancer, and ECOG 1-3 had higher average pain levels during treatment (all $p<0.05$) Nasopharynx, paranasal sinus and oropharynx tumour sites and higher radiation dose were associated with worse dysgeusia (all $p<0.05$).

Conclusions: Head and neck cancer patients experience significant side effects during radiotherapy. The most severe symptoms reported were dysgeusia, pain and mucositis. Oropharynx cancer patients reported the highest symptom scores during radiotherapy.

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ASSESSMENT OF INTER-FRACTIONAL ANATOMICAL AND DOSIMETRIC TRENDS IN A RETROSPECTIVE COHORT OF 200 HEAD AND NECK CANCER PATIENTS

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Purpose: We assess the anatomical and dosimetric changes over the course of radiotherapy treatment for a large cohort of head and neck cancer patients treated with chemoradiation. These results provide an update of typical during-treatment changes based on current standards of care.

Materials and Methods: We examined a cohort of 200 advanced-stage head and neck cancer patients treated with radical chemoradiotherapy with VMAT between Nov 2015 and May 2018. Pre-treatment structure volumes and initial plan parameters were measured on the simulation CT and patient plan. Inter-fractional anatomical and dosimetric changes were calculated by comparing the simulation CT to the last-acquired CBCT (median acquisition: fraction 28). Deformable image registration automatically calculated the anatomical changes. Principal components analysis was performed on during-treatment anatomical and dosimetric changes and verified by pairwise application of Kendall's rank correlation test. Collection of toxicity measures from physician notes, diagnostic tests, and patient reported outcomes is underway.

Results: The average CTV volume loss was smaller for this cohort than some reported in the literature: average high-dose CTV volume change of -5.2% (range: -123.85 cm^3 to 25.16 cm^3). Average change in weight was more in line with published results, at -8.4% (-21.7% to 8.4%). Parotid gland Dmean increases resulted in patients receiving a dose exceeding planning objectives by 7.8% on average for the end-of-treatment fraction analyzed. Similarly, the pharyngeal constrictor Dmean exceeded the planning objective by 1.4%. The largest variation in dose deviations across the cohort occurred for the submandibular glands with a range of 0.7 Gy/fraction. Principal component analysis and Kendall's rank correlation test indicated positive correlations between: change in BMI; change in target, parotid gland and submandibular gland volumes; and parotid gland and high-dose CTV centre of mass shifts. This group of parameters was negatively correlated with: initial BMI; initial low-dose CTV volume; increases in spinal cord Dmax, target hotspot, submandibular Dmean, and pharyngeal constrictor Dmean deviations. Additional statistical methods will incorporate pre-treatment characteristics, stratification of patients according to "risk-profiles", and toxicity measures.

Conclusions: Generally, patients lost weight and tumour volume during treatment which resulted in average planning objective violations of 0.5% for CTV and up to 7.8% for organ-at-risk volumes. Patients with larger pre-treatment BMI exhibited greater volumetric changes and larger dose deviations in central-axis structures (spinal cord and pharyngeal constrictors), parotid glands, and submandibular glands.

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RESPONSE ASSESSMENT WITH 18F-FDG PET/CT SCAN IN PATIENTS WITH ANAL CANCER TREATED WITH RADICAL RADIOTHERAPY

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Purpose: Functional imaging like positron emission tomography (PET) in combination with computed tomography (CT) has been found to be an important tool in post-treatment response assessment in several malignancies. The objective of this study was to identify the utility of early post-treatment response assessment with ^{18}F-Fluorodeoxyglucose PET/CT (FDG PET/CT) scan in patients with squamous cell carcinoma (SCC) of anal canal primarily treated with radical radiotherapy.

Materials and Methods: We reviewed the provincial population database for anal cancer patients who were treated with radical radiotherapy (2005-2015) and subsequently underwent post-treatment FDG PET/CT scans (majority within 12-17 weeks after treatment completion) for response assessment. Information related to pt and tumour characteristics, treatment regimen were collected. Disease free survival (DFS) and cancer specific survival (CSS) were estimated using Kaplan-Meier product limit method.

Cox multivariable regression model was used to determine the association of post-treatment maximum standardized uptake value (SUVmax) as a continuous variable with DFS and CSS after adjustment for age at diagnosis, stage, radiotherapy dose, use of concomitant chemotherapy, use of salvage surgery, sex and performance status.

Results: A total of 287 patients were treated with radical radiotherapy over the time period of the study and 56 had post-treatment response assessment with PET/CT. Median age of the study cohort was 60.5 years (IQR, 53-66). Median radiotherapy dose was 54Gy (IQR, 53.6-54). Among a total of 56 patients, concurrent chemotherapy was offered in 53 (95%) patients. Mean post-treatment SUVmax for the primary tumour and node were 2.6(±3.9) and 4.3(±6.7). On multivariable analysis (MVA), post-treatment SUVmax for the primary tumour had a significant association with CSS (hazard ratio (HR): 1.39, 95% confidence interval (CI): 1.13-1.70, p=0.002). The HR for post-treatment nodal SUVmax was 1.09 (95% CI: 0.88-1.36, p=0.4). The association of post-treatment SUVmax of primary (HR: 1.01, 95% CI: 0.86-1.18, p=0.88) or node (HR: 1.10, 95% CI: 0.92-1.31, p=0.31) with DFS was not statistically significant.

Conclusions: The current population-based study shows significant correlation of presence of FDG avid residual tumour with CSS. Every one unit increase in post-treatment SUVmax of the primary tumour was associated with 39% increase in the relative risk of death. Although post-treatment nodal SUVmax showed similar direction of association, the overall association was not statistically significant which could be attributed to the limited sample size. The study highlights the importance of post-treatment PET based response assessment in patients with anal SCC and early institution of salvage treatment in presence of FDG avid residual tumour to avoid potentially fatal consequences. Further validation of this finding with randomized clinical trial is warranted.

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CAN WE USE HOUNSFIELD UNIT RANGES AS SURROGATES FOR FUNCTIONAL LUNG AVOIDANCE IN 4-DIMENSIONAL COMPUTERIZED TOMOGRAPHY SIMULATION DATASETS: A PILOT STUDY

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Purpose: Radiation pneumonitis (RP) is a common toxicity following radiation therapy (RT) to the thorax. Research is ongoing to establish 3-dimensional maps of functional lung for the purpose of avoidance in RT planning to reduce the risk of significant RP. We investigate various combinations of Hounsfield Unit (HU) ranges in 4-dimensional computerized tomography (4DCT) datasets versus known measures of lung function based on spirometry, in an effort to develop a readily available CT density surrogate for areas of healthy functional lung.

Materials and Methods: Our local Research Ethics Board (REB) approved this pilot study in 2016. All patients who had a 4DCT simulation for RT planning of lung cancer were screened. Only patients with pulmonary function tests (PFT) or spirometry available within 90 days of 4DCT were included. Patients were excluded if 4DCT was inadequate due to the presence of artifacts, or scan length is too limited. Total of 91 consecutive patients met the selection criteria for analysis. The PFT data were tested for correlation with various 4DCT variables to assess the strength of possible relationships. This included the standard approach of contouring the entire lung seen in the average intensity pixel (Ave-IP), as well as assessing subsets of this volume based on HU range, i.e. excluding the low attenuation areas (LAAs) regions (defined as any pixel with HU < -860) or looking at various HU ranges (e.g. -800 to -600 HU). Analysis was via linear regression, and GNU PSPSS was used to calculate Pearson's and Spearman rank correlation and p-values.

Results: There were 42 males and 49 females with average age of 71 years (range 53-92). The mean FVC was 2.66L (0.94-4.70, SD=0.80) and mean FEV1 was 1.79L (0.54-3.23, SD=0.60). Linear regression plots of FVC or FEV1 versus Ave-IP showed weak correlation for FVC (R^2=0.23), and no association for FEV1 (R^2=0.01). Pearson and Spearman rank correlations were 0.48 and 0.47 for FVC, and 0.12 and 0.15 for FEV1 respectively with p-values significant for FVC (p<0.00001) but not FEV1 (p=0.259). By excluding LAA regions, FVC correlation improved from low to moderate (Spearman r values went from 0.47 to 0.57). When focusing on lung tissue in the HU range between -800 and -600, the FEV1 correlation with 4DCT data went from negligible to a low strength correlation, bordering on moderate (Spearman r values went from 0.15 to 0.46, p<0.001).

Conclusions: Our work suggests 4DCT "total lung" volumes poorly correlate with FVC and not at all with FEV1. Further study is required to validate the link between lung contoured on 4DCT plans and functional lung to allow sparing.

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HYPOFRACTIONATED RADIOTHERAPY FOR SOFT TISSUE SARCOMAS - EARLY EXPERIENCE WITH 35GY IN 5 FRACTIONS

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Purpose: Radiotherapy (RT) plays an important role in the management of soft tissue sarcoma (STS). STS have a low alpha/beta ratio and so are sensitive to fraction size. This together with the practical advantages of a shorter treatment schedule for both the patient and the healthcare system prompted us to investigate the use of 35Gy in 5 fractions given on alternate days over two weeks, an EQD2 of 70Gy, using an alpha/beta ratio of three. We report here our initial experience.

Materials and Methods: Twelve patients with newly diagnosed or metastatic STSs were treated between January 2018 and February 2019. Treatments were planned using VMAT or SBRT and delivered with image-guidance with daily CBCTs. No patient received concomitant systemic therapy.

Results: The most prevalent histologies were liposarcoma and angiosarcoma. Five patients received neoadjuvant radiotherapy for newly diagnosed STS and, the remainder, palliative RT for oligometastatic disease for pain and/or radiological progression. RT was a well-tolerated treatment. Among those treated with palliative intent, one patient with a lesion in the manubrium presented pain flare after 2 fractions and dermatitis Grade 1 at the end of RT, while six patients presented dermatitis Grade 1 during the month following RT. No progression of disease was seen during follow-up. Of the patients treated pre-operatively, one to the popliteal region developed a wound infection and dehiscence while two patients treated to the upper limb had no wound healing issues following surgery. The two other patients are waiting for surgery.

Conclusions: A treatment schedule of 35Gy in 5 fractions appears to be well tolerated, with only mild acute side-effects and good control of the disease. These hypothesis-generating findings should be taken with caution given the small number of patients and short follow-up. We will open a phase I/II trial for preoperative RT for patients with newly diagnosed STS.*oligometastatic*

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IMPROVING WAIT-TIMES FOR RADIATION ONCOLOGY INTRA-TREATMENT VISITS

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Purpose: AOPSS survey conducted in the Cedar's Cancer Centre (CCC) waiting room showed that 63 % of patients wait longer than expected for their radiation intra-treatment visits. The purpose of this study is to objectify wait times at the CCC and identify factors affecting them. This data will be used to implement the first improvement as part of a Plan-Do-Study-Act (PDSA) cycle in an effort to decrease wait times, thereby improving patient satisfaction.

Materials and Methods: A management system in waiting rooms was used to obtain time stamp data from four samples (taken from August 4, 2018 to January 16, 2019). The outcome measure was time from check-in for appointment to beginning of intra-treatment visit. Employing a standard statistical approach, results were tabulated and stratified according to physician, time of day, day of the week and wait time experience. A root cause analysis was also performed.

Results: Baseline data from 1054 patients was analyzed, of which 10 patients with wait-times >5 hours were excluded. Median time from check in to beginning of intra-treatment visit was 46 minutes, mean 53 minutes. Almost all patients (94%) were seen within two hours, with the majority seen within one hour (63%). There was variation between wait times by treating physician, time of day and by day of the week. Wait-times vary between physicians, ranging from 38 minutes to 76 minutes. For check-ins after 7:00, wait-times tended to increase throughout the morning, from 16 minutes to a peak of 73 minutes. After that there was a steady decline during the afternoon to 10 minutes. The longest average wait times were encountered by patients who were checked-in on Monday (66 minutes) while the shortest occurred on Friday (39 minutes). A root-cause analysis showed coordinator unavailability, confusion with names of rooms, and poor communication between physicians and treatment machines to be amongst contributory factors to prolonged wait times.

Conclusions: Our analysis showed that 37% of patients wait >1 hour for their intra-treatment visit. The goal is to decrease this number to <25% within two months of implementation of new workflow and check-in process for the intra-treatment clinic. Lengthy wait times can be prevented using classic quality improvement methodology. As such, PDSA cycles will be used to implement a series of interventions, and changes in wait time will be tracked. For the first cycle of PDSA changes, we will act on three of the main contributory factors to prolonged wait times – we will aim to clarify signage in waiting rooms to decrease the likelihood of patients waiting in the wrong place, aim to increase communication between physicians and machines, and aim to have regularly scheduled intra-treatment visits rather than schedule them on the go so patients are less affected by coordinator unavailability. These results will be analyzed in two months time (after the first cycle of improvements) and presented at CARO.

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A COMMUNITY- BASED ORTHOPEDIC RADIATION ONCOLOGY CLINIC (OROC): AN EARLY EXPERIENCE REPORT

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Purpose: Skeletal related events (SREs) reduce life and increase health care costs (1,2). Practice guidelines recommend a multidisciplinary approach to management of Metastatic Bone Disease (MBD) to improve outcomes and reduce clinical morbidity (3). Prophylactic orthopedic fixation for high-risk MBD enhances quality of life and reduces health care cost (2,4). A fracture risk assessment includes radiographical assessment of the of the size, type and location of the lesion and a clinical examination to assess functional pain (5,6,7). Prior to OROC, on call orthopaedic evaluation was required based on the radiographic report of pending fracture risk. The use of orthotic devices was limited only to spinal braces, Radiation Oncology follow-up care and rehabilitation services were lacking for patients with bone metastases of the appendicular skeleton. This report describes a provincial survey on the use of multidisciplinary care for SREs and a preliminary review of the OROC clinic experience.

Materials and Methods: An email survey of four questions was sent to fourteen Ontario Radiation Therapy Department Managers regarding current practices for the treatment of long bone metastases at their cancer centre.OROC Charts were reviewed retrospectively from April to July 2018 and information regarding fracture risk category and interventions including referrals, orthotics and patient education material were collected.

Results: A response rate of 71% (10/14) demonstrated that 30% (three of 10) of Radiation Oncology Departments currently offer a dedicated Bone Metastases clinic that operates on a weekly or biweekly basis. One radiation oncology department provides a combined multidisciplinary assessment with a Radiation Oncologist and Orthopedic Surgeon in their MBD Clinic. The remaining respondents (n=5) indicated that orthopedic surgeon resources are utilized on an as needed or on call basis for fracture risk assessment of long bone metastases. From April to July 2018, 29 patient consultations and nine follow-up visits occurred in the weekly OROC clinic. Eleven out of 29 (38%) patients were identified as high risk of pathologic fracture and received restricted weight bearing instructions. Five out of 29 (17%) patients were offered prophylactic orthopedic fixation and 20/29 (69%) received palliative radiation therapy. Four out of 29 (14%) patients were referred for prosthetic/orthotic devices and three out of 29 (10%) for physiotherapy services.

Conclusions: Preliminary data supports the interdisciplinary OROC objective of providing rapid access to centralized coordinated care in order to improve patient education, time to treatment, provide follow-up and rehabilitation services. Future partnership with a community-based rehabilitation program and OROC will ensure consistency of post-treatment care for patients with SREs of the appendicular skeleton. Further research is needed to measure the outcomes of this patient population in addition to establishing best practices for patients with SREs.

