2) This variation will relate to patient factors, disease-related factors, and treatment factors.

3) That regional variation in need for radiotherapy for lung cancer predicted by the MALTHUS model will be greater than that seen with a benchmark approach to optimal utilization.

Methods: The MALTHUS model for radiotherapy demand will be utilized in order to investigate factors associated with regional variation in need for radiotherapy for lung cancer patients. MALTHUS decision trees for 23 disease sites have been established. The proximal branches of the tree encodes for cancer site, stage distribution, and treatment modality indication. Distal branches contain detailed information about how radiation is delivered, such as fractionation. MALTHUS takes into account 1) variation in cancer incidence, disease stage, performance status, and co-morbidity. It draws on high-quality cancer incidence data collected from national Cancer Registries and the National Cancer Intelligence Network (NCIN). It simulates demand at local, regional and national levels, and draws comparisons with actual radiotherapy activity from the British National Health Service’s (NHS) Radiotherapy Dataset (RTDS). The resulting data can be used to study the effects of differences in clinical opinion over best practice, and can assist local oncologists and service managers in developing and assessing business plans.

We will update the British data with direct access to the National Cancer Intelligence Database that, from previous work, has been properly curated for the use of this model. Data will be stratified for age, tumor characteristics, stage distribution, and region subdivided at the county level. The model will then be adapted to the appropriate treatment indications and dose fractionations using national evidence based best practice guidelines. We will quantify the influence of patient-related factors (age, sex, comorbidity, functional status), disease-related factors (cancer incidence, cancer stage), and treatment factors (hypofractionation including usage of SBRT) on regional (NHS Primary Care Trust level) demand for radiotherapy for lung cancer. In univariate analysis, factors will be defined categorically and demand for radiotherapy by variable category will be described. The influence of these factors will be further investigated in univariate sensitivity analysis. The consequences of applying regional extremes in each variable’s distribution on national radiotherapy demand will be considered. For multivariate sensitivity analysis, a Monte Carlo (MC) simulation model will be used. Probability distributions based on population-based data from the Ontario Cancer Registry (OCR) will be utilized. This will include data on cancer incidence, and collaborative stage information. Data on age distribution by county from OCR will be used to estimate regional differences in performance status and comorbidity.

Significance: A primary benefit of this model is its potential to elucidate what influences demand for radiotherapy patients. Demand, and by the same token, wait lists, are affected by an increase in the incidence of cancer, by the increase in the referral of patients for radiotherapy, and by an increase in dose fractionation per course of radiotherapy. All of these factors are reflected in the MALTHUS. As the public system has a fixed global budget and lacks the reserve needed to expand capacity quickly in radiotherapy, an accurate prediction of future demand is vital in our situation. Comparing Canadian and British data utilizing MALTHUS should increase generalizability in its projections and may identify national differences in the impact of key factors driving demand. Reliable, well-characterized models are needed, as it can take years in working closely with policy makers in order to influence officials to provide adequate capacity for high-precision radiotherapy.

Radiation therapy has major oncological benefits, and small incremental gain in health system performance can translate into large societal benefits. Health Services Research in its nascent stages in the field of Radiation Therapy, therefore there is a significant amount of knowledge and skills that can be gained by young investigators. Results of this research program will have a direct link to many global institutions. ESTRO and QUARTS are currently exploring optimal infrastructure for radiation therapy around Europe, a project funded by the European Commission. Moreover, this comparative analysis will supplement data utilized for Activity Based Costing and Cost Benefit research that ESMO is currently undertaking.

43 PHASE I-II ON THE USE OF DUAL-ENERGY COMPUTED TOMOGRAPHY (DECT) FOR ASSESSMENT OF DIFFERENTIAL PULMONARY FUNCTION IN RADIOTHERAPY PLANNING

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Purpose: Current lung parenchyma dose reduction strategies do not take into account the relative contribution of different lung regions. The addition of functional information at the time of treatment planning could preferentially save the most functional parts and reduce the risk of toxicity. The purpose of this study was to quantify lung function based on a DECT-derived iodine map in patients treated with radiotherapy for lung cancer, as well as to assess the dosimetric impact of its integration in radiotherapy planning.

