THE IMPACT OF A CENTRAL NERVOUS SYSTEM EVENT ON COGNITIVE FUNCTION AFTER RADIATION TREATMENT IN PATIENTS WITH ONE-TEN BRAIN METASTASES

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Purpose: The cognitive side effects of whole brain radiotherapy (WBRT) are well recognized, as is the importance of local disease control on neurocognitive function. We therefore set out to assess the neurocognitive impact of a central nervous system (CNS) event in patients that received volumetric radiosurgery (VRS) and with the aid of defining a subgroup of patients receiving radiosurgery that may preserve cognition with WBRT.

Methods and Materials: This multicentre Phase 2, single-arm study accrued 60 patients with one to ten brain metastases. Eligible patients received 47.5 Gy in 5 fractions VRS to their metastases concurrent with 20 Gy in 5 fractions to the whole brain. Cognitive assessment was a secondary endpoint in the trial. Neurocognitive function was assessed using the Mini-Mental State Examination (MMSE). It was analyzed at baseline and at three-month intervals, until the 12-month follow up point. An MMSE drop of 3 points, which is the minimal clinically significant difference, was defined as a cognitive event. A CNS event was defined as local recurrence, distant brain relapse or radionecrosis.

Results: From July 2010 to May 2013, 60 patients, with a median age of 62 years, underwent treatment. Median survival was 10.1 months. Twenty-seven patients (45%) had a CNS event in the first 12 months after treatment. Sixteen patients (59%) developed distant brain relapse, five (19%) local relapse, and six (22%) radionecrosis. On univariate analysis, the risk of a CNS event was significantly associated with local recurrence, distant brain relapse or radionecrosis. On multivariate analysis, both age (HR = 4.5, p = 0.03) and CNS event (HR = 11.6, p = 0.00) with the risk of first 3 point drop in MMSE. On multivariate analysis, the risk of a CNS event was significantly associated with local recurrence, distant brain relapse or radionecrosis. On univariate analysis, the risk of a CNS event was significantly associated with the risk of first 3 point drop in MMSE. On multivariate analysis, both age (HR = 4.5, p = 0.03) and CNS event (HR = 11.6, p = 0.00) with the risk of first 3 point drop in MMSE was significantly associated with the risk of first 3 point drop in MMSE. On multivariate analysis, both age (HR = 4.5, p = 0.03) and CNS event (HR = 11.6, p = 0.00) was significantly associated with a cognitive event.

The risk of a first 3-point drop in MMSE was found to be highest in patients above median age that experienced a CNS event. This study showed that control of CNS events is the most important factor in maintaining neurocognitive function in patients with one to ten brain metastases. It determined that a clinically significant drop in MMSE was associated with local recurrence, distant brain relapse or radionecrosis, as well as older age. In patients treated with WBRT, it highlights the importance of age on neurocognitive function, as older patients with a CNS event were more at risk of a cognitive event. Using WBRT adjuvantly to preserve cognitive function, should be considered in younger patients with a high-risk of distant brain relapse.

123 USING EFORMS TO ADDRESS DATA MANAGEMENT CHALLENGES: AN IAEA TRIAL

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Introduction: Randomized Controlled Trials (RCT), particularly of rare tumour groups, often have issues with patient accrual, which necessitates a multicentre approach to achieve accrual targets. Logistically, investigators of multicentre trials face issues in efficient data management in terms of accuracy, transfer, security, and quality assurance. Historically, paper-based report forms to collect patient baseline and regular follow up data have made these issues challenging.

Purpose: To discuss the use of electronic forms (eForms) used for our glioblastoma multiforme (GBM) trial study. Various limitations and advantages of the use of eForms are discussed and compared to paper based and internet based data collection methods

Methods and Materials: Specially formatted computer based PDF forms were completed to gather patient by the investigators for screening and eligibility data (eForm A and B), as well as baseline QOL eforms (quality of life data according to EORTC QLQ-C30 and QLQ-BN20 questionnaires). After randomization, radiation treatment details (eForm C) and QOL data were collected. eForm D was used to collect follow up data. All of these forms were completed by the participating centre and then emailed as an attachment to the Data Management Centre (DMC). A short satisfaction survey was sent to the physicians of the participating centres after the completion of the study.

Results: For this study, there were 12 participating centres from across the world. There were no issues overall with data collection using the eForms. The costs associated with the development of the eForms were minimal as well. The forms were a convenient way of sending patient trial data via email to the DMC. The results of the survey agreed with our experience. About 90% of the participating sites found the design of the forms to be user-friendly, and did not have any problems accessing, completing, and submitting the files from their computer. Most of the participants found the eForms to be very practical, efficient, and standardized. About 20% of the participants found the need for a guide to be associated with the eForms for better standardization and minimizing bias. We did not find any problems with the security of using eForms as well.