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THE CLINICAL SIGNIFICANCE OF BONE MINERAL DENSITY CHANGES FOLLOWING LONG TERM ANDROGEN DEPRIVATION THERAPY IN PROSTATE CANCER PATIENTS ENROLLED IN THE PCS V TRIAL

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Purpose: Treatment for advanced prostate cancer includes long term androgen deprivation therapy (ADT), which has been associated with decreased bone mineral density (BMD). It is unclear whether this translates to a clinically significant change in bone density status. Some evidence suggests that there is no impact on fracture risk despite a decrease in BMD. We quantified changes in BMD when all patients on ADT were mandated to take Calcium and Vitamin D (CaVitD) in the setting of a phase III randomized clinical trial and compared the findings to historical data.

Materials and Methods: BMD analysis was conducted for high-risk prostate cancer patients enrolled in the PCS V study (NCT01444820), a randomized phase III trial comparing conventional and hypofractionated radiotherapy regimens. Patients received 24 months of ADT and were prescribed CaVitD supplementation (Carbocal D 1 tablet twice daily; 500mg of Calcium + 400 IU of Vitamin D3). Long-course ADT consisted of luteinizing hormone-releasing hormone agonist therapy, with 14 days of bicalutamide (50mg per day) with the first injection only. BMD reports at baseline and at 30 months of follow-up had the areal density and T-scores (spine, femoral neck, and total femur) extracted and the absolute change calculated. The results were then compared to the BMD decline of CaVitD control groups in bisphosphonate trials. Clinical bone density status (normal, osteopenia, versus osteoporosis) was monitored.

Results: In total, BMD reports were obtained from 329 patients. Patient data was further analyzed if a 24-month follow-up BMD data was present for a given site - 226 (spine), 231 (femoral neck), and 173 (total femur). The mean change (standard deviation) in the areal density was -2.65% (5.78), -2.76% (5.59), -4.27% (4.41), respectively. The difference was statistically significant for all three sites ($p<0.001$). The average decrease in BMD across all three sites was -3.2% after 24 months of ADT, compared to a historical figure of -2.1% following 12 months of ADT. For most patients (n=140, 83%), there was no clinically significant decline in bone density status. Eight patients (5%) with osteopenia prior to ADT became osteoporotic, 18 patients (11%) who had normal BMD became osteopenic, and no patients with normal BMD developed osteoporosis.

Conclusions: In comparison to historical data for one year of ADT, our analysis of the prospectively collected BMD data showed minimal further deterioration with two years of ADT. Despite the drop in BMD, the change in bone density status remains low. This is in accordance with data from bisphosphonate trials using CaVitD as a control group, which showed that there is no clinically significant difference in fracture risk despite changes in BMD. As such, mandating patients to take CaVitD alone while on prolonged ADT may suffice, and we propose that steps should be taken to standardize dosing and encourage patient compliance.

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PEER REVIEW OF TARGET CONTOURS: UTILIZING FORCED FUNCTIONS WITHIN ARIA TO IMPROVE COMMUNICATION, COMPLIANCE, AND PROCESSES

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Purpose: Peer review (PR) is a key quality indicator (CPQR) and Accreditation Canada requirement, defining good clinical practice in Radiation Oncology. Several PR steps are imbedded into the care path of our electronic medical record (ARIA®). Currently, for target volume review, a "Contour Peer Review" ("CPR") task is automatically generated in ARIA® for all adjuvant and radical cases as well as for high precision palliative cases. The "CPR" task must be completed before a case can be advanced to the planning phase. Currently the Radiation Oncologist (RO) has the option to cancel the task, however documentation is not always provided as to why the task is cancelled. Quarterly internal audits help to determine compliance with national PR standards and to identify barriers. Current audits have shown that up to **22%** of "CPR" tasks are cancelled without documentation. The objective of this Quality Improvement project is to utilize the existing EMR along with Forced Functions to better track and document rates of task completion and reasons for task cancellation. Information gained from improved documentation may allow our department to further develop and improve our peer review process efficiency.

Materials and Methods: Utilizing ARIA® an existing "CPR" task, which will be enhanced to include a new questionnaire created that (as a Forced Function) must be completed prior to completing the task. The (RO) will be directed to complete all "CPR" tasks and will not have option to cancel the task. The Forced Function questionnaire will include 4 options to communicate why the task has been completed.

1. Contour peer review completed by second RO
2. Contour peer review **not** needed as case is palliative
3. Contour peer review **not** completed as no second RO available
4. Contour Peer review **not** completed as case is urgent and cannot be held up.

Results: Trial of the new "Contour Peer Review" Forced Function is anticipated to begin April 1, 2019 and run until June 30 2019. Utilizing reports/reporting functions within ARIA® descriptive results (including % of plans with completed "Contour Peer Review"; breakdown and frequencies for reasons why "Contour Peer Review" was not completed) will be analyzed by July 26, 2019.

Conclusions: As we are working towards peer review as a mandatory task for all cancer patients requiring radiation therapy prior to first treatment, This Quality Improvement project will: 1) improve target contour PR compliance prior to treatment planning; 2) decrease number of required re-plans identified during Full Plan peer review step; and 3) improve local process based on identified barrier(s) to completing "Contour Peer Review".

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ESTABLISHMENT OF 1ST BOARD-CERTIFIED RADIATION ONCOLOGY RESIDENCY PROGRAM IN A WAR-TORN NATION: EXPERIENCE FROM IRAQ

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Purpose: Board-certified residency programs are important for safe and competent radiation oncologists in the developed stable nations. In a war-torn nation, like Iraq, there was a gap in this field for many years.

Materials and Methods: Descriptive report of the steps, challenges and outcomes after graduation of two batches of the first board-certified radiation oncology program in Iraq.

Results: After 18 months of technical and logistical preparations, a group of local and external faculty members were invited by an external board-certified radiation oncologist to establish the required syllabus of the first board-certified program in radiation oncology, which comes with a total of 100 post-graduate academic credits along four calendar years after internship (25 theoretical and 75 practical credits; each credit equals 15 theoretical hours or 45 practical hours). After passing the entry exam, accepted residents were four in 2013 and two in 2014. Evaluation included regular in-term practical assessments and quizzes, seven papers at the first in-house annual assessment (in radiation oncology, cancer and radiation biology, medical physics, radiological anatomy, tumour pathology, onco-pharmacology, medical statistics/research methodology and cancer epidemiology), followed by a comprehensive examination (in tow papers) at the board headquarter. Annual evaluations with enrolling in the American College of Radiology In-Training examination in radiation oncology were arranged. The final assessment included logbook and skills' review, graduation thesis or publication, two-papers written exam, and an exit practical examination conducted by external examiners.

Conclusions: It was a challenge in Iraq to build its human resources in modern radiation oncology. In spite of these difficult circumstances, 1st certified board residency program in radiation oncology was successfully started in Iraq and six of its graduates became specialists by 2017 and 2018 and they became qualified to help in addressing the shortage of radiation oncologists in this war-torn nation.

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CHARACTERIZING THE INITIATION, COMPLETION, AND INTEGRATION OF ENTRUSTABLE PROFESSIONAL ACTIVITY ASSESSMENTS IN RADIATION ONCOLOGY RESIDENCY TRAINING AND CLINICAL WORKFLOW: AN INSTITUTIONAL PILOT OF COMPETENCE BY DESIGN

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Purpose: Canadian Radiation Oncology residency training will transition to Competence by Design (CBD) in July 2019. However, little is known about the initiation and completion of CBD's Entrustable Professional Activity (EPA) assessments in practice and their impact on clinical workflow in Radiation Oncology. A pilot of CBD was designed to: 1) characterize the initiation and completion of EPA assessments by residents and staff radiation oncologists; 2) characterize the perceived impact of assessments on clinical workflow; and 3) ascertain the perspectives of residents and staff on how the implementation of assessments can be improved.

Materials and Methods: Six residents (PGY2-5) and eight staff radiation oncologists were recruited at our centre. All participants received an orientation to CBD. The Core of Discipline stage was piloted for one block and four clinical EPAs were assessed using online evaluation forms. Anonymized evaluations were analyzed to characterize completion. Participants were asked to complete anonymized pre-post intervention surveys. Focus groups were conducted with staff and residents separately to qualify the survey data.

Results: Surveys were completed by four of six residents and five of eight staff. Four out of four residents requested assessments at least once a week. All staff and residents reported no declined resident assessment requests. The staff-reported percentage of direct observations based on part of an interaction (66%, SE 9.27) was significantly greater than the percentage based on all of an interaction (34%, SE 9.27) ($p<0.05$). Five out of five staff gave verbal feedback after a direct observation by the end of clinic and four out of five staff completed the corresponding assessment forms by the end of the week. Five out of five staff reported completing assessments at least once per week, though the average number of evaluations completed per block was 3.66 (range: 3-5, mode: 3). 31.8% of evaluations did not contain narrative comments. Three out of six staff-resident dyads had evaluations lacking narrative comments (range: 33%-75%, mean: 56%). One out of 15 narrative comments contained justifications for numerical ratings, three out of 15 contained specific examples, and zero out of 15 provided recommendations for improving performance. Three out of five staff agreed that integrating assessments into their clinical workflow was stressful. Three out of five staff stated that EPA assessments have a negative impact on clinical workflow. The need for a culture of coaching and improved assessment tool accessibility arose as themes in the focus groups.

Conclusions: EPA assessments were successfully piloted over one block, with weekly initiation and completion by residents and staff, respectively. Ongoing challenges include improving the frequency and quality of written narrative feedback and decreasing the stress and perceived negative impact of integrating assessments into clinical workflow. Developing mobile-accessible online assessment tools and a culture of coaching for residents and staff may help optimize the transition to CBD in Radiation Oncology residency training.

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THYROID CANCER PATIENT INTERNET USE PATTERNS

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Purpose: Thyroid cancer incidence rates and Internet use are both increasing. Thyroid cancer is common in young patients, who are most likely to use the Internet.

Objectives: The purpose of this study is to characterize thyroid cancer patient Internet use and search patterns, the perceived quality of online resources, and their effects on clinical care.

Materials and Methods: From May to December 2017, patients with thyroid cancer attending new patient and follow-up radiation oncology appointments at two tertiary cancer centres were invited to complete a survey about Internet use. At these tertiary centres, radiation oncologists see all thyroid cancer patients from low- to high-risk for surveillance only, radioactive iodine, and external beam radiotherapy, in consultation and long term follow-up. The patient survey included closed- and open-ended questions about demographics, Internet usage, search patterns, and the usefulness of the Internet as a resource.

Results: The response rate was 54% (39/72). Respondents were of varied ages (28% aged 19-39, 44% aged 40-59, and 28% aged 60-79), predominantly female (69%), and mostly diagnosed with thyroid cancer in the past five years (75%). Almost all

participants (97%) used the Internet, and 87% had searched for thyroid cancer information. The majority (94%) used the search engine Google. Patients most often looked for information about treatment (94%) and symptom management (76%). Patients most often read websites from non-profit organizations (62%), academic or healthcare institutions (48%), or commercial websites (41%). Patients evaluated content quality by comparing several resources (71%), discussing with a physician (56%) or using a credible academic or government site (53%). Online information was somewhat hard to understand for 32% of respondents, but 91% found it useful. More than half (60%) of patients reported that treatment decisions were affected by web resources, and information helped 50% of patients make decisions with their physicians. Respondents highlighted a lack of resources on survivorship and less common tumours such as medullary or anaplastic cancer.

Conclusions: This is the first study to examine thyroid cancer patients' Internet use. Clinicians should recognize that patients overwhelmingly access online information that often impacts their treatment decision-making. Many patients do not simply select the first search results, and actively assess website quality. However, there are gaps between what information patients seek, and what they find. Clinicians can play a key role in guiding thyroid cancer patients through the abundance of web-based information and assisting them in interpretation. Educators can also use this information to guide resource development, tailoring content and design to thyroid cancer patients' needs.

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QUESTIONING THE QUALITY OF ONLINE THYROID CANCER INFORMATION

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Purpose: Thyroid cancer is the cancer with the highest incidence amongst young people in Canada. As such, many thyroid cancer patients likely use the internet to seek information which may sway decision-making. Thus, it is essential to understand the quality of web-based thyroid cancer resources.

Objectives: This project aims to evaluate the quality of online information for thyroid cancer patients.

Materials and Methods: "Thyroid cancer" was searched on Google and meta-search engines Yippy and Dogpile. The "top 100" websites with patient information on thyroid cancer were evaluated with a previously-validated structured rating tool assessing quality markers such as website currency, attribution, interactivity and content. Content was assessed based on comprehensiveness, accuracy, and readability. Responses to general and personal "patient" questions were evaluated for promptness and accuracy. Two reviewers independently coded the first 20 sites to ensure inter-rater reliability, then one reviewer coded the remaining sites.

Results: A search for "thyroid cancer" returned 4,760,000 hits on Google and 610,759 on Yippy; Dogpile provided no total. Only 26% of the top 100 websites disclosed authorship and 56% cited sources. 18% contained bias or opinion. 74% had dates of creation or last update, with only half of those dates occurring within the past two years. Only 2% of websites were comprehensible without high school education based on the Flesch-Kincaid Grade Level. Seventy-six percent of websites included information on at least six of the eight content categories examined. Websites most often discussed the definition (94%), diagnosis (92%) and treatment (94%) of thyroid cancer. Least common were prevention, on 37% of websites, and incidence or prevalence on 57%. While diagnosis and treatment were among the most frequently presented topics, they were also the most often incomplete or inaccurate: only 50% of diagnosis explanations were complete and accurate, and 47% of treatment. Eighty-three websites were contacted with "patient" questions, and 50 replied, 48 within one week. Seventeen responses answered the general question, and nine of these also addressed the personal one. Two responses addressing both questions contained potentially harmful information. Forty-one responses referred patients to their healthcare providers, and 29 linked to online resources.

Conclusions: Websites about thyroid cancer are abundant, but their quality is variable. This is the most comprehensive examination of English resources to date. It shows that many websites lack quality markers that patients can use to assess information themselves, such as authorship, citations and dates. Further, information is difficult to comprehend, and often incomplete with respect to topics of importance to patients, including diagnosis and treatment. Knowing this, educational resource developers can remedy these deficiencies, and healthcare providers can aid thyroid cancer patients in finding trustworthy online resources.

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BRIDGING THE GAP: IDENTIFYING BARRIERS TO ENABLE THE INTEGRATION OF TOBACCO CESSATION INTO CANCER PATIENT CARE

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Purpose: Evidence-based practice is an expectation in healthcare. However, practicing in this manner is not always achievable. This can lead to gaps between what is known to be best practice and what is actually done. Tobacco cessation in cancer care is a good example of this kind of gap. Tobacco use can render treatment less effective and can have a negative impact on outcomes. Despite this knowledge, many patients continue to use tobacco after their diagnosis and during treatment. Knowledge to Action (KTA) frameworks are beneficial in closing knowledge gaps by aiding in implementing and sustaining evidence-based practices and policies. It is the goal of this study to identify the barriers to tobacco cessation within the local context of this centre and use this information in conjunction with a KTA framework to form a successful and sustainable tobacco cessation model.

