

2019 RSS ANNUAL SCIENTIFIC MEETING MARCH 21-23, 2019 • SHERATON • SAN DIEGO



BRIDGING THE GAP

the
Radiosurgery
Society

ADVANCING VALUE-BASED CARE THROUGH RADIOSURGERY

CLINICAL SESSION ABSTRACTS



2019 RSS Scientific Meeting
Bridging the Gap: Advancing Value-Based Care Through Radiosurgery
March 21-23, 2019 | San Diego, CA
www.therss.org

Interactions between Dose, Cavity Size, and Histology in the Prediction of Local Control following Stereotactic Radiosurgery for Resected Brain Metastases

Chengcheng Gui BSE, Jimm Grimm PhD, Joseph Moore PhD, Lawrence Kleinberg MD, Todd McNutt PhD, Chetan Bettgowda MD PhD, Michael Lim MD, Kristin Redmond MD MPH

Objectives: In the treatment of resected brain metastases with stereotactic radiosurgery (SRS), recent randomized controlled trials observed local control rates considerably lower than suggested by previous large retrospective studies. To better understand potential methods of improving local control, we constructed quantitative models to evaluate local control as a function of dosimetric and tumor characteristics.

Methods: Patients with brain metastases treated with resection and SRS to the cavity at our institution were evaluated retrospectively. Melanoma, sarcoma, and renal cell carcinoma were considered radio-resistant histologies. Local failure was defined by pathologic confirmation or radiographic progression leading to further overlapping radiation therapy. The dependence of 1-year local control on dose was evaluated with logistic regression. Predictors of local recurrence over time were evaluated with Cox regression. Doses were converted to 3-fraction equivalents, using the linear quadratic model with $\alpha/\beta = 12$ Gy.

Results: Among 150 resection cavities, the most common histologies were lung (40.7%), melanoma (12.7%), renal (12.7%), and breast (11.3%). Forty-one cavities (27.3%) were radio-resistant by histology. Resection was subtotal in 11 cases (7.3%) and gross total in the remainder. The median prescription was 21 Gy (range 15-25) delivered in 3 fractions (range 1-5). The median prescription isodose line was 68% (range 50-74). Median CTV and PTV volumes were 9.1 mL (range 0.7-50.2) and 14.6 mL (range 1.3-65.4), respectively. Five cases (3.3%) of biopsy-proven radionecrosis were observed. Local recurrence occurred in 20 cases (13.3%), at median 6.3 months (range 0.7-43.1) after SRS. Larger cavities were associated with poorer local control. Stratifying by a threshold PTV volume of 12 mL, 63 (42%) and 87 (58%) cavities were categorized as small and large, respectively. When controlling for D₉₅ and gross versus subtotal resection, Cox regression demonstrated significantly greater risk of local failure among large cavities (HR=4.1, 95% CI=[1.4-11.9], p=0.01). Logistic regression identified relationships between maximum dose (D_{max}) and local control among small and large radio-resistant cavities. For small radio-resistant cavities, D_{max} of 30, 35, and 40 Gy were associated with 86%, 95%, and 98% 1-year local control. For large radio-resistant cavities, D_{max} of 30, 35, and 40 Gy were associated with 69%, 79%, and 86% 1-year local control, consistent with overall higher rates of recurrence among large cavities. Among large radio-resistant cavities, similar dose-response relationships were appreciated with D₅₀ instead of D_{max}, but not with D₉₀, D₉₅, D₉₉, or D_{min}. Furthermore, Cox regression demonstrated that greater D_{max} was significantly associated with lower risk of local recurrence among large radio-resistant cavities, when controlling for D₉₉ (HR=0.34/Gy, 95% CI=[0.12/Gy, 0.96/Gy], p=0.04).

Conclusions: In the treatment of resected brain metastases with SRS, local control among small and large cavities of radio-resistant histology may be improved with greater maximum dose. Understanding the risks of toxicity established by previous studies, cautious investigation of dose escalation based on cavity size and histology may be warranted.

Tumor Control and Survival in Patients with Ten or More Brain Metastases Treated with Stereotactic Radiosurgery: A Retrospective Analysis

Matthew I. Ehrlich, B.S., Elliot Schiff, B.S., Jonathan P.S. Knisely, M.D., Jengwa Chang, Ph.D., Xin Qian, Ph.D., **Anuj Goenka, M.D.**, Michael Schulder, M.D.

Objectives: To assess tumor control and survival in patients who were treated with stereotactic radiosurgery (SRS) for 10 or more metastatic brain tumors.

Methods: Patients treated with SRS for 10 or more total brain metastases at this institution between March 2014 and April 2018 were retrospectively identified. Patient records were reviewed for clinical follow-up data, and post-treatment magnetic resonance imaging (MRI) studies were used to assess tumor control. For tumor control studies, patients were separated into two groups: those who received treatment for 10 or more synchronous metastases and those who received several treatments for 10 or more metachronous lesions. Tumor control was then assessed at intervals of three, six, and nine months. Overall survival was calculated from the first SRS treatment date. The Kaplan-Meier method was used to fit survival curves for the data, and log-rank and Cox proportional-hazards regression were employed to analyze the influence of age, sex, primary tumor histology, number of metastases treated, total tumor volume treated, brain volumes treated with 12 Gy (V12 Gy), and prior whole-brain radiation therapy (WBRT).

Results: Fifty-five patients were treated for 10 or more total brain metastases with SRS. The median patient age was 61.4 years, with patients ranging from 15.2 to 89.6 years. On average, patients were treated for a total of 17.5 metastases, with a median of 10 metastases treated per encounter. Forty patients received synchronous treatment, while 15 patients received metachronous treatment. Overall tumor volume treated ranged from 0.3167 cm³ to 54.86 cm³. Median overall survival was 10.9 months. NSCLC was the dominant primary tumor (47%), while breast cancer (22%) and melanoma (16%) were the next most common. Eight patients (14%) had prior WBRT, and ten patients (18%) required post-SRS WBRT. Cox proportional-hazards analysis revealed a significant association between patients receiving larger brain volumes irradiated with 12 Gy and decreased overall survival ($p=0.0406$); however, significance was lost on multivariate analysis. Among patients who received synchronous treatment for 10 or more metastases, the median percentage of tumors controlled was 100%, 91%, and 82% at 3, 6, and 9 months, respectively. Among patients who received metachronous treatment for 10 or more metastases, the median percentage of tumors controlled after each SRS encounter was 100% at all three time points.

Conclusions: SRS can be used to treat patients with 10 or more total brain metastases with an expectation of tumor control and overall survival that is equivalent to that reported for patients with four or fewer tumors. Development of new metastases leading to repeat SRS is not associated with worsened tumor control or survival. Survival may be adversely affected in patients having a higher volume of normal brain irradiated.

Management of Brain Metastases from Large Cell Neuroendocrine Carcinoma of the Lung: Improved Outcomes with Radiosurgery

Shaakir Hasan, Richard Williamson, Stephen M. Karlovits, Russell Fuhrer, **Rodney E. Wegner**

Objectives: Large Cell Neuroendocrine Carcinoma (LCNEC) of the lung is a rare pulmonary tumor characterized by the presence of both neuroendocrine morphology and immunohistochemical evidence of neurochemical markers, not meeting criteria for the better recognized small cell lung cancer (SCLC) but having similar natural history and management strategy. As such, the management of brain metastases in these patients has mirrored that of SCLC through the use of whole brain radiation therapy (WBRT) as opposed to stereotactic radiosurgery (SRS). We used the National Cancer Database (NCDB) to look at predictors of SRS and any potential differences in outcomes for patients with brain metastases from LCNEC.

Methods: We queried the NCDB from 2004-2015 for patients with LCNEC of the lung with brain metastases at diagnosis that received brain radiation. Univariable and multivariable analyses were performed to identify sociodemographic, treatment, and tumor characteristics predictive of SRS use and overall survival (OS). Propensity-adjusted Cox proportional hazard ratios for survival were used to account for indication bias.

Results: Out of 9,970 patients with LCNEC of the lung we identified 348 with brain metastases at time of diagnosis. Sixty-eight patients were treated with up front SRS and 280 were treated with WBRT. Patients that were treated at an academic facility or received chemotherapy as part of up front treatment were more likely to receive SRS. Of note, comorbidity score, age, and absence of other extracranial metastases were not predictive of SRS utilization. Univariable analysis revealed improved outcomes with SRS compared to WBRT, with a median overall survival of 11 months compared to 6 months, respectively ($p=0.007$). Multivariable Cox regression with propensity score confirmed SRS to have an improved survival (HR: 0.68, 95%CI: 0.51-0.91, $p=0.0093$). Multivariable Cox regression with propensity score also identified younger age, receipt of chemotherapy, absence of extracranial disease, and non-rural locations as additional predictors of improved overall survival.

Conclusions: In this NCDB analysis, treatment of brain metastases from LCNEC of the lung with SRS was associated with improved survival. For the appropriate patient (younger, absence of extracranial metastases, and ability to receive chemotherapy) up front treatment of limited brain metastases with SRS may be appropriate.

High-Grade Toxicity after Combination Radiosurgery Anti-PD-1 Immunotherapy for Brain Metastases

Roman L Travis, Samuel R Marcrom, MD, James M Markert, MD, MPH, Kristen O Riley, MD, Robert Conry MD, Christopher D Willey, MD, PhD, Markus Bredel, MD, PhD, Mayank P Patel, John B Fiveash, MD

Objectives: Prior studies have produced mixed conclusions regarding whether anti-PD-1 therapy increases radiosurgery toxicity. The objective of this study is to determine the high-grade toxicity of radiosurgery and anti-PD-1 immunotherapy for patients with renal cell carcinoma (RCC), non-small cell lung cancer (NSCLC), and melanoma brain metastases (BM).

Methods: This study retrospectively assessed high grade toxicity in patients treated at UAB since 2014 for NSCLC, RCC, and melanoma BM with radiosurgery and anti-PD-1 immunotherapy. Similar to the dose-limiting toxicity definition in RTOG 9005, high grade toxicity was defined as irreversible grade 3 or any grade 4/5 neurologic events. Patients undergoing salvage resection with a pathologic mixture of necrosis and viable tumor were scored as both grade 4 toxicity and local failure. All patients received pembrolizumab and/or nivolumab and radiosurgery for at least one brain metastasis. No patient had whole brain radiation or prior radiosurgery to the index lesion(s). Median follow-up was 11.3 months (1-32.4), and the majority of patients received immunotherapy within 1 month of radiosurgery.

Results: Forty-three patients with median 2 (1-21) tumors each for a total of 126 tumors were followed for median 11.3 (0.7-32) months. Median tumor volume was 0.16 (0.01-24) cc and median radiation dose was 20 Gy (single fraction) and 30 Gy (five fractions). Thirty-six patients received single fraction radiosurgery, and 7 received hypofractionated therapy, most commonly 6 Gy x 5 fx. Five patients (11.6% of patients, 4% of tumors) experienced high-grade CNS toxicity including three patients requiring resection and two patients with irreversible brain edema associated with a decline in performance status and initiation of palliative care. All of these patients had melanoma with largest tumor volumes of 24.0 cc, 4.2 cc, 12.0 cc, 3.8 cc, and 2.3 cc with 3 of 5 receiving single fraction treatment. All but one event occurred within the first month of radiosurgery. In all five cases, patients worsened when treating physicians minimized or limited steroids due to concerns regarding the impact on immunotherapy.

Conclusions: Combination radiosurgery-immunotherapy (anti-PD1) appears tolerable for RCC, NSCLC, and melanoma BM with a level of high-grade toxicity that should not change treatment recommendations. Traditional factors such as treatment volume continue to drive the risk of high-grade toxicity, but variations in steroid prescribing patterns for immunotherapy patients may exacerbate toxicity.

Dosimetric Comparison of Protons versus Photons for Treatment of Pituitary Adenoma

Shivani Sud, Thomas Botticello, Andrzej Niemierko,
Jillian Daly, Marc Bussiere, Helen A Shih



Objectives: To compare the dosimetric advantages and limitations of protons (PRT) versus photons (XRT) in stereotactic radiosurgery for pituitary adenomas.

Methods: Nine patients with pituitary adenomas were selected among patients receiving single-fraction stereotactic proton radiation therapy (PRT) between 2016 and 2017. These cases were re-planned with XRT volumetric-modulated arc therapy (VMAT) with 2.5mm and 5mm multileaf collimators (2.5XRT and 5XRT, respectively). PRT using a dedicated passive scattering stereotactic proton unit with collimated and range compensated ports was delivered via three equally or unequally weighted isocentric fields. XRT VMAT plans were constructed with up to 6 partial arcs to minimize dose to organs at risk (OAR) and avoid direct irradiation or exit dose through the eyes. Plans were generated using the original total treatment dose delivered in one fraction.

Results: Plans were evaluated for clinical target volume (CTV) dosimetry and estimated clinical toxicity. Average target volume was 2.51ml (range 0.57 - 7.88) treated to an average dose of 17.5 Gy(RBE) (range 15-20). There was no statistically significant difference in V100% (91.0%, 93.3%, 95.3%), V95% (93.9%, 95.9%, 97.2%) or V90% (96.3%, 97.3%, 98.3%), Homogeneity index (1.11, 1.12, 1.11) or Gradient index (1.12, 1.08, 1.05) between PRT, 5XRT, 2.5XRT, respectively. 5XRT offered equal or superior V90%, V95% or V100% compared to PRT for 7, 5 and 8 of 9 cases, respectively. 2.5XRT offered equal or superior V90%, V95% or V100% compared to PRT for 9, 9 and 8 of 9 cases, respectively. The Dmax%, highest percent of prescription dose to a 0.1ml volume of CTV, was lower with PRT compared to 5XRT and 2.5XRT (99.7%, 112.2% and 110.9%), $p < 0.001$. The Conformity index was significantly higher for PRT (1.97) than 5XRT (1.63, $p = 0.046$) and 2.5XRT (1.63, $p = 0.017$). The maximum dose to OAR, highest dose in Gy delivered to a 0.1ml volume, was significantly lower with PRT compared to 5XRT and 2.5XRT for optic nerves (4.72, 5.73, 5.67), cochlea (0.01, 1.53, 1.49) and hypothalamus (1.71, 3.94, 3.77), $p < 0.002$. The maximum dose to OAR did not significantly differ for the eye globe, optic chiasm, temporal lobes, brain stem or whole brain. The average whole brain volume receiving 12Gy was higher for PRT than 2.5XRT (4.69ml versus 4.14ml, $p < 0.05$), however, there was no significant difference in the whole brain volume receiving 16Gy, which is predictive of radiation necrosis.

Conclusions: PRT, 5XRT and 2.5XRT demonstrate comparable target volume dosimetry. VMAT typically provides equal or superior CTV coverage but with higher Dmax%. PRT has a higher >1 conformity index indicating that the irradiated volume is greater than the CTV. The maximum dose to OAR including critical proximal structures such as the optic nerve and hypothalamus was significantly lower with PRT. The V16Gy was comparable between modalities, however, the V12Gy was lowest for 2.5XRT. In clinical scenarios where dose to critical OAR is limiting, PRT may offer superior organ sparing.

Primary and Repeat Linac Radiosurgery for Cerebral Arteriovenous Malformations in Pediatric Population

Slawomir Blamek, Dorota Gabrys, Marek Mandra, Jan Baron, Dawid Larysz

Objectives: To evaluate response rates and toxicity of the treatment in patients under 18 years old treated with stereotactic radiosurgery or hypofractionated stereotactic radiotherapy for arteriovenous malformations (AVMs) of the brain.

Methods: A group of 30 patients aged 5 - 18 years (mean age 13.8, median 14) treated between 2002 and 2017 with a linear accelerator equipped with a micromultileaf collimator or with the CyberKnife system. There were 4 Spetzler-Martin grade I, 8 grade II, 11 grade III, and 6 grade IV lesions. In the group treated with single dose there were 3 patients in each of grade I-III groups. Hypofractionated treatment was applied in 1, 5, 8, and 6 patients with AVM of grade I-IV, respectively. Four patients were irradiated for the second time 5-7 years after the initial treatment. All of them were followed-up for at least one year after the second treatment. The doses applied varied between 16 and 20 Gy for single fraction treatment or 16-24 Gy delivered in 2-3 fractions.

Results: Actuarial total obliteration rates were 35%, 42%, 56% and 85% at 2, 3, 5 and 7 years respectively. Actuarial response rates (total and partial obliteration) were 43%, 55%, 66% and 92% at 2, 3, 5 and 7 years respectively. Actuarial 5-year total obliteration rates in patients with grade I and II AVMs and grade II and IV AVMs were 72% and 32%, respectively. No significant difference in outcome between single-fraction and fractionated treatment was found. No bleeding was recorded during follow up. In 6 patients MR imaging abnormalities (in one symptomatic) were recorded. In two patients new epileptic seizures occurred (currently they are fits-free), in another two we observed aggravation of preexisting hemiparesis (in both after the second treatment).

Conclusions: Linac-based radiosurgery for pediatric AVMs provides satisfactory outcome. In case of large or involving critical organs lesions, application of fractionated treatment can be considered without jeopardizing the outcome. Repeat treatment is feasible but associated with increased risk of side effects.

Systemic Therapy as a Risk Factor Associated to Complications in SBRT for Spine Metastases

Christian Arias, Philip Wong, Mathilde Nahmiash, David Donath,
David Roberge, Laura Masucci



Objectives: The benefits of SBRT in pain control await confirmation in 2 large North American trials (RTOG0631 and CCTG SC24) but SBRT is already commonly used to improve local control. We hypothesized that systemic therapy may influence the efficacy of spine SBRT in controlling pain and increase the risk of vertebral compression fracture (VCF).

Methods: We retrospectively reviewed the clinical data of 155 patients treated with SBRT between June 2009 and June 2016. In the current analysis, we included the 127 patients for which SBRT was administered in a context of oligometastatic or oligoprogressive disease (either alone or postoperatively). Outcomes were calculated actuarially and comparisons were performed using log-rank tests (significance set at <0.05).

Results: Patient, disease and treatment characteristics are summarized in Table 1. The mean age was 64 (range: 22.67-81.82). Forty-nine patients (39%) had cancers considered radio-resistant (kidney 16%, thyroid 9%, melanoma 3 %) and 63 patients had breast (26%), prostate (14%) or lung (13%) cancers. Prior to SBRT and surgery, 33%, 63% and 3% had stable (SINS 0-6), potentially unstable (SINS 7-12) and unstable vertebrae (SINS 13-14). Postoperative SBRT was administered in 41%. Pain was present in 78% of patients prior to SBRT. Forty-two percent of the patients received systemic therapy during or within 7 days of SBRT. The median BED10 was 48. Median local recurrence free survival, distant progression free survival and overall survival were 20.5 months, 9 months and 25 months, respectively. There were 14 VCFs. No case of radiation myelopathy was reported. On univariate analysis, patients who were receiving systemic treatment were significantly at a higher risk of developing VCF ($p=0.014$) or pain recurrence ($p=0.001$). SINS score, Bilsky scale and pre-SBRT stabilization surgery were not significantly associated with VCF, local recurrence or pain.