Methods and Materials: Patients treated with stereotactic ablative radiotherapy (SABR) for locally advanced lung cancer were prospectively enrolled in this study. A DECT in treatment position was obtained at time of treatment planning. Single Photon Emission Computed Tomography / Computed Tomography (SPECT/CT) and pulmonary function tests were obtained for validation purposes. Relative contribution of each voxel to the total lung function was based on iodine concentration. Composition of each voxel was determined with a Matlab (MathWorks) script based on a three material decomposition. The functional map was integrated in treatment planning system using 6 sub-volumes of varying iodine concentration levels. Percent lung volume receiving 5 Gy (V5), V20 and mean dose (MLD) to whole lungs (anatomical) versus functional lungs were compared using bilateral paired Student T tests.

Results: Results from 20 consecutive patients, including 16 patients treated with SABR and four patients with IMRT, are presented. Forty percent had known chronic obstructive pulmonary disease. Median forced expiratory volume in one second was 62% of predicted (29-113%) and median diffusing capacity of the lung for carbon monoxide was 56% (39-91%). There was a strong correlation between DECT and SPECT/CT-derived lung function (r = 0.8, p = 0.0001). Mean V5, V20 and MLD variation between functional (weighted dosimetry) and anatomical lung volumes was 16% (0-48%, p = 0.03), 5% (1-15%, p = 0.12) and 15% (1-43%, p = 0.047), respectively.

Conclusions: DECT-derived iodine map correlates well with SPECT/CT and its integration in treatment planning is associated with significant differences in V5 and mean dose to functional lungs. Future work will focus on selection of patients most likely to benefit from function-sparing IMRT.

44 PREDICTING IQ AND THE RISK OF HEARING LOSS FOLLOWING PROTON VERSUS PHOTON RADIOTHERAPY FOR PEDIATRIC BRAIN TUMOUR PATIENTS

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Purpose: Intensity modulated proton therapy (IMPT) allows for the delivery of ionizing radiation over a well-defined range with minimal exit dose compared to photons, and may further improve dose conformity compared to other proton modalities. IMPT is not available for brain cancer treatment in Canada. Instead, patients who would likely benefit from proton over photon therapy are evaluated on a case-by-case basis for referral to US facilities. Improved neurocognitive outcomes would certainly constitute a strong argument. As such, tools were developed to estimate the intelligence quotient (IQ) and the risk of hearing loss post radiotherapy and to compare outcomes of proton against photon in pediatric brain tumours on a case-by-case basis.

Methods and Materials: Pediatric patients who had received cranial photon intensity modulated radiation therapy (IMRT) were randomly selected from our retrospective database: 10 cases each of craniopharyngioma, ependymoma and medulloblastoma, and 20 cases of glioma. The existing planning CT and contourd structures were used to generate IMRT plans employing a robust optimization procedure. The RBE-corrected dose to brain structures and the cochleas were calculated for both IMPT and IMRT. A dose dependent IQ model was applied to estimate IQ using a Markov chain Monte Carlo technique. Cumulative probability distributions (CDF) were calculated to perform a statistical interpretation and to compare proton versus photon outcomes. The reported incidence of hearing loss as a function of cochlear dose in the literature was used to estimate the probability of occurrence.

Results: The average dose to the brain was less in all IMPT plans compared to IMRT: ranging from a 6.7% reduction (p = 0.003) in the case of medulloblastoma to 38% (p = 0.007) for craniopharyngioma. This dose reduction translated into a gain in IQ of 1.9 points on average for protons versus photons for the whole cohort at five years post-treatment (p = 0.011). In terms of specific diseases, the gains in IQ points were 0.8, 1.6, 2.3, and 2.7 for medulloblastoma, ependymoma, glioma and craniopharyngioma, respectively. When estimating the IQ using dose to the temporal lobes, these gains increased to 3.1 to 6.0 IQ points. Overall, the probability for IQ deficits > 7.5 points was estimated to be 32% for IMPT compared to 48% for IMRT, an absolute reduction of 16% for the whole cohort (p = 0.014). Hearing loss probability was evaluated on a per-ear-basis and was found to be systematically less for proton versus photon: 2.9% versus 7.2% (p < 10^-7).

Conclusions: IQ predictions post IMPT and IMRT were found to be very similar, but a modest gain was systematically observed for proton in all patients. Given the uncertainties within the IQ model used and our reinterpretation, the predicted gains may be underestimated. Additional long-term clinical studies are needed to improve our understanding of radiation on the developing brain.