Methods and Materials: Radiation oncologists (n=4), radiation therapists (n=7) and radiation oncology nurses (n=2) were invited to participate in uniprofessional focus groups and semi-structured interviews. Questions regarding barriers to providing cessation support were used to help guide the discussions. Audio recordings were taken of each group and interview and transcribed verbatim. These transcripts were analyzed by a coding process which was utilized to identify themes within the data. Information gathered from a local tobacco cessation working group and a review of tobacco cessation processes in neighbouring provinces was used to support the data from this study.

Results: Insufficient recourses and unclear roles and responsibilities were the main themes identified in the data by all three professional groups. Data from the provincial working group and neighbouring centres showed a large variation in tobacco cessation practices.

Conclusions: The consequences of continued tobacco use during cancer treatment highlights the need for a tobacco cessation model within our department. Identifying the barriers to tobacco cessation within the context of this centre and applying the information to a knowledge to action framework outlined a plan for the development of a tobacco cessation model. This framework also outlined methods to evaluate this model, monitor it's use, and propose ways to ensure its sustainability. The goal of this

process is to ensure that our patients are receiving care based on the best available evidence.

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EVALUATION OF A JUNIOR FACULTY MENTORSHIP PROGRAM IN A RADIATION ONCOLOGY DEPARTMENT
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Purpose: Although the value of mentorship in academic medicine has been established, the specific components essential to program success remain unclear.

Objective: To evaluate and explore the impact of a junior faculty mentorship program within an academic radiation oncology department.

Materials and Methods: In 2016, our institution implemented a Mentorship Program for junior faculty (on staff <5 years) consisting of: 1) an orientation handbook; 2) educational faculty development sessions; and 3) direct, one-to-one selection and declaration of a mentor. Formal confidentiality agreements are signed, a goals/expectations template is provided, and meeting dates are tracked. Mentors and mentees were invited to participate in a program evaluation using mixed-methodology: a questionnaire followed by a one-on-one semi-structured interview to explore perceptions of the mentorship program. Interviews were conducted by an experienced qualitative researcher who is not a radiation oncologist (ST). Descriptive statistics were used to summarize questionnaire results. Thematic analysis will be used to summarize interview results.

Results: Eleven junior faculty members have selected 11 mentors. None of the participants have requested changes. To date, 15 participants (68%) have completed the program evaluation questionnaire: 10 mentees (six male, four female) and five mentors (four male, one female). The majority (12/15) have participated in the program for >2 years. Duos typically meet formally 2-3 times per year but do report monthly contact. Meetings are primarily arranged by the mentee and occur in-person, either at work or outside. The majority (11/15) report not using or being aware of the goals/expectation template. Although the majority of mentees report having additional mentors, 30% report this as their sole mentorship relationship. Interviews are on-going.

Conclusions: Design and implementation of a junior faculty mentorship program is feasible. Increased education regarding the goals/expectations template is required. Although many junior faculty have additional mentors, some do not, which further highlights the importance of this program for professional development.

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NON-ONCOLOGIST PHYSICIAN AWARENESS OF RADIATION THERAPY AT AN URBAN COMMUNITY HOSPITAL
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Introduction: Appropriate referral for radiation therapy (RT) is crucial for cancer care. Previous work suggests that many non-radiation oncologists who care for cancer patients are uncomfortable referring for RT. We surveyed physicians in a community hospital in Bronx, New York to assess their training in RT and understanding of RT.

Materials and Methods: Invitations to complete an online questionnaire were sent to all faculty and resident physicians at St. Barnabas Hospital. The questionnaire asked about previous training in oncology, RT knowledge self-rating and an objective knowledge assessment of RT indications and effectiveness. Statistical analysis used Pearson chi-square and Fisher's exact test for categorical variables and Student's t-test and ANOVA for interval variables.

Results: Two hundred and forty-seven participants received the invitation email, and 87 responded (35% response rate). Among responders, 19 were attending physicians (22%) and 66 (76%) were residents (two failed to disclose). Fifty-one respondents (59%) were from Internal Medicine (IM) and 20 (24%) from Emergency Medicine. Seventy-two percent of respondents reported caring for >5 cancer patients in the past month, but 45% (37% of IM respondents) never refer patients for RT. Seventy-one percent of respondents stated they received no formal radiation oncology training in medical school, and 47% reported no oncology training at all. Pluralities believed themselves to be "somewhat knowledgeable" about RT indications (49%), benefits (53%), and side effects (55%). Objective assessment mean score was 6.2/12 (median 7) for all respondents. IM respondents scored higher than others (mean 7.7 versus 3.5; $p<0.001$), but only 28% of IM respondents (0% of others) scored 10/12 or higher. Scores did not differ between attending and resident physicians ($p=0.75$), resident PGY level ($p=0.43$), or receiving oncology training in medical school ($p=0.54$). Factors cited by >50% as affecting RT referral decisions either "somewhat" or "a lot" were: type of cancer, patient wishes, family wishes, poor functional status, and life expectancy.

Conclusions: Many physicians are unaware of RT effectiveness or indications, which may affect referral patterns. Previous oncology training was not associated with higher knowledge score.

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SURVEY FOR CHILDREN WITH CANCER UNDERGOING RADIATION THERAPY AND THEIR FAMILIES: ASSESSING WHICH TOOLS ARE MOST EFFECTIVE TO IMPROVE PATIENT EDUCATION AND REDUCE ANXIETY
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Purpose: The purpose of the study was to improve our understanding of the radiation therapy (RT) experience of pediatric patients and their families. Specific objectives were to understand which components of RT are anxiety-provoking; to assess the current tools aimed at helping pediatric patients and their families through RT; and to determine the patient, disease and treatment factors associated with helpfulness of specific tools.

Materials and Methods: The study population consisted of pediatric patients receiving RT and their parents. Parents and patients older than seven years of age were invited to participate. A survey was distributed to study participants asking them to rate on a five-point scale how worrisome they found specific components of RT. They were also asked to rate pediatric treatment tools based on their helpfulness in improving the overall experience. In addition, participants could provide suggestions on how to improve the patient experience in the form of free text. Basic demographic information was captured. A preliminary analysis was conducted using descriptive statistics.

Results: Nine of the 10 families who were approached about the study agreed to participate, yielding a response rate of 90%. The nine participating families consisted of nine parents and two children. The percentages of participants who "strongly agreed" or "agreed" that specific components of RT were worrisome were: 87.5% for masks, 87.5% for "not knowing what to expect" and 37%

for tattoos. The tools during treatment that were most frequently selected as "extremely helpful" or "very helpful" were: having the same therapists treating daily (90%), receiving information about what to expect (89%), warm blankets (78%), daily stickers (60%) and child appointment cards (55%). The education that was most commonly found to be "extremely helpful" or "very helpful" was the information received from the radiation oncologist (82%) and the radiation therapist (80%). Most participants (70%) felt they received enough education.

Conclusions: Most pediatric patients undergoing RT and their families felt they received sufficient education. Masks and not knowing what to expect were the most worrisome aspects of radiation treatment for families. Consistency of care was very important.

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PAN-CANADIAN SURVEY OF MEDICAL RADIATION TECHNOLOGIST'S VIEWS TOWARDS EVIDENCE-BASED PRACTICE, RESEARCH, BARRIERS, AND ENABLERS

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As medical radiation technologist (MRT) professions grow and adapt to rapidly evolving technology, MRTs are challenged to be more active in research. From research, professionals build a body of knowledge and this repository of knowledge is the pre-cursor for evidence-based practice (EBP).

Objectives: To determine the attitudes, perceptions, enablers and/or barriers and level of uptake of EBP and research within the MRT community in Canada. Canadian results will be compared with a similar cohort of MRTs in Spain who have completed the same survey in their country.

Materials and Methods: Utilizing the Canadian Association of Medical Radiation Technologists' (CAMRT) email distribution list, all registered members were sent an invite and link to an on-line electronic survey. The electronic survey included a demographics section, followed by questions asking participants about their perceptions of EBP, research, and barriers. Descriptive statistics including frequencies, descriptives and crosstabs were utilized to analyze data.

Results: Eight-hundred and twenty-seven were surveys submitted (384 were incomplete) resulting in 443 completed surveys available for analysis. Respondents' demographics included: 56.2% RTR, 25.7% RTT, 11.3% RTMR and 6.8% RTNM. The majority of respondents were female (79.7%) and ≥42 years old (56.3%). MRTs strongly agreed that they had a solid understanding of what EBP was (73% RTMR, 80% RTR, 82% RTNM, 95% RTT). Despite agreeing/strongly agreeing (82.4%) that research is important and that there is a solid link between research and EBP (79.9%), just over half of respondents indicated that they were not interested in being active in research (52.7%). Most frequently identified extrinsic barriers to EBP/research included: lack of time, heavy workload, lack of management/physician support, and workplace attitudes/culture. Intrinsic barriers included: research competence/knowledge and confidence in being successful in research. Extrinsic success factors identified included: access to a mentor, enrollment in post-secondary education, dedicated time, support from management, and support from coworkers. Intrinsic success factors were: self-motivation, sense of inquiry/curiosity and satisfaction with collaborating with others. *(note: at time of abstract submission, both Canadian and Spanish surveys were closed with initial, local results analyzed separately only as of Feb 18 2019. Full, international comparison of the two countries will be performed March-June 2019).*

Conclusions: This pan-Canadian interprofessional survey highlights the current landscape with respect to perceptions and uptake of EBP and research amongst MRTs. Further analysis and dissemination of results may offer MRTs, employers, educational facilities and professional bodies' insight into strategies that can be undertaken to improve MRT research participation. Comparison of Canadian and Spanish results offers a novel examination of this topic from an international perspective.

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ADDRESSING THE NEED FOR IMPROVED PROSTATE CANCER PATIENT PRE-SIMULATION EDUCATION

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Purpose: Radiotherapy for prostate cancer requires careful management of bladder and rectal filling, and poor compliance with bladder and rectal instructions results in inefficient use of CT simulator time and other impacts on patient care. This study's purpose was to assess if watching an instructional video and meeting with a radiation therapist (RTT) improved: 1) the patient's understanding of the importance of compliance with the required preparation; 2) the understanding of the potential problems with non-compliance; and 3) recall of the information.

Materials and Methods: Prostate cancer patients were given department specific full bladder and empty rectum instructions both written and verbal at time of consultation. Data was collected on how many prostate cancer patients being planned for radiotherapy complied with the instructions and how many required re-simulation or re-scanning. To improve compliance rates, a short instructional video was made outlining bladder and bowel preparation instructions. Post consultation, the patient would watch the video with an RTT, review the instructions and discuss the impact of not being ready for simulation. Data was then re-collected to assess if these interventions improved compliance rates.

Results: Prior to video teaching implementation, 41.4% (39/94) patients were not ready for simulation. Post-video teaching implementation, 36.2% (34/94) were not ready for simulation. Rebooking a second simulation prior to the video implementation was 7.4% and rebooking a second simulation after video implementation was 6.4%.

Conclusions: The addition of the video teaching with a radiation therapist at time of consult did not result in a decrease in re-bookings or re-simulations. Further study is required for new approaches to prostate preparation and to seek patient feedback on how to improve processes.

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DEVELOPING A STRATEGIC PLAN FOR A PROVINCIAL RADIATION TREATMENT PROGRAM TO ADVANCE THE QUALITY OF CARE FOR PATIENTS

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Purpose: The Radiation Treatment Program (RTP) at Cancer Care Ontario, improves the access, safety and quality of radiation treatment (RT) for patients. In the past, the RTP strategic planning initiatives were focused on the provincial RT capital investment needs. However, the increasing complexity of the healthcare

system and advancements in technology make it imperative for clinical programs, such as the RTP, to proactively identify strategic priorities to improve the quality of care for patients. The objective of this initiative is to develop the first provincial RTP Strategic Plan to define the future state of the program's vision, goals, and strategic priorities to improve the quality of care in Ontario.

Materials and Methods: RTP led a mixed-methods strategic planning process that assessed the current and future state of RT in Ontario, through semi-structured interviews with over 130 clinicians, administrators, regional partners, and patient family advisors. An international environmental scan guided the process. Provincial RT operational data were used to understand the current environment and support priority identification. Triangulation of data sources informed the strategic priorities and how the program will define success over the next four years.

Results: Preliminary results suggest the mixed-methods strategic planning process was successful in identifying five strategic priorities and associated actions for how the program will advance the quality of care. The identified priorities included understanding and improving integrated wait times (time from diagnosis to first day of cancer treatment), developing an equitable, quality-focused, and sustainable funding model for radiation services, improving access to care in marginalized populations, standardizing peer review of RT plans, and assessing and supporting innovative treatment approaches.

Conclusions: The strategic planning process can be effectively applied to the development of a provincial strategic plan to outline strategic opportunities and build consensus and support amongst stakeholders. The process results in identifying a program's desired future state to improve the quality of care for patients.

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PATIENT REPORTED OUTCOMES USED IN RADIATION PROGRAMS ACROSS CANADA

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Purpose: The Canadian Partnership for Quality Radiotherapy (CPQR) supports the use of patient reported outcomes (PRO) as an essential component of quality patient care and is committed to developing processes that promote the use of PRO. The overall aim is promote PRO as both a point-of-care tool and a cancer system performance tool in population-based learning.

Objectives: To conduct a pan-Canadian environmental scan to determine what PROs are in place; how they are being used; barriers and facilitators to their use and implementation, as well as the potential utility of guidance from CPQR regarding PRO use in the radiotherapy (RT) setting.

Materials and Methods: A multidisciplinary PRO Working Group within the CPQR was assembled to provide guidance on the collection and use of (RT) specific PRO measures in radiation oncology programs (ROPs) across Canada both to support local uptake and facilitate pan-Canadian learning and knowledge mobilization. An interview framework was developed by the working group to determine what PRO tools are in use, barriers and facilitators to PRO use and implementation, and to elicit if centres have an interest in guidance from CPQR on PRO. Semi-structured telephone interviews were held (July to October 2018) with select members of Radiation Oncology Programs across Canada. Participants were identified by members of the CPQR National Quality Advisory Committee as the most knowledgeable individual(s) with regards to the use of PROs within their centre, particularly in the RT setting. Purposeful sampling was done to ensure representation by pan-Canadian geographic region, centre size and academic status. Interviews were held by telephone, audio-recorded and coded for common themes.

Results: Interviews were held with individuals from 20 centres across Canada at which time we determined saturation had been reached. Participating centres represented Ontario, Quebec, Atlantic Provinces, Alberta, Manitoba and British Columbia. Use of PROs varies considerably across the country from no current PRO use to PRO use being standard of care for every patient and multiple PROs in place. A total of 13 different PRO instruments were identified and their use within the centre described. A multitude of facilitators and barriers (e.g. lack of resources, patient/physician buy-in, patient burden, IT infrastructure) were reported. All centres expressed a strong desire to learn from other Canadian centres and endorsed guidance from CPQR on the use of PROs in the radiotherapy setting.

Conclusions: The use of PROs varies across Canadian Radiation Oncology Programs. The CPQR will continue to take a pan-Canadian approach to support consistent use and expansion of PRO use. Development of a CPQR Guidance Document on Patient Reported Outcomes is underway to inform PRO use and implementation of PROs into clinical care programs across Canada.