Conclusions: In our single center retrospective review, we observed that patients on systemic treatments prior to spine SBRT were at high risk of developing VCF and pain recurrence/progression. These results suggest that pain response analyses in ongoing trials need to take into account concurrent systemic treatments as a potential confounding factor. Patient and clinician expectations as to the risk of VCF may also need to be modulated.

Initial Observation of Vestibular Schwannomas: A Modern Institutional Experience

Janet Leon, DO¹; Larry Lundy, MD²; Kaisorn Chaichana, MD³;
Prasanna Vibhute, MD⁴; **Aditya Patibandla, BS¹**; Laura Vallow, MD¹;
Henry Ruiz-Garcia, MD¹; Austin Hadley, DMP¹; Steven Herchko, DMP¹;
Daniel M. Trifiletti, MD^{1,3}; Jennifer Peterson, MD^{1,3}



1 Department of Radiation Oncology, 2 Otolaryngology, 3 Neurological Surgery, 4 Radiology

Objectives: Vestibular schwannomas are benign, slow growing, tumors that arise from the Schwann cells in the vestibulocochlear nerve. Although benign, these tumors can cause significant symptoms and the optimal initial treatment paradigm is controversial. In this study we review the outcomes of patients undergoing initial observation alone.

Methods: The clinical characteristics including presenting symptom (asymptomatic, hearing loss, imbalance, headache, other) of 360 consecutive patients with radiographically diagnosed vestibular schwannoma were reviewed by researchers at one institution for those who opted against any initial intervention. All the patients diagnosed after 1989 and the actuarial rates of tumor control, freedom from definitive therapy, and survival were calculated at last known follow up. Radiographic local control was determined by a neuroradiologist.

Results: Of the 360 patients seen, 243 opted for initial observation (67.5%). Median age at diagnosis was 59.9 years and median follow up time was 39.9 months from diagnosis. Of these observed patients, 118 (48.6%) were female and 125 (51.4%) were male. Hearing loss was the most common symptom at presentation of observed patients (55.1%). Local control at 1, 5, and 10 years was 92%, 70%, and 58%, respectively. The freedom from local therapy rate while under observation at 1, 5, 10 years were 91%, 74%, and 65%, respectively. Overall survival at 1, 5, and 10 years was 100%, 95%, and 95%, respectively. Patient gender, age, and initial presenting symptom did not impact the time to local failure after observation ($p = 0.13, 0.08, 0.64$, respectively).

Conclusions: Over half of patients with vestibular schwannoma who undergo initial observation at diagnosis will maintain local radiographic tumor control at 10 years. Although surgery and radiosurgery are common options for treating vestibular schwannomas, observation can still be considered in appropriate, minimally-symptomatic patients.

Clinic Feasibility of Frameless Functional Radiosurgery with a Virtual Cone

John B Fiveash MD, Markus Bredel MD, Barton Guthrie MD, Evan Thomas MD PhD,
Michael C Dobelbower MD PhD, Elizabeth Covington PhD¹, Richard Pople PhD

Objectives: The Virtual Cone is a multi-leaf collimator (MLC) delivery sequence designed to replicate the dose profile of a standard cone or 4 mm Gamma Knife helmet. Unlike other MLC-based techniques, this delivery sequence has the advantage of not requiring patient specific quality assurance measurements. In this series we describe the preliminary experience utilizing this technique for frameless functional radiosurgery for trigeminal neuralgia and tremor.

Methods: The Virtual Cone includes five different table positions delivering two different collimator angles (ten total partial arcs for trigeminal neuralgia and twenty partial arcs for tremor) with a fixed size aperture of 2.1 mm x 5 mm but a variable dose rate of up to 2400 MU/min. During treatment patients are immobilized with a two-piece open face aquaplast mask. Infrared surface imaging is utilized to detect deviations in intrafraction position. RAD 1502 includes 80 Gy to the dorsal root entry zone for trigeminal neuralgia. RAD 1601 delivers 130 Gy to the ventral intermediate nucleus for tremor. This report includes patients enrolled in these trials and patients treated without enrollment in a clinical trial.

Results: Forty-six patients have been treated utilizing the Virtual Cone technique including thirty-eight patients with trigeminal neuralgia and eight patients with tremor (essential or Parkinsonian). Approximately 27,000 MUs are required for trigeminal neuralgia and 43,000 MUs for tremor. Typical treatment time from onset of imaging to completion of treatment varies from 30 to 60 minutes with 10X FFF. Two patients had repeated intrafraction motion over 1 mm and were unable to complete treatment that same day. With variable follow-up no patient has developed grade 3 or greater toxicity related to treatment.

Conclusions: The Virtual Cone is clinically feasible for frameless functional radiosurgery. The efficacy and long-term toxicity of this technique will require longer term follow-up of ongoing clinical trials. A small minority of patients may be unable to remain immobile during the entire frameless procedure. Options being explored for this group include use of anesthesia, modifications to the mask system, and automating couch movement to further reduce treatment time.

The Dancing Cord: Inherent Spinal Cord Motion and its Effect on Cord Dose in Spine Stereotactic Body Radiation Therapy

Murat Alp Oztek, Nina Mayr, Mahmud Mossa-Basha, Matthew Nyflot, Patricia Sponseller, Christoph Hofstetter, Rajiv Saigal, Stephen Bowen, William Yuh, Simon Lo

Objectives: Stereotactic body radiation therapy (SBRT) is an emerging treatment option for spine tumors. Because spine tumors are in close proximity of the spinal cord, adherence to strict dose limits is essential to prevent neurologic complications. Generally accepted spinal cord dose constraints have been established. However, while inherent CSF and spinal cord motion are known phenomena, their dosimetric effects on the spinal cord have not been explored.

Methods: In addition to conventional MR imaging, dynamic cardiac-gated balanced fast field echo sequences were obtained as part of routine treatment planning imaging for VMAT-based spine SBRT in 17 patients with spine tumors. Dosimetric data and images were retrospectively analyzed in this IRB approved study. Planning CT data sets, static T2-weighted (cordstat), and each of 15 phases of the dynamic MRI images (corddyn) were coregistered. Motion on the dynamic imaging was compared to the static T2-weighted images using Dice coefficient, and the amount of distance the centroids of corddyn moved with respect to cordstat. The maximum dose between cordstat, and corddyn was compared. The maximal cord dose was compared between corddyn, cordstat and cordstat with various planning organ at risk volume (PRV) margins.

Results: Dice coefficients between cordstat vs. corddyn ranged from 0.70 to 0.96 (mean, 0.85 ± 0.07). In 13 of the 17 patients, the maximal dose to corddyn exceeded that of the dose per treatment plan by 0.1 - 12.8% (mean $2.3 \pm 4.1\%$). Compared to the planning contour, corddyn spatially extended outside the 1 mm PRV margin in 12 of the 17 patients (70.6%). The maximum dose received by corddyn exceeded the maximum dose the cordstat +1 mm PRV margin in 6 of the patients (35.2%). In none of the patients did the maximum corddyn dose exceed that of the dose to cordstat +1.5 mm PRV margin. Corddyn did not extend outside the 1.5 mm PRV margin of cordstat.

Conclusions: The spinal cord shows inherent motion, resulting in measurable dosimetric effects which should be considered during SBRT dosimetry. Maximum dose received by the moving spinal cord exceeds that calculated using static planning images, even if 1 mm PRV margin is included. A 1.5 mm PRV margin surrounding the cord, always included the inherent spinal cord motion and did not underestimate the maximum spinal cord dose. We advise incorporating a 1.5 mm PRV margin or dynamic imaging to assess individual patients' cord motion during SBRT planning.

Efficacy and Safety of Robotic Radiosurgery for Spinal Metastases

Markus Kufeld, Lucas Mose, Christoph Fürweger, Stefan Zausinger,
Alfred Haidenberger, Alexander Muacevic

Objectives: Aim of this study was to analyze the efficacy and safety of frameless robotic radiosurgery for spinal metastases of various histologies with regard long-term tumor and pain control.

Methods: 301 patients with spinal metastases had been treated consecutively over a period of 10 years. Clinical and radiological follow-up data was available for 247 patients with 286 metastases. The Kaplan-Meier method and life tables were used to analyze freedom from local failure and overall survival. Pain as a main symptom was classified using the visual analogue scale (VAS) score.

Results: Median age was 62 years, ranging from 16 to 88 years. 20 percent of the patients received repeated radiosurgical treatments for new lesions. All tumors were treated in a single session, apart from two lesions which have been treated in 3 and three lesions in 5 fractions. The median target volume was 22 ccm. The median applied dose was 20 Gy (range, 12-40 Gy) prescribed to the 70 % isodose line. Median follow-up was 16 months (range, 3-147 months). The actuarial rates of freedom from local failure were 94 % at 6 months, 91 % at 12 months and 83 % at 24 months. Primary tumor and prescription dose have been identified as significant contributors to local control in uni- and multivariate analysis, showing the highest control rate in prostate cancer and lowest in renal cancer. The median overall survival after radiosurgery was 20 months. 59 patients suffered from pain before radiosurgery (median VAS 6). The VAS score dropped significantly after the treatment to median VAS of 2 ($p=0,001$). No CTCAE grade III or higher toxicities were observed, of particular note no additional myelopathy or radiation induced neurological deficits were recorded.

Conclusions: Robotic radiosurgery is an efficient and safe treatment option for spinal metastases offering long-term local tumor control and reducing tumor-induced pain syndromes effectively.

Dose-Response Modeling the Risk of Carotid Bleeding Events after Stereotactic Body Radiation Therapy for Previously-Irradiated Head and Neck Cancer

Diane C. Ling MD, Rachel J. Grimm, Brian J. Gebhardt MD, David A. Clump MD PhD, Robert L. Ferris MD PhD, James P. Ohr DO, Dwight E. Heron MD MBA FACRO FACR

Objectives: Stereotactic body radiation therapy (SBRT) has been increasingly used as a treatment option for recurrent, previously-irradiated head and neck cancer, although early reports suggested higher rates of carotid blowout syndrome (CBOS) after SBRT compared with conventional re-irradiation techniques. We previously reported on a cohort of patients treated at our institution and were unable to identify a significant association between carotid dose and CBOS. Given the lack of clear dose constraints for the carotid to guide SBRT treatment planning, we sought to create dose-response models to better quantify the risk of any grade carotid bleeding events following SBRT.

Methods: We retrospectively reviewed 186 patients with recurrent, previously-irradiated head and neck cancer treated between January 2008 and March 2013, of which 75 patients with 150 carotid arteries had complete dosimetry data available and were included for analysis. The median follow-up was 37 months for surviving patients (range: 31-91 months). Patients were treated with conventional linear accelerator-based SBRT to a median dose of 44 Gy (range, 40-50 Gy) in 5 fractions delivered every other day. Eight patients (10.7%) received more than 1 course of SBRT, and the cumulative carotid doses from fused summary plans of all SBRT treatments were recorded. At our institution, only small volumes of the carotid artery were allowed to exceed 20 Gy in 5 fractions, a constraint selected based on treating physicians' clinical experience. Dose-response models were created based on the 75 cases using the DVH Evaluator software (DiversiLabs, LLC, Huntingdon Valley, Pa). Dose-volume descriptors analyzed included carotid artery D0.1cc, D1cc and D2cc. A carotid bleeding event was defined as a rupture and hemorrhage from the carotid artery or its major branches after re-irradiation in the absence of residual or progressive local disease.

Results: Out of 75 patients, a total of 4 (5.3%) carotid bleeding events occurred, 2 of which were fatal. According to the logistic models, the risk of a carotid bleeding event with a D0.1cc of 20Gy is 0.8% (95% CI 0.1%-3.9%), whereas the risk is 2.7% (95% CI 0.8%-6.5%) with a D1cc of 20 Gy, and 4.0% (95% CI 1.5%-8.2%) with a D2cc of 20 Gy. The risk is reduced to 0.2% with a D0.1cc of 10 Gy, but rises to 5.0% with a D0.1cc of 50 Gy, a value that may be reached when a patient receives more than 1 course of SBRT. Similarly, the risk of a bleeding event is reduced to 1.8% with a D2cc of 5 Gy, but rises to 5.0% with a D2cc of 30 Gy. No patient experienced a carotid bleeding event with a cumulative D0.1cc <39.4 Gy, D1cc <28.3 Gy, or D2cc <10.1 Gy.

Conclusions: Based on our logistic dose-response models, the risk of a carotid bleeding event following SBRT for recurrent, previously-irradiated head and neck cancer is less than 1% with a cumulative D0.1cc of 20 Gy from SBRT. Dose-response models can be used to quantify the relationship between carotid bleeding events and carotid artery dose, even in the context of multiple courses of SBRT re-irradiation.

Unconventional SBRT-Based Partial Irradiation of Unresectable Bulky Tumors Exploiting The Bystander and Abscopal Effect

Slavisa Tubin, MD

Objectives: Patients with bulky unresectable tumors have a poor prognosis and are usually destined to receive palliative treatments. Such "heavyweight" tumors, due to their large volume, very intimate and infiltrating relationship with surrounding OAR and greater hypoxic compartments cannot be successfully treated by the available conventional treatments, representing complicated mostly un-treatable clinical situation. In response to such challenging clinical situations we have applied the non-targeted effects of radiotherapy with the aim to improve the results of radiotherapy. Our pre-clinical studies on focused bystander (BE)- and abscopal effect (AE)-induction, have shown for the first time that high-dose partial (vs. whole) tumor irradiation, targeting exclusively the hypoxic (vs. normoxic) tumor resulted in significant radiation-hypoxia-induced BE and AE. Those findings were translated to clinic leading to development of our novel SBRT approach for partial tumor irradiation (PTI). We hypothesized that high-dose PTI targeting exclusively the hypoxic segment would generate an effective tumor-abscopal signaling and antigen release leading to immune-mediated regression of whole partially-irradiated tumor (due to BE) but also of unirradiated metastases (due to AE). Primary endpoints were BE and AE response rates. Secondary endpoints included overall survival (OS), progression-free survival (PFS) and assessment of toxicity.

Methods: This study involved 35 oligometastatic patients whose bulky tumors of the lung, head and neck, pancreas, kidney, skin, adrenal glands and lymph nodes were partially irradiated. We defined "Bystander Tumor Volume (BTV)" (hypoxic segment) using PET-CT, as a hypovascularized-hypometabolic junctional zone between the central necrotic and peripheral hypermetabolic tumor segment. Based on tumor site and volume, BTV was irradiated with 1-3 fractions of 10 or 12 Gy prescribed to 70% isodose. No patient received chemotherapy or immunotherapy. The immunohistochemistry was performed on the available tissue samples after surgery following neoadjuvant SBRT-PTI to study the mechanisms behind the clinical results and modifications within the tumor microenvironment.

Results: On an average, the BTV corresponded to 30% of the bulky tumors. With median follow-up of 12 months (range: 2-22) OS and PFS were 70% and 87%, respectively. BE response rate was 97%. Average bulky shrinkage was 60% with 4 complete responses. AE response rate was 51% with mean reduction of unirradiated metastases of 50% (range: 30-100%). No patient experienced acute or late toxicity of any grade. The immunohistochemical findings after neo-adjuvant SBRT-PTI showed that apoptosis-inducing factor was massively upregulated in the partially irradiated bulky and also at the abscopal site, whereas a dense immune reaction was observed only at the border of the partially irradiated tumor but not at the abscopal site indicating an important role of the tumor-abscopal signaling.

Conclusions: SBRT-PTI for bulky tumors was feasible, effective and safe, showing high potential for induction of BE and AE, resulting in improved local control and prolonged PFS. Relevance: high neoadjuvant potential to convert unresectable into resectable lesions; very convenient palliative 1-3 days treatment for patients in worse general conditions, offering an improved cost-effectiveness profile; safe option as a salvage re-irradiation in case of relapses.

Trends of Stereotactic Body Radiation Therapy Utilization in the United States from 2004-2015

Eric J. Lehrer, MD, MS; Niraj Gusani, MD; Vonn Walter, PhD; Stephen Ko, MD;
Daniel M. Trifiletti, MD; Nicholas G. Zaorsky, MD

Objectives: Stereotactic body radiation therapy (SBRT) is defined as a high dose of highly conformal radiation therapy (RT) administered in 1-5 fractions. The purpose of this analysis is to characterize the use of SBRT among disease sites. We hypothesized that SBRT use is increasing for localized cancers of the brain, breast, liver, lung, pancreas, and prostate.

Methods: The National Cancer Database (NCDB) was queried from 2004-2015 for patients diagnosed with brain, breast, liver, lung, pancreas, and prostate cancers of all stages. SBRT was defined as = 5 Gy/fraction in = 5 fractions, excluding common palliative doses and non-photon modalities. Linear regression models were utilized to model usage trends for each of these cancers by year; the null hypothesis was rejected for $p < 0.05$.

Results: Between 2004-2015 there were 5,935,798 patients diagnosed with cancer among all subsites with 78,143 (1.3%) of these patients receiving SBRT. Among these, SBRT was used in cancers of the brain (.78%, 1,606/204,705), breast (.04%, 988/2,445,870), liver (.93%, 1,589/171,013), NSCLC (4.3%, 60,427/1,393,073), pancreas (.79%, 2,679/340,780), and prostate (.79%, 10,854/1,380,357). For brain cancers, median SBRT dose was 21 Gy (range: 10-76 Gy in 2 fractions); breast median dose was 24 Gy (range: 10-80 Gy in 2 fractions); liver median dose was 40 Gy (range: 10-80 Gy in 5 fractions); NSCLC median dose was 50 Gy (range: 10-97.5 Gy in 4 fractions); pancreatic median dose was 30 Gy (range: 8-72 Gy in 5 fractions); prostate median dose was 36.25 Gy (range: 9-95 Gy in 5 fractions). The use of SBRT increased from .01% in 2004 to .07% in 2015 for breast cancer ($p < 0.001$), .05% to 1.5% for liver cancer ($p < 0.001$), .5% to 9.2% for NSCLC ($p < 0.001$), .02% to 1.5% for pancreatic cancer ($p < 0.001$), and 0.07% to 1.7% for prostate cancer ($p < 0.001$). The use of SBRT declined during this time for brain cancer 1% to 0.7% ($p = 0.005$).

