prostate ultrasound images with either a Foley or gel were fused and analyzed. The catheter tends to take a path of least curvature and is thus located in the anterior urethra. At mid-prostate the difference is most pronounced with the posterior aspect of the gel-filled urethra. Urethra V115% was higher when the urethra was defined with gel. Median V115% was 0 cc (0.0-0.03) with catheter compared to 0.03 cc (0.0-0.53) with gel (p = 0.02) and translated to a median V115% of 0% (0.2-14) versus 3.23% (0.20-20.95) (p = 0.003), respectively. Only one patient when analyzed with the gel had a V115% > 10%(16.6%) and three had a V125% > 0 cc (p = 0.31). The urethral volume was 1.4 cc (1.04-1.85) using the 6mm circle and was 1.22 cc (0.7-2.53) when using aerated gel (p = 0.522). At the prostate base and apex the smaller diameter of the catheter makes visualization with gel alone difficult.

Conclusions: Using a Foley catheter for urethral identification and dose prescription underestimated the dose that is actually received by some patients. Urethral curvature differs from the Foley catheter, especially at mid gland where the catheter rides anteriorly. A standard 6 mm circle does not represent the entire urethral volume. Although we have not observed unexpected toxicity, we will continue to monitor actual urethral dose to correlate with toxicity in future patients. In the meantime, use of a catheter is the most reliable means of visualizing the entire length of the prostatic and membranous urethra. Consideration could be given to expanding the 6 mm circle in the posterior direction in mid-gland.

39  LONG-TERM OUTCOMES OF A PHASE II TRIAL OF MODERATE HYPOFRACTIONATED IMAGE-GUIDED INTENSITY MODULATED RADIOTHERAPY (IG-IMRT) FOR LOCALIZED PROSTATE CANCER
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Purpose: To evaluate long-term biochemical control (bRFR) and radiation toxicity for men with localized prostate cancer treated with two moderately hypofractionated IG-IMRT regimens.

Methods and Materials: Eligible consenting men with T1c-T3a Nx Mo prostate cancer were enrolled in a Phase II trial and received IG-IMRT to a a modified prostate volume that included proximal seminal vesicles at 3 Gy per fraction, 5 days per week in sequential cohorts to a total dose of either 60 Gy or 66 Gy. Late gastrointestinal (GI) and genitourinary (GU) toxicity were recorded at each follow up using the Radiation Therapy Oncology Group criteria and biochemical failure was scored using the PSA nadir+2 criteria. Outcome estimates were calculated using the Kaplan-Meier method and log rank test. Early stopping rules terminated accrual to the 66 Gy cohort due to excessive Grade 3-4 late toxicity.

Results: Ninety-six men received 60 Gy and 28 received 66 Gy. Androgen deprivation therapy (3-36 months duration) was used in 10% of men in both cohorts. For each cohort, the median age was 71 years (60 Gy) and 70 years (66 Gy). Low or intermediate-risk presentation was respectively 27% and 65% (60 Gy) and 25% and 75% (66 Gy). Median follow up was 128 months (60 Gy) and 108 months (66 Gy). The five- and eight-year bRFR for 60 Gy and 66 Gy were respectively 83% and 67% versus 88.5% and 73.4% (p = 0.224). For each cohort, five (60 Gy) and one (66 Gy) subjects died from disease. Overall five- and eight-year cumulative late Grade 1-4 GI toxicity for 60 Gy versus 66 Gy were respectively 21.2% and 21.2% versus 44.6% and 48.9% (p = 0.004). Cumulative late Grade 1-4 GU toxicities were respectively 23.8% and 32.8% versus 40.4% and 51.4% (p = 0.048). Cumulative five- and eight-year late Grade 3-4 GI toxicity for 60 Gy and 66 Gy were respectively 1.1% and 1.1% versus 11.5% and 11.5% (p = 0.01). Cumulative five- and eight-year late Grade 3-4 GU toxicity for 60 Gy and 66 Gy were respectively 0 and 1.5% versus 3.7% and 3.7% (p = 0.41). At last follow up in the 60 Gy cohort there were no Grade ≥ 3 late GI toxicities and one Grade 3 late GU toxicity. In the 66 Gy cohort there was one Grade 4 late GI toxicity and one Grade 4 late GU toxicity.

Conclusions: Moderate hypofractionation to 60 Gy was associated with modest late toxicity and provided excellent five-year bRFR for our patients, although failures continued to be observed with subsequent follow up. Dose escalation to 66 Gy was associated with significantly worse late GI and GU toxicity without an apparent improvement in bRFR.