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90-DAY MORTALITY AFTER RADICAL RADIOTHERAPY FOR HEAD AND NECK CANCER: A POPULATION-BASED COMPARISON BETWEEN RURAL AND URBAN PATIENTS

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Purpose: We previously demonstrated a 3.6% 90-day mortality in patients treated with radical radiotherapy for head and neck cancer. This study assesses whether this rate differs between patients living in rural and urban areas, as we hypothesized decreased access to supportive care services (e.g. speech-language-pathologists, dietitians) in rural areas could result in higher rates of treatment-related death (e.g. dehydration, aspiration pneumonia).

Materials and Methods: All head and neck cancer patients treated between 1998-2014, with radiotherapy with or without chemotherapy and/or surgery in British Columbia were included. Two classification systems (Statistics Canada [SC] and Modified Statistics Canada [mSC]) were used to divide patients into rural and urban centres, because of the controversy in which is most appropriate. In SC, rural areas are defined as a population <1,000 and a density of <400 people/km2 or 1,000-30,000 people with a density ≥400/km2 and urban areas as population of ≥30,000 or more and density ≥400/km2. mSc classifies a population <30,000 as rural and ≥30,000 as urban. Multivariable logistic regression analyses were performed to assess associations between 90-day mortality and rurality and other patient or treatment characteristics.

Results: 5,554 patients were included in this study. Median age was 63 years, 76% was male and 77% of patients was treated with ≥60 Gy. According to the SC and mSC definitions, 53% and 68% of patients, respectively, lived in urban centres. Neither definitions were associated with 90-day mortality in univariate or multivariable analyses (SC: OR 0.95, 95%CI 0.68-1.31, p=0.74;

mSC: OR 1.23 95%CI 0.86–1.77, p=0.26). In both models, factors associated with a lower 90-day mortality were age <60 years, Stage I/II, radiation dose of ≥70Gy and initial surgery (p<0.05). Factors associated with higher early mortality were oral-cavity primary tumour, Stage IVb, radiation doses between 0-39 Gy, 40-49 Gy and 50-59 Gy (p<0.05).

Conclusions: After controlling for potentially confounding factors, we did not find an association between 90-day mortality and rurality in patients that were treated with radiotherapy for head and neck cancer in British Columbia.

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POPULATION-BASED OUTCOMES OF PARAGANGLIOMAS IN BRITISH COLUMBIA

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Purpose: Paragangliomas are rare neuroendocrine tumours located along the sympathetic or parasympathetic paraganglia. This study assessed population statistics, treatments and outcomes for patients diagnosed with paragangliomas and related neuroendocrine tumours in our province.

Materials and Methods: A retrospective chart review was performed of 138 consecutive patients diagnosed with paragangliomas and related neuroendocrine tumours in our province from 1998 to 2018. Patient, disease, and treatment outcomes were assessed. Survival analysis was performed using the Kaplan-Meier method.

Results: The median age at diagnosis was 55 years and 82 patients were female (59%). The most common presenting symptoms were hearing loss or tinnitus (n=47) for jugulotympanic tumours or a palpable mass (n=30) for neck tumours. The most common primary tumour sites involved the juguolotympanic paraganglia (44%) and carotid body paraganglia (30%). Forty-two patients had multicentric disease (30%). Twenty-four patients had malignant tumours (17%), including lymph node involvement (n=5), bone metastases (n=10), organ metastases (n=3) and both bone and organ metastases (n=6). Initial treatment was surgery for 49% (n=68), radiation therapy for 39% (n=54), embolization for 2% (n=3) and chemotherapy for 1% (n=2). Eleven patients were managed solely via observation. Ten-year overall and local recurrence-free survival was 96% and 42%, respectively, for patients initially receiving surgery and 97% and 83%, respectively, for patients initially receiving radiation therapy. With respect to benign and malignant tumours, overall and local recurrence-free survival at 10 years was 92% and 72%, respectively, for patients with benign tumours and 67% and 24%, respectively for patients with malignant tumours.

Conclusions: We found that paraganglioma patients in our province were most often female, were typically diagnosed at age 50-60, and often developed tumours involving the jugulotympanic and carotid body paraganglia. Long-term overall survival for paraganglioma patients were favourable after both surgery and radiation therapy, although patients initially receiving surgery had poorer 10-year local recurrence-free survival (42%) compared with those initially receiving radiation therapy (83%).

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PATTERNS OF HEREDITARY REFERRAL AND IDENTIFICATION OF GENETIC MARKERS FOR PARAGANGLIOMAS IN BRITISH COLUMBIA

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Purpose: Paragangliomas are rare neuroendocrine tumours with a strong genetic component. Recent estimates suggest that 30-50% of paragangliomas may be hereditary. The purpose of this study was to examine the: 1) frequency and patterns of hereditary referrals; and 2) genetic test results in patients diagnosed with paragangliomas or related tumours at our institution.

Materials and Methods: A retrospective chart review was performed to collect and analyze genetic details regarding 138 patients with paragangliomas and related tumours in our province from 1998 to 2018. Parameters collected included: age at diagnosis, sex, family history of paragangliomas or related tumours, the frequency of hereditary referrals, and the outcomes of hereditary testing. Analysis was performed using SPSS.

Results: Fourteen patients reported a known family history of paragangliomas or related tumours (10%). 39 patients were referred for hereditary testing (28%). Variables associated with referral included: family history of paragangliomas (n=14), bilateral paragangliomas (n=17), and multicentric paragangliomas (n=18). Referred patients had a median age at diagnosis of 41 years, compared to 55 years in the population studied. 31 patients completed testing (23%). Of those tested, 20 patients showed evidence of genetic markers (65%). There were 13 cases of SDHD mutations, three cases of SDHB mutations, and one case each of SDHA, SDHC, HIF2A and Von-Hippel Lindau disease. Variables associated with genetic markers included: family history of paragangliomas (n=12), bilateral paragangliomas (n=14), and multicentric paragangliomas (n=16). The median age at initial diagnosis of those with positive results was 38 years.

Conclusions: In our study, 14% of patients showed evidence of genetic markers, which represented 65% of those actually tested. Only 28% of patients were referred for hereditary testing, although annual rates increased to greater than 50% in the past five years. These results suggest a history of under-referral for hereditary testing for paraganglioma patients in our province.

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THE IMPACT OF ROUTINE ESAS USE ON EMERGENCY DEPARTMENT VISITS AND HOSPITALIZATIONS: A POPULATION-BASED RETROSPECTIVE MATCHED COHORT STUDY

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Purpose: The Edmonton Symptom Assessment System (ESAS) is a standardized instrument to measure symptoms among ambulatory cancer patients in Ontario. The aim of the current study was to examine the effect of ESAS use on visits to emergency department (ED) and hospitalizations in cancer patients.

Materials and Methods: This was a retrospective matched cohort study conducted in Ontario, Canada. The study included

all patients aged 18 or older who were diagnosed with cancer between January 2007 and December 2015. Patients were considered exposed if they were screened with ESAS at least once during the study period and their first ESAS screening date was defined as the index date. Each exposed patient was matched randomly to a cancer patient without ESAS using a combination of hard matching (birth year ± 2 years, cancer diagnosis date ± 1 year, cancer type and sex) and propensity score matching (14 variables including cancer stage, treatments received, and comorbidities). Each patient's follow-up time was divided into three phases of care: initial, continuing, or palliative care. A multivariable Andersen-Gill recurrent event model was used to evaluate the effect of ESAS on the rate of healthcare use.

Results: The analysis included 128,893 matched pairs that were well balanced on baseline measures. After adjusting for other variables, patients with ESAS had lower rates of both ED visits (HR: 0.92, 95% CI: 0.91-0.93) and hospitalizations (HR: 0.86, 95% CI: 0.85-0.87) compared to patients without ESAS. ESAS screening was associated with lower rates of ED visits and hospitalizations in the initial and palliative phases of care but slightly higher rates in the continuing phase of care.

Conclusions: ESAS use is independently associated with decreased rates of both ED visits and hospitalizations in the initial and palliative phases of care.

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SECONDARY MALIGNANCY AFTER RADIOTHERAPY FOR TESTICULAR CANCER: DOES THE RISK PERSIST IN THE MODERN ERA?

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Purpose: Secondary primary malignancy (SPM) is a significant concern in men with testicular cancer (TC), noting the excellent long-term prognosis. The trend in recent years has been for more judicious use of radiotherapy (RT), smaller and more conformal treatment fields, and lower doses. The purpose of this study is to determine if the SPM risk persists in the modern era.

Materials and Methods: We evaluated SPM and long term survival rates in men diagnosed with TC between 1973 and 2010, as reported to the SEER registry. Kaplan Meier survival (KM) and Cox regression analyses were performed, dividing patients into cohorts diagnosed 1973-1980, 1981-1990, 1991-1995, 1996-2000, 2001-2005, and 2006-2010. Propensity score matching analysis was performed at a 1:1 ratio, matching patients treated with and without RT.

Results: 41,010 men were included in the study; 943 men with non-germ cell histologies were excluded. 30 year SPM rate was 14.7% (no RT) versus 22.4% (RT). RT was associated with a significantly higher SPM rate on multivariate analysis when assessing non-seminoma and seminoma patients separately, for all time cohorts evaluated, and on assessment of the propensity score matched population. Despite the assumed modernization in radiotherapy, the SPM risk for all time cohorts strictly superimposed, suggesting that improved radiation techniques did not had any effect on the prevention of SPM. Chemotherapy was significantly associated with SPM in the non-seminoma cohort, but not the overall, seminoma, or propensity matched cohorts.

Conclusions: This study confirms the high rate of SPM in men treated with RT for TC with an absolute increase of 7.7% compared to patients treated without RT. There is no improvement using modern techniques, and therefore the use of techniques with less scatter dose, for example proton therapy, should be considered.

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HOW SCIENTIFIC EVIDENCE IS USED TO ADOPT COMPLEX INNOVATIONS IN CANCER CARE: A MULTIPLE-CASE STUDY FROM NOVA SCOTIA, CANADA

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Purpose: Health care delivery and outcomes can be improved by using innovations (i.e., new technologies and practices) supported by scientific evidence. However, scientific evidence may not be the foremost factor in adoption decisions. We sought to examine the role of scientific evidence in decisions to adopt complex innovations in cancer care.

Materials and Methods: Using an explanatory, multiple case study design, we examined the adoption of complex innovations in five purposively-sampled cases in Nova Scotia, Canada. Cases were sampled to obtain variation on three criteria: 1) type of innovation; 2) evidentiary base; and 3) contextual factors (e.g., setting, timing, individuals involved). Data were collected via documents and key informant interviews. Data analysis involved an in-depth analysis of each case, followed by a cross-case analysis to develop theoretically informed, transferable knowledge on the role of scientific evidence in innovation adoption that may be applied to similar settings and contexts.

Results: The cases selected included prognostic and therapeutic innovations, including Intensity Modulated Radiation Therapy. Across the five cases, data were collected from 32 key informants and >100 documents. The analyses identified key concepts alongside important caveats and considerations. Key concepts were: 1) scientific evidence underpinned the adoption process; 2) evidence from multiple sources informed decision-making (scientific evidence, clinical experience, local data, patient experience, and information from other jurisdictions); 3) decision-makers considered three key issues when making decisions (expected budgetary and operational implications, expected impact on patients, and equitable access to care); and 4) champions were essential to eventual adoption. Caveats and considerations were: 5) urgent problems may compel innovative solutions; 6) short-term financial pressures may expedite decisions; and 7) adopting later in time (relative to peer organizations) minimizes risk.

Conclusions: The findings revealed the different types of issues decision-makers consider while making these decisions and why different sources of evidence are needed in these processes. Future research should examine how different types of evidence are legitimized and why some types are prioritized over others.

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RADIATION INDUCED SECONDARY LUNG CANCER IMPACTS MAINLY EARLY STAGE BREAST CANCERS

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Purpose: Using a modified BEIR-VII model, we previously reported an excess of lifetime attributable risks of secondary lung cancer (SLC) after breast radiotherapy (RT), with a 4.3% excess risk for a patient treated at age 50 years. The SLC risk was low the first 10 years and raised sharply after 20 years. This long delay makes difficult assessing this risk in trials and meta-analysis. We also reported that the SLC risk is 4-folds smaller using APBI compared to whole breast RT.

Objective: To confirm the long-term excess risk of SLC due to radiotherapy for various stages of breast cancers.

Materials and Methods: Patients from the SEER registry diagnosed for breast cancer between 1988 and 2012 were accrued in the study. Extracted variables included the date of breast cancer diagnosis, cancer stage, patient's age, radiotherapy delivery, survival, status at study cut-off, and date of lung cancer. Kaplan Meyer statistics was used to calculate the SLC free survival and log-rank test to compare survival with or without RT for each cancer stage.

Results: A total of 641,000 cases were identified, with 325,852 patients (51%) treated with radiotherapy. There was 11,416 DCIS (2%), 325,646 Stage I (51%), 224,748 Stage II (35%), and 79,190 Stage III (12%). Early stages had a longer median survival and a significant excess of SLC risk when treated with RT compared to higher stages. For DCIS the 28 years SLC risk was 8% with RT and 4% without RT (p=0.002). This corresponds to a predicted excess of mortality of 3.2%.

Conclusions: Early stage breast cancers have an excess of long term SLC after RT, which is not significant for advanced stages. APBI reduces the lung exposure to radiation and may reduce this risk.

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IMPACT OF DISSEMINATION OF CHOOSING WISELY CANADA (CWC) RECOMMENDATIONS ON UTILIZATION OF PALLIATIVE SINGLE FRACTION (SFRT) FOR BONE METASTASES IN MANITOBA

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Purpose: Despite level 1 evidence supporting palliative SFRT for management of symptomatic bone metastases, Multiple Fraction Radiotherapy (MFRT) use persists. In 2015, in order to reduce MFRT use, a provincial cancer program disseminated CWC recommendations which endorsed SFRT for symptomatic bone metastases to each radiation oncologist. This study aimed to determine the impact of dissemination of CWC guidelines on uptake of SFRT, and identify patient/treatment/disease factors associated with use of MFRT.

Materials and Methods: This retrospective population-based study identified all patients treated in a Manitoba from January 1, 2016 to December 31, 2016 with palliative RT for a bone metastasis using the provincial electronic medical record. Patient, treatment, and disease characteristics were extracted and tabulated by fractionation schedule. Univariable and multivariable logistic regression analyses were performed in order to identify risk factors associated with the receipt of MFRT.

Results: Eight-hundred and seven patients received palliative RT for bone metastases with a mean age of 70 (range 35-96), of whom 40.5% were female, and 61.3% had uncomplicated bone metastases. The most common treatment sites were spine (43.9%), pelvis (30.6%), and lower extremity (9.7%), and the most common primary malignancies were prostate (27.1%), lung (20.6%), and breast (15.9%). MFRT was used in 62% of cases, which was unchanged from 2015 (MFRT use was 61.9% in 2015). On Multivariable analysis, gastrointestinal (OR 5.3, 95% CI 2.2 to 12.4) or lung (OR 3.3, 95% CI 1.8 to 6.1) primary, presence of a complicated bone metastases (OR 4.3, 95% CI 2.8 to 6.5), and treatment at a subsidiary site (OR 4.4, 95% CI 2.1 to 9.1) were associated with increased odds MFRT.

Conclusions: Dissemination of CWC recommendations alone was ineffective at increasing use of palliative SFRT by radiation oncologists in a Manitoba. Coordinated knowledge translation efforts are therefore warranted in order to encourage increased uptake of SFRT in Manitoba.