Conclusions: SBRT is becoming more widely used in localized cancers in the United States with a 13-14 fold increase between 2004-2015. Future studies will aim to further characterize these usage trends by treatment intent and disease stage.

Long-Term Results of Stereotactic Thermal Destruction Drug-Resistant Temporal Lobe Epilepsy

Slobina Elena Khlebokazov Fedor Dokukina Tatyana Korolevich Pavel Misyuk Nikolay Shamruk
Irina Makhrov Michail Martynenko Alexandr Dudarchik Anastasia

Objectives: To present the results of clinical application of stereotactic thermal destruction in patients with pharmaco-resistant epilepsy, and to assess the feasibility, tolerability of this kind of local treatment.

Methods: Functional stereotactic surgical interventions were performed in 163 patients with medically-resistant forms of temporal epilepsy and with registered bilateral temporal foci, of which 79 men and 84 women. The age of patients at the time of surgery was 17 to 62 years (median - 34 years). In total since 2001. to 2006. 326 stereotactic operations were carried out. The destruction of the epileptic focus was carried out by a thermal defect generator.

Results: The effectiveness of stereotactic operations was assessed based on observations of the nature and frequency of seizures. The duration of the catamnesis was from 1 to 5 years. Thermal destruction of the tonsils on both sides was performed in 147 patients (90%), bilateral destruction of the anterior sections of the hippocampus in 71 patients (43.6%). Any complications or side effects associated with symmetric destruction of the nuclei of the limbic system of the brain were not noted in the postoperative period. In 44.2% of cases in the postoperative period, positive dynamics in the course of mental processes, favorable changes in the emotional and personal sphere were detected. The frequency of excellent and good results (group 1 and group 2 patients) decreased over time: 75.5% after 1 year, 70% after 2 years, 59.8% after 3 years, 46.3% after 4 years, after 5 years - 40%.

Conclusions: The achieved results (a positive effect in 5 years continues to persist in 70% of patients) suggest that this method in most cases allows to precisely localize and destroy foci of epileptic activity and the ways of its spread in the brain.

Clinical Outcomes following Stereotactic Body Radiation Therapy (SBRT) for Small-Cell Lung Carcinoma: A Preliminary Analysis from the RSSearch® Patient Registry

Raj Singh, Hayden Ansinelli, Jan Jenkins, Joanne Davis, John Austin Vargo, Sanjeev Sharma

Objectives: To utilize the RSSearch Patient Registry (RSSPR) to examine local control (LC) and overall survival (OS) following stereotactic body radiation therapy (SBRT) for small-cell lung carcinoma (SCLC) and evaluate potential prognostic factors relating to LC and OS.

Methods: We searched the RSSPR for SCLC patients treated with SBRT from January 2008 to July 2018. Patients that had previously received radiation therapy were excluded. Potential predictive factors of LC and OS (including patient age, initial Karnofsky Performance Score (KPS), gross tumor volume (GTV), gender, receipt of adjuvant chemotherapy, and BED10) were estimated using time-to-event analysis and log-rank t-tests with the Kaplan-Meier method. Dose escalation was defined as a BED10 > 100 Gy₁₀ among all fractionation schedules, > 54 Gy for 3-fraction SBRT, and > 50 Gy for 5-fraction SBRT. The relationship between toxicity incidence and dose escalation was examined with univariate binary logistic regressions.

Results: Forty-nine patients with 50 treated lesions were identified that met study criteria. Twenty-five patients had information on LC. Median patient age was 73 years (range: 48-91), median pre-treatment KPS was 80% (range: 50%-100%), and the median GTV was 9.65cc (range: 0.72- 124.18). One patient was treated with one-fraction (dose of 19.89 Gy), twenty-two patients with three-fractions (median dose of 54 Gy (range: 24 Gy - 71.12 Gy)), ten patients with four-fractions (median dose of 48 Gy (range: 36 Gy- 60 Gy)), and sixteen patients with five-fractions (median dose of 50 Gy (range: 30 Gy - 53 Gy)). The median BED10 was 109.18 Gy₁₀ (range: 43.2 Gy₁₀ - 239.72 Gy₁₀). For the cohort, 1- and 2-year OS rates were 66.39% (95% CI: 45.58% - 80.77%) and 28.45% (95% CI: 11.92% - 47.6%), respectively. No factors evaluated were found to be associated with OS. The 1-year LC rate was 83.2% (95% CI: 55.5% - 94.4%), with a median time to failure of LC of 7.4 months (range: 2.27 - 7.43). No predictive factors for LC were identified. Acute and late toxicities were reported by 14.3% of patients that were all Grade 1-2 (57% acute and 43% late), with the most common being fatigue, dyspnea, and cough. Dose escalation was not found to be associated with toxicity incidence.

Conclusions: SBRT was well-tolerated in the treatment of SCLC, with minimal toxicity including no > Grade 2 complications. No dose-response for LC, OS, or toxicity was identified.

Stereotactic Body Radiotherapy for Pulmonary Non-Small Cell Neuroendocrine Tumors

Anand Mahadevan, M.D., David D'Ambrosio, M.D., Paul Chomiak, M.D., Heidi McKeller, M.D.,
Sanjeev Sharma, M.D., John Pablo, M.D., Frank Kimsey, M.D. Joanne N. Davis, Ph.D.

Objectives: Non Small cell neuroendocrine tumors of the lung are rare and are usually treated with surgical resection. When surgery is not feasible or desirable, there is little data on the efficacy of other treatment options. Here we report the outcomes after stereotactic body radiotherapy (SBRT) for pulmonary neuro endocrine tumors (NET).

Methods: The RSSearch® Patient Registry was screened for non small cell pulmonary NETs diagnosed between May 2004 and May 2015 and treated with SBRT. Benign carcinoids were not included. Descriptive analyses were completed for patient, lesion characteristics, and SBRT . Overall survival (OS), local control (LC) and distant disease control (DC) were calculated using the Kaplan-Meier method.

Results: 20 patients with non carcinoid, no small cell pulmonary NETs were included in the study. Median follow-up was 16 months (1-38 months). Median age was 78 years (range 50-90 years) , and 11 were female and 10 were male. Median SBRT dose was 50 Gy (range, 24-60 Gy) delivered in a median number of 3 fractions (range 3-5). There were 8 deaths with a median OS of 19 months. There was 1 local failure at 19 months. There were no Grade 3 or more toxicity.

Conclusions: SBRT seems to be a safe and effective nonsurgical treatment for non-small cell neuroendocrine tumors.

Early Feasibility Study for Cardiac Radiosurgery: Evaluation of Novel 3-D Treatment Planning Software and Safety Data on First Three Patients

Brad Pollard, **Douglas Rivera**, Paul C. Zei, Amin Al-Ahmad

Objectives: Cardiac radiosurgery to treat ventricular tachycardia is being evaluated in an IDE approved Early Feasibility Study. Our objective was to evaluate proprietary 3-D software for contouring of myocardial ventricular targets and review three-month safety data on the first three patients.

Methods: A cardiac electrophysiologist contoured ablation targets in the left ventricle using proprietary cardiac treatment planning software. The target data was imported into the radiosurgical treatment planning software and the radiosurgical team created the treatment plans with a target dose of 25 Gy. A margin was placed on the targets and critical structures to allow for cardiac motion (assessed in a cardiac, four-dimensional CT). Plans were judged deliverable based on efficacy (assessed through target coverage) and safety (assessed through dose to critical structures). The radiosurgical team delivered the treatment plans with a robotic radiosurgical system. Stereotactic x-ray images of a cardiac pacing lead placed temporarily in the right ventricle were used to align the patient in the radiosurgical system. This lead was also used for tracking respiratory motion of the heart.

Results: The proprietary 3-D contouring software was used adjunctively by the electrophysiologist. In all treated subjects, the proprietary software enabled the initial definition of the target based on a 3-D rendering of the cardiac surface. All three treatments were developed and delivered as planned, with treatment volume 153.2 ± 49.7 cc, treatment time 89.3 ± 2.5 min.

Conclusions: In this first FDA approved Early Feasibility Study for the treatment of ventricular tachycardia with stereotactic radiosurgery, three patients completed three-month follow-up as of June 9, 2018. There have been no deaths and no unanticipated serious or non-serious adverse events, with close clinical follow up and imaging. Efficacy at three months cannot be adequately assessed, and will be evaluated in the future.

Ten Year Final Results of the TROG 03.04 (Radar) Randomised Phase 3 Trial with an Analysis of the Relative Benefit of Radiation Dose Escalation and Longer Hormone Duration to Prevent Distant Progression with Locally Advanced Prostate Cancer

David John Joseph, James W Denham, Allison Steigler, David S Lamb, Nigel A Spry, John Stanley, Tom Shannon, Gillian Duchesne, Chris Atkinson, John Matthews, Sandra Turner, Lizbeth Kenny, Keen-Hun Tai, Nirdosh Kumar Gogna, Rachel Kearvell, Judy Murray, Martin Ebert, Annette Haworth, Brett Delahunt, Christopher Oldmeadow, John Attia

Objectives: The relative effects of radiation dose escalation (RDE) and androgen suppression (AS) duration on distant progression (DP) remain unclear.

Methods: We addressed this by incorporating a RDE program by stratification at randomisation ie. in 66, 70 and 74 Gy external beam (EBRT) dosing subgroups and a 46 Gy EBRT plus high dose rate brachytherapy boost (HDRB) subgroup. Participants were randomised to 6 or 18 months AS ± 18 months zoledronic acid (Z). The primary endpoint was PCSM. Cumulative incidence at 10 years for each RDE group was estimated using Fine and Gray competing risk modelling adjusting for AS duration, use of Z, age, tumour stage, Gleason grade group, PSA, and site.

Results: Compared to 6 months AS, 18 months AS significantly reduced DP sHR=0.69 (0.55-0.88) p=0.002. At 10 years, adjusted cumulative incidences were 21.5, 22.5, 21 and 16% for DPs in the respective dosing groups. Compared to 70Gy, HDRB significantly reduced DP, sHR=0.68 (0.49-0.93) p=0.015 independently of AS duration.

Conclusions: RDE and longer AS independently reduced DP. The risks and benefits to the individual must be balanced when selecting radiation dose and AS duration. We now propose replacing HDR brachytherapy with virtual brachytherapy utilizing CyberKnife.

Clinical trial information: NCT00193856

Ten Year Final Results of the TROG 03.04 (Radar) Randomised Phase 3 Trial Evaluating Duration of Androgen Suppression ± Zoledronate for Locally Advanced Prostate Cancer

David John Joseph, David S Lamb, James William Denham, Christopher Oldmeadow, John Attia, Allison Steigler;

Sir Charles Gairdner Hospital, Perth, Australia;
University of Otago, Wellington, New Zealand; University of Newcastle, Callaghan, Australia;
Hunter Medical Research Institute, Newcastle, Australia;
University of Newcastle, Newcastle, Australia; University of Newcastle School of Medicine

Objectives: We investigated whether 18 months of androgen suppression (AS) plus radiotherapy (RT) ± 18 months of zoledronate (Z) is more effective than 6 months of neoadjuvant AS plus RT ± Z.

Methods: Eligible men with T2a-4, N0, M0 prostatic adenocarcinomas with PSA ≤10 and Gleason score (GS) ≤7 in T2a cases were randomly allocated in a 2x2 factorial trial design to 6 months neoadjuvant AS using leuprolide (22.5mg i.m. 3 monthly) and radiation (control arm) or followed by treatment factor 1- 12 months AS (22.5mg i.m. 3 monthly), or accompanied by the second treatment factor 2- 18 months Z (4mg i.v. 3 monthly) starting at randomisation, or by both treatment factors. Patients were stratified by centre, baseline PSA, tumour stage, GS, and use of a brachytherapy boost. The primary endpoint was prostate cancer-specific mortality (PCSM). Secondary endpoints included time to PSA, local, distant, bone and soft tissue progressions (PSA, LP, DP, BP and STP) and time to secondary therapeutic intervention and all-cause mortality (STI and ACM). Endpoints were analysed by intention to treat using competing risks methodology. ACM was analysed using Cox regression.

Results: Between October 2003 and August 2007 1071 men were randomised with median age 68.7 years. Median follow-up was 10.4 years (IQR 7.9-11.7). No significant interaction was observed between AS and Z. Significant reductions were observed favouring 12 months AS for the primary endpoint: PCSM sHR 0.70 (0.50-0.97), $p = 0.035$; and for the secondary endpoints: BP sHR 0.61 (0.45-0.83), $p = 0.001$; DP sHR 0.71 (0.56-0.90), $p = 0.004$; PSA sHR 0.65 (0.53-0.78), $p < 0.001$; LP sHR 0.60 (0.39-0.92), $p = 0.021$; and STI sHR 0.66 (0.53-0.81), $p < 0.0001$. There were also non-significant reductions favouring 12 months AS in STP (sHR 0.85 [0.62-1.16], $p = 0.30$) and ACM (HR 0.84 [0.69-1.03], $p = 0.10$). The addition of 18 months Z did not influence any outcome significantly.

Conclusions: 18 months AS+RT is an effective option for locally advanced prostate cancer but the use of 18 months Z is not beneficial.

Clinical trial information: NCT00193856

Outcomes of Stereotactic Body Radiotherapy Delivered by Gantry-Based Linear Accelerators for Low- and Intermediate-Risk Prostate Adenocarcinoma: A Multi-Institutional Study

Audrey Dang, Christopher R. King, David Shabsovich, Constantine A. Mantz, Kevin L Stephans, Andrew Loblaw, Luca Cozzi, Albert DeNittis, Amar U. Kishan



Objectives: Stereotactic body radiotherapy (SBRT) is increasingly being used to treat low- and intermediate-risk prostate cancer (PCa). Much of the available published data are derived from patients treated with robotic-arm mounted linear accelerators (LINACs). However, SBRT can also be delivered using gantry-mounted LINACs. We sought to review the efficacy and safety of gantry-based SBRT for localized PCa from a multi-institutional consortium pooled analyses.

Methods: Individual patient-level data from six institutional prospective phase II trials of gantry-based SBRT from 2006-2017 were obtained. Patients were stratified into low- and intermediate-risk cohorts, as defined by the National Comprehensive Cancer Network guidelines. Biochemical relapse (BCR) was defined as PSA rise >2 ng/ml above nadir. Toxicity data was scored according to the CTCAE v 4.0 or Radiation Therapy Oncology Group scoring system. Kaplan Meier analysis was used to analyze freedom from BCR (FFBCR) and overall survival (OS) rates.

Results: 928 men were eligible for analysis, (506 [54.5%] with low risk and 422 [45.5%] with intermediate risk PCa). The median follow-up was 3 years (range, 0.5-10.8 years). Fractionation schemes ranged from 7-8 Gy in 5 fractions. 21 patients (2.3%) received ADT with SBRT. 31 patients (3%) experienced BCR, 5 patients (0.5%) experienced distant metastases, and 0 patients (0%) died of PCa. The 5-year FFBCR rate was 97% in low-risk patients and 87% in intermediate-risk patients. Corresponding 5-year OS rate was 99% in the low-risk group and 98% in the intermediate-risk group. Toxicity rates are displayed in table 1. 10 patients (1.1%) experienced acute grade 3 genitourinary (GU) toxicities, including urinary frequency, retention, dysuria, and bladder outlet obstruction. Two (0.2%) acute grade 3 gastrointestinal (GI) toxicities (diarrhea) were observed. 7 patients (0.8%) experienced late grade 3 GU toxicities, including urinary retention, obstruction, mixed urinary incontinence, frequency, dysuria, and urethral necrosis. Three (0.3%) late grade 3 GI toxicities (radiation proctitis) were observed. One (0.1%) late grade 4 GU toxicity (necrosis) and two (0.2%) late grade 4 GI toxicities (fistula-in-ano and necrosis) were observed.

Conclusions: To the best of our knowledge, this is the largest analysis of gantry-based SBRT for localized PCa. The results indicate a favorable efficacy and toxicity profile that is equal to robotic-arm mounted LINACs, though longer term follow-up is warranted to draw firm conclusions regarding comparative efficacy. Table 1. Physician-Scored Toxicity (CTCAE or RTOG)

Grade	1	2	3	4
Acute GU	306 (33%)	117 (12.6%)	10 (1.1%)	1 (0.1%)
Acute GI	127 (13.7%)	39 (4.2%)	2 (0.2%)	1 (0.1%)
Late GU	223 (24%)	63 (6.8%)	7 (0.8%)	1 (0.1%)
Late GI	99 (10.7%)	28 (3%)	3 (0.3%)	2 (0.2%)

Implications for Appropriate Margins in Radiosurgery of Bone Oligometastases from Prostate Cancer: An Analysis of Sodium Fluoride (NaF) PET/CT Response Assessment in the POPSTAR Clinical Trial

Shankar Siva Michael Hofman Nicholas Hardcastle

Objectives: Bony metastases are common in advanced prostate cancer and impact on quality of life through pain and skeletal related events. Prostate cancer bone metastases are largely sclerotic; RECIST response assessment is not valid for bone metastases and visual response assessment using conventional bone scan and CT can be unreliable (1). ¹⁸F-NaF-PET-CT images osteoblastic activity with superior sensitivity and resolution compared to conventional bone scintigraphy whilst enabling accurate uptake quantification (2). We report on ¹⁸F-NaF uptake before and after stereotactic ablative body radiotherapy (SABR) to prostate cancer bony metastases.

Methods: All patients with bony metastases enrolled in the POPSTAR (Trial ID: U1111-1140-7563) trial received an ¹⁸F-NaF-PET-CT prior to and 6 months post-SABR. All patients received a single 20 Gy fraction to one or more lesions with 3D-conformal or intensity modulated techniques. The gross tumour volume (GTV) was contoured using the ¹⁸F-NaF-PET-CT and planning CT, and a 5 mm planning target volume (PTV) margin was applied to non-spine lesions. Spine clinical target volumes were derived using the International Spinal Radiosurgery Consortium guidelines and a 3 mm PTV margin applied. The ¹⁸F-NaF-PET-CT uptake was measured in the GTV, and non-GTV bone receiving 2-24 Gy in 2 Gy increments.