40  RADIATION PNEUMONITIS IN PATIENTS WITH INTERSTITIAL LUNG DISEASE TREATED WITH LUNG STEREOTACTIC RADIATION THERAPY
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Purpose: To determine the impact of pre-treatment interstitial lung disease (ILD) on radiation pneumonitis and overall survival (OS) in patients treated with lung SBRT.

Methods and Materials: Patients treated with lung SBRT between October 2004 and July 2015 at our institution were included. Pre-treatment CT scans were reviewed by experienced thoracic radiologists and interstitial changes including ground glass opacities (GGO), reticulations and honeycombing were scored and involvement to the nearest % was used to calculate Washko and Kazerooni scores. Radiation pneumonitis (RP) was prospectively documented using the CTCAE V4.0 criteria. Pre-treatment imaging characteristics, lung and heart dose parameters and clinical variables including smoking status and pulmonary function were assessed by univariate (UVA) and multivariate analysis (MVA). OS was assessed by log rank test and impact of ILD on overall survival was assessed by Cox regression.

Results: Five hundred and forty-two patients were assessed with 56 having evidence of interstitial changes on pre-treatment scans. These included 12 cases of usual interstitial pneumonia (UIP), 18 cases of possible UIP, nine cases of non-specific interstitial pneumonia and 17 cases of age-related reticulations thought to be unrelated to ILD. RP was significantly higher in the 39 patients with ILD (Grade ≥ 2 20.3% versus 5.8%, p < 0.01; Grade ≥ 3 10.3% versus 1.0%, p < 0.01). Of the three cases of Grade 5 RP observed in our series, two had imaging features of ILD. On UVA, radiographic evidence of ILD, Washko score, lung parameters (V5/V10/V15/V20/mean lung dose) and performance status were significant predictors of Grade ≥ 2 RP. Age-related reticulations were not associated with increased toxicity. On MVA, ILD (OR 5.18, p < 0.01) and mean lung dose (OR 1.003, p < 0.01) were predictors of RP. ILD did not significantly affect OS on UVA or MVA. Median survival was 26.5 months in the ILD cohort and 36.6 in the ILD negative cohort (p = 0.09).

Conclusions: Radiographic evidence of ILD is a significant risk factor for RP in patients treated with lung SBRT, but did not impact OS. CT scans should be reviewed for evidence of ILD prior to SBRT and involvement of respirology for management is essential. If ILD patients are treated with SBRT, they should be monitored closely for RP.

41  EVALUATION OF AN AUTOMATED DEFORMABLE REGISTRATION ALGORITHM FOR MRI-GUIDED FOCAL BOOST INTEGRATED WITH ULTRASOUND-BASED HIGH DOSE-RATE BRACHYTHERAPY IN THE TREATMENT OF PROSTATE CANCER
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Purpose: Real-time transrectal ultrasound (TRUS) image guidance for prostate high dose-rate brachytherapy (HDR-BT)
enables a high degree of accuracy in dose delivery. Nevertheless, the identification of a dominant intraprostatic lesion (DIL) on TRUS is challenging. With the advent of multiparametric magnetic resonance imaging (mpMRI), it is possible to identify a location of excess of tumour cells location that are especially aggressive. Unfortunately the geometry of the prostate on TRUS and on mpMRI may be different, requiring a deformable fusion to map a DIL identified on mpMRI. This study evaluates a novel automated deformable registration algorithm developed in-house for mpMRI-to-TRUS DIL fusion.

Methods and Materials: Five patients with low- and intermediate-risk prostate cancer treated as part of a Phase II clinical trial approved by our institutional research ethic board were included in this study. All patients had a predominant PIRADS 4-5 intraprostatic nodule identified on mpMRI. An automated deformable registration was then accomplished as a three-part process: 1) convert each of the two datasets into distance maps; 2) register the MRI distance map to the TRUS distance map using a rigid affine transformation; and 3) perform a basis-spline (B-spline) deformable registration between the two datasets. An MRI assisted TRUS based real-time prostate HDR-BT was delivered afterward. A single fraction of 19 Gy prescribed as a minimal dose to the prostate was delivered with the DIL to receive a D90 ≥ 23 Gy up to 28 Gy (tertiary objective).

To evaluate the accuracy of the automatic deformable registration algorithm, a radiation oncologist was asked to cognitively register the lesion on mpMRI onto the intraoperative TRUS dataset. Correlation between the observer’s contours and the automated contours were compared using the Dice similarity coefficient. The average distance from the edges of the observer and automated contours were reported in each of the cardinal directions.