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IMPLEMENTATION OF A PROSPECTIVE MULTIDISCIPLINARY CLINICAL DATABASE FOR HEAD AND NECK CANCER AT THE OTTAWA HOSPITAL

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Purpose: Head and Neck cancers represent approximately 3% of all cancers diagnosed in North America with an increasing incidence. With the constantly changing landscape and multidisciplinary approach required for the care of these cancers, patient outcome must be documented with utmost precision without the biases and inaccuracies which accompany retrospective medical chart reviews. To address this, we built a prospectively maintained Multidisciplinary Head and Neck Cancer database initialized by the specialist at the first patient consultation and updated at each subsequent visit for later retrospective analysis. Here we describe challenges encountered during a trial run of this database as well as lessons learned.

Materials and Methods: This database was created using Microsoft SQL with the help of the Ottawa Hospital Research Institute and allows for the storage of demographic, socioeconomic, diagnostic, intraoperative and postoperative information including management plan, complications as well as side-effects. We simulated prospective data gathering by using data for patients treated in 2015 and 2016 for oropharyngeal cancer at the Ottawa Hospital in order to assess future feasibility in a clinical setting.

Results: One hundred and seven cases were entered into the database between June and August 2018. Challenges encountered included: 1) software restraints, control and security checks limiting efficacy; 2) difficulty meeting the vast array of database needs from differing specialties while maintaining software simplicity in user interface; as well as 3) streamlining data entry to minimize utilization of free text; 4) determining who would be responsible for data entry in a prospective fashion. We are planning a quality assurance analysis of data entered to ensure reliability of database.

Conclusions: The use of a multidisciplinary head and neck database prospectively maintained by each physician will allow for accurate collection of patient diagnoses, treatment outcomes and toxicities for use in correlative, long term outcome and validation studies. Challenge to address during the inception of such multidisciplinary databases include simple user interface and ease of access in order to avoid compromising clinical efficiency and drop-down menus encompassing all possibilities in order to minimize need for free text.

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A SINGLE CENTRE'S REVIEW OF EMERGENT AND URGENT PALLIATIVE RADIOTHERAPY: ARE WE COMPLIANT WITH PROVINCIAL POLICY?

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Purpose: There is little information in the literature and no national guidelines regarding timeliness of palliative radiotherapy (RT)

based on indication. This study aimed to report on a single centre's experience with RT prioritized as "emergent" and "urgent", including review of indications for, and timing of such RT considering provincial quality assurance (QA) guidelines.

Materials and Methods: A retrospective chart review was conducted of patients coded by physician as requiring "emergent" or "urgent" RT from January 2016 to December 2017. Extracted data included details of patient demographics, disease and treatment. The province of New Brunswick has a Cancer Treatment Access Repository (CTAR) QA guideline, specifying indications/definitions of urgent and emergent RT as well as expected timelines for delivery (<=24 hours for emergent RT: cord compression, superior vena cava obstruction (SVCO), hemorrhagic syndromes and symptomatic cerebral metastases, <=72 hours for urgent RT: all other palliative cases). The centre has a category of "CT Sim/Start" for MD request of same day RT.

Results: A total of 307 RT cases were included: 97 coded as "emergent" and 268 "urgent". Over half (50/97, 52%) of the "emergent" cases would have been classified as urgent by CTAR definition. Of the 47 emergent cases appropriately prioritized by CTAR definition, 57.4% were cord compressions and 19.1% were SVCO. Only 11 of the 268 (4%) "urgent" cases would have been classified as emergent by CTAR definition. Physicians requested 186 same day CT Sim/Starts: 35/74 categorized as "emergent" did not meet CTAR definition to require treatment within 24 hours, and only eight out of 112 cases categorized as "urgent" would have met CTAR definition of emergent to require same day RT. A total of 22 patients were treated outside of clinical hours (15 "emergent", seven "urgent"). Of the cases classified as per CTAR definitions, 91.5% and 81.3% of emergent and urgent cases respectively, met the provincial wait time target.

Conclusions: The results of this single centre study show gaps in clinical practice versus provincial QA guidelines for categorization of emergent and urgent palliative RT. Factors beyond emergent RT should be considered as potential indications for same day Sim/Start in order to properly implement a policy, such as patient convenience and simulator availability. Given the potential impact on centre resources and patient care, further investigation is warranted to determine whether local clinical practice should further align with policy or whether the provincial guidelines of 2012 requires modification.

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IMPROVING PATIENT EXPERIENCE IN HEALTH CARE AND ONCOLOGY: A SCOPING REVIEW

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Purpose: Patient-reported experience measures (PREMs) gather information directly from patients and capture their perspectives on their health care. This includes what matters to them and how they experience care. Health care deficiencies and gaps identified by PREMs can lead to quality improvement interventions. The purpose of this review was to identify published and unpublished evidence on initiatives aimed to improve patient experience and to identify areas of application in health care, measurement tools and overall impact on patient experience.

Materials and Methods: We conducted a systematic literature review using MEDLINE (Ovid), Evidence Based Medicine (EBM) Reviews, HealthStar, PsycINFO, PubMed, PubMed Central, CINAHL, MEDLINE (Ebsco), Psychology & Behavioral Sciences, Turning Research into Practice (TRIP), EMBASE and Web of Science databases. We also reviewed the grey literature using the local health authority Insite, Google, Google Scholar, Open Archives Initiative (OAISter), Canadian Cancer Society, American Society of Clinical Oncology (ASCO), and European Society for Medical Oncology (ESMO) websites. Inclusion criteria required the studies to evaluate an intervention or a systematic change aimed to improve patient experience and measured by a specific PREM. The search was limited to English language reports published between 1998 and 2018. Out of initial yield of 695 articles, 204 were included in abstract reviews. One hundred and eighty-three abstracts were excluded for the following reasons: 23 did not include a PREM, 147 lacked an intervention, 71 described the development or validation of a PREM and 71 were descriptive only. A total of 21 records were included in the full text review.

Results: Ten records were included in the final analysis (nine published articles and one report). Included studies were published between 2010 and 2018 in the USA, UK, Belgium and Bangladesh. There were five quality improvement (QI) initiatives, two randomized studies, two national patient experience models and quality improvement and one mixed method study. The areas of focus included hospital inpatients (four records), oncology (two records), all patients within the health care system (two records), orthopedic surgery (one record), and patients with chronic illnesses (one record). Six interventions were programmatic/multimodal and four included a specific intervention, such as patient navigators or CHEMO-SUPPORT. All but one study showed positive effect on the patient experience.

Conclusions: There is paucity of published data about specific or system-wide initiatives in health care and oncology primarily aimed to improve patient experience. Such initiatives are needed to evaluate and understand their impact on patient experience and person-centered care. One such department-wide initiative (PROSE = Person-centered Radiation Oncology Service Enhancement) is currently underway at our institution.

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RADIATION DOSES TO THE LEFT ANTERIOR DESCENDING ARTERY AND HEART IN LEFT-SIDED BREAST CANCER PATIENTS TREATED WITH DEEP INSPIRATION BREATH HOLD AND FREE BREATHING TECHNIQUES

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Purpose: For adjuvant breast radiation therapy, recent protocols recommend aiming to reduce heart dose to as low as possible and typically a mean heart dose constraint of 4Gy. It is suggested that doses to the coronary arteries, particularly to the left anterior descending artery (LAD), may be a more relevant in relation to the risk of late cardiac toxicity. However, there have been no established dose limit guidelines or recommendations for LAD and there is paucity of published data on achievable or safe LAD doses. The aim of this study was to report on and compare radiation doses to the whole heart and the LAD in patients with breast cancer treated within the last five years with adjuvant radiation in either free breathing (FB) or deep inspiration breath hold (DIBH).

Materials and Methods: In this retrospective analysis, all left-sided breast patients with identified LAD structures and who were treated with 4250cGy in 16 fractions at a tertiary cancer centre between 2013 and 2018 were included. This analysis included patients treated with both standard tangent fields (whole breast radiation alone) and 4-field (locoregional radiation to whole breast and regional lymph nodes) techniques. Whole heart and LAD volumes were contoured as per the centre's established contouring guidelines. For heart and LAD structures, the mean (Dmean) and maximum (D0.03cc) doses were calculated separately for patients treated with the DIBH and FB techniques.

Results: A total of 362 patients treated with DIBH and 125 patients treated with FB were included. The LAD mean dose (± standard deviation) for patients treated with DIBH and FB were 361.8cGy (±191.5 cGy) and 462.0cGy (± 437.7cGy), respectively. The heart Dmean for patients treated with DIBH and FB were 99.3cGy (± 28cGy) and 106.4cGy (± 40.6cGy), respectively. The mean D0.03cc (± standard deviation) to the LAD for patients treated with DIBH and FB were 660.8cGy (± 365.5cGy) and 870.6cGy (± 736.7cGy), respectively. For maximum point dose, the mean D0.03cc to the heart for patients treated with DIBH and FB were 1250.8cGy (±797.7cGy) and 1744.8cGy (±1186.0cGy), respectively. For the DIBH and FB cohort, a two-tailed t-test identified all metrics were statistically lower (p-value<0.05) for patients treated with DIBH compared to FB. For the LAD, 95% of patients treated with DIBH and FB had D0.03cc values below 1074.9cGy and 3242.3cGy, respectively.

Conclusions: The mean and the maximum radiation doses to the heart and LAD were low in both groups of patients, with statistically lower values for all metrics in patients treated with DIBH compared to free breathing. More studies are needed to determine the appropriate LAD dose constraint and its' correlation with cardiac toxicity outcomes.

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DYNAMIC TUMOUR TRACKING (DTT) FOR HEPATOCELLULAR CARCINOMA USING A GIMBALED LINAC STEREOTACTIC BODY RADIATION THERAPY (SBRT) SYSTEM

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Purpose: To determine the feasibility and benefit of treating patients with primary hepatocellular carcinoma (HCC) using real time dynamic tumour tracking stereotactic body radiotherapy (DTT-SBRT) on the Brainlab VERO gimbaled mounted linac.

Materials and Methods: Twenty-two patients (18 male, four female) with HCC were treated between October 2017 and February 2019. Prescription doses were 40 - 45 Gy in 3 or 5 fractions based on the effective liver volume irradiated. Baseline patient demographics and dosimetric data were collected. A biological equivalent dose assuming an α/β of 10 (BED_{10}), was calculated to allow for dose comparison. The percentage reduction in DTT planning target volume ($PTV_{TRACKING}$) was compared to the conventional motion encompassing internal target volume (ITV) approach (PTV_{ITV}) as determined by the amplitude of fiducial movement on a four-dimensional computed tomography (4DCT) and fluoroscopy.

Results: Median follow-up for this cohort was 3.4 months (range, 0.1 – 10.1). The median age was 71 years (range, 36 – 86 years) with baseline ECOG performance status 0 or 1 in 77.3% of patients. The baseline Childs-Pugh Score was A5/6 in 90.9 % and B7/8 in 9 % and ALBI Grade 1, 2 and 3 in 45.5%, 50% and 4.5% of patients respectively. Underlying liver cirrhosis was present in 17 patients (77.3%). Nineteen patients (86.4%) had hepatitis, of which 45.5% had hepatitis C and 40.9% hepatitis B. Fifteen patients (68.2 %) had received previous liver directed therapy prior to SBRT (median number of treatments, 1 (range, 0 – 5)). The median prescribed biologically effective dose (BED_{10}) was 112.5Gy with 16 patients (72.7 %) treated with 45Gy in 3 fractions. The median GTV and PTV (cm^3) was 18.8 (range, 1.6 – 154.9) and 120.1 (range, 24.9 – 357.4) respectively. Median BED_{10} to 95% of the PTV (D95) was 109.9 Gy_{10} (range: 64.8-112.5Gy_{10}). BED_{10} D95 for the PTV was ≥100Gy_{10} in 16 patients (72.7%) and ≥80Gy_{10} in 18 patients (81.8%). The mean liver (minus gross tumour volume) dose (MLD) was 10.1Gy (range, 3.4 – 15.9 Gy) and 16.1Gy (range, 7.6 – 19.5) in 3 and 5 fractions respectively. Twenty-one out of 22 patients completed treatment as prescribed. There was a significant PTV reduction using DTT with a median volume reduction of 38.4 % (range 2.4 – 64.1; P<.001) relative to the PTV_{ITV}.

Conclusions: DTT is feasible and resulted in a considerable PTV reduction compared to the ITV approach. Work on calculating NTCP to estimate the clinical gain expected from this volume reduction is ongoing and will be presented at the meeting.

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OUTCOMES OF 34 GY IN SINGLE-FRACTION STEREOTACTIC ABLATIVE RADIATION THREAPY (SABR) IN LUNG TUMOURS

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Purpose: Single-fraction SABR for lung tumours is convenient, shown to be effective in RTOG 0915 trial, but still not widely used. To our knowledge, there is no report on the use of this regimen in Canada. We reviewed the outcomes of patients with lung tumours treated with 34Gy in single-fraction SABR (1x34Gy) in our institution.

Materials and Methods: A retrospective analysis was performed including all patients with lung tumours treated in our institution with 1x34Gy. All tumours were located >2cm from proximal bronchial tree and treated according to RTOG-0915 trial. Location of the tumour (vicinity to the chest wall) was not a contraindication. Outcomes including tumour control rate, overall survival, and toxicity (scored according to CTCAEv3) were assessed.

Results: Between 2010 and 2018**,** 82 patients with 91 lung lesions (71 primary tumours and 20 metastasis) were included in this analysis. Median follow-up is 17.6 months (range 0-89). The median age is 72 years. PTV was abutting chest wall (CW) in 60% of treated lesions. The one-year and two-year tumour-control rates were 97.8% and 92%, respectively. The overall survival rate was 93% at one year and 85% at two years. Concerning toxicity, no Grade 3 or 4 toxicities were noted. For Grade 1 and 2, the most common adverse events were chest wall pain in six patients (7%) and rib fracture in two patients (2%). Of those eight patients, PTV was abutting CW in 6 patients and within 0.5 cm from CW for the other two patients. For all eight cases, the maximum rib dose ranged from 30Gy to 40Gy (median=36Gy).

Conclusions: Our outcomes with 1x34Gy for lung tumours are encouraging and similar to fractionated SABR. 60% of our patients had the PTV adjacent to CW but <10% had Grade1/2 CW toxicity. Prospective data and longer follow-up are warranted.

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OUTCOMES OF LIVER TRANSPLANTATION FOLLOWING STEREOTACTIC BODY RADIOTHERAPY FOR HEPATOCELLULAR CARCINOMAS

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Purpose: Stereotactic body radiotherapy (SBRT) is an emerging curative treatment modality for hepatocellular carcinomas (HCC). However, little is known regarding the outcomes of its use for downstaging or as a bridge to liver transplantation. The objectives of this study are to report the provincial demographics, toxicity and outcomes of HCC patients who underwent SBRT and subsequent orthotopic liver transplantation.

Materials and Methods: We conducted an analysis of all provincial HCC patients who underwent SBRT from 2013 to 2017, and subsequent liver transplantation. Baseline patient, tumour, treatment and clinical outcome data were collected through retrospective review. Progression-free survival (PFS) and overall survival (OS) were analyzed by Kaplan-Meier method.