Results: Twenty-one patients with 33 bony metastases were included with a mean \pm st. dev. 7.4 ± 1.0 months follow-up ¹⁸F-NaF-PET-CT scan. The SUV_{mean} of normal, un-irradiated bone was consistent between pre and post-treatment scans, with a mean \pm st. dev. ratio, post/pre of 0.98 ± 0.08 . Reduction in GTV SUV_{max} was observed in 30/33 lesions, with 2/3 lesions without reduction arising in the same patient. Four patients had increased SUV immediately adjacent to the treated volume, suggesting marginal failure. No loss in SUV_{mean} was observed in non-tumour bone receiving < 10 Gy; above 10 Gy uptake decreased with increasing radiotherapy dose to a mean \pm S.E.M loss of $24 \pm 6\%$ for non-tumour bone receiving 24 Gy.

Conclusions: ¹⁸F-NaF-PET-CT detected response in 90% of lesions treated with single fraction SABR. Surrounding normal bone receiving > 10 Gy demonstrated loss of normal bone osteoblastic activity. Possible marginal failures can occur with the use of a direct 5mm expansion from GTV, suggesting a CTV margin could be appropriate to account for occult at the disease margin.

References: 1. Brown MS, Chu GH, Kim HJ, Allen-Auerbach M, Poon C, Bridges J, et al. Computer-aided quantitative bone scan assessment of prostate cancer treatment response. Nucl Med Commun. 2012;33(4):384-94.

2. Beheshti M, Rezaee A, Geinitz H, Loidl W, Pirich C, Langsteger W. Evaluation of Prostate Cancer Bone Metastases with ¹⁸F-NaF and ¹⁸F-Fluorocholine PET/CT. J Nucl Med. 2016;57(Suppl 3):55S-60S.

Radioablation of LR and IR Prostate Cancer. Single Center Results of Consecutive 500 Patient Treatments

Miszczyk Leszek, Napieralska Aleksandra, Kraszkiwicz Malgorzata, Namysl-Kaletka Agnieszka, Wozniak Grzegorz, Stapor-Fudzinska Malgorzata, Miszczyk Marcin

Objectives: An evaluation of effectiveness and toxicity of low risk (LR) and intermediate risk (IR) prostate cancer patients (PCP).

Methods: Consecutive 500 PCP (LR 264 and IR 236) were irradiated with fd 7.25 Gy to TD 36.25 Gy. Median FU was 32 months. PSA, ADT uptake and toxicity using EORTC/RTOG scale were checked (acute effects to 4 months, next late ones). ROC curves were created and appropriate AUC were calculated for different PSA values as predictors of failures.

Results: During FU 15 failures appeared (6 biochemical failures, 2 local relapses and 7 locoregional nodal disseminations). Median time to failure was 19.9 months (22.5 to relapse and 17.5 to dissemination). Percentage of patients without ADT increased from 44.6% before RT to 100% 56 months later. In this period PSA median decreased from 2.8 to 0.12. Percentage of patients without gastrointestinal (GI) toxicity varied from 90.2% at the RT end to 100% 56 months later. There was one G4 toxicity: rectourethral fistula revealed 26 months after RT. Percentage of patients without genitourinary (GU toxicity) was smaller and varied from 74.5% 1 month after RT to 97.9% 44 months after RT. No G4 GU toxicity was noted. Higher PSA values during FU (even not filled Phoenix criterion), before failure appearance were connected to high risk of failure later on.

Conclusions: Radioablation of LR and HR PCP is save and very effective treatment modality. Higher value of PSA during first part of FU is strong predictive factor for a treatment failure.

Utilization of Stereotactic Body Radiation Therapy for Localized Prostate Cancer at Georgetown University Hospital: An Analysis of Patient Demographics and Travel Distance

Nima Aghdam, MD; Malika Danner, M.D., Marilyn Ayoob, MSN;
Thomas Yung, MSN; Brian Collins, M.D., Deepak Kumar, PhD, Simeng Suy, PhD;
Sean Collins, MD, PhD; Jonathan W. Lischalk, MD

Objectives: Stereotactic Body Radiation Therapy (SBRT) offers definitive treatment for localized prostate cancer with comparable efficacy and toxicity to conventionally fractionated radiotherapy. Decreasing the number of treatment visits from over forty to five may ease treatment burden and increase accessibility for logistically challenged patients. Travel distance is one of the factors that affects a patient's access to treatment and is often related to demographic factors, specifically geographic location and socioeconomic status. In this study, we review the demographic and geographic factors of patients treated with SBRT for prostate cancer for a single institution with over a decade of experience.

Methods: One thousand and thirty-five patient zip codes were derived from a large prospectively maintained quality of life database for patients treated for prostate cancer with SBRT from 2008 to 2017. The geospatial distance between the centroid of each zip code to our institution was calculated using the R package Geosphere. Seven hundred and twenty one patient's specific characteristics were evaluable at the time of analysis including race, age, and insurance status. Subsequently to assess the geographic reach of our institution, we evaluated the demographic features of each zip code using US census data. Statistical comparisons for these features and their relation to distance traveled for treatment was performed using the Mann-Whitney U test. Finally, an unsupervised learning algorithm was performed to identify distinct clusters of patients with respect to median income, racial makeup, educational level, and rural residency.

Results: Patients traveled from 246 distinct zip codes at a median distance of 11.35 miles. Forty percent of patients were African American, 6.9% resided in a rural region, and 22% were over the age of 75. Using K-means cluster analysis, four distinct patient zip-code groups were identified based on the aforementioned demographic features: suburban/high-income (45%), urban (30%), suburban/low-income (17%), and rural (8%). For each of the clusters, the average travel distance for SBRT was significantly different at 14.8, 10.8, 17.5 and 54.7 miles, respectively ($p < 0.001$).

Conclusions: Distinct demographic features are related to travel distance for prostate SBRT. Despite longer travel distance, a small but significant rural cohort is able to access this new technology. Additionally, travel distance does not preclude access for a large African American and/or elderly cohort. Prostate SBRT offers a diverse population modern treatment for their localized prostate cancer, and particularly those who live significant distances from a treatment center.

Liver Function Abnormalities Twelve Months after Stereotactic Body Radiation Therapy (SBRT) for Hepatocellular Carcinoma (HCC)

Justin Tang, M.D., Nitin Ohri, M.D., M.S., Rafi Kabarriti, M.D., Aneesh Pirlamarla, B.A., Madhur Garg, M.D., Andreas Kaubisch, M.D., Shalom Kalnicki, M.D., Milan Kinkhabwala, M.D., Chandan Guha, M.B.B.S., Ph.D.

Objectives: To report clinical outcomes and liver function abnormalities following treatment with stereotactic body radiation therapy (SBRT) for hepatocellular carcinoma (HCC) at our institution.

Methods: We reviewed all patients treated with SBRT for liver-confined HCC between 2010 and 2015 at our institution. Clinical records, including patient characteristics, treatment details, and clinical outcomes were reviewed. Follow-up imaging was obtained every 2-3 months. Local control (LC), progression-free survival (PFS), and overall survival (OS) were assessed using the Kaplan-Meier method. All patients completed treatment with prescription doses ranging from 25 to 54 Gy in 5 fractions based on mean liver dose and tumors' proximity to organs at risk. Liver function was assessed after SBRT using CTCAE, Child-Turcotte-Pugh (CTP), Albumin-Bilirubin (ALBI), and MELD-Na score. Toxicity data were censored at the time of disease progression. Adverse outcomes over time were assessed with the Wilcoxon signed-rank test for CTP and using mixed-effects models for ALBI and MELD-Na score.

Results: Sixty-nine patients were included in the analysis. Fifty-five patients had CTP scores of 5 or 6, while eleven patients have CTP score of 7, and three patients have CTP scores of 8 or 9. The actuarial LC rate at 24 months for the entire cohort was 92% (95% CI, 81%-97%). The PFS rate at 24 months was 50% (95% CI, 36%-61%). The OS rate at 24 months was 80% (95% CI, 67%-88%). Over the initial 3 months after SBRT, none of the patients experienced overt liver dysfunction by CTCAE criteria. However, we observed a statistically significant decline in liver function as assessed by CTP, ALBI, and MELD-Na score. Seventeen patients (27%) had an increase in CTP score of 2 points or more after 3 months. The median increase in CTP score at 3 months was 1 (IQR 0 to 2, $p < 0.001$). Three months after SBRT, the median MELD-Na score increased by 1 point from baseline ($p = 0.43$). Patients at baseline had a mean ALBI score of -1.89 (SD 0.66); this worsened to -1.54 (SD 0.34, $p < 0.001$) 3 months after SBRT. We further assessed ALBI score longitudinally over a 12 months period and we noted continued worsening of ALBI score at 6 months (-1.38, SD 0.28). The ALBI score subsequently stabilizes at 9 (-1.48, SD 0.29) and 12 months (-1.47, SD 0.46), but the score did not return to the baseline value.

Conclusions: In accordance with other institutional experiences, we observed excellent overall LC rates following SBRT for HCC. The majority of this cohort had CTP class A at the time of treatment, which may explain why there was no overt clinical liver dysfunction observed. However, there was a persistent subclinical decline in liver function detected even 12 months after initial treatment. The subclinical liver dysfunction may limit future treatment options in the event that the patient progresses locally. Therefore, further studies on strategies to mitigate liver injury and dysfunction after SBRT may be warranted.

Adjuvant Pancreatic SBRT for Close or Positive Margins

Philip Sutura, Mark Bernard, Kimmen Quan, Steven Burton, Nathan Bahary,
Melissa Hogg, Amer Zureikat, Dwight Heron



Objectives: Patients with close or positive margins after surgery for pancreatic carcinoma are at a high risk of recurrence. Stereotactic Body Radiation Therapy (SBRT) allows for safe dose escalation with great conformity and short duration of treatment. Herein, we report initial results of a phase II clinical trial to evaluate the efficacy and safety of this treatment option.

Methods: Patients eligible for the study had pathologically-proven T1-4N0-1M0 pancreatic adenocarcinoma with a positive margin ($\leq 1\text{mm}$) or a close margin defined as less than 2.5mm. Patients were treated with either neoadjuvant and/or adjuvant chemotherapy, if eligible for systemic therapy. All patients received 36 Gy in 3 fractions to the close or positive margin site.

Results: From February 2013 to January 2018, 50 patients were enrolled with 49 treated on protocol and included in analysis. The median age was 71years. Median CTV was 11.3cc and median PTV was 22.0 cc. Median overall survival was 23.7 months (95%CI, 13.6-33.8). Local progression-free survival at 1- and 2-years was 85 and 77%, respectively. Regional progression-free survival at 1-year and 2 years was 73% and 73%, respectively. Distant metastases-free survival was 57% and 49% at 1 and 2 years, respectively. Grade 3+ radiation toxicity was only 4.1% occurring in 2 patients.

Conclusions: Adjuvant pancreatic SBRT was shown to be a safe and feasible treatment option for high-risk pancreatic adenocarcinoma patients with close or positive margins. This is the first prospective trial to study SBRT in high-risk post-operative pancreatic cancer. Our results yielded significant local and regional control with low rates of acute toxicity. This technique does not interrupt administration of systemically dosed multi-agent chemotherapy and can be safely interdigitated between cycles given it is only 1 week of treatment.

Stereotactic Body Radiation Therapy with Immunotherapy in the Treatment of Oligometastatic Disease: A Subset Analysis of a Prospective Phase II Trial

Philip Sutera, Ronny Kalash, David Clump, Dwight Heron

Objectives: Metastatic disease represents the cause of approximately 80-90% of cancer-related deaths. Patients with oligometastatic disease may experience significantly improved outcomes when treated with aggressive local therapies such as stereotactic body radiation therapy (SBRT). Targeted immunotherapies have also improved outcomes in those with metastatic disease. It is currently hypothesized that combining radiation with immunotherapy (IO) may lead to a synergistic effect potentially mediated by the abscopal effect. Here we report an analysis of a prospective phase II trial assessing SBRT for treatment of oligometastatic disease followed by IO.

Methods: Patients with a pathologically-proven solid malignancy with oligometastatic disease (1-5 metastases) were prospectively recruited between 2011-2017. SRS/SBRT dose and fractionation was dependent upon the lesion location and size. Following treatment with SBRT patients received immunotherapy under the care of a medical oncologist. Patient follow-up occurred at 6 weeks following completion of SBRT and at 3-month intervals for 3 years. Patients received FACT-G questionnaire at baseline and at each follow-up to assess for quality of life (QOL). Total FACT-G scores were compared to baseline using Wilcoxon signed rank test. Median follow-up was calculated by reverse Kaplan-Meier method. Overall survival (OS), local progression-free survival (LPFS), and distant progression-free survival (DPFS) were calculated using Kaplan-Meier estimation to either date of last follow-up/death or local/distant failure.

Results: 18 patients were enrolled with oligometastatic disease treated with SBRT followed by IO. Primary tumors included, non-small cell lung cancer (55.6%), squamous-cell carcinoma of the head and neck (16.7%), colorectal adenocarcinoma (11.1%), renal-cell carcinoma (11.1%), or malignant melanoma (11.1%). Median age at enrollment was 64.3 years (IQR: 60.8-73.3). Patients received SBRT to either 1 (50.0%), 2 (33.3%), 3 (5.6%), or 5 (5.6%) metastatic sites. Following SBRT patients received either nivolumab (77.8%), pembrolizumab (11.1%), atezolizumab (5.6%), or ipilimumab (5.6%). With a median follow-up of 32.0 months, median OS was 43.3 months (95% CI: 39.3-47.3) with a 5-year OS of 32%. At 2-year LPFS and DPFS were 69% and 6%; respectively. Acute grade 2 toxicity was observed in 16.7% of patients with no acute grade 3+ toxicity. No significant change in QOL was identified as compared to baseline within 12 months of SBRT.

Conclusions: SBRT followed by immunotherapy is a feasible and safe treatment strategy for patients with oligometastatic cancer. These results indicate enhanced overall survival and LPFS, and a preserved quality of life following aggressive local treatment.

Prognostic Factors for SBRT in Pancreatic Cancer: Analysis of the Multi-Institutional RSSearch® Patient Registry Database

Amanda Rivera, Rafi Kabaritti, Patrik Brodin, Shalom Kalnicki, Madhur Garg

Objectives: Local control of pancreatic cancer treated with radiation is of large importance for both tumor control and local symptom control. The use of pancreas SBRT is emerging as an alternative to standard fractionated courses for borderline resectable or unresectable pancreatic cancer. Local control remains of utmost importance given the use of localization, smaller margins, and unlikely surgical intervention in this setting. We sought to identify factors associated with local control following pancreas SBRT in a large registry database.

Methods: The RSSearch® Patient Registry was queried for patients with pancreatic cancer treated with SBRT for a primary pancreatic malignancy. Patients were excluded if TNM staging was unavailable. The database was analyzed for clinical and treatment parameters, as well as, local control outcomes. Clinical characteristics assessed included weight, TNM stage, operable status, chemotherapy, gender, and ethnicity. Treatment parameters assessed included prescription dose, maximum dose, and number of fractions. Outcomes data assessed were local control and death. Multivariable logistic regression modeling was used to analyze the risk of local failure.

Results: A total of 95 patients met inclusion criteria and were available for statistical analysis. The median age of patients was 77 years (IQR: 68-83). Fifty six patients were considered to be surgically operable and thirty nine patients were considered surgically inoperable. The majority of patients were Caucasian (86%), with a small minority of patients being African American (5%), Hispanic (4%), Asian (1%) or other/unknown (4%). The median weight was 153 lb (IQR: 122-176 lb) and the median prescription dose was 30 Gy (IQR: 25-35 Gy), with a median maximum dose of 42.2 Gy (IQR: 31.3 - 50 Gy). All treatment courses were delivered in one to five fractions. Maximum dose was significantly associated with decreased local failure. Specifically, maximum dose > median yielded a HR of 0.12 (95% CI: 0.02 - 0.85), $p=0.033$. Furthermore, weight was significantly associated with increased local failure. Weight > median yielded a HR of 13.3 (95% CI: 1.72 - 103), $p=0.013$. T-stage was not significantly associated with local failure ($p=0.40$), though higher T stage trended toward a higher risk of local failure. Operable status, chemotherapy, and gender were not significantly associated with local control.

Conclusions: Using a large, multi-institutional database, we found a strong association between weight and increased local failure, and maximum dose and decreased local failure, following SBRT for pancreatic cancer. More research is warranted regarding obesity and the underlying mechanisms relating to local control for pancreas SBRT.

Real-Time Magnetic Resonance Guided Liver Stereotactic Body Radiation Therapy

Aharon M. Feldman, MD; Ankit Modh, MD; Carri K. Glide-Hurst, PhD; Jadranka Dragovic, MD; Munther Ajlouni, MD; Newton Hurst, MD, PhD; Benjamin Movsas, MD; **Jennifer L. Dolan, PhD**

Objectives: Stereotactic body radiation therapy (SBRT) is a proven and effective modality for treatment of hepatic primary and metastatic tumors. However, these lesions are challenging for planning and treatment execution due to large excursion and hysteresis exhibited during respiration. Often, generous margins are required to ensure appropriate tumor volume coverage. Magnetic Resonance Imaging (MRI) offers superior soft tissue contrast resolution and the ability for real-time image guided treatment delivery and lesion tracking. We report our initial clinical experience treating hepatic tumors with MR-guided gated radiation therapy on an MR linear accelerator (MR-linac) platform.

Methods: Treatment data from 16 consecutive patients treated with SBRT were reviewed. All deliveries were performed using a step and shoot technique to one or more liver lesions on an MR-linac platform. Patients received 45 Gy prescribed to at least 95% of the planning target volume (PTV) in five fractions except for two patients who received 27-30 Gy in three fractions. CT and MRI simulation were performed in the supine position prior to treatment in the free-breathing, end exhalation, and end inhalation breath-hold positions to determine patient tolerability and potential dosimetric advantages of each technique. Immobilization consisted of using anterior and posterior torso MRI receive coils embedded in a medium sized vacuum cushion. Gating was performed using sagittal cine images acquired at 4 frames/second. Gating boundaries were defined in the three major axes to be 0.3 to 0.5 cm. An overlapping region of interest (ROI), defined as the percentage volume allowed outside the boundary for beam-on to occur, was set between 1 and 10%. The contoured target was assigned a 5 mm PTV expansion. The prescribed liver dose constraint was no more than 700 cc to receive a maximum of 21 Gy.