Conclusions: In the setting of multicentre trials, using eForms for data management proved to be efficient, convenient, and reliable. Future multicentre trials may benefit from similar data management systems to improve data collection and analysis.

124 DETECTION OF LOCAL CANCER RECURRENT AFTER STEREOTACTIC ABLATIVE RADIOTHERAPY (SABR) FOR LUNG CANCER: PHYSICIAN PERFORMANCE VERSUS RADIOMIC ASSESSMENT

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Purpose: Stereotactic ablative radiotherapy (SABR) is a guideline-specified treatment option for early-stage lung cancer. However, significant post-treatment fibrosis can occur and confound the detection of local recurrence. The goal of this study was to assess physician ability to detect timely local recurrence on computed tomography (CT) imaging, and compare physician performance with that of a radiomics tool. Radiomics aims to extract more complex information from medical images, including features not easily visible with the naked eye.

Methods and Materials: CT scans of 45 patients (15 with proven local recurrence matched to 30 with no local recurrence) were used to measure physician and radiomic performance in assessing response. Scans were individually scored by three thoracic radiation oncologists and three thoracic radiologists, all of whom
were blinded to clinical outcomes. Radiomic features (first-order, second-order grey-level co-occurrence matrix, and size- and shape-based) were extracted from the same images. Performance of the physician assessors and the radiomics signatures were compared.

**Results:** A total of 182 follow up CT scans were analyzed with a median imaging follow up of 20 months. When taking into account all CT scans during the entire follow up period, median sensitivity for physician assessment of local recurrence was 83% (range 67-100%) and specificity was 75% (range 67-87%), with only moderate inter-observer agreement (kappa=0.54). The median time to detection of recurrence across all observers was 15.5 months. When predicting recurrence using images acquired < 6 months post-SABR, physicians assessed the majority of images as benign injury/no recurrence, with a mean error of 35%, false positive rate (FPR) of 1%, and false negative rate (FNR) of 99%. At the same time point, a radiomic signature consisting of five post-SABR image appearance features in the consolidative and surrounding peri-consolidative regions demonstrated excellent discrimination, with an area under the receiver operating characteristic curve of 0.85, leave-one-out cross-validation classification error of 24%, FPR of 24%, and FNR of 23%.

**Conclusions:** These results suggest that radiomics can detect early changes associated with local recurrence that are not typically considered by physicians. Patients with recurrence tend to have increased presence of ground-glass opacity surrounding consolidative changes compared to patients with benign injury at this early follow up time point. These appearances detected by radiomics may be early indicators of the promotion and progression to local recurrence; our ongoing studies include using correlative histology to determine their composition. This has the potential to lead to a clinically useful computer aided decision support tool based on routinely acquired CT imaging, which could lead to earlier life-saving salvage opportunities for patients with local recurrence following SABR.

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**ON THE PHYSICAL AND DOSIMETRIC PROPERTIES OF 3D PRINTED ELECTRON BOLUS FABRICATED USING POLYLACTIC ACID**

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**Purpose:** A fused deposition modeling three dimensional printer is currently being commissioned at our centre for fabrication of electron bolus. The main advantage in using a 3D printer for this purpose is that virtually any shape can be produced, potentially providing a more accurate way to compensate for irregular surfaces that can change the dose distribution within the patient. PLA is one of the most commonly used 3D printer materials. Compared to ABS, PLA is less likely to warp due to heating and cooling during printing. For less expensive printers which may not have heated printing beds or thermally controlled environments, it is especially appealing. Before PLA boluses can be clinically used, their physical and dosimetric properties must be characterized. The purpose of this study was to characterize the density, dimensional accuracy, uniformity, and attenuation of PLA boluses fabricated with our printer.

**Methods and Materials:** Several uniform solid square slabs were printed with specific requested dimensions and 100% infill using concentric and rectilinear fill patterns. These pieces were imaged using an x-ray flat panel imager in order to check for uniformity of the print. The PLA slabs were placed on solid water and irradiated with a 12 MeV electron beam. Percentage depth doses (PDDs) were measured downstream of the slabs using a parallel plate chamber and compared to measurements in water. The dimensions of the PLA slabs were measured using digital calipers in several locations, and the average was compared to design values. The slabs were also weighed using a digital scale to find their average density relative to water.