Results: Twelve cases were identified (age median 58.5, range 45.6 - 68.6; median ECOG performance status 0, median age-adjusted Charlson comorbidity index score 7). All patients had cirrhosis (four [33.3%] hepatitis B, six [50%] hepatitis C, one [8.3%] alcohol, one [8.3%] nonalcoholic steatohepatitis). Ten [83.3%] patients had invasive liver directed therapies (liver resection, ablation, chemo / bland embolization) prior to SBRT, with a median of three interventions prior to SBRT. The median Child-Pugh score (CPS) before SBRT was A6 (5 [41.7%] A5, 3 [25%] A6, 3 [25%] B7, 1 [8.3%] B8) and the median Albumin-Bilirubin (ALBI) score was -2.16, Grade 2 (4 [33.3%] Grade 1, 7 [58.3%] Grade 2, 1 [8.3%] Grade 3). 45Gy in 3 fractions (BED_{10} 112.5Gy) was prescribed in 7 (58.3%) cases, 45Gy in 5 fractions (BED_{10} 85.5 Gy) in four (33.3%) cases and 40Gy in 5 fractions (BED_{10} 72 Gy) in one (8.3%) case. Five (41.7%) patients were outside of the Milan transplantation criteria at the time of SBRT. The median GTV size was 23.0cc (range 4.3 - 329.1 cc). Three (25%) patients developed acute CTCAE V5 Grade 3 toxicities, with ascites requiring drainage. There was no Grade 4-5 toxicity. Within 6 months post-SBRT, four (33.3%) patients had a rise in CPS of 2 or higher and 4 (33.3%) had an increase in ALBI Grade of 1. The median time from SBRT to transplantation was 9.3 months (range 2.0 - 26.4 months). On pathological analysis, the SBRT target lesion remained viable in six (50%) cases. There was discordance between pre-transplantation imaging and pathology for the treated lesions in three (25%) cases, with imaging showing partial response as per mRECIST criteria and pathology revealing complete response. The median follow-up after transplantation was 22.4 months. The two-year PFS and OS after transplantation were respectively 71.3% and 91.7%.

Conclusions: SBRT can selectively provide a safe means of treatment prior to liver transplantation for HCC, capable of achieving good post-transplantation outcomes.

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OUTCOMES OF STEREOTACTIC ABLATIVE RADIOTHERAPY FOR LYMPH NODE OLIGOMETASTASES

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Purpose: Stereotactic ablative radiotherapy (SABR) for the treatment of oligometastases is being investigated in ongoing prospective studies, with available phase II data suggesting favorable outcomes. However, there is little data regarding the use of SABR for oligometastatic lymph nodes (LNs). The objectives of the study are to report the demographics, toxicity and outcomes of all patients treated provincially with SABR to oligometastatic LNs.

Materials and Methods: We conducted an analysis of all patients who underwent SABR to oligometastatic LNs in our provincial program, from 2013 to 2017. Some of the patients were treated on clinical trials, and data was prospectively collected. For the remaining majority of the patients, baseline patient, tumour, treatment and clinical outcome data were collected through retrospective review. Local control (LC), progression-free survival (PFS) and overall survival (OS) were analyzed by Kaplan-Meier method. Cox regression analysis was used to identify predictors of outcomes.

Results: Twenty-four patients underwent SABR to 35 LNs (median 1 and mean 1.5 LNs per patient). The primary sites were colorectal eight (22.9%), kidney six (17.1%), esophagus four (11.4%), gallbladder four (11.4%), stomach three (8.6%), lung three (8.6%), skin two (5.7%), pancreas two (5.7%), liver one (2.9%), duodenum one (2.9%), and unknown origin one (2.9%). Four (11.4%) LNs were in the neck / supraclavicular regions, 14 (40.0%) in the hilum / mediastinum and 17 (48.6%) in the abdomen / pelvis. All patients had treated and controlled primary sites at the time of SABR. The median follow-up post-SABR was 31.7 months. The SABR dose fractionation ranged between 30-60 Gy in 5-10 fractions, with median BED_{10} of 72Gy (range 41.3-105 Gy). All patients were treated with VMAT technique, with 4DCT and respiratory gating used for motion management in 19 (54.3%) cases. The one- and three-year LC were 85.4% and 62.7%. The median PFS was 7.6 months, with one-year PFS at 25.7% and three-year at 18.4%. The median OS was 45.0 months, with one-year OS at 91.3% and three-year at 55.7%. Thirteen (54.2%) patients initiated systemic therapy after SABR, at a median time for these patients of 10.0 months following completion of SABR. The median systemic therapy-free survival (STFS) for all patients after SABR was 17.8 months. There was no Grade 3-5 toxicity as per CTCAE V5 criteria. On multivariate analysis, younger age (p=0.019) and female gender (p=0.046) were found to be factors predictive of improved OS.

Conclusions: SABR to oligometastatic LNs achieves meaningful STFS, without significant toxicity. While the treatment yields moderate rates of long-term LC, the PFS was limited in this cohort. Further evaluation of patient and tumour selection is warranted.

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SINGLE-FRACTION STEREOTACTIC RADIOSURGERY ALONE VERSUS HIPPOCAMPAL-AVOIDANCE WHOLE BRAIN RADIOTHERAPY FOR PATIENTS WITH 10-30 BRAIN METASTASES: A DOSIMETRIC ANALYSIS

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Purpose: RTOG 0933 recently confirmed a neurocognitive benefit favoring hippocampal-avoidance whole brain radiotherapy (HA-WBRT) versusconventional WBRT for patients with multiple brain metastases; however, there are no comparative data for HA-WBRT versusstereotactic radiosurgery (SRS) alone. Our objective was to compare normal tissue dosimetry between HA-WBRT versusSRS in patients with 10-30 brain metastases and describe a novel SRS strategy: Spatially Partitioned Adaptive RadiosurgEry (SPARE).

Materials and Methods: A retrospective review identified SRS treatment plans with >10 brain metastases located >5mm from the hippocampi. Our Gamma Knife Icon SPARE (GKI-Spr) technique treats multiple brain metastases with single-fraction SRS partitioned over consecutive daily treatments that are limited to no more than 60 minutes per day. For each identified case, hippocampal and normal brain dosimetry were compared between 3 treatment strategies: GKI-Spr, single-fraction single-day GKI (GKI-Sfr) and 30Gy in 10 fractions HA-WBRT. All of the following dose metrics were converted to equivalent dose in 2Gy fractions (EQD2). The maximum point dose (Dmax), mean dose (Dmean) and dose to 40% of the hippocampi (D40) were determined for the contoured hippocampi. The rationale for selecting these dose metrics were as follows: Dmax is a dose constraint from RTOG 0933, the Dmean is a useful parameter that is frequently reported in other planning studies and the D40 has been previously correlated with delayed memory recall. Normal brain contours were evaluated using the Dmean, the volume of brain receiving 30Gy (V30) and

the volume of brain receiving 2Gy (V2). The V30 was selected as it is the EQD2 value corresponding with 10Gy in 1 fraction which is a dosimetric predictor of radiation necrosis, while the V2 was selected to compare low dose volumes delivered to the brain.

Results: Ten cases were eligible for inclusion and subsequently analyzed. Compared to HA-WBRT, GKI-Spr significantly reduced the median EQD2 hippocampal Dmax, Dmean and D40 by 86%, 93% and 93%, respectively (p=0.014), and similarly for GKI-Sfr by 81%, 92% and 91%, respectively (p=0.014). The normal brain median Dmean, V30 and V2 were reduced by 95%, 99%, and 83%, respectively with GKI-Spr and 94%, 99%, and 76%, respectively with GKI-Sfr. Compared with GKI-Sfr, GKI-Spr further reduced the median EQD2 hippocampal Dmax, Dmean and D40 by 30%, 27% and 20%, respectively (p=0.014). GKI-Spr also reduced the normal brain Dmean, V30 and V2 by 20%, 8% and 30%, respectively (p=0.014).

Conclusions: GKI yields superior hippocampal and normal brain dosimetry compared to HA-WBRT, and the novel GKI-Spr strategy may provide further dosimetric advantages compared with traditional GKI-Sfr.

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PREDICTORS OF LEPTOMENINGEAL DISEASE AFTER HYPOFRACTIONATED STEREOTACTIC RADIOTHERAPY FOR INTACT AND RESECTED BRAIN METASTASES

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Purpose: Hypofractionated stereotactic radiotherapy (HSRT) for patients with resected or large intact brain metastases is increasing in clinical practice; however, reporting on patterns of failure, specifically leptomeningeal disease (LMD) is lacking. In this study we identify patterns of LMD and determine predictors for developing LMD in patients with intact or resected brain metastases treated with 5-fraction HSRT.

Materials and Methods: A single-institution retrospective review of a prospective database identified patients receiving HSRT for intact brain metastases or surgical cavities. Patient, tumour and treatment factors were extracted. Patterns of LMD were stratified into four groups based on their radiographic presentation: focal classical, diffuse classical, focal nodular and diffuse nodular. Univariate and multivariable analyses were conducted to determine potential predictors for developing LMD.

Results: HSRT was delivered to 320 intracranial lesions (57% intact and 43% surgical cavities) in 235 patients with a median follow-up of 10.5 months (range, 0.2 to 60 months). The most common dose regimen was 30Gy in 5 fractions (65%). Overall, the incidence of developing LMD was 19% and the most common radiographic presentation of LMD was a diffuse nodular pattern (44%). The six-month and one-year rates of LMD were 6% and 12%, respectively. On multivariable analysis for the entire cohort, cavity lesions were statistically significant predictors of LMD compared with intact metastases (24% versus7%; hazard ratio=0.47; p=0.01). For cavities alone, radiosensitive tumours were the only statistically significant predictor of LMD (p=0.041), with a trend towards significance observed for increasing max tumour diameter (p=0.076). For intact metastases alone, the use of a targeted agent was predictive of LMD (p=0.023). From the date of LMD diagnosis, the median, six-month and 12-month overall survival rates for the entire cohort were 3.8 months (range, 0.2 to 20.8 months), 40% and 15%, respectively. No statistically significant difference in survival was observed between the four patterns of LMD (p=0.203) or between nodular and classical patterns (p=0.74).

Conclusions: For patients treated with a 5-fraction HSRT regimen, surgical cavities are at increased risk of developing LMD compared to intact brain metastases. These findings suggest that despite the capability of HSRT to safely escalate tumour dose compared with single-fraction SRS, it may still be insufficient to mitigate the risk of LMD. Further research is required to determine optimal strategies to reduce LMD rates.

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A PHASE II STUDY TO DETERMINE EFFICACY OF STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR SPINAL/ PARA-SPINAL METASTASES FOR PATIENTS AT PRINCESS MARGARET HOSPITAL FROM 2011 TO 2015.

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Purpose: Spine SBRT is defined as the precise delivery of high dose per fraction radiotherapy in 1-5 fractions to a spinal target. The use of image guided technology and advanced inverse planning techniques allow treatment plans with steep dose gradients between targets and OAR. Principle is to target with a high BED to involved vertebra in contrast to conventional radiation where a low BED is used, and a vertebral margin is targeted.

Objectives: To evaluate the efficacy of spine SBRT as an alternative to conventional radiation for patients in three cohorts – no prior radiation, prior radiation and post-operative patients. Primary endpoint: efficacy based on imaging and symptom-based criteria. Secondary endpoint: pain and functional outcome using brief pain inventory; quality of life using EORTC QLQ-BM22; pain flare using pain diary; neurologic outcomes using ASIA classification, toxicity using NCIC common toxicity criteria v3.0

Materials and Methods: Three cohorts with pretreatment H&P and a variety of standard neurologic physical evaluation components. Baseline Imaging conducted. Standard oncologic diagnoses and imaging characteristics recorded. Primary endpoint based on follow-up MRI and recorded as partial response (PR), complete response (CR), progressive disease (PD) or stable disease (SD). Second endpoints based on follow-up assessment of symptom response.

Results: From 2011 until 2015 at Princess Margaret Hospital 69 patients in three cohorts were recruited, treated with SBRT and followed for up to four years. Patients divided into: 31 patients no previous radiation; 17 patients previously irradiated; 21 post-operative patients. Data collected in spreadsheet format and clinical notes to be analyzed for both efficacy primary endpoint and functional outcome secondary endpoints.

Conclusions: Will be meaningful for practitioners of SBRT and conventional spinal radiation to guide expectation of efficacy and functional outcomes in patients treated with spinal SBRT.

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AUTO-GENERATED TEMPLATE TRAJECTORIES FOR RADIOSURGERY THAT RELY ON CRANIAL ANATOMY: A CASE STUDY

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Purpose: Stereotactic radiosurgery (SRS) is commonly treated with volumetric modulated arc therapy (VMAT) that depends on a template arrangement of four trajectories. 4π radiotherapy is a novel treatment planning technique that permits the freedom to

automatically design trajectories that leverage the full degrees of motion of a linac. The aim of this research was to use 4π maps to develop a set of anatomically aware trajectories for radiosurgery and compare them with the standard template. The hypothesis is that the optimal number of arcs can be automatically chosen, as compared to necessary manual selection for the standard template.

Materials and Methods: The template was made anatomically aware by using the Montreal Neurological Institute's (MNI) average human brain. The MNI brain was then filled with 2cm diameter spherical targets (n=247), and 4π overlap maps were calculated based on OAR-PTV overlap in the beams-eye-view (BEV). This was done in six regions that encompassed the complete cranial anatomy (frontal, medial, and posterior with laterality dependence) to give six anatomically specific 4π maps. A shortest path algorithm was then applied to each 4π map to guide arc placement through minimization of BEV overlap, unrestricted by arc number corresponding for each of the six cranial regions. For this case study a VMAT plan was generated from these trajectories and then compared with a VMAT plan generated from the standard template using a test patient created in the Eclipse treatment planning system (v. 13.6, Varian Medical Systems, Inc., Palo Alto, USA). A case-specific arc trajectory VMAT plan was also generated from the case-specific 4π map for further comparison. All planning objectives were kept consistent to highlight the effect of optimized arc placement.

Results: According to the SRS dose constraints outlined in our clinic, for this difficult case the standard VMAT template did not meet constraints of maximum dose to brainstem (16.2Gy), or optic chiasm (12.3Gy). Using arcs chosen from an anatomically aware template, these doses were reduced to 13.7Gy and 5.4Gy respectively. Finally, using arcs chosen from the case-specific 4π overlap map, these doses were reduced to 12.2Gy and 5.6Gy respectively.

Conclusions: In this case study, using arcs generated from anatomically informed templates reduced dose to the optic chiasm to within tolerance however the brainstem remained outside tolerance. The case-specific arcs brought both OARs within tolerance. This demonstrates that although an anatomically informed template offered some OAR sparing, case-specific optimization was superior.

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STEREOTACTIC BODY RADIOTHERAPY FOR HEPATOCELLULAR CARCINOMA WITH MACROVASCULAR INVASION

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Purpose: In patients with hepatocellular carcinoma (HCC), macrovascular invasion (MVI) is associated with a poor prognosis. The purpose of this IRB approved study is to describe long-term outcomes of patients with HCC and MVI treated with stereotactic body radiation therapy (SBRT).

Materials and Methods: Patients with HCC and MVI who were treated with SBRT from January 2003 to December 2016 were eligible for analysis. Patients who had extrahepatic disease, had a previous liver transplant, or were treated with palliative intent were excluded. Demographical, clinical, and treatment variables were collected, under IRB approval. The degree of vascular invasion was quantified into two categories: mainportal vein branch/IVC and distal portal/hepatic vein.