Results: Sixteen patients, 12 males and 4 females, with 18 lesions, successfully completed the prescribed treatment with minimal treatment breaks or delays. The mean number of beams on during treatment was 9.2 (6 - 10; STD 1.3) and the mean beam segments used was 23.2 (10 - 39; STD 7.3). The mean monitor units per fraction was 2079.1 MU (1549.1 - 2613.1; STD 358.0). Based on patient compliance, 11 lesions were treated at end-exhalation while 7 were treated at end-inhalation. The average liver volume receiving 21 Gy was 119.3 cc (5.1 - 236.6; STD 75.0). Total delivery time, defined as the time interval from the first beam on to the end of the last beam on, was 10.4 minutes (5.8 - 25.2; STD 3.5). Beam on time was a mean of 73.5 percent (46 - 92; STD 8.6). Follow up imaging ranged from 1 month to 9 months post treatment and confirmed either stable or decreased size of treated lesions. Toxicities included nausea and vomiting in one patient and one case of abdominal pain with bloody diarrhea requiring a brief treatment break and resolved without any intervention. Three patients died due to complications from liver cirrhosis unrelated to radiation effect.

Conclusions: Gated SBRT treatment on a MR-Linac has been successfully demonstrated and offers potential to allow for tighter margins and reduced toxicity. Further follow up is needed to identify potential toxicities associated with treatment and more studies are warranted to identify the benefits and risks associated with MR-guided SBRT.

Stereotactic Body Radiotherapy (SBRT) for Colorectal Liver Metastasis - Clinical Outcomes from the International Multi-Institutional RSSearch® Patient Registry

Pollyanna Leite, Andrew Gaya, Oliver Blanck, Rachele Lanciano, Jun Yang, Joanne Davis and Anand Mahadevan

Objectives: We investigated factors associated with clinical outcome for liver metastases from colorectal primary tumors treated with Stereotactic Body Radiotherapy (SBRT) from a multi-center, international, prospective patient registry.

Methods: A subgroup of patients with colorectal liver metastases treated with SBRT was identified from the RSSearch® Patient Registry. Patient, tumor and treatment characteristics associated with outcome were evaluated. Dose fractionations were normalized to BED10. Overall survival (OS) and local control (LC) were evaluated using Kaplan Meier analysis and log-rank test.

Results: 200 patients with 221 liver metastases from primary colorectal cancer treated with SBRT between 2005-2017 and enrolled in the RSSearch Patient Registry were included. Median age was 68 years (31-90 years) with a median KPS of 90% (40-100%). The median follow-up was 15 months (1-75 months). 7% of patients received prior or concurrent chemotherapy. Median tumor volume was 21.95 cm³ (0.5 - 638 cm³), median SBRT dose was 45 Gy (16 - 60 Gy) delivered in a median of 3 fractions (1-5). Median number of liver metastases was 1 (1-8). Median overall survival (OS) was 27 months and median local control (LC) was 41 months. One and two-year OS was 75% and 56%, respectively. One and two-year LC was 74% and 64%, respectively. Higher BED10 was associated with improved LC with median LC of 44 months for BED10 = 100 Gy compared to 39 months for BED10 < 100 Gy (p=0.0016). One-year LC rates for BED10 = 100 Gy and BED10 < 100 were 87% and 59%, respectively and 2 year LC rates were 52% for BED10 <100 Gy and 77% for BED10 = 100 Gy . Higher BED10 was also associated with improved OS with median OS of 32 months for BED10 = 100 Gy compared to 19 months for BED10 < 100 Gy (p=0.0003). One-year OS for BED10 = 100 Gy and BED10 < 100 was 83% vs 62%, respectively. Two-year OS for BED10 = 100 Gy and BED10 < 100 was 66% vs 39%, respectively. Smaller tumor volume was associated with improved OS, with median OS of 33 months for tumor volume < 27 cm³ vs 21 months for tumor volumes = 27 cm³ (p=0.0021). One year OS was 80.5% vs 67% for tumor volume < 27 cm³ vs = 27cm³, respectively. Local control was also associated with a small tumor volume: median LC for tumor < 27 cm³ vs = 27 cm³ was 44 months vs 27 months, respectively (p=0.034). Prior or current chemotherapy was correlated with decreased OS, with median OS of 26 months for patients who received chemotherapy vs 44 months for patients who did not receive chemotherapy (p=0.0188). The use of systemic chemotherapy did not correlate for LC in this cohort.

Conclusions: In this multi-institutional prospective cohort, OS and LC were favorably correlated with small tumor volume and higher BED10. The decreased OS observed with chemotherapy use may be related to more advanced disease in that cohort.

Stereotactic Body Radiation Therapy for Early Stage Breast Cancer using a Robotic Linear Accelerator-5 Year Results from the NYU Winthrop Hospital Trial



Jonathan Haas, MD, Seth Blacksborg, MD, MBA, Owen Clancey, PhD,
Donna Catell, MD, Astrid Sanchez, Diane Accordino, RN,
Elaine Castellano, RN, Gizem Demircioglu, MA,
Alec Haber, Matthew Witten, PhD

Objectives: Standard radiation therapy for patients with breast cancer desiring breast conservation typically consists of lumpectomy followed by radiation. Radiation can either be delivered to the whole breast or to part of the breast. Whole breast radiation is typically given daily for 3-6 weeks depending on the dose/fractionation scheme. When partial breast irradiation is given, often an implanted catheter is used to deliver a conformal dose of radiation to the lumpectomy cavity in an accelerated manner twice daily over one week. In properly selected patients, the results for partial breast irradiation appear comparable to results for conventional whole breast radiation. We examined the safety and efficacy of using Cyberknife for selected patients with early stage breast cancer after lumpectomy and report on our technique and 5 year results.

Methods: 50 consecutive patients with Stage I/II breast cancer were enrolled on the NYU Winthrop Hospital IRB approved CyberKnife breast protocol. Eligibility included Stage I/II (< 3 cm) Age >45, margins negative. 1 patient had fiducial markers placed by the surgeon. The other 49 patients had fiducial markers placed by the treating radiation oncologist using image guidance on a CT simulator with coordinate placement determined by the physics/dosimetry staff for optimal location. Patients were immobilized either using a thermoplastic cast with a hole removed around the areola to allow for reproducibility daily or with an alpha cradle to allow the breast to remain in its natural position. All patients received a dose of 3000cGy in 5 fractions of 600 cGy each given on five consecutive days. The median number of beams was 86. The median prescription isodose line was 71%. This isodose was chosen to allow for a more rapid fall of dose beyond the target volume to more accurately emulate HDR treatment.

Results: With a median followup of 64 months, (range 14-96 months) all 50 patients (100%) remain locally controlled with no evidence of disease following treatment. RTOG Grade 1 dry skin desquamation occurred in 1 of 50 patients. Minimal erythema involving a small portion of the breast was reported by 2 patients. 1 patient reported temporary pain at the lumpectomy site 10 months post treatment. The cosmesis was excellent in 48 and good in 2 patients using the Harvard cosmesis scale.

Conclusions: With 5 year followup, Cyberknife radiosurgery for early stage breast cancer remains very well tolerated and efficacious for selected patients desiring breast conservation after lumpectomy. Further followup will be required to see if these results remain durable.

2019 RSS ANNUAL SCIENTIFIC MEETING MARCH 21-23, 2019 • SHERATON • SAN DIEGO



BRIDGING THE GAP

the
Radiosurgery
Society

ADVANCING VALUE-BASED CARE THROUGH RADIOSURGERY

POSTER SESSION ABSTRACTS

CLINICAL



2019 RSS Scientific Meeting
Bridging the Gap: Advancing Value-Based Care Through Radiosurgery
March 21-23, 2019 | San Diego, CA
www.therss.org

Acoustic Neuroma Radiosurgery Delivery Factors, including Treating Staff and Time on Table, are Associated with Improved Functional Outcomes: A Single-Institution Retrospective Review

John Byun, MD

Objectives: To assess the role of stereotactic radiosurgery treatment delivery factors and long-term functional outcomes on patients diagnosed with acoustic neuroma.

Methods: A single center, retrospective chart review of all cases treated with stereotactic radiosurgery at the Robert Wood Johnson University Hospital

We are working with the author to get the full text of this abstract.
We will update the file as soon as possible.

A Dosimetric Analysis comparing Preoperative with Postoperative Stereotactic Radiosurgery for Brain Metastases

Chase C. Hansen, MD, MBA; Jonathan J. Paly, DO; Jiangtao Gou, PhD; Xiaoming Chen, PhD; Kerry Januszka, RN, BSN; Shelly Hayes, MD; Stephanie E. Weiss, MD

Objectives: Stereotactic radiosurgery (SRS) or radiotherapy (SRT) is emerging as an effective alternative to surgery or whole brain radiation for the treatment of brain metastases. It is commonly accepted as the standard of care in the postoperative setting. However, there is increasing interest exploring the role of SRS prior to surgical resection. Decreased rates of leptomeningeal disease, improved target delineation, in addition to smaller treatment volumes are all theoretical advantages of preoperative SRS/SRT. Our aim is to compare dosimetric and volumetric endpoints for preoperative and postoperative SRS/SRT treatment plans on the same patient.

Methods: Using our departmental IRB approved database of patients treated with SRS/SRT, we identified five patients that were treated with SRS/SRT following resection of a brain metastasis in 2018. Preoperative MR imaging was reviewed, with "mock" contours and radiation treatment plans generated for each patient. Actual postoperative treatment plans were generated for comparison. A planning target volume (PTV) was created for the postoperative plans by adding 2 mm to the resection cavity. This volume was compared to the gross tumor volume (GTV) for the preoperative plans which included the tumor only without a margin. Volumetric and dosimetric analyses compared each patient's plan for both preoperative and postoperative treatment. To the author's knowledge, this is the first analysis comparing preoperative and postoperative SRS/SRT treatment plans in the same patient.

Results: Actual postoperative SRS/SRT plans were compared to "mock" preoperative SRS/SRT plans for 5 patients. In this small cohort, four lesions were based in the supratentorial region and one in the infratentorial region. All treatments used the dose 24 Gy given in three fractions prescribed to the 70% to 80% isodose line. Each patient had a different disease histology, including melanoma, breast, colorectal, and both squamous and adenocarcinoma of lung. Mean target volumes were 17.3 cc (SD 12.0) and 9.5 cc (SD 5.44) ($p=0.031$) for pre- and postoperative SRS/SRT, respectively. Similarly, the mean volume of tissue encompassed by the 12 Gy isodose line (V_{12}) was 47.3 cc (SD 27.9) and 32.6 cc (SD 16.2) ($p=0.138$). As a measure of normal brain tissue treated, a surrogate for the risk of neurotoxicity, the V_{12} minus GTV (V_{12} -GTV) was calculated and was 30.0 cc (SD 16.2) and 26.9 cc (SD 13.0) ($p=0.318$). Two patients with preoperative target volumes < 11 cc showed smaller V_{12} -GTV volumes favoring preoperative therapy. The remaining patients had preoperative target volumes measuring > 14 cc and larger V_{12} -GTV volumes when compared to postoperative volumes.

Conclusions: Not surprisingly, this study demonstrates that for a given patient, preoperative treatment volumes are larger than postoperative volumes, which makes sense given that the main reason for surgery in these patients was a large, symptomatic tumor. The amount of normal brain tissue receiving ablative doses is not significantly different between treatment techniques. Patients with smaller, asymptomatic tumors stand to benefit most from preoperative SRS/SRT with lower V_{12} -GTV volumes.

A Study of Brain Metastases' Responses to Frameless SRS Treatments by Using Modified RANO-BM Criteria

Katie Xue, Nimisha Deb, David Andolino, Xiaoling Song, Rong Ding Li,
Tianyou Xue, Hugh Moulding

Objectives: The aim of this study was to evaluate the response of each brain metastasis lesion to frameless stereotactic radiosurgery (SRS) treatments by using a modified Response Assessment in Neuro-Oncology Brain Metastases (RANO-BM).

Methods: This is a retrospective study of 87 patients with a total of 149 brain metastases lesions that were treated with frameless SRS from February 2015 to March 2017. The RANO-BM criteria are modified as following for each metastasis lesion: Complete Response (CR): Disappearance of the target lesion; Partial Response (PR): At least a 30% (or 3 mm for lesions with baseline longest diameters between 5 mm and 10 mm) decrease in the longest diameter of the target lesion (no PR for lesions less than 5 mm due to relative large measurement uncertainty); Progressive disease (PD): At least a 20% increase (or 3 mm for lesions with baseline longest diameters between 5 mm and 10 mm) in the longest diameter of the target lesion; Stable disease (SD): Neither sufficient shrinkage to qualify for partial response, nor sufficient increase to qualify for progressive disease. All measurements are based on T1 MR images with contrast. Follow up MR scans are from 2 to 16 months after treatments.

Results: Of the 95 patients treated during the study period, 7 patients did not have planning MRI or follow up MRI scans; the lesion of another patient was next to a surgical cavity. Those 8 patients were excluded from the study. 50 patients had single metastases lesions; 37 patients had 2 to 9 metastases lesions. A total of 149 lesions were studied. The results are 62 (41.6%) CR, 21 (14.1%) PR, 58 (38.9%) SD, and 8 (5.4%) PD.

Conclusions: Our retrospective study shows a 94.6% local control (CR, PR and SD) rate to frameless SRS.

Clinical Evaluation for Setup Accuracy of OSMS Data over CBCT Matched Values for Brain Metastasis with SRS

Amol Babu Pawar Anand Jadhav Ankita Nachankar Prasad Dandekar

Objectives: To evaluate the accuracy of a video-based optical surface imaging system for motion monitoring during stereotactic treatment of brain metastasis. Precise patient positioning and thus of the PTV is a prerequisite for effective treatment with SRS for brain metastasis. The intra fraction motion should at least be within the CTV-PTV margin used. Conventional imaging modalities used to ensure exact positioning for treatment typically involve additional radiation exposure of the patient. Patient alignment and monitoring during treatment, without additional exposure, is provided by optical 3D surface scanning and registration systems. Typical SRS brain treatments with multiple couch angels limits the ability of CBCT verification during treatment. This paper aims to correlate the data obtained by the OSMS system with the internal shifts observed by the offline CBCT matches pre and post treatment.

Methods: Patients treated with stereotactic radiosurgery (SRS) and fractionated stereotactic radiotherapy (FSRT) were immobilized with a thermoplastic double shell open face mask and a SRS immobilisation system (Encompass ? Immobilisation System and Encompass ? SRS Fiberplast Qfix). During treatment a video-based three-dimensional optical surface monitoring system was used to monitor the motion of a region of interest. This motion monitoring was done in 6 dimensions. A tolerance of 0.2 cm for linear directions and 0.5 degrees for rotational directions was set. If the optical surface monitoring system detected an exceeding of the set tolerance, treatment stopped automatically. If necessary, the physician decided to take a new CBCT. A total of 13 patients were followed for SRS or FSRT treatment between January 2016 and May 2018 with a total of 19 fractions evaluated for intra fractional uncertainties. Both CBCT and snapshots obtained with the OSMS were acquired at the start and stop of every treatment to compare both methods. In addition the average motion and SD during treatment was monitored to investigate the validity of pre- and post-measurements for assessing intra fractional motion.

Results: A pre-treatment mean intra fractional shift for of 0.12 cm in vertical (STDEV of 0.08), 0.11 cm in longitudinal (STDEV of 0.11), 0.17 in lateral direction (STDEV of 0.14). Only in one patient, set tolerance was exceeded and a new CBCT was taken which showed a lateral shift of 0.47 cm. Pre-treatment Delta Values Delta Vrt Delta Lng Delta Lat Delta Pitch Delta Roll Delta Rtn median 0.11 0.09 0.17 1.02 0.30 0.90 mean 0.12 0.11 0.17 0.97 0.85 1.17 SDEV 0.08 0.11 0.14 0.74 0.98 0.68 max 0.28 0.29 0.47 2.60 3.25 2.22 A post-treatment mean intra fractional shift for of 0.04 cm in vertical (STDEV of 0.05), 0.05 cm in longitudinal (STDEV of 0.05), 0.04 in lateral direction (STDEV of 0.05). None of the patient were exceeded set tolerance during treatment. Post-treatment Delta Values Delta Vrt Delta Lng Delta Lat Delta Pitch Delta Roll Delta Rtn median 0.03 0.04 0.03 0.30 0.16 0.36 mean 0.04 0.05 0.04 0.39 0.41 0.43 SDEV 0.05 0.04 0.05 0.34 0.42 0.30 max 0.21 0.13 0.15 1.20 1.25 1.00.

Conclusions: The CBCT data clearly shows that the intra fractional offset of all brain metastasis patients treated with SRS or FSRT was below the institution's predefined threshold. The OSMS data obtained during treatment still needs a more detailed evaluation. For further analysis the approach was changed and real time data during treatment is now continuously triggered, obtained, mathematically analysed and compared with the CBCT offline calculated offset.

Conformal Arc Informed VMAT for Multiple Brain Metastases Radiosurgery

Will Giles, Obed Laryea, Fang-Fang Yin, John Kirkpatrick, Justus Adamson

Objectives: Linear accelerator based radiosurgery is often performed using either dynamic conformal arcs or VMAT. For multiple brain metastases, multifocal conformal arc techniques can struggle to deliver the desired dose and high conformity for all targets simultaneously. While VMAT can achieve better coverage and conformity, it can result in highly modulated, non-intuitive MLC trajectories. The complex MLC trajectories can often struggle with blocking between targets and may leave MLC gaps between targets. Our purpose is to develop a technique for multiple brain metastases that combines the intuitive MLC trajectories of dynamic conformal arcs with the flexibility of VMAT.

Methods: A Conformal Arc Informed VMAT (CAVMAT) planning technique was developed in which conformal arcs are assigned subgroups of targets to maximize blocking between targets. Arc weights are optimized to achieve desired dose per target while minimizing the variation in MU per arc. The optimized conformal arc plan then serves as the starting point in a VMAT inverse optimization to fine tune the dose to each target and optimize conformity. Eight multiple brain metastases cases - originally planned with VMAT - were re-planned with CAVMAT. The following metrics of plan quality were used to compare the VMAT plans with the CAVMAT plans: volume of healthy brain receiving 6Gy, 12Gy, and 16Gy, conformity index, and total number of monitor units.

Results For the CAVMAT plans, the average decrease in V6Gy, V12Gy, and V16Gy was $3\pm 11\%$ (range: 16% lower to 18% higher), $7\pm 3\%$ (range 12% lower to 4% lower), and $6\pm 5\%$ (range 14% lower to 1% lower), respectively. The number of monitor units changed little on average ($0.6\pm 21\%$ increase), but varied widely by plan (to 42% lower to 22% higher) compared to VMAT plans, beam on time has an average difference of 1% compared to VMAT plans. The conformity index was 1.27 ± 0.12 for CAVMAT compared to 1.22 ± 0.12 for VMAT.

