RADIATION DOSE MAPPING OF THE STOMACH IN TRIMODALITY THERAPY FOR ESOPHAGEAL CANCER

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Purpose: Esophageal cancer remains a difficult cancer to cure despite aggressive therapy. A common strategy aimed at achieving cure in locally advanced esophageal cancers is to use neoadjuvant concurrent chemoradiotherapy followed by surgery (“trimodality” therapy). Post-operative complications following esophagectomy with gastric pull-up are significant events when they occur, including possible anastomotic leaks. Our goal is to investigate whether a relationship exists between these complications and the radiation dose to specific sub-regions of the esophagus and stomach.

Methods and Materials: An ethics board-approved retrospective analysis was performed on 37 consecutive patients at our institute who underwent neoadjuvant chemoradiotherapy followed by a radical esophagectomy. Patients were treated between January 1, 2008 and December 31, 2012. For each case, the 3D conformal plan was re-calculated once the stomach was contoured. Gastric contouring consisted of an overall organ contour from the gastro-esophageal junction to the pylorus. A series of sub-contours were then devised dividing the stomach into thirds: superior, middle and inferior third. The superior third was further subdivided into medial and lateral sub-components. At the time of simulation, patients were not given any specific instructions for food avoidance, and a subset were asked to drink oral contrast (< 100 ml). The mean radiation dose and V40 were computed for specified regions of the stomach.

Results: A total of 37 patients were analyzed. The study cohort included 31 cases of esophageal adenocarcinoma and six cases of squamous cell carcinoma. Thirty-five of 37 cases involved the lower third of the esophagus. All surgeries were performed with a transthoracic approach, with minimally invasive (15) or open techniques (22). Radiation dose varied between 4500-5040 Gy, given 180-200 Gy per day, often with a two phase approach with a smaller boost volume. The mean (range) dose of the medial superior, lateral superior, middle and inferior thirds of the stomach were 3819 Gy (46-5193), 2587 Gy (40-5077), 2569 Gy (27-4713) and 1304 Gy (14-4265) respectively. The calculated V40 for each gastric sub-segment was 72.3%, 34.0%, 34.7% and 12.5% respectively.

Conclusions: There is no radiation sparing of the distal 2/3 of the stomach in patients treated with neoadjuvant radiotherapy for esophageal cancer. In some cases, doses approach or are equal to the prescribed dose. Surgeons may not be aware that tissues used to form an anastomosis with the proximal esophagus may have received significant dose. There is rationale to investigate a relationship between dose to the stomach and potential anastomotic complications in this patient population.

RADIIUM-223 IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER: SINGLE-INSTITUTION ANALYSIS OF FACTORS ASSOCIATED WITH TREATMENT COMPLETION AND SURVIVAL

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Purpose: Radium-223 (Ra-223), an alpha particle-emitting radionuclide, is the first bone-targeted therapy demonstrated to improve survival in metastatic castration-resistant prostate cancer (mCRPC). We report our institution’s experience with this therapy, exploring the association between mCRPC therapies received prior to Ra-223 and treatment outcomes.

Methods and Materials: The outcomes of patients with progressive, symptomatic mCRPC with bone metastases treated with Ra-223 between October 2009 and December 2015 were analyzed. The association between baseline characteristics and outcomes following treatment were analyzed using descriptive statistics while overall survival (OS) was estimated using the Kaplan-Meier method. Toxicities were assessed using NCI CTCAE v4.0.

Results: A total of 36 patients were analyzed. Median follow up was 6.8 months (range, 1.5-34.7). Median age was 75 years (range, 49-88). Prior to commencing Ra-223, 14 patients (39%) were treated with abiraterone acetate (abi), 17 patients (47%) with enzalutamide (enza), and 14 patients (39%) with docetaxel; 16 patients (44%) received more than one of these agents and seven (19%) received none. The median number of Ra-223 injections received was five (range, 1-6). Nineteen patients (53%) discontinued therapy prematurely. Median OS for the total cohort was 10.0 months (95% CI, 4.5-15.0). There was a non-significant trend towards shorter OS in those patients that had received prior abi or enza versus those that had previously received neither of these agents (median 6.8 versus 14.0 months; HR 2.67; 95% CI, 0.87-8.20; log-rank p = 0.087). Forty-four percent of patients that had received prior abi/enza completed all six planned injections of Ra-223 versus 55% of those that had not received prior abi/enza. There were differences in the baseline characteristics of those that had received prior abi/enza versus not: mean PSA 272 versus 114 mcg/L, and proportion with ≥ 20 metastases 64% versus 44%, respectively. Cumulative incidence of Grade ≥ 3 hematologic toxicity during or after treatment with Ra-223 was as follows: anemia 19%, neutropenia 0%, and thrombocytopenia 11%.