Results: One hundred and twenty-eight eligible patients with HCC and MVI were treatedwith SBRT. The median age was 61 years (39 to 90 years). Underlying liver disease was hepatitis B in 23%, hepatitis C in 45%. Baseline Child-Pugh (CP) score was A5 in 67%, A6 in 20%, B7 or higher in 13%. Thirty-five percent received previous liver-directed therapies. Median gross tumour volume (GTV) was 153.7mL (range: 3.9 to 1,813.5 mL). Median AFP was 205ug/L (range 1 to 171,154). Median SBRT dose was 33.3Gy (range: 27 to 54 Gy) in 6 fractions. Local control at one year was 82.4% (95% CI 72.8 to 88.8%); SBRT dose, GTV volume, or treatment era were not statistically significant on univariate analysis. Median overall survival (OS) was 18.3 months (95% CI 11.2 to 21.4 months) for which baseline ECOG PS >1 (HR:1.73, p=0.02), baseline CP score (HR: 1.66, p=0.03), and treatment between 2003 and 2010 (HR: 2.28, p=0.0009) were significant on multivariate analysis; SBRT dose, GTV volume, and degree of vascular invasion were not statistically significant for survival. In 35 patients who received sorafenib following SBRT, median survival was 38.5 months (95% CI 17.23 to 43.16 months). Regarding toxicity, five patients developed GI bleeding and from 112 patients with liver function evaluable at baseline and three months, 27 patients experienced a deterioration of their CP class.

Conclusions: SBRT was associatedwith excellent outcomes for patients with HCC and MVI, compared to historical controls treated with Sorafenib alone. Randomized phase III trials of SBRT with systemic and/or regional therapy are warranted and ongoing.

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SMALL BOWEL TOLERANCE IN STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR)

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Purpose: The tolerance of small bowel is still not clear and fear of significant toxicity has limited the use of ablative regimens of SABR in targets located close to small bowel (SB). One review (one) shows a risk of 6.5% of severe SB toxicity for Dmax=21Gy/3 (BED_3 = 70Gy). We started a regimen of 36Gy in 6 fractions with SB-Dmax BED_3 = 129Gy to prospectively assess tolerance. We report that experience.

Materials and Methods: SABR was delivered in our institution to metastatic tumours close to SB the following way: PTV = 36Gy in 6 daily fractions. Constraints: SB-Dmax<40Gy (BED_3=129Gy); D15cc<35Gy. Spinal cord=max 26Gy. Bladder and rectum=D>40Gy< 20cc. Kidney=D200cc<19Gy; V>17Gy<50%. Toxicity was assessed (CTCv3) during treatment and follow-up.

Results: Twenty-nine patients with metastatic nodes were treated. Primary tumour was prostate (19); lower GI (five), melanoma (two), kidney (one), sarcoma (one), esophagus(one). Median age=72 years oold (29-86 years). Location: R iliac= eight; L iliac= three, pre-sacral or low paraortic nodes=18 patients. Median SB-Dmax dose=34Gy (5- 40 Gy). Median Volume PTV=33cc (4-119 cc). Median SB-D15cc=17Gy (12-34 Gy). Median f-up=308 days (0-1099 days). Tolerance: except for some mild fatigue (Grade 1), there was no acute or late toxicity. None of the tumours treated with SABR seemed to progress during f-up, but patients received different systemic treatments after SABR.

Conclusions: SB-Dmax BED_3=129Gy looks safe (similar BED_3 dose was suggested by QUANTEC and COMET trial). No significant toxicity was observed during and in the first few months following treatment in our cases. These patients with oligo-metastatic cancer subsequently received systemic treatments making assessment for late-effect difficult. Challenge increases with the growing use of immunotherapy. Higher doses of SB-Dmax should be tested to allow real ablative SABR doses in tumours surrounding the SB.

(1). LaCouture TA et al. Small Bowel Dose Tolerance for SBRT. Semin Radiat Oncol. 2016;26(2):157-64.

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RADIATION NECROSIS FOLLOWING FIVE DAILY FRACTIONS OF STEREOTACTIC RADIOTHERAPY FOR SURGICAL CAVITIES AND INTACT BRAIN METASTASES

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Purpose: There is increasing use of hypofractionated stereotactic radiosurgery (HSRS) for the treatment of intact brain metastases and surgical cavities. Unlike single fraction stereotactic radiosurgery (SRS), limited data exist quantifying the risk of radiation necrosis (RN) specific to HSRS. We present our analyses of the risk of RN following 5 daily fraction HSRS to surgical cavities and intact metastases and respective predictors.

Materials and Methods: Eighty-seven consecutively treated patients with 118 surgical cavities and 132 intact metastases were retrospectively reviewed. All patients were treated with thermoplastic mask immobilization using a cone-beam CT (CBCT) image-guided linac with a multi-leaf collimator (MLC) and six-degrees-of-freedom treatment couch. All patients were treated with 5 daily fractions with a 2mm planning target volume (PTV) applied. Clinical and dosimetric variables were assessed to identify predictors of RN including the total volume of the brain minus the CTV (BMC) receiving 5 to 30 Gy in 5Gy increments, where the CTV was the surgical cavity for resected lesions and equaled the GTV for intact lesions.

Results: The median total dose was 30Gy (range 20 to 35 Gy) and median follow-up was 13.5 months (range 2 to 85). One hundred forty-four patients (77%) received treatment to a single target, otherwise the median number of simultaneously treated targets was two per patient (range 2-4). The most common histologies were lung cancer (48%), breast cancer (21%) and melanoma (10%). Median PTV volumes for cavity and intact metastases were 24.9cc and 7.7cc, respectively. RN was observed in 53 targets (21.2%) and the median time to RN was eight months (range 1 to 41). Time to RN was <6 months for 20 (38%), six to 12 months for 23 (43%) and >12 months for 10 (19%) targets. The rate of RN specific to cavities was 16%, of which 47% were symptomatic, and 26% for intact metastases of which 53% were symptomatic. RN was determined by surgical pathology in 29 cases (57%) and serial MRI in 23 cases (43%). Multivariable analysis (MVA) identified intact metastases versus cavities [OR 3.7 (95% CI, 1.33 to 10)] as a significant predictor of symptomatic RN. Specific to cavity HSRS, prior WBRT [OR 7.73 (95% CI, 1.67 to 35.69)] and prior SRS [OR 8.66 (95% CI, 1.14 to 65.7)] were significant predictors of symptomatic RN. For intact metastases, the BMC30Gy [OR 1.21 (95% CI, 1.02 to 1.43)] was a significant predictor of symptomatic RN and a threshold of 10.5cc was identified with an OR of 7.21 (95% CI, 1.31 to 39.45).

Conclusions: The overall risk of RN with HSRS is modest and about half of affected patients are symptomatic. The risk of RN was greater for intact metastases compared to cavities following HSRS. In intact lesions, the BMC30Gy was predictive for symptomatic necrosis and a threshold of 10.5cc may guide treatment planning and/or dose selection.

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STEREOTACTIC PELVIC ADJUVANT RADIATION THERAPY IN CANCERS OF THE UTERUS (SPARTACUS) - A PLANNING STUDY

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Purpose: Standard adjuvant pelvic radiation in uterine cancer involves the delivery of 25 daily fractions. Advances with stereotactic body radiotherapy (SBRT) techniques have allowed for hypofractionated treatment with increasing conformality. There is potential to leverage these advances to reduce treatment times in uterine cancer. This dosimetric planning study of adjuvant pelvic radiotherapy examines three elective nodal (CTV_N) dose levels [25 (DL25), 27.5 (DL275) and 30Gy (DL30) in 5 fractions], each in conjunction with a simultaneous integrated boost of 30Gy to the central target volume of upper vagina and parametrial tissue (ITV_T).

Objective: To characterize the dosimetry of stereotactic delivery of adjuvant radiotherapy for uterine cancer.

Materials and Methods: Twenty consecutive patients treated with adjuvant pelvic radiotherapy were selected for study. Included patients must have been simulated with bladder full and empty and contoured according to RTOG 0418 recommendations. Patients were excluded on the basis of hip arthroplasty, absence of bladder or rectum or treatment of para-aortic lymph nodes. Planning was identical for each dose level. Planning target volumes (PTV) were generated using 7mm isotropic expansions of both CTV_N and ITV_T. Organs-at-risk (OAR) included rectum, bladder, bowel (delineated as loops) and femoral heads (left/right). Dose evaluation metrics were constructed apriori according to existing pelvic SBRT literature, including: PTV_N V95% > 95%; ITV_T V100% >98%; PTV_T V105% <10%; bladder V30Gy <20%, rectum V29Gy <20% and femoral heads V28Gy <5%. As there is limited long-term data on bowel toxicities in this context, evaluative lower-dose constraints were set at V25Gy < 40cc. A maximum point dose (Dmax) for each OAR was set at 32Gy. The D2cc was also recorded for each OAR. Planning was completed on Varian Eclipse (v13.6) utilizing a class solution optimization, without individual plan adjustment.

Results: For DL25, DL275 and DL30, 16, two and one patients met all planning metrics, with bowel V25Gy being the primary limitation. The median (interquartile range: 75th - 25th) bowel V25Gy for DL25, DL275 and DL30 were 26, 88.7 and 143.4cc (26.4, 106.4 and 133.5cc); median bladder V30Gy were 11.7, 11 and 13.6% (5.5, 5.4, 3.7%); median rectum V29Gy were 10.9, 11.4 and 13.5% (8.3, 7.1, 7.7%). The target coverage and femoral head metrics were met in all plans across all dose levels. The Dmax and D2cc did not exceed 32Gy for any OAR in any dose level.

Conclusions: The elective nodal dose is an important dosimetric variable in adjuvant pelvic radiotherapy with an SBRT approach. The bowel V25 represented the primary limiting OAR across dose levels for the assigned planning aim. Prospective dosimetric improvement could reasonably be expected with dedicated motion management, image-guidance, PTV margin reduction and individual plan optimization. Phase I/II evaluation of toxicities are required to establish high-volume dose metrics for bowel.

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STEREOTACTIC RADIOTHERAPY TO SPINE AND NON-SPINE BONE METASTASES IN NOVA SCOTIA

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Purpose: Stereotactic radiation (SBRT) is a commonly used form of high precision radiotherapy demanding high precision image

guidance and tumour localization. Review of patients treated is important to ensure that high degree of local control is being achieved, with reasonable toxicity.

Objectives: To perform a quality assurance review of patients treated to date, and to report the local control and survival in the patients treated.

Materials and Methods: Retrospective chart review, was performed, after local quality board / REB approval to review patient records for the purpose of quality assurance. The Varian ARIA database was queried to find patients treated with SBRT.

Results: Thirty-nine sites in 34 patients were treated between April 2015 and January 2019, using linac-based SBRT with the Varian Trubeam, and the Brainlab Exactrac imaging system. The average age of patients treated was 67.4 (range: 42 to 86). Thirty-one sites received SBRT to spine, the remainder received SBRT to non-spine bone lesions. The origin of the metastases and number of sites were as follows: prostate (17), lung (nine), kidney (seven), thyroid (four), sarcoma (one), and melanoma (one). From 39 sites, 34 were controlled at last assessment (87.2%). The modal dose utilized was 24 Gy in 2 fractions. Local control at three years was significantly better for prostate metastases versus non-prostate metastases (100% versus 50%, log-rank p-value = 0.043). One patient treated with spinal SBRT for Kidney cancer has suffered a vertebral fracture, using a dose of 24 Gy in 2fr. Overall survival for all patients is 82.7% at three years. Overall survival is significantly better in the patients with prostate cancer versus other primary sites at three years (100 versus 65%, log-rank p-value = 0.0339)

Conclusions: SBRT for bone metastases appear to result in high rates of local control, especially for patients with prostate cancer.

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STEREOTACTIC BODY RADIOTHERAPY FOR OLIGOMETASTATIC CANCER: A RAPID REVIEW OF THE CLINICAL EFFECTIVENESS AND COST-EFFECTIVENESS

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Purpose: The National Cancer Institute defines oligometastasis as a "type of metastasis in which cancer cells from the original (primary) tumour travel through the body and form a small number of new tumours (metastatic tumours) in one or two other parts of the body." One potential treatment for patients with oligometastatic cancer is stereotactic body radiotherapy (SBRT, also known as stereotactic ablative radiotherapy).

Objective: To summarize the evidence regarding the clinical effectiveness and cost-effectiveness of SBRT for patients with oligometastatic cancer.

Materials and Methods: A limited literature search was conducted of three academic databases and the grey literature, and titles and abstracts of the retrieved publications were reviewed. Full-text publications were evaluated for final article selection according to predetermined selection criteria (population, intervention, comparator, outcomes, and study designs). Studies that did not directly describe the target population as patients with oligometastatic cancer were excluded.

Results: The literature search of the academic databases identified 798 citations, with one additional article identified from the grey literature. After screening the abstracts, 79 were deemed potentially relevant, and four met the criteria for inclusion in this review – three retrospective cohort studies that compared SBRT to usual care for patients with adrenal metastatic tumours or pulmonary (lung) oligometastases, and one economic evaluation. Overall, the clinical evidence was of limited quality. One cohort study found local control for adrenal metastasis in patients with oligometastasis was most effective with real-time tumour-tracking radiotherapy (RTRT) versus SBRT, although there were more adverse events with RTRT. The other two cohort studies considered patients with pulmonary metastases (comparing SBRT to pulmonary metastasectomy) and did not find any significant differences in the outcomes investigated (overall survival rates, progression-free survival, freedom from failure of local strategy, and freedom from local progression). The economic evaluation assessed the cost-effectiveness of initial management strategies including SBRT for pulmonary oligometastases in patients with melanoma, non-small cell lung cancer (NSCLC; three types), and colon cancer. For melanoma and NSCLC adenocarcinoma, SBRT was the most cost-effective; for the other NSCLC subtypes examined, systemic therapy was more cost-effective; and, for colon cancer, video-assisted thoracic surgery (VATS) wedge resection was more cost-effective. However, it is unclear whether these findings can be applied to a Canadian setting.

Conclusions: Given the limited availability and low quality of evidence, the effectiveness and use of stereotactic body radiotherapy for oligometastatic cancer remains uncertain.

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PROSPECTIVE CASE SERIES IN THE USE OF NON-LIVER ABDOMINAL AND PELVIC SBRT IN THE CONTEXT OF OLIGOMETASTATIC DISEASE

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Purpose: There is emerging evidence for an "Oligometastatic" state where local therapy to a limited number of metastatic lesions may provide progression-free survival (PFS), overall survival (OS), and potentially quality of life benefits. Stereotactic Body Radiotherapy (SBRT) is an emerging therapy in the treatment of oligometastatic disease but there is a paucity of published data on SBRT to intra-abdominal and pelvic targets outside of the liver.

Materials and Methods: We analyzed all patients treated with 5-fraction SBRT to the abdomen and pelvis for oligometastatic disease in 2014 - 2018. Patients treated with SBRT to the liver, periportal area and local recurrence after Whipples' type procedure were excluded. Radiotherapy was delivered VMAT using Varian planning software in 5 fractions on alternative days with abdominal compression employed to reduce breathing amplitude of upper abdominal targets. Patients were categorized in terms of primary diagnosis, target location, target size, prescribed dose, PFS and OS from SBRT and time to next treatment. Local control was evaluated using cross – sectional imaging. Toxicity was assessed using CTCAE version 4. Data analysis was undertaken as part of an institutional Quality Assurance Process.