Conclusions The CAVMAT planning technique provides smaller low dose spill to normal brain tissue compared to VMAT, with comparable conformity, monitor units, and treatment times. Future work will focus on automation and further investigation of the consequence of target size.

High Resolution (1mm) Magnetic Resonance Imaging (MRI) is More Sensitive Than Lower Resolution MRI for Detecting the Number of Brain Metastases in Patients Undergoing Stereotactic Radiosurgery

Pacitti D, Stross W, Waddle MR, Malouff TD, Ko S, Vallow L, Miller R, Trifiletti DM, Peterson JL

Objectives: Magnetic Resonance imaging (MRI) with 2.5mm - 5mm slice thickness (2.5 - 5mm MRI) is routinely used for detection of brain metastases. Stereotactic Radiosurgery (SRS) is a treatment which requires highly accurate image resolution, and thus at our institution an additional MRI with 1mm slice thickness (1mm MRI) is typically obtained prior to treatment. The aim of this study is to characterize the frequency that 1mm MRI changes management when compared to 2.5mm - 5mm MRI.

Methods: Patients that were treated with brain metastases from 1997 - 2018 at Mayo Clinic Florida were reviewed. Patient characteristics, disease details, screening and planning MRI information, radiotherapy treatment, and disease control information were collected. Patients without both a 2.5mm - 5mm MRI and a 1mm MRI, or patients with greater than 30 days between scans were excluded. MRIs were reviewed by a radiation oncologist to identify the number, location, and size of brain metastases. The frequency that 1mm MRI detected more or less brain mets than 2.5mm - 5mm MRI was then determined as the primary endpoint. Factors such as disease site, size of the largest lesion, and time between planning and treatment MRI were assessed between the two groups. Sensitivity and positive predictive were also calculated.

Results: A total of 86 patients were treated for brain metastases from 1997 to 2018. We identified 25 (29%) instances when 1mm MRI changed management, 18 (21%) times by detecting more lesions and 7 (8%) times by detecting less lesions. This conferred a sensitivity of 74% and positive predictive value of 88% to the 2.5mm - 5mm MRI. The average age was 64 years (66 median) and most patients (55%) were treated after 2014. Lung, breast, and melanoma were the most common primary disease sites at 50%, 14%, and 14% of patients. Breast cancer was noted to have a high rate (58%, N=7/12) of change in management with 1mm MRI.

Conclusions: High resolution 1mm MRI was more sensitive at detecting brain metastases than larger slice thickness MRIs. Additionally, 1mm MRI found a significant number of false positive brain metastases. Our findings suggest that 1mm MRI should be standard of care for SRS treatment, and physicians may consider the use of 1mm MRI for routine screening in patients with known brain metastases.

Mask-Based Cranial Stereotactic Radiosurgery: Practical Considerations for an Innovative Approach

1) Ke Nie PhD 2) Shabbar Danish MD, FAANS 3) Simon Hanft MD 4) Arthur Carminucci MD
5) Ma Rhudelyn Rodrigo MA RN CCRN 6) Irina Vergalaso PhD BS 7) Joseph P. Weiner MD

Objectives: The use of stereotactic radiosurgery (SRS) is widely employed to treat intracranial pathology. For decades, patients treated via isotope-based radiosurgical units were immobilized via the placement of an invasive head frame. More recently, the introduction of the Gamma Knife Icon allows for a frameless, mask-based approach to immobilization. Despite the attractiveness of a non-invasive mask, technical and practical considerations still remain given the novelty of this system. The purpose of this study is to investigate our experience with the frameless system and to identify ideal patient selection criteria.

Methods: We performed a retrospective review of all patients treated with SRS at our institution since the introduction of our newest unit with mask capabilities, from January 2017 to May 2018. Treatments included both single fraction radiosurgery as well as hypofractionated radiosurgery (HF-SRS). Descriptive statistics were used to analyze these patients.

Results: There were 221 patients treated in this time frame with SRS, of which 13 patients (5.9%) were recommended to undergo at least one treatment fraction via the frameless system. Patients were treated for different pathology including brain metastases (n=7, 53.8%), meningioma (n=3, 23.1%), pituitary adenoma (n=1, 7.7%), acoustic neuroma (n=1, 7.7%) and recurrent high grade glioma (n=1, 7.7%). The median number of brain metastasis treated was 4 (range 1-37 metastasis). Of the total cohort of 13 patients, 10 patients (76.9%) were able to complete their entire frameless treatment as prescribed resulting in 28 fractions delivered. Two patients were converted to a framed procedure (15.4%), as one was unable to tolerate the mask due to baseline respiratory dysfunction which repeated triggered our gating system, and another patient was found to have an increased burden of disease on MRI requiring a longer treatment duration. One final patient declined radiation. Of the completed patients, 3 patients (30%) were treated with single fraction SRS (median dose 18 Gy, range 15-20 Gy) and 7 patients (70%) were treated with HF-SRS. Of those treated with HF-SRS, the median number of fractions was 3 (range 2-6 fractions) and the median dose was 24 Gy in 3 fractions. For lesions treated with HF-SRS, the median volume was 15.4 cc (range 0.9-76 cc). During the course of treatment 3 of the 7 patients (42.9%) undergoing HF-SRS needed to have a new mask created mid-treatment due to mask shrinkage. Sixteen fractions (57.1%) were able to be completed without triggering a treatment interruption (median duration 23.4 minutes), though 12 fractions (42.9%) needed at least one interruption, median 1, range 1-5, (median duration 46.0 minutes).

Conclusions: Frameless radiosurgery via an isotope-based radiosurgical unit is a viable option for well selected patients, especially those needing either hypofractionated radiosurgery or limited treatment time. A small percentage of patients will be unable to tolerate the mask and will need conversion to frame-based immobilization. Longer treatment times are associated with increased treatment interruptions.

Multi-Session Radiosurgery for Jugular Foramen Schwannomas: Long-Term Outcomes

Enmin Wang M.D. Ph.D., Xin Wang M.D., Huaguang Zhu M.D., Xiaoxia Liu M.D.,
Yang Wang M.D., Li Pan M.D. Ph.D., Jiazhong Dai M.D.

Objectives: Jugular foramen schwannomas (JFSs) are rare lesions. Complete resection is possible but may be associated with significant morbidity. Stereotactic radiosurgery (SRS) is a minimally invasive alternative or adjunct to microsurgery. The authors reviewed clinical and imaging outcomes of multi-session SRS for patients with these tumors.

Methods: Fifty-nine patients with JFSs underwent multisession cyberknife radiosurgery between January 2008 and January 2015. Thirteen patients had previous microsurgical resection, one patients had recurrent tumor post Gamma Knife, the rest 45 patients underwent multi-session cyberknife radiosurgery based on their neuroimaging and clinical manifestations. Fifty-four patients had preexisting cranial nerve (CN) symptoms and signs. The median tumor volume was 15.1 cm³ (range 2.6-36.0 cm³), and 39 of them was larger than 10cm³ in volume. The radiation dose prescribed to the tumor margin and the number of fractions depend on the tumor volume. Twelve patients with large tumors were treated in 4 fractions, 31 patients were treated in three fractions and 16 patients in two fractions.. The median margin dose was 19.2 Gy/2 fractions, 21.1Gy /3 fractions and 24.5Gy /4 fractions-. Patients with neurofibromatosis were excluded from this study.

Results: The median follow-up was 58 months (range 24-105 months). Tumors regressed in 41(69%) patients, remained stable in 9 and progressed in 4. At last follow-up, one patients with large tumor was dead owing to the tumor progression . The progression-free survival (PFS) was 93% at 5 years, Preexisting cranial neuropathies improved in 32 patients, remained stable in 9, and worsened in 18.. Three patients underwent resection at a median of 25 months after multi-session SRS (range 18-36 months).

Conclusions: Multi-session stereotactic radiosurgery proved to be a safe and effective primary or adjuvant management approach for JFSs. Long-term tumor control rates and stability or improvement in CN function were confirmed.

Patients with Cystic Brain Metastases had Similar Local Control and Survival Time compared with Solid Tumor underwent Radiosurgery Treatment

Hui Wang, Xiaoye Liu, Yuhan Zhang, Zhiyong Yuan

Objectives: We aimed to compare the survival between cyst and solid brain metastases and assess risk factors for BMOS (overall survival after brain metastases) in patients underwent radiosurgery treatment.

Methods: A total of 356 patients (including 498 brain metastases) were enrolled and analyzed in our study. The Kaplan-Meier method and multivariate Cox regression analysis were used to compare survival time and evaluate risk factors for BMOS.

Results: A total of 67 patients (67/356, 18.8%) developed 75 cyst brain metastases. There is no statistical significance in BMOS between patients with cyst (3-64 months) and solid (1-65 months) brain metastases ($p=0.148$). However, the volume of cyst brain metastases decreased more slowly than solid brain metastases ($p<0.05$). The results indicated that high RPA classification ($p = 0.006$), large volume of brain metastases ($p=0.006$) and different primary lesion (especially Gastrointestinal tract tumor) ($p=0.001$) were associated with poor prognosis in patients with brain metastases.

Conclusion: There is no difference in prognosis between patients with cyst and solid brain metastases. However, the rate of tumor shrinkage was lower in cyst brain metastases after radiotherapy. Patients with larger volume of brain metastases had shorter survival time, regardless of cyst or solid brain metastases.

Phase I Time to Event Continual Reassessment Method (TITE-CRM) Dose Finding Study of Fractionated Stereotactic Radiation Therapy (FSRT) for Large Brain Metastases

Orisamolu Abimbola, Baliga Sujith, Kabarriti Rafi, Bodner William, Ohri Nitin, Garg Madhur

Objectives: Fractionated radiation therapy (FSRT) has emerged as an alternative to whole brain radiation for patients with large brain metastases. The optimal dose and fractionation schedule for FSRT in the treatment of brain metastases is not known. Here we describe an ongoing prospective phase I trial to determine the maximum tolerated dose (MTD) of FSRT for brain metastases.

Methods: This is a prospective phase I TITE-CRM dose escalation study. Our primary objective is to determine the maximal tolerated dose (MTD) associated with a 20% probability of dose-limiting toxicity (DLT), defined as radiographic or clinical diagnosis of radionecrosis that occurs within 1 year from the start of FSRT. Other objectives include to 1) determine the percentage of patients who have achieved a complete response, partial response, or stable disease in response to FSRT; and 2) determine if molecular biomarkers in the blood circulation, prior to, during the course of treatment and at first follow up after treatment predicts overall survival. Patients with a pathologically proven diagnosis of a non-hematological malignancy other than small cell carcinoma in the past five years and who have brain metastases visible on gadolinium contrast enhanced MRI are eligible. Patients must be age \geq 18 years with Karnofsky performance status = 60 or ECOG \leq 2 and life expectancy greater than 3 months. A detailed neurological examination, including mini mental status examination and MD Anderson Symptom Inventory - Brain Tumor (MDASI-BT), is conducted immediately prior to protocol treatment to assess treatment morbidity. The LENT-SOMA scale will be used to assess late toxicity. This study employs a continual; reassessment methodology (CRM) to determine the MTD. Information for the proper dose level for each subsequent patient enrolled will be determined based on DLTs from previous patients enrolled in the trial. This approach is particularly advantageous for accrual of patients when the primary endpoint is a delayed event. The RT dose level for each subsequent design will be determined using a TITE-CRM statistical approach. Our initial starting dose is 35 Gy in 5 fractions delivered to the planning target volume (PTV) every other day. 30 Gy, 32.5 Gy, 37.5 Gy, or 40 Gy may be delivered in 5 fractions to subsequent patients depending on the DLT's seen in patients who are already enrolled. The PTV is defined on planning CT simulation with aid of fused MRI and is a 2-3 mm expansion of GTV. Critical organs such as optic pathway, brainstem, cochlea, and spinal cord will be delineated and constrained. Response will be assessed based on WHO criteria as complete response (CR), partial response (PR), stable disease (SD), and progression (P).

Results: This protocol has been approved by the relevant IRB and has accrued 3 patients. The accrual goal is 30.

Conclusions: This protocol has successfully been implemented at our institution. Once mature data has been collected we will have new information about the optimal dose and fractionation schedule for FSRT.

Radiosurgery versus Stereotactic Radiotherapy for Hemorrhagic Brain Metastases

Jonathan Paly DO, Ambrosia Simmons PhD, Shelly Hayes MD,
Chase Hansen MD, Stephanie E. Weiss MD

Objectives: To compare single fraction stereotactic radiosurgery (SRS) with hypofractionated stereotactic radiotherapy (SRT) for differences in adverse events and local control in patients with hemorrhagic brain metastases.

Methods: We queried our IRB approved departmental database for prospectively enrolled patients with brain metastases who had pre-treatment intratumoral or peritumoral hemorrhage between Jan 2009 and June 2018. To be eligible, patients required treatment to intact lesions, and at least two months of follow-up if surviving greater than two months after therapy. Student's t-test was used to evaluate differences in incidence of rebleeding, new or increased post-treatment steroid use, recurrence in treated metastases verified by imaging or pathology, or additional local intervention.

Results: Forty four patients with forty seven hemorrhagic metastases were identified. Primary tumor histology was 43% non-small cell lung cancer, 19% melanoma, 11% renal cell carcinoma, 9% small cell lung cancer, and 18% other. Median follow-up after SRS/SRT was 4.5 months. Twenty seven metastases were treated with SRS to a median dose of 20Gy (range 15-22Gy) and 20 metastases received SRT with a median dose of 25Gy (range 24-30Gy) in a median of 5 fractions (range 3-10 fractions). Pre-treatment whole brain radiation therapy was delivered in 48% of the SRS group and 20% of the SRT groups ($p=0.048$). Rebleeding after radiotherapy occurred in 22% of the SRS group and 30% of the SRT group ($p=0.6$). New or increased post-procedural steroid requirement likely attributable to the treated lesion occurred in 41% of the SRS and 60% of the SRT groups ($p=0.2$). Probable recurrence of the treated lesion occurred in 22% of the SRS and 30% of the SRT groups ($p=0.6$). Subsequent local intervention with surgery or radiation for the treated lesion occurred in 19% of the SRS and 20% of the SRT groups ($p=0.9$).

Conclusions: To our knowledge, this is the first study to compare adverse events and local control of hemorrhagic brain metastases for patients treated with SRS versus SRT. There were no significant differences in either local control, incidence of rehemorrhage, treatment-associated steroid need, or subsequent local intervention based on fractionation schedule. Multivariate regression and correlation of tumor size to outcomes will be explored to evaluate potential prognostic indicators and determine whether other confounding tumor or treatment factors effected outcomes.

Repeated Stereotactic Radiosurgery in the Treatment of Brain Metastases

Stankiewicz Magdalena, Ksiezniak-Baran Dorota, Blamek Slawomir

Objectives: The aim of the study was to assess efficacy and safety of robotic stereotactic radiosurgery (SRS) in the treatment of brain metastases in patients who were previously treated with the use of SRS.

Methods: A retrospective analysis of clinical data of a group of 38 patients who underwent SRS at least twice. All patients were in good performance status (mean and median Karnofsky Performance Status - 80). Mean age was 57 years (range 34 - 79 years), 66% of patients were female. In 32% of patients location of primary tumor was lung, in 29% - breast, in 13% - kidney. Median time between the diagnosis of the primary tumor and brain metastases was 26 months, mean - 43 months (range 0 - 185 months). In 13% of patients brain metastases were found prior to diagnosis of the primary tumor. Planned dose was delivered in 1 - 3 fractions, 55% of patients were treated with single fraction. Mean total tumor volume of brain lesions was 8.86 mL, median - 4.62 mL (range 0.06 - 52.2 mL). Radiological evaluation of the treatment effects was performed in 82% of patients. For statistical analysis Kaplan - Meier estimator and log-rank test were used.

Results: Median overall survival (OS) in the whole group was 21 months. Longer OS was observed in patients with single brain metastasis as compared to those with multiple lesions ($p = 0.001$). Median OS calculated from the second treatment - nearly 11 months. Acute toxicity (including headache, dizziness, and fatigue) was observed in 10% of patients. Additional whole brain radiotherapy was not associated with longer OS, neither was systemic treatment. Significantly shorter OS was observed in patients with progressive systemic disease ($p = 0.037$). Higher total tumor volume (>7 mL) was associated with shorter OS ($p = 0.019$). Median progression free survival was 17.5 months. In multivariate analysis statistically significant predictors of OS were multiple brain metastases ($p = 0.0037$) and total tumor volume ($p = 0.018$).

Conclusions: Repeated stereotactic radiotherapy in patients with brain metastases is a well-tolerated and effective treatment. In patients suitable for repeated treatment the extent of brain invasion is the main adverse prognostic factor.

Stereotactic Radiation Surgery: The Impact of Tumor Size/Shape, Margin and Prescription on Normal Tissue Brain V12Gy

Tatsiana Reynolds, Mustafa Ozer, Ellen E Bellairs

Objectives: 12-Gy radiosurgical volume of normal brain tissue is a predictor for radionecrosis (RN) in intracranial tumors. Different prescription (Rx) doses, target margins are utilized in stereotactic radiosurgery (SRS) of various target sizes and shapes. This study aimed at investigating the dosimetric effect of these four factors on V12Gy for CyberKnife (CK) SRS cases.

Methods: The plans for two hundred fifty-four brain cancer patients, previously treated with CK SRS in our institution between March 2015 and May 2018, were analyzed for this study. All SRS planning was carried out with MultiPlan (5.3.0). SRS dose varied from 15 to 22 Gy with mean (median) Rx is 19.8 (20) Gy. The plans were divided into four groups, with the Rx doses less than 20 Gy (G1), 20 Gy (G2), 21 Gy (G3) and 22 Gy (G4). The target margin sizes ranged between 0 and 2 mm (with increment 0.5 mm), depending on the tumor type, size and uncertainty in contouring. To evaluate the effect of tumor size and shape on V12Gy, SRS plans were separated into six groups with respect of tumor size (Group I (0-1cc), II (1.0-3.0cc), III (3.0-5.0cc), IV (5.0-10.0cc), V (10.0-15.0cc), and VI (15.0-40.0cc)), and four groups with respect of tumor shape: (A) regularly shaped lesions distant from any organs at risk (OARs) except for normal brain tissue, (B) any shape lesions adjacent to radiosensitive OARs, (C) irregularly shaped lesions distant from any OARs, and (D) two or more lesions in the same plan.