Conclusions: This cohort of patients receiving Ra-223 spans the era prior to the advent of abi and enza and thus included patients with and without prior exposure to these agents. Patients receiving abi and/or enza prior to commencing Ra-223 were less likely to complete the 6 planned injections and had a non-significant trend toward shorter survival, raising the hypothesis that earlier integration of Ra-223 in the mCRPC disease course may be preferred. This apparent association may simply reflect greater disease burden in more heavily pre-treated patients rather than diminished efficacy of Ra-223 in this setting. Prospective trials of Ra-223 in early mCRPC are underway. Finally, the toxicity profile of Ra-223 observed in this real-world setting was relatively favourable and comparable to that seen in the Phase III trial that led to regulatory approval.

ADJUVANT RADIOTHERAPY FOR PROSTATE CANCER: DID GUROC RECOMMENDATIONS INFLUENCE PRACTICE TRENDS?

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Purpose: In 2008, the Genito-Urinary Radiation Oncologist of Canada (GUROC) published a guideline recommending adjuvant RT (aRT) for the treatment of prostate cancer patients with high-risk features (HRF; pathologic margins, extracapsular extension [ECE], or seminal vesicle invasion [SVI]). To determine the association between the guideline and the patterns of practice, we compared the rate of aRT offered prior to and following this GUROC recommendation.

Methods and Materials: All patients treated with radical prostatectomy (RP) in 2005 (pre-GUROC cohort) and 2012 (post-GUROC cohort), who were eligible for aRT (HRF and post-operative PSA < 0.2ng/mL) and were referred to a radiation oncologist in a particular Canadian province were identified retrospectively from the cancer registry. Demographics, pathology, commodities, and treatment data were extracted from patients’ electronic medical record. aRT was defined as radiation given within six months of RP with the last PSA before
radiotherapy < 0.2 ng/mL. Salvage RT was defined as radiation delayed until PSA rose above a threshold (≥ 0.2 ng/mL). All patients were followed for three years.

Results: Forty-nine patients (pre-GUROC: n = 20, post-GUROC: n = 29) met the inclusion criteria. Age, clinical, and pathological factors were similar between the two cohorts, including rates of ECE, SVI and post RP PSA (p > 0.05), however, there were more patients with positive margins in the post-GUROC cohort (50% versus 79%, p = 0.03). Rate of aRT offered was not significantly different between the pre- versus post-GUROC cohort, 65% versus 69%, (p > 0.05). Furthermore, no differences were noted between the rate of salvage RT or no RT offered between the cohorts: 15% versus 10% (p = 0.05), and 20% versus 21% (p > 0.05), respectively.

Conclusions: Two-thirds of eligible prostate cancer patients referred to radiation oncologists in a particular Canadian province were offered aRT. This practice pattern did not significantly change after the publication of the GUROC recommendations.

224 RADIOTHERAPY OF THE PRIMARY TUMOUR FOR METASTATIC PROSTATE CANCER
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Purpose: The standard treatment for men with newly diagnosed metastatic prostate cancer (mPCA) is androgen deprivation therapy (ADT). Local radiotherapy (RT) to the prostate has traditionally been reserved for men who require symptomatic relief in patients with metastatic disease. However, local RT may have other benefits in addition to symptomatic relief. This study investigates the impact of local RT on overall survival (OS) in men with newly diagnosed mPCA.

Methods and Materials: This is a retrospective, population-based study of patients age > 18 years diagnosed with metastatic (M1) prostate cancer in Manitoba between 2004-2013. Patients with neuroendocrine or small cell histology were excluded. Data was collected from Cancer Registry and electronic charts including age, T/N/M stage, PSA, Charlson comorbidity score, RT, surgery, systemic therapy, Gleason score, and ECOG performance status. Cox regression was used to predict OS. Likelihood ratio testing was used to identify factors associated with OS. A p value < 0.05 was considered significant.

Results: A total of 321 patients were included and 25 (7.7%) received RT to the prostate within one year of diagnosis. The median follow up was 2.21 years. The mean age was 71.9 years. Clinical T stage included T1 (9.3%), T2 (26.6%), T3 (21.7%) and T4 (10.5%) and TX (31.9%). N stage ranged from NO (21.4%), N1 (37.5%), NX (41.2%). M stages consisted of M1a/M1b (63.5%), Mt1c (14.2%) or MX (22.3%). Of the 25 patients who received prostate RT, 15 received high dose (≥ 50 Gy) and 10 low dose (< 50 Gy). Multivariable analysis showed a hazard ratio (HR) for death of 1.09 (95% CI 0.64-1.85, p = 0.75) for patients receiving prostate RT (any dose) compared to those without prostate RT. Furthermore, the HR for high dose RT was 0.73 (95% CI 0.35-1.53, p = 0.41) and 1.77 (95% CI 0.89-3.52, p = 0.1) for low dose RT.

Conclusions: In this cohort of patients with newly diagnosed mPCa, there was no association between RT to the prostate and OS. However, this study was limited by statistical power and additional investigation in a larger population is needed.