Results: The mean Dice coefficient for the prostate volumes was 0.88 ± 0.01. The mean Dice coefficient for the DIL was 0.76 ± 0.04. The mean difference in the anterior and posterior edge of the automated versus human contours was 0.93 ± 0.89 mm and 0.26 ± 0.26 mm respectively. The mean difference in the superior and inferior edge of the automated versus human contours was 2.19 ± 1.72 mm and 1.55 ± 1.44 mm respectively. The mean difference in the lateral edge of the automated versus human was 1.13 ± 0.38 mm as opposed 2.58 ± 1.8 mm in the medial edge.

Conclusions: The automated deformable registration algorithm objectively and reliably transposes the DIL identified on mpMRI into the TRUS based prostate HDR-BT workflow. Caution should be exercised when using automated contour based algorithms, with careful QA of the resultant co-registration. Particular scrutiny should be directed at the sup-inf and med-lat extents of the DIL resulting from the fusion.

42 CARO FELLOWSHIP

STAGGING ON TARGET: OPTIMIZING UTILIZATION OF PRECISION RADIOTHERAPY

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Background: Radiotherapy is an effective and comparably low-cost cancer treatment. It has been estimated that 50% of cancer patients require radiation treatment. Lung cancer is the most commonly diagnosed cancer globally, and 77% of patients diagnosed with lung cancer will need radiotherapy. Despite this, evidence from around the world suggests that radiotherapy for lung cancer and other cancers continues to be under-utilized for reasons unrelated to patient need. Traditionally in radiation oncology, the majority of research has been focused on improving scientific knowledge and technical aspects of therapy. However, achieving the outcomes that these innovations allow is often hampered by system factors such as the complexities of matching demand for radiotherapy with supply of radiotherapy services. Consequently, there is a great need to measure actual and optimal use of radiotherapy and to identify and research modifiable factors that contribute to sub-optimal utilization of multimillion-dollar high-precision radiation treatment centres. The lack of availability of comprehensive information on characteristics that influence the performance of radiotherapy programs has limited the design and management of their services. As a result, planning has often been directed by expert opinion rather than objective evidence. The consequences of such an approach can be unpredictable, which in turn can lead to inefficient and inadequate care. In an era of high-precision radiotherapy, the greatest impediment is still failing to deliver radiotherapy when it is indicated.

We propose a study to begin to address this, focusing on lung cancer as an example. Recently, Cambridge University has developed The MALTHUS Project: An application of mathematical models of radiotherapy demand for local and national capacity planning using Monte-Carlo simulation techniques. The MALTHUS model is a form of Evidence-Based Requirements Analysis (EBRA). EBRA identifies indications for radiation therapy for a specific population based on systematic literature reviews. It then used an epidemiologic approach to calculate how frequently these indications for radiotherapy occurred in the population. This information is synthesized in order to estimate an appropriate rate of radiotherapy utilization. Delaney, Barton et al. expanded its use to all cancer sites and EBRA-type models are now broadly used for resource planning. Compared to some historical EBRA models, the MALTHUS model has the advantage of taking into consideration treatment complexities and dose fractionation of radiotherapy, which results in a more accurate demand quantification.

A second method of demand estimation, “Benchmarking,” draws from the business world practice of comparing outcomes against the toughest competitor. In a radiotherapy context, benchmarking utilizes regions with cancer centres without major access barriers as the standard. This method assumes that experts are making “perfect” decisions about radiotherapy indications and that patients have access to optimal treatment services. Criticism of the benchmarking method to assess health outcomes lies in its assumption of optimal structures, processes and practices, all of which have not been proven.

The overall population’s need for radiotherapy will change according to the different proportions of cancers and stages of cancer found in different populations, geography, as well as patient factors such as functional status, age, and comorbidity. To tailor the model to a specific country or health setting requires data on the distribution of tumour types and stages as well as geographical and demographic factors. The MALTHUS model can be used to examine factors associated with regional variation in current demand and can also be used to predict future demand.

Proposed Study: We propose a comparative analysis between Ontario and England of the estimated need for lung radiotherapy for lung cancer based on the MALTHUS model. The analysis will provide insights characterizing the extent to which patient-related and disease-related factors that drive the need for radiotherapy resources.

This study will build on previous models of radiotherapy utilization and will be a collaborative approach with multiple international stakeholders. The results of this study will aim to optimize utilization of high-precision radiotherapy in quantifying the impact of patient factors, disease factors, and treatment factors on estimating demand of radiotherapy.

Hypotheses:

1) That evidence-based estimates of need for radiotherapy for lung cancer will vary widely between health delivery units