Results: Conservative assumption V12Gy <7 cc (V12Gy Pass) was adapted at our institution as a safe guideline for the healthy brain tissue receiving radiation dose. Overall, 81% of SRS plans passed the criterion for the healthy brain tissue receiving radiation dose. The mean (median) V12Gy were 3.3 (4.6) cc for all 254 SRS treatments. The biggest effect on V12Gy played target size and shape. The percentage of plans meeting V12Gy criterion decreased dramatically with increasing the target size from 100% (Group I) to 0% (Group VI), with the major reduction from 93% to 24% between groups II and III, corresponding to the target sizes of radius 2 cm. The highest percentage of plans failing V12Gy criterion is shown for the irregularly shaped targets (50%), and multilesions (33%). The percentage plans for the regularly shaped and adjacent to OARs targets meeting V12Gy criteria is 93% and 100%, respectively. The percent of SRS plans meeting V12Gy criterion decreased from 90% (G1) to 79% (G2 and G3) to 75% (G4). No relations between the target margin on V12Gy was found. Indeed, the SRS dose was prescribed according to the size of the lesion according to RTOG 9508.

Conclusions: The largest impact on V12Gy of normal tissue brain were target size and shape. Majority of the plans with target size greater than 2 cm failed the V12Gy normal tissue brain guidelines. Therefore, the dose to the larger targets (> 2 cm) are recommended to fractionate to reduce the risk of RN. The lesions of irregular shapes and multilesions lead to the increased V12Gy. There was minor reduction on percentage of plans passing V12Gy dose criteria with increasing Rx dose, while no correlation was observed with target margin.

Stereotactic Radiosurgery and Hypofractionated Stereotactic Radiotherapy for Vestibular Schwannomas: A Comparison of Clinical Outcomes from the RSSearch® Patient Registry

Raj Singh, Hayden Ansinelli, Jan Jenkins, Joanne Davis, Sanjeev Sharma, John Austin Vargo

Objectives: To utilize the RSSearch® Patient Registry (RSSPR) to compare local control (LC) and related toxicities in patients treated with either hypofractionated stereotactic radiation therapy (HSRT) or stereotactic radiosurgery (SRS) for vestibular schwannomas (VS).

Methods: We searched the prospectively-maintained RSSPR for VS patients treated with SRS and HSRT from January 2008 to November 2016. Patients that had received previous surgery or radiation therapy were excluded. Potential factors predictive of toxicity and local control (LC) were estimated using time-to-event analysis and log-rank t-tests with the Kaplan-Meier method and a propensity-score weighted Cox proportional hazards model. Toxicity incidence was also analyzed with univariate and propensity-score weighted binary logistic regressions adjusting for all observable covariates.

Results: Sixty-four patients were identified that met study criteria. Twelve patients were treated with SRS (median prescription dose of 12.25 Gy (range: 6-18 Gy)), 41 patients with 3 fractions (median prescription dose of 18 Gy (range: 18-22.5 Gy)), and 11 patients with 5 fractions (median prescription dose of 25 Gy (range: 18-25 Gy)). Median patient age was 60.5 years (range: 31-88) with a median time to last follow-up of 30.43 months (range: 7.53 - 106.97 months). The median GTV was 1.089cc (range: 0.00784 - 34.782). Sixty-one of 64 patients (95.3%) had radiographic local control at last follow-up. SRS (100%) and HSRT (94.2%) resulted in similar rates of LC ($p = 0.33$). Acute and late toxicities were reported by 35.9% of patients that were all Grade 1-2. HSRT was associated with a significantly higher likelihood of experiencing toxicities than SRS on time-to-event analysis (42.3% vs. 8.33%; $p = 0.038$). The relationship between toxicity incidence and HSRT was maintained following a propensity score weighted binary logistic regression ($p = 0.039$) as well as a propensity score weighted Cox regression ($p = 0.039$; hazard ratio (HR) = 8.85 (95% CI: 1.12 - 70.10)).

Conclusions: SRS and HSRT in a multi-institutional cohort resulted in comparable LC consistent with prior single-institutional reports with fewer patients reporting toxicities following SRS.

Systemic Therapy as a Prognosticator in Patients Receiving Radiosurgery for Melanoma

Francesco Seddo, Narine Wandrey, MD,
Richard Crownover, MD, PhD, Mohamad Fakhreddine, MD

Objectives: Traditionally, metastatic melanoma has been treated with chemotherapy (chemo) or targeted therapy. Immunotherapy (IT), however, has redefined treatment of extracranial metastatic disease by increasing overall survival (OS) 1-5). Recently, it has been investigated in patients with melanoma brain metastasis (MBM). Studies so far have investigated IT used concurrently with SRS or with undefined time frames (6,7). The purpose of our study is to determine how administration of systemic therapy, including IT, prior to receiving SRS, affects OS. This information could serve as a potential modifier to the GPA Index and other tools, to select those who are most likely to benefit from SRS with MBM.

Methods: Patients were identified from the National Cancer Data Base (NCDB) who were diagnosed from 2004-2014. An initial selection was done for those with metastatic disease from a melanoma primary, who were also treated with SRS (GammaKnife, Linac based, etc.). Additional selection criteria included receiving systemic therapy before SRS. Kaplan-Meier curves were generated to plot OS. Univariate (UVA) analysis was done with the log-rank and Wilcoxon tests for significance. Analyzed variables included age, grade, Charles Deyo score, race, gender, and treatment prior to SRS. Treatment was classified as one of: chemo, IT +/- chemo, and no therapy. A multivariate (MVA) analysis was done for the same variables.

Results: 1287 patients received SRS for MBM and 291 were alive at last follow-up. Of these, 347 patients received only chemo, 219 received IT +/- chemo, and 721 received no systemic therapy prior to SRS.

The use of IT +/- chemo rose rapidly from 2004 to 2014 (2.3% vs 63%, $p < 0.0001$). The use of IT +/- chemotherapy superseded chemotherapy alone starting in 2013-2014. Older patients were more likely to receive no systemic therapy at all, as were patients with a higher Charles-Deyo score.

The median OS was 10.6 months (95% CI 9.3-11.96 months) with chemo, 19.7 months (95% CI 16.89-24.02) with IT +/- chemo, and 9.8 months (95% CI 9.07-10.55 months) for those without systemic therapy, $p < 0.001$.

On UVA, increasing age, increasing Charles Deyo score, and year of diagnosis were all significantly associated with worse OS.

On MVA, only age and treatment remained significant predictors of OS in this population. Compared to chemo, IT +/- chemo was associated with a significantly improved relative risk of death (RR 0.604, $p < 0.0001$). However, receiving no therapy was not associated with a significantly different risk ratio compared to chemotherapy (RR 0.99, $p = 0.84$).

Conclusions: For MBM, administration of IT +/- chemo for patients receiving SRS was associated with greater OS. Patients who received IT had a median OS of 19.8 months compared to 10.6 months for those who received only chemo. Thus, patients with MBM who received IT may be

especially likely to benefit from the diminished long-term side effect profile of SRS compared to WBRT.

Additionally, IT +/- chemo was used more often compared to chemo alone starting in the 2013-2014 cohort, however, the majority of patients still received no systemic therapy prior to SRS.

The brain met-GPA Index and other prognostication tools should take into account the notably higher survival in patients who may receive IT.

The Accuracy of Stereotactic Radiosurgery with Cone Beam Computed Tomography Image Guidance for Refractory Trigeminal Neuralgia

Joon K. Lee, MD, Karen C. Snyder, MS, Haisen Li, PhD, Yimei Huang, PhD,
Ning Wen, PhD, M. Salim Siddiqui, MD, PhD

Objectives: Trigeminal neuralgia (TN) causes intense pain along the branches of the fifth cranial nerve. Stereotactic radiosurgery (SRS) may be offered to patients who do not achieve adequate pain response to medical or surgical management. We provide data on the accuracy of SRS with cone beam computed tomography (CBCT) image guidance for refractory TN on a linear accelerator-based treatment system.

Methods: We identified nine patients with refractory TN. A stereotactic head frame was placed by a neurosurgeon for patient immobilization. Planning computed tomography (CT) images were acquired (512 x 512 pixels, 120 kVp, 501 mAs, 1 mm slice thickness) and the image set was co-registered with high-resolution 1 mm thin magnetic resonance (MR) images obtained in the T1- and T2-weighted, and fast imaging employing steady-state acquisition (FIESTA) sequences. The radiosurgical target was defined as a short length of the cisternal segment of the involved trigeminal nerve as demonstrated on the FIESTA sequence. Contouring was performed by the treating radiation oncologist. SRS was delivered in a single fraction using 14 partial arcs with a 4 mm conical cone and 6 MV flattening-filter-free photon energy performed on a linear accelerator-based treatment system. All patients were positioned on a 6 degree of freedom couch. CBCT images were obtained for initial localization. Positional corrections were made for deviations > 0.5 mm or 0.5 degrees followed by further image verification prior to initiating radiosurgery. Midway through treatment, intrafractional motion was assessed with a mid-verification CBCT. Positional corrections were repeated as needed followed by a mid-shift verification CBCT prior to completing the radiosurgical procedure. Clinical response was determined using the Barrow Neurological Institute (BNI) pain intensity score.

Results: All nine patients successfully completed the prescribed SRS treatment without complications. Median radiosurgical target volume was < 0.004 cc (range, < 0.004-0.200 cc). Median isocenter dose was 85 Gy (range, 80-90 Gy). Median brainstem dose to 0.035 cc and to 0.5 cc was 10.94 Gy (range, 5.41-14.19 Gy) and 3.15 Gy (range, 2.13-3.70 Gy), respectively. Median monitor units (MUs) delivered was 20,060 (range, 19,266-21,909 MUs). Median treatment delivery time (including image-guided positional corrections and beam on time) was 56 minutes (range, 50-82 minutes). Median number of CBCT images obtained was 4 (range, 3-7). Median translational and rotational positional deviations were 1 mm (range, 0-0.7 mm) and 0 degrees (range, 0-0.4 degrees), respectively. Only 1 patient required a positional correction for a translational deviation of 0.7 mm. Median follow-up time was 2 months (range, 2-15 months). Median BNI pain intensity score was III (range, I-V). Four patients (44.4%) achieved complete pain response, another 4 patients (44.4%) achieved partial pain response, and 1 patient (11.1%) achieved no pain response. Follow-up MR images were available for 4 patients, all of which demonstrated stable to improved radiographic findings.

Conclusions: SRS with CBCT image guidance for refractory TN can achieve sub-millimeter positional accuracy with acceptable treatment delivery times and favorable clinical outcomes. Long-term follow-up is needed to assess safety and efficacy of treatment.

CyberKnife Radiosurgery for Drop Metastases of Non-Neurogenic Origin

Shinichiro MIZUMATSU¹, Manabu HATANO¹, Hiroshi RYU², Kei NOMURA²,
Satoshi YOSHIKAWA², Norio INOUE³

1) CyberKnife Center, 2) Cerebrospinal Center,
3) Recovery Rehabilitation Center, Aoyama General Hospital, Toyokawa, JAPAN

Objectives: Intradural extramedullary spinal metastases that arise from intracranial lesions are called drop metastases (DM). We evaluated efficacy and toxicity of CyberKnife Radiosurgery (CKR) for drop metastases from solid cancers of non-neurogenic origin.

Methods: We treated with CKR for 10 patients with 27 DM from September 2009 to May 2014 at Aoyama General Hospital CyberKnife Center in Japan. Primary site were lung cancer (6 cases), ovarian cancer (2 cases), breast cancer (1 case) and cervical cancer (1 case). The lesions were located at cervical (7 lesions), thoracic (13 lesions), lumbar (6 lesions) and sacral cord (1 lesion). Four patients were symptomatic (2 local pain, leg weakness, leg numbness) due to DM. Lumbar and sacral large lesions (> 1mL) had caused these symptoms. Prior therapies for brain metastases included whole-brain radiation therapy (4 cases), surgery (3 cases), gamma knife or CyberKnife radiosurgery (5 cases) and no radiation therapy (1 case). The median target volume was 0.29 mL (range, 0.08 - 2.63 mL). The median marginal dose was 16Gy (range, 8 - 30Gy) and the median fractions were 1 (range, 1 - 5 fractions). The median maximum dose and isodose line were 29Gy and 58%.

Results: The median follow-up time was 2.8 months (range, 1.0 - 5.8 months). All patients had died during the observation. The cause of death were meningeal carcinomatosis (5 cases), primary lesions (4 cases, all lung cancer), lung metastasis (1 case) and hematemesis (1 case). The 50% survival time, 3 months and 6 months survival rate from CKR were 2.7 months, 30% and 0%. All two local pains improved completely and leg weakness slightly during the CKR treatment, but the leg numbness continued to the end. The treated lesions had no developing new symptoms after CKR. CKR treatment caused no adverse event.

Conclusions: Non-neurogenic origin DM were extremely poor prognosis. The therapeutic purpose should not life extension but palliative. CKR was useful as a non-invasive palliative pain relief and halt tumor progression in DM of advanced cancer patients.

Investigation of SRS Spine Treatment Plan Quality on a Magnetic Resonance Image Guided Linear Accelerator

Jennifer L. Dolan PhD, Josh P. Kim PhD, Karen C. Snyder MS, Indrin J. Chetty PhD, Ning Wen PhD

Objectives: To investigate the treatment plan quality and adherence to Radiation Therapy Oncology Group (RTOG) 0631 Protocol for Spine Stereotactic Radiosurgery (SRS) planned for delivery on a Magnetic Resonance Imaging Guided Linear Accelerator (MR-Linac).

Methods: Two previously treated Spine SRS patients were re-planned on a Monte Carlo-based MR-Linac commercial treatment planning system (TPS). The MR-linac system combines a 0.345 T magnet with a 6 MV flattening filter free (FFF) beam delivered at a nominal dose rate of 600 MU/min. The treatment technique utilized in this study was step-and-shoot IMRT using a double-stacked MLC that can achieve field sizes down to 0.2 x 0.4 cm². Beam geometries consisted of 7-9 posterior beams spaced at 20-25 degrees. Treatment plans were optimized to achieve the coverage and constraints dictated by RTOG 0631. Following planning, ion chamber and absolute film dosimetry (3%/1mm global gamma analysis) patient specific quality assurance (PSQA) measurements were performed to assess the deliverability and dosimetric accuracy of the treatment plans.

Results: The Monte Carlo-based TPS was capable of managing target and critical tissue constraints to result in plans that achieve prescription dose to 95% of the PTV, greater than the 90% required by RTOG 0631. Treatment plans were normalized to cover 95% of the contoured vertebral body with the 18 Gy single-fraction prescription dose. Critical tissues included conventional/partial spinal cord, esophagus, aorta, liver, and kidneys. RTOG 0631 constraints on these tissues were met (e.g. on average < 5% of the partial spinal cord receives 10 Gy, and the spinal cord max dose remains below 13 Gy). In addition to meeting the RTOG 0631 plan quality metrics, efforts were made to minimize the complexity of the delivery (less than 6 segments per field on average) and, furthermore, the delivery time. During PSQA measurements, delivery duration was monitored and averaged less than 30 minutes. PSQA ion chamber and film analysis results agreed with the TPS at 1.8 % and 92% gamma (3%/1 mm), respectively, which are within institutional tolerances.

Conclusions: This study demonstrated the feasibility of planning RTOG 0631 compliant Spine SRS treatments on an MR-Linac using the MC-based TPS. In addition to plan quality, PSQA measurements validated the deliverability and dosimetric accuracy of the planned MR-Linac deliveries.

Spinal SABR: An Analysis of Optimum Target Voluming Technique

Dr Christy Goldsmith, Dr Robert Urwin, Mr Andrew Edwards, Mr Timothy Cross,
Mrs Melanie Green, Dr Nicholas Plowman, Prof Pat Price

Objectives: To evaluate Spinal SABR treatment outcomes (toxicity and local control) in a UK centre defining the treatment target by GTV to PTV margin expansion.

Methods: The Harley Street Clinic, London was the first UK centre to deliver Spinal SABR. Target definition described in the treatment protocol specifies outlining of the Gross Tumour Volume (GTV) seen on MRI co-registered to Planning CT, in conjunction with PET where appropriate. This is expanded by a margin to define the PTV (Planning Target Volume). Spinal SABR is now delivered in many UK centres. NHS England (NHSE) have drafted "Standards for the Provision of SABR" guidelines. These guidelines include target volume outlining guidance for contouring spine lesions based on the International Spine Radiosurgery consortium guidelines. These advocate delineating a Clinical Target Volume (CTV) based on the anatomical location of the tumour, and then expanding to PTV. The aim of this study was to evaluate local control, patterns of relapse and toxicity in the Spinal SABR patients treated at the Harley Street Clinic, London. The study population was limited to patients with vertebral metastases. Patients being treated as re-irradiation, were excluded from the analysis. Toxicity and outcome data were prospectively collected at 3 months after treatment, then 6-monthly intervals thereafter. Toxicity was assessed using Common Toxicity Criteria Adverse Events version 3 (CTCAEv3). Post-treatment imaging schedule was at the discretion of the referring Consultant. Local recurrence was defined as recurrence on imaging in the treated vertebra during the study period. A total of 48 patients suitable for analysis were treated with Spinal SABR between March 2009 and Oct 2016. Treated patients had a median age of 68 years (range 35-97 years). The median follow up period was 11 months (range 3 - 52 months). Median GTV/CTV volume = 13cc (range 0.27cc - 246.8cc). Tumour target was expanded by a median 2mm margin (range 0-5mm). Median PTV volume = 22.7cc (range 2.9-331cc). Treatment dose was prescribed to a median 27Gy (range 16-36Gy) in a median of 3 fractions (range 1-5). Median BED = 51.3Gy10. Treatment was prescribed to a median prescription isodose of 61% (range 49 - 77).

Results: Treatment was well tolerated, 7 patients experienced post-treatment toxicity (15%). This was largely limited to grade 1-2 toxicity, with side-effects of pain/fatigue. A single patient experience grade 3+ toxicity (vertebral crush fracture experienced 8 weeks post treatment). This patient was treated to 18Gy/3# (BED1029), the PTV size was 9.43cc. The disease was lytic, and was situated in L4: both predisposing factors to increase fracture risk. There were no local recurrences documented during the study period (Local control 100%). 12 patients died (25%), of these the median interval between Spinal SABR and death was 18 months (range 6 - 36 months).

Conclusions: Spinal SABR planned using a GTV to PTV margin expansion is well tolerated and effective. Where a tumour occupies much of a vertebral body the NHSE guidelines provide excellent outlining guidance. However, our data demonstrate that for a patient with a small defined GTV within vertebra, margin expansion may be adequate for local control, and may be associated with less risk of vertebral fracture.