45 VOLUMETRIC MODULATED ARC THERAPY OF HIGH-GRADE GLIOMAS USING 18F-FDOPA POSITRON EMISSION TOMOGRAPHY FOR DOSE PAINTING

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Purpose: Patient outcomes with dose escalation for high-grade gliomas have been disappointing because of non-central relapses and radionecrosis. Dose-painting can maximize central disease control, while minimizing the risk of radionecrosis. This study aimed to determine whether dose painting with volumetric modulated arc therapy (VMAT) for high-grade gliomas using 3,4-dihydroxy-6-[18F]fluoro-L-phenylalanine (18F-FDOPA) positron emission tomography (PET) could achieve dose-escalated coverage of biological target volumes (BTVs) without increasing the dose to cranial organs at risk (OARs).

Methods and Materials: Computed tomography, magnetic resonance imaging (MRI) and 18F-FDOPA PET/CT images were obtained for post-operative radiation therapy planning of 10 patients with high-grade glioma. The gross tumour volume (GTV) was contoured by a radiation oncologist using gadolinium-enhanced T1 and T2 FLAIR MRI. The clinical target volume (CTV) was defined as a 2 cm expansion of the GTV and surgical cavity. The planning target volume (PTV) was defined as a 0.5 cm expansion of the CTV. Two VMAT plans (Eclipse version 11.01, Varian Medical Systems, Palo Alto, CA) were generated for each patient: a conventional VMAT plan without dose escalation with a prescribed dose of 60 Gy in 30 fractions in the PTV and a plan with dose escalation up to a maximum dose of 80 Gy. The BTVs were created by thresholding the 18F-FDOPA uptake on PET/CT using a linear quadratic model that assumed tracer uptake was linearly related to tumour cell density in each image voxel and required the number of surviving tumour cells in each voxel to be the same. The treatment planning OARs were: brainstem, optics (combined optic nerves and chiasm), anterior chambers, and retinas. Dose conformity was quantified using van’t Reit’s conformation number. Mean OAR and maximum doses were compared using two-sided paired t tests (α = 0.05).

Results: The mean volume of the PTV receiving 95% of the prescribed dose (V95%) was 99.1% with and 99.1% without dose-painting (p = 0.6). The average PTV conformation number was high for plans with (0.92) and without (0.93) dose painting. The mean V95% was 98.7% for BT65, 94.6% for BT70 and 97.2% for BT75. The patient-averaged mean doses were 64.3 Gy for BT65, 68.5 Gy for BT70, and 73.9 Gy for BT75. The patient-averaged maximum doses to the brainstem (43.6 Gy versus 44.5; p = 0.9), optics (25.8 Gy versus 25.9 Gy; p = 0.8), anterior chambers (5.8 Gy versus 5.9 Gy; p = 0.2) and retinas (8.7 Gy versus 8.6 Gy; p = 0.9) did not differ significantly between the types of plans.

46 FACTORS AFFECTING ACCESS TO RADIOTHERAPY FOLLOWING PROSTATECTOMY FOR PROSTATE CANCER PATIENTS IN ONTARIO IN A CONTEMPORARY COHORT

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Purpose: Evidence-based guidelines confirm a survival advantage of adjuvant radiotherapy (ART) for prostatectomy (RP) patients with high-risk pathologic features. Delayed referral for salvage radiotherapy is under evaluation as an alternative strategy, and current Ontario guidelines recommend radiation oncology (RO) referral of high-risk cases for discussion of options. We sought to evaluate factors associated with referral and use of ART after RP for patients with adverse pathology in a recently diagnosed cohort.

Methods and Materials: This retrospective study used electronic treatment records linked to Ontario’s population-based cancer registry and pathology records. Multivariable regression analysis was used to evaluate factors clinical and health systems factors associated with radiation oncology (RO) consultation and ART use within six months post-RP.

Results: From January to November 2012, 2663 prostate cancer patients (mean age 61.3, s.d. 6.6 years) received RP in Ontario. Following RP, 1130 (42.3%) had at least one high-risk pathologic feature as a guideline indication for referral: extracapsular extension (ECE, 33.2%), seminal vesicle invasion (SVI, 10.1%), or positive margins (20.4%). Of these, 466 (41.2%) were seen by RO within six months of RP, of which 52.6% received ART. Of the 885 patients with adverse pathologic risk factors who did not receive ART, 75.0% were never assessed by RO. Multivariate analysis confirmed that RO assessment within six months was more frequent amongst patients with adverse pathology, including