Results: A total of 22 patients with 26 courses of SBRT met inclusion criteria, with median age 60 years (range 24 – 82 years) with targets including para-aortic lymph nodes (nine cases), abdominal wall (five cases), adrenal gland (four cases), iliac lymph nodes (four cases) and others (four cases). Primary tumour types included colorectal (five patients), hepatocellular carcinoma (four patients), endometrial (two patients), lung (two patients), ovary (three patients), renal cell carcinoma (two patients) and others (four patients). Median SBRT prescription dose was 35 Gy in 5

fractions to the PTV (range 25 - 50Gy) with the mean ITV size 46.3cc (range 0.44-398cc). Estimated local control rate was 80% at one year and 60% at two years, respectively. Median PFS following SBRT was 331 days (95% CI 116 - 546 days), with estimated one-year PFS 43%. Median overall survival was 745 days (95% CI 573-917 days), with estimated one-year overall survival of 89% and two-year survival 64%. Median treatment-free time following SBRT was 506 days (95% CI 303 - 709 days), with an estimated 64% of patients being chemotherapy-free at one year. One Grade 3 GI toxicity was observed with dyspepsia. No Grade 4 or other Grade 3 toxicities were seen. There was no association between LC rate or PFS and different cancer types, ITV size or prescribed doses.

Conclusions: Abdominal and pelvic SBRT to non-liver oligometastatic targets was well tolerated in this patient series. It can allow the either a period of time off chemotherapy or the continuation of existing chemotherapy thereby potentially increasing the remaining chemotherapy options available to the patient.

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FEASIBILITY AND ACCEPTABILITY OF MEASURING CERVIX CANCER SPECIFIC PATIENT-REPORTED OUTCOMES IN CLINICAL PRACTICE

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Purpose: The use of patient-reported outcomes (PROs) in oncology positively impacts clinical outcomes, including overall survival. Most studies have used generic PROs and data pertaining to implementation of disease-specific PROs in clinical practice is limited. The objective of this study was to implement a cervix cancer-specific PRO instrument, the European Organization for Research and Treatment of Cancer Quality-of-Life questionnaire cervical cancer module (EORTC QLQ-CX24), into routine clinical practice and evaluate acceptability by patients and oncologists.

Materials and Methods: This was a prospective, multi-institutional study involving three Canadian cancer centres. Cervix cancer patients treated with definitive chemo-radiation attending routine follow-up clinic were approached between January 2017 and August 2018. Consenting patients completed the EORTC QLQ-CX24 on paper prior to their appointment and reviewed it with their oncologist. A Feedback Survey evaluated acceptability of EORTC QLQ-CX24 implementation, from the perspective of both patients and oncologists, using a 5-point Likert scale (strongly disagree to strongly agree). Descriptive statistics were used to summarize the results.

Results: Of the 82 patients who consented to participate in the study, 80 (97.5%) completed the EORTC QLQ-CX24 and 76 (92.6%) completed the Feedback Survey. Median age was 52 years (range: 27-82). The majority of items had high completion rates (93-98%); however, items pertaining to vaginal symptoms and sexual health were low (34-35%). Patients strongly agreed/agreed that the instrument was useful (80%), easy to understand (97%), easy to complete (97%), facilitated discussion of symptoms (76%) and improved communication (68%). The majority (80%) recommended use of this instrument, with only 11% reporting it as time-consuming and 1% upsetting to complete. All eligible oncologists participated and completed the Feedback Survey (n=9). Oncologists strongly agreed/agreed that the instrument was clinically relevant (89%), improved communication (89%) and identified symptoms (100%); however, most (78%) reported it increased visit length.

Conclusions: Implementation of the EORTC QLQ-CX24 into routine clinic was feasible and positively endorsed by cervical cancer patients and oncologists. However, the high rates of incomplete responses for vaginal/sexual items requires further exploration. Future directions will assess implementation and evaluation of electronic platforms.

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RESPONSE AND INTERVENTION TO ELEVATED ESAS SCORES: A CHART AUDIT OF GYNECOLOGIC ONCOLOGY CLINICS

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Purpose: While the incorporation of patient-reported outcomes (PROs) in oncology has several benefits, data pertaining to symptom management practices are limited. The objective of this study was to evaluate health care professional (HCP) documentation of elevated PRO symptom scores and subsequent intervention.

Materials and Methods: This was a retrospective chart review of gynecologic oncology patients within a single institution. The Edmonton Symptom Assessment System (revised version) (ESAS-r) is a validated, PRO tool that evaluates 9 common symptoms and is completed prior to each clinic visit. Symptom management intervention guidelines exist for each symptom based on severity: mild (1-3), moderate (4-6) and severe (=/>7). Biopsy-proven gynecologic oncology patients with any ESAS symptom score =/>4 were eligible. A stratified sampling method was used: 100 patients were randomly selected with 20 per year from 2012 to 2016. Patient, tumour and treatment characteristics were collected. HCP documentation of symptoms with score =/>4 and subsequent interventions were assessed by two independent oncologists. Interventions were categorized as: counselling, investigation, treatment or referral. Descriptive statistics were used to report symptom prevalence, HCP documented response and intervention. Fisher's exact test evaluated documentation and intervention rates according to individual symptom severity and total ESAS score.

Results: Between January 2012 and December 2016, a total of 5849 patients completed the ESAS. Symptoms scores were =/>4 in 3216 patients (55%) and >7 in 1446 (25%). In our sample of 100, ovarian malignancies were most common (42%), followed by endometrial (34%). Median age was 55 years (range 47-63). The median total ESAS score was 24 (range: 17-39). The most prevalent symptoms were tiredness (70%), anxiety (61%) and poor appetite (40%). Overall, documentation of a least one symptom =/> 4 occurred in 50 patients (50%), most commonly for pain (71%) and tiredness (36%) and least commonly for depression (11%) and nausea (4%). An intervention was offered to only 32 patients (32%), most commonly for pain (56%) and least commonly for nausea (4%). The primary intervention was a treatment recommendation (12/32; 38%). Higher median total ESAS score was associated with higher rate of documentation ($p=0.002$) and higher rate of intervention ($p<0.001$). Similarly, higher symptom severity was significantly associated with higher rate of documentation, except for anxiety and nausea, and higher rate of intervention, except for anxiety, nausea and tiredness.

Conclusions: A significant proportion of gynecologic oncology patients report elevated symptom scores that should prompt an intervention. However, HCPs document symptoms in only half of patients and offer interventions in only one third, warranting further evaluation. A study exploring the barriers and facilitators of optimal ESAS use is underway.

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LATE EFFECTS IN SURVIVORS TREATED FOR LYMPHOMA AS ADOLESCENTS AND YOUNG ADULTS

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Purpose: There is a relative lack of literature documenting late effects in oncology patients treated as adolescents and young adults (AYA) compared to as pediatric patients. The objective of this study was to describe and quantify the incidence of treatment-induced late effects in AYA patients treated for lymphoma.

Materials and Methods: Patients diagnosed with Hodgkin lymphoma (HL) at 15-24 years of age or non-Hodgkin lymphoma (NHL) at 15-29 years of age were identified in the Lymphoid Cancer Database. All patients in the province who received RT as part of their lymphoma management from 1974-2014 with a minimum five-year survival post-RT were included. Late effects were defined as documented health complications persistent or arising beyond five years post-RT. For the analysis of cardiac disease, patients who received mediastinal RT and/or anthracycline chemotherapy were included. For infertility, patients who received pelvic RT and/or chemotherapy agents with the risk of infertility were included. Analyses of all other late effects included only survivors who received RT to the relevant anatomical site. Late effects were analyzed using Kaplan-Meier method and reported as cumulative incidence (CI) ± standard error.

Results: Of the 378 patients studied, 226 patients (60%) were diagnosed with HL and 152 patients (40%) with NHL. Median follow-up was 7.2 years (range, 0.2-37). Median age at diagnosis was 22 years. 34 patients (9%) were treated with RT only and 344 patients (91%) were treated with RT and chemotherapy. 305 patients (81%) received one course of RT and 73 patients (19%) received ≥2 courses. Eighty-five patients (22%) had at least one relapse of lymphoma and 59 patients (16%) were deceased by last follow-up. Of the late effects studied, radiation-induced (RI) hypothyroidism was the most prevalent, with a CI of 19.8±2.5% at five years and 30.4±3.3% at 10 years. The CI of in-field second malignancy was 0.4±0.4% at five years and 1.1±0.8% at 10 years, of which the most common types were skin cancer (n=4) and sarcoma (n=3). The five-year CI of symptomatic RI lung damage was 4.8±1.4% and 10-year CI was 6.8±1.8%. RI esophageal complications occurred at a CI of 1.2±0.7% at five years and 1.9±1% at 10 years. CI of RI xerostomia and/or dental decay was 5.2±1.7% at five years and 7.1±2.1% at 10 years. Treatment-induced cardiac disease occurred at a CI of 1.9±0.8% at five years and 3.7±1.3% at 10 years. CI of reported infertility was 6.9±1.5% at five years and 11.1±2.1% at 10 years.

Conclusions: Even with relatively limited follow-up, this study demonstrates that survivors of AYA lymphoma are significantly affected by long-term complications of treatment. The diverse clinical presentation and high incidence of late effects in a young population necessitate focused follow-up and screening when appropriate. Patients and primary care providers need to be informed to ensure proper management.

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EVALUATING THE DISCUSSION OF LATE EFFECTS AND SCREENING RECOMMENDATIONS IN SURVIVORS OF ADOLESCENT AND YOUNG ADULT (AYA) LYMPHOMA

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Purpose: Survivors of lymphoma treated as AYAs are at risk of developing late effects (LEs) of radiotherapy (RT) and chemotherapy. The study objective was to assess the quality and quantity of late effects (LEs) discussion and screening recommendations (SRs) provided to survivors of AYA lymphoma and their primary care professionals (PCPs).

Materials and Methods: Eligible patients were diagnosed with lymphoma at 15-29 years of age, received RT between 1974-2014 in the province, and survived for at least five years post-RT. Charts were reviewed for patient, disease and treatment characteristics, and for documented counseling of LEs risks and SRs prior to discharge from BC Cancer. Individual susceptibility to specific LEs was determined based on each patient's RT and chemotherapy exposure.

Results: The study cohort consisted of 378 patients, including 226 survivors of HL and 152 survivors of NHL. Median age at diagnosis was 22 years. The total percentage of patient charts with any specific LEs discussed was 70.4%, while the total percentage of patients receiving any specific SRs was 38.9%. Accounting for individual patient susceptibility to LEs, the most commonly discussed LEs risks were radiation-induced (RI) infertility (discussed in 48.7% of those susceptible), RI lung damage (33.1% of those susceptible), and RI thyroid disease (31.0% of those susceptible). The least commonly discussed LEs risks in susceptible patients were RI bowel cancer (3.1%), RI meningioma (1.9%), and RI carotid artery stenosis (0.4%). The most common SRs in susceptible patients were for RI breast cancer (43.2%) and RI thyroid disease (23.5%). SRs were discussed with 53.1% of patients who had a discharge appointment versus 29.9% of patients who did not have a discharge appointment ($p<0.0005$). LEs were discussed for 87.7% of patients diagnosed between 1996-2009 compared to 51.9% of patients diagnosed between 1959-1996 ($p<0.0005$). SRs were made for 46.7% of patients diagnosed between 1996-2009 30.6% of those diagnosed between1959-1996 ($p=0.001$). SRs were given to a greater proportion of patients who were ≥29 years versus <29 years old at discharge (44.0% versus 33.5%, respectively; $p=0.036$), while there was no significant difference in LEs discussion between these two groups.

Conclusions: Most survivors of AYA lymphoma received some discussion of LEs, but each relevant LEs risk was discussed in only a minority of susceptible patients; the discussion of SRs was even less common. SRs were more likely given to patients who had a formal discharge appointment. The frequency of LEs discussion and SRs increased over time, but there is room for further improvement. Overall, written documentation to PCPs lacked adequate LEs education and SRs. Recall of this cohort of AYA lymphoma survivors should be considered to assess the presence of LEs and long-term follow-up needs.

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LONG-TERM OUTCOMES FOR PATIENTS WITH LIMITED STAGE FOLLICULAR LYMPHOMA: AN UPDATE OF THE BC CANCER EXPERIENCE

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Purpose: Follicular lymphoma (FL) is the most common indolent lymphoma and most frequently presents as advanced stage disease. Radiotherapy (RT) is integral in the treatment of limited stage FL and potentially curative. However, given the long natural history, mature follow-up is needed to accurately define the relapse risk. We previously reported on the long-term outcome of 237 patients with limited stage FL treated with curative intent RT with a median follow-up of 7.3 years. Herein, we report the outcome with now a median follow-up of 13.1 years and also re-evaluated the impact of involved node with margins ≤5cm (now

known as involved site RT (ISRT)) on relapse rates.

Materials and Methods: Patients diagnosed with Stage 1A/IIA, Grade 1–3A FL from 1986–2006 and treated with curative-intent RT alone were previously identified. Computed tomography scans but not positron emission tomography scans were used for staging. RT was categorized as IRRT versus ISRT; IRRT encompassed the involved lymph node (LN) group plus ≥1 adjacent, uninvolved LN group(s) and ISRT covered the involved LN(s) with margins ≤5 cm. Survival rates with standard errors were calculated using the Kaplan-Meier method and comparisons made using the log-rank test. Cox regression was used for multivariable analysis (MVA).

Results: Of the 237 patients, 48% were men, 54% were >60 years old at diagnosis, 76% had Stage IA disease, 12% had Grade 3A disease, 19% had LN size ≥5 cm, and 7% had elevated lactate dehydrogenase. IRRT was used in 60% and ISRT in 40%. Median follow-up was 13.1 years (range, 0.3-28.9 years) and 80% were followed for over seven years. Freedom-from-progression (FFP, unrelated deaths censored) was 65.9±3.1% at five years, 49.5±3.4% at 10 years and 43.8±3.6% at 15 years. Five-year progression-free survival (PFS, all deaths counted) was 61.8±3.2%, 10-year PFS was 40.1± 3.2% and 15-year PFS was 28.0±3.1%. Overall survival was 86.5±2.2% at five years, 70.9±3.0% at 10-year and 57.2±3.2% at 15 years. Of the 124 first relapses, 11 (9%) occurred beyond 10 years and three (2%) occurred beyond 15 years. First failures were distant alone in 107 patients (45%), in-field alone in 4 patients (1.6%) and both distant and in-field in 11 patients (4.6%). Of the 95 patients treated with ISRT, only one (1%) had a first failure that was regional-only (i.e., out-of-field but would have been covered by an IRRT approach). Ten-year FFP was 45.9±4.3% after IRRT and 55.4±5.4% after ISRT (p=0.26). On MVA, RT field size did not impact FFP; significant factors for FFP included only sex and stage, with hazard ratio [HR]=1.5 for male versus female (p=0.028), HR=3.7 for LN size ≥5cm versus complete excision (p=0.007), and HR=2.7 for nodal size <5cm versus complete excision (p=0.032).

Conclusions: In patients with limited stage FL, disease recurrence was uncommon after 10 years and rare after 15 years. At 15 years, 44% of patients remained disease-free, confirming that a cure is possible. Reduction of RT fields to ISRT did not appear to impact relapse risk in the long-term.

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