225 ASSESSMENT OF BIOCHEMICAL OUTCOME WITH INCREASING DOSE ESCALATION IN LOCALIZED PROSTATE CANCER (PCA) WITH PRECISION IMAGE-GUIDED RADIOTHERAPY (IGRT)
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Purpose: Dose escalation (DE) increases biochemical and local control in PCA. Addition of image guidance improves outcomes of highly conformal techniques. However, the benefit of DE and optimal fractionation in the context of IGRT remains unknown. Herein, we determine biochemical outcomes in three patient cohorts treated with progressively DE schemes and daily image-guidance (IG).

Methods and Materials: We analyzed prospectively collected data from a single Institution. Departmental standard included three sequential prostate-only schedules, A: 75.6 Gy (1.8 Gy/d); B: 79.8 Gy (1.9 Gy/d); C: 78 Gy (2 Gy/d). Daily IG consisted of fiducial markers and daily orthogonal imaging (predominantly A and B) or cone beam CT (mainly C). Patients were categorized into NCCN risk categories, and intermediate-risk (IR) subdivided into favourable and unfavourable (Zumsteg’s criteria). Primary endpoint was biochemical recurrence (BCR) by Phoenix definition (PSA nadir + 2 ng/mL). Biochemical relapse-free rates (bRFR) were compared between three dose schedules and risk groups using Cox proportional hazard models and Kaplan-Meier method.

Results: Nine hundred and eighty-seven patients were included with a median age of 71.7 years. Risk category distribution was 18% (low), 68% (IR) and 13% (high). Of IR patients (673), 62% were unfavourable. Two hundred and ninety-three (30%), 315 (32%) and 379 (38%) patients were treated with A, B and C, respectively. Overall, 11% of patients received ADT. Age, initial PSA, T-stage, Gleason score, use of ADT and risk category distribution were not different between three groups. Median follow up was 5.9 years (0.1-16.5): 9.0 years (0.1-16.5), 9.6 years (0.1-14.3) and 4.9 years (0.2-9.5) for A, B and C. bRFR was significantly different between A, B and C (p < 0.0001) with five year rates of 76%, 82%, 91% and eight year rates of 54%, 64% and 80%, respectively. Overall, compared to C, those treated with A and B had a HR of 2.67 (95% CI 1.87-3.81, p = 0.001) and 1.93 (95% CI 1.34-2.77, p < 0.001) for BCR, respectively. In low-risk category, group A had a higher risk of BCR compared to C (HR 4.1, 95% CI 1.18-14.32, p = 0.027), but no difference between B and C was observed (p = 0.17). For favourable IR, A and B had increased risk of BCR (HR 4.38, 95% CI 1.68-11.4, p = 0.0025 and HR 3.05, 95% CI 1.68-9.4, p = 0.022, respectively) compared to C. Findings were similar for unfavourable IR group (HR 2.24, 95% CI 1.36-3.67, p = 0.0015 and HR 1.88, 95% CI 1.13-3.14, p = 0.015 for A and B versus C, respectively). In high-risk category, no difference in BCR rates was observed.

Conclusions: We observed a possible continuous dose response and bRFR improvement with progressive DE in the context of daily IG, particularly significant for IR categories. With long-term follow up, we observed a continuous occurrence of BCR. Given the limitations of retrospective studies, our results justify further dosimetric- and technique-related factors analyses. Prospective validation of these findings and consideration for higher DE-IGRT seem warranted to improve outcomes for PCs.

226 Abstract withdrawn

227 PROGNOSTIC SIGNIFICANCE OF TONSIL EXPRESSION AND THE HOMOLOGOUS RECOMBINATION PATHWAY IN INTERMEDIATE-RISK PROSTATE CANCER RECURRENTNESS
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Purpose: The standard of care for men with newly diagnosed mPCA is androgen deprivation therapy (ADT). Local radiotherapy (RT) to the prostate has traditionally been reserved for men who require symptomatic relief in patients with metastatic disease. However, local RT may have other benefits in addition to symptomatic relief. This study investigates the impact of local RT on overall survival (OS) in men with newly diagnosed mPCA.

Methods and Materials: This is a retrospective, population-based study of patients age > 18 years diagnosed with metastatic (M1) prostate cancer in Manitoba between 2004-2013. Patients with neuroendocrine or small cell histology were excluded. Data was collected from Cancer Registry and electronic charts including age, T/N/M stage, PSA, Charlson comorbidity score, RT, surgery, systemic therapy, Gleason score, and ECOG performance status. Cox regression was used to predict OS. Likelihood ratio testing was used to identify factors associated with OS. A p value < 0.05 was considered significant.

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Conclusions: In this cohort of patients with newly diagnosed mPCa, there was no association between RT to the prostate and OS. However, this study was limited by statistical power and additional investigation in a larger population is needed.