The Use of SBRT for Spine Metastases from Breast Cancer using Volumetric Arc Therapy

Beatriz E. Amendola, MD Naipy Perez, MSc Jose M. Torices, MD Xiaodong Wu, PhD
James Melotek, MD Marco Amendola, MD

Objectives: Breast cancer patients may experience a long survival despite the presence of metastatic disease. Our purpose is to evaluate our results using stereotactic body radiosurgery (SBRT) for the treatment of spine metastases from breast cancer with special attention to pain control, toxicity and tolerance to treatment in a single institution experience.

Methods: This is a retrospective review of the records of 27 patients (42 procedures) treated with SBRT to the spine from November 2011 to August 2018. There were 27 patients (26 females and 1 male) ages ranging from 28 to 83 years of age (median = 69). All patients were treated by the same team following our in-house protocols. They were planned with CT and MRI fusion. Treatment was delivered with LINAC-based radiosurgery systems using volumetric modulated arc therapy (VMAT). Patients were immobilized using thermoplastic masks. The site most frequently treated was Thoracic Spine (16 patients). The prescription dose to the PTV ranged from 13 Gy to 30 Gy using from 1 to 5 fractions. The most common dose scheme that was used in 50 % of the procedures was three fractions of 7 Gy/tx to the PTV with a simultaneous integrated boost of 10 Gy/tx to the GTV. The PTV volumes ranged from 2.3 cc to 641.4 cc (median 76.45 cc). In all procedures, we subtracted the spinal canal from the PTV. Pain relief was evaluated using a pain scale of 11 points (from 0 to 10) before and after treatment of radiosurgery and reported at the last procedure and one month and 3 months thereafter. Toxicity was evaluated following Toxicity Criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC).

Results: The procedures were well tolerated in all patients. No acute or late toxicity was observed. Out of 33 treated sites evaluated for pain control; 79 % responded to treatment with pain reduction of more than 50 %. Total pain control was achieved in 52 % of the sites treated reported by the patient as pain level 0 in the follow-up evaluation. The average treatment time was 2.7 minutes and did not exceed 5.7 minutes.

Conclusions: In our experience, a high rate of pain control was achieved after spinal SBRT in this group of patients with no acute or late toxicity observed. Spinal radiosurgery offered a significant decrease in treatment time, reducing treatment uncertainties and intra-fractional motion. This technique appears especially suited for patients presenting with quality-of-life altering pain. It is also a safe and well-tolerated treatment modality to be used in patients with more than one affected vertebra and higher target volumes.

Single Institution Experience in the use of Lattice Radiosurgery in Voluminous Tumors

Beatriz E. Amendola, MD Naipy Perez, MSc Marco A. Amendola, MD Xiaodong Wu, PhD

Objectives: Locally advanced voluminous tumors present a challenge for the physician as the use of surgery, standard radiation therapy and or systemic treatment are frequently not a viable option. Failure to achieve initial local control of the primary tumor or of a local recurrence may result in an extremely poor quality of life. To evaluate tolerance and toxicity of the use of Lattice Radiotherapy (LRT) in various locations in patients presenting with voluminous tumors in order to prime conventional radiation.

Our second objective was to evaluate local control in patients that otherwise were deemed hospice candidates, or were at preterminal phase of disease.

Methods: During a 7-year period 51 patients presenting with bulky, unresectable tumors of the chest, abdomen, pelvis, and head and neck, were treated using a single or 3 fractions of LRT followed by conventional fractionation or with stereotactic body radiosurgery (SBRT). Patients received initial lattice fractions of 10 Gy to 18 Gy in the lattice vertices and 3 Gy in the periphery. The descriptions and grading scales found in the revised NCI Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 were utilized for toxicity assessment

Results: All patients tolerated the treatment well and achieved tumor response ranging from partial to complete. None of the patients treated experienced any significant acute or chronic toxicity. Follow up ranged from 1 to 85 months with a median of 6 months.

Conclusions: This retrospective review demonstrates the safety and efficacy of this technique using modern radiotherapy for inoperable tumors. LRT was safely delivered without significant morbidity or mortality directly attributed to LRT and resulting in a statistically significant reduction in tumor size. Some improvement in overall survival was observed in patients otherwise deemed hospice candidates. This experience may be useful to establish prospective studies and guidelines in order to improve the lattice planning process.

Four Years Experience with Intraoperative Electron Radiation Therapy for Early Stage Breast Cancer

S. Goetsch, K. Shimizu, M. Wilde, A. Koka, C. Olson, K. Glover, L. Mendenhall

Objectives: This paper reports the first four years of a clinical program using a mobile electron linear accelerator to treat patients at time of surgery for early stage breast cancer. The program began with 10 Gy boost and has now progressed to 21Gy monotherapy.

Methods: An electron linear accelerator (Mobetron 2000, Intraop Corporation) was acquired in March 2014. The unit moves on rubber tires into the operating room at time of surgery. It is self shielded with electrons of 6, 9 and 12MeV at dose rates of roughly 1100 MU/minute. The unit began treating selected patients in December, 2014. A total of 62 patients were treated with a 10 Gray "upfront boost" dose and expanded to treat patients with a monotherapy dose of 21Gy in November 2016. A total of 56 patients have now been treated with the higher dose. A copper shield (later replaced with a newly fabricated steel shield) is inserted distal to the treatment volume to act as internal shielding for X-rays generated by electrons stopping in the target.

Results: Only early stage breast cancer patients (Stage I, no positive lymph nodes, imaged tumor size = 2.5cm) were admitted. Some patients with DCIS have also been treated. A total of 114 patients have now been treated, 4 of them with bilateral disease. Electron cone beam sizes of 4.5 to 7.0cm diameter have been used (median size 5.5cm). Bolus of 0.0 to 1.0cm was inserted in the electron beam path (median thickness 0.5cm). The 9MeV energy was used 69% of the time.

Conclusions: Early stage breast cancer is highly curable with long term disease free survival rates exceeding 96%. The breast IOERT program offers a reduction or total elimination of outpatient radiation therapy treatment following surgery. Early results are encouraging, with no reported recurrences and good cosmetic results.

Stereotactic Body Radiotherapy for Lung Oligometastases: A Single Institutional Study

Rashad Rzazade, MD, Mehmet Dogu Canoglu, MD, Esra Kucukmorkoc, PhD,
Emre Sanli, PhD, Nadir Kucuk, PhD, Hale Basak Caglar, MD

Objectives: To evaluate the efficacy and safety of lung oligometastases treated with hypofractionated stereotactic radiosurgery in a single institution.

Methods: Between August 2013 and January 2017, we treated 86 lung metastases from 61 patients. All lesions except one was treated with linear accelerators. Motion management strategy for linear accelerator based treatments was the internal tumor volume formation with 4 dimensional computed tomography. The median SBRT dose was 55 Gy(range, 54-60) delivered in 5 fractions(range, 3-8). The response evaluations were performed with PET-CT after median 4 months and thorax CT every 3 months afterwards. Local control was defined as metabolic response of the first PET-CT imaging and no progression in size afterwards.

Results: The local control and survival analyses were performed on the patients who have at least 3 months of follow up. A total of 61 patients [45 men and 16 women; median age 62 (range 32-81)] with 86 lung oligometastases. Primary sites and patient numbers were as follows: lungs, 35; gastrointestinal tract, 15; and others 11. The median follow up was 25 months (range, 5-46 months). Forty patients were alive during the analysis. In 3 patients local progression was detected after 11 and 15 months (1 patient 10 months, 2 patients 15 months). Twelve, 18 and 24 months local control rates were %98, %96 and %96 respectively. Disease progression after SBRT, 12, 18 and 24 months were %89, %75 and %70 respectively. Overall survival rates of 12, 18 and 24 months were %98, %85 and %83 respectively from the time of the first diagnosis and %90, %78 and %73 from the diagnosis of lung metastases. Four patients (6.5%) developed Grade 2 radiation pneumonitis. One patient (1.6%) developed rib fracture. No other late adverse events.

Conclusions: Stereotactic Body radiotherapy for lung oligometastases is a non-invasive, safe and effective local treatment strategy without any compromise in systemic therapy. It is being used as a standard approach in our hospital.

Lung Stereotactic Body Radiotherapy (SBRT) in Stage IV Non-Small Cell Lung Cancer (NSCLC): Durable Survival for the Incurable Patient

Rodney Wegner, Sidney Anderson, Shaakir Hasan, Athansios Colonias

Objectives: Non-small cell lung cancer (NSCLC) oftentimes presents with metastatic disease. The concept of oligometastasis has arisen in recent years, with ongoing investigations into aggressive local therapy in addition to traditional systemic therapy showing potential for long term survival in a subset of patients.

Methods: We retrospectively reviewed the charts of 20 patients treated between 2009 and 2016 with lung stereotactic body radiotherapy (SBRT) in the setting of limited stage IV NSCLC. Seventeen (85%) of 20 patients had oligometastatic disease (defined as ≤ 5 sites) and 16 (80%) received some form of systemic therapy prior to or after SBRT. The majority (65%) of patients presented with limited brain metastases at diagnosis. Outcomes that were analyzed included local control in lung and brain, distant progression, overall survival, and rate of treatment-related toxicity.

Results: Fifteen men and 5 women underwent lung SBRT to a median dose of 48 Gy (35-50) in 5 fx (4-5), yielding a median BED₁₀ of 100 Gy (59.5-105.6). Median lung PTV volume was 36.56 cc (7.5-152.0). Eleven of 13 patients with brain metastases had a solitary lesion resected followed by resection bed radiosurgery at a median dose of 15 Gy (14-27.5) in 1 fraction (1-5). Ninety-five percent of patients had chest imaging in follow up for review. All patients with brain metastases had follow up MRIs available for review. The median follow up from diagnosis was 16.5 months (3-109). Median overall survival was 24 months with 2 year and 5 year survival rates of 45% and 23%, respectively. Local control for the lung lesions was 89% at 2 years. Local control in the brain was 85% at 1 year and 68% at 2 years. One patient had grade 2 hemoptysis after lung SBRT which resolved on its own. One patient had grade 3 radiation necrosis after intracranial SRS at 11 months, requiring resection.

Conclusions: In this series NSCLC patients with limited metastatic disease at presentation had durable survival and long term control with SBRT to the primary lung lesion. As systemic therapy and targeted therapy continue to improve and be tailored to the individual patient, the importance of safe and effective local therapy in the form of SBRT will increase as well. The treatment approach presented here is currently being evaluated in multiple phase II studies.

A Single Institution Case Series of Liver Reirradiation with Hypofractionated Stereotactic Body Radiation Therapy (SBRT)

Berkowitz A, Ohri N, Garg M, Kalnicki S

Objectives: To evaluate the safety of reirradiation in a series of patients treated with multiple courses of liver SBRT at our institution.

Methods: We queried an institutional database for patients treated with at least two courses of liver SBRT between 2013 and 2018. We collected the dose statistics from each treatment plan. We also collected survival outcomes, acute and late toxicity data, and liver function tests for each patient. Late toxicity was defined as any toxicity occurring at least 30 days after completion of treatment. All toxicities were graded according to CTCAE 4.0.

Results: We identified 8 patients who were treated with at least 2 courses of liver SBRT in the abovementioned timeframe. These patients had a total of 22 treated lesions. Two patients received 3 courses of SBRT, and 6 patients received 2 courses of SBRT. Seven patients were treated for primary liver cell carcinoma, and one patient was treated for metastatic colon cancer. All patients received a dose of 45-60 Gy in 3-5 fractions during each course. The median age at first treatment was 69 (range 60-78). Five patients had at least 1 prior transarterial chemoembolization (TACE), and 4 patients had at least 1 radiofrequency ablation (RFA) or microwave ablation procedure. Pre-treatment Child Pugh scores ranged from 5 to 8. Child Pugh scores between courses 1 and 2 of SBRT ranged from 5 to 8. Scores after the second course of SBRT ranged from 5 to 10. Since completion of treatment, 1 patient died due to sequelae of metastatic hepatocellular carcinoma, and 1 patient died of unrelated causes. The median time interval between treatment courses was 17.3 months (range 3.9-44.2). The mean liver dose (defined as Liver-GTV) for each treatment course ranged from 3.0-14.9 Gy. There were no Grade 2-4 acute or late toxicities for any patient. Five patients experienced acute Grade 1 nausea with or without vomiting, 2 patients experienced acute Grade 1 dermatitis, 2 had acute Grade 1 fatigue, and 1 had acute Grade 1 abdominal pain. Only one patient experienced late toxicity which included Grade 1 abdominal pain and dermatitis.

Conclusions: Liver reirradiation with SBRT may be delivered safely and with a very low toxicity profile. Further study is required to identify applicable normal tissue constraints to guide patient selection and treatment planning in this setting.

Evaluation of Stereotactic Body Radiation Therapy Pancreas Patient Plans Delivered Using Magnetic Resonance-Guided Radiotherapy

Josh Kim PhD, Kate Aldridge CMD, Dongsu Du PhD, Anthony Doemer MS, Carri Glide-Hurst PhD, Ning Wen PhD, Indrin J Chetty PhD, Jadranka Dragovic MD, Benjamin Movsas MD

Objectives: To evaluate the plan quality of a set of stereotactic body radiation therapy (SBRT) pancreatic cancer treatments using a combined magnetic resonance imaging and linear accelerator system (MR-linac).

Methods: Since commissioning the system, six SBRT pancreatic cancer patients were treated on an MR-linac using a breath-hold approach. Five patients were treated to a prescription dose of 30 or 35 Gy in 5 fractions, while one was treated using a simultaneous integrated boost approach with 21 Gy planned to the planning target volume (PTV) and 27 Gy planned to the gross tumor volume (GTV). The MR-linac comprises a 0.345 T magnet and an S band, standing wave linac capable of delivering a 6 MV flattening filter free (FFF) beam. The beam is shaped using a double-stacked MLC with physical leaf width of 0.83cm. MLC banks are shifted to provide an effective leaf thickness of 0.415cm. An integrated treatment planning system (TPS) that utilizes a fast Monte Carlo dose prediction algorithm for plan optimization and dose calculation was used for plan generation. Patients were simulated on a wide bore (85cm bore) CT scanner and on the MR-linac. During CT-simulation, free-breathing, end-exhale and end-inhale breath hold, and 10-phase 4DCT images were acquired. Similarly, during MR-simulation in the MR-linac, free-breathing, end-inhale, and end-exhale scans were acquired. After simulation, the physician assessed patient compliance during breath hold scans and image quality and determined which breath hold to use for dose calculation. The system uses a step-and-shoot approach for intensity modulated radiation therapy (IMRT). The GTV was contoured on the selected breath hold image and expanded 5mm isotropically to generate the PTV. Dose was normalized so that 95% of the PTV would receive the prescription dose, and conformity index (CI) and R50 (ratio of 50% prescription isodose volume to the PTV) were evaluated. Organ-at-risk (OAR) constraints given by AAPM TG101 were used during optimization. Patient specific quality assurance (PSQA) was performed by mapping generated plans onto a phantom consisting of a stack of solid water and comparing to measurements acquired using a micro-ion chamber and radiochromic film.

Results: The end-exhale phase was selected for all patients for treatment planning and delivery since it represented the most reproducible respiratory state. An average of 10 fields (range: 9-12) spaced 15-30 degrees apart were used. Depending on the volume (32.2 ± 23.5 cc) and location of surrounding OARs, the number of segments needed to generate an acceptable plan ranged from 24 to 49 (average: 36) to deliver an average of 2019.1 MU (range: 1254.4-2876.2 MU). Average CI for the patient set was 1.08 ± 0.08 , and R50 values were 4.02 ± 0.91 . All OAR constraints were met according to AAPM TG-101 report criteria. Extra attention was given to avoid small bowel and duodenum. For PSQA, ion chamber measurements averaged $-0.4 \pm 1.1\%$ difference from the value calculated in the TPS. For radiochromic film, absolute gamma analysis results using 3%/1mm (global dose difference/distance-to-agreement, 10% dose threshold) criteria were $96.8 \pm 1.8\%$.

Conclusions: Six pancreatic cancer patients were effectively treated using an SBRT regimen on an MR-guided linac. TPS generated plans met constraints given in TG101 and other plan quality metrics comparable to those treated with SBRT on other linacs. PSQA measurement results were within 1% of calculations.

Repeated High-Dose SBRT for Primary and Metastatic Liver Tumors

Dorota Gabrys Roland Kulik Lukasz Dolla Agata Roch-Zniszczol Slawomir Blamek

Objectives: Liver can tolerate a high dose of radiation if a sufficient volume of healthy tissue is spared. In the repeat therapy setting the available approaches typically involve stereotactic body radiation therapy (SBRT). However, data on repeat liver irradiation are scarce. In the current paper we examined the safety and tolerability of liver reirradiation and dose volume histograms (DVH) of combined treatment plans.

Methods: A group of 22 patients treated at least twice with high-dose liver SBRT was identified. One patient had a primary liver carcinoma (HCC), the remainder - metastatic (15 colorectal, 2 ovarian, 2 breast, 1 kidney, and 1 pharynx), recurrent or new liver tumors. With the use of a treatment planning evaluation system we integrated for each patient the imaging data and isodose distributions from all treatment sessions. As a result, spatial reconstructions of the summed-up dose distribution and combined dose-volume histograms were available for review. Several fractionation schemes were used during study period. In primary therapy a total dose of 36-48 Gy was given in 3 fractions of 12-15 Gy, for second course of irradiation fraction doses of 10-15 Gy were used and the total dose 30-48 Gy was given, third (8 patients) of 3-15 Gy to the total dose 15-50 Gy. Median cumulative prescribed dose was 90 Gy (range 72-209). Median highest total radiation dose to one GTV volume was 48 Gy (range 36-95). All patients were treated with photons with respiratory gating technique (19 patients) or with the CyberKnife system (3 patients). 28 tumors treated during the second course were new lesions, 6 were local recurrences in the previously irradiated volume. Median interval from the initial SBRT to first retreatment was 8.5 months (range 3.4-50.8). Patients who underwent third radiotherapy were irradiated for a recurrent tumor after the first treatment (4 GTV) or after the second course (4 GTV), and 3 patients underwent radiotherapy to a previously not irradiated volume. Six patients are still alive and median time from the first radiotherapy to the last visit was 19.5 months (range 3.5-60).

Results: We did not notice significant decrease in mean liver volume which was 1516 cm³ at the time of first radiotherapy and 1458 cm³ at last treatment. The cumulative mean dose to the liver was 20.2 Gy (range 10.2-32.7). Mean volume receiving 10 Gy was 61.5 % (range 26-80.2), and 21 Gy was 36.3 % (range 13.5-54.9). Grade 1 increase in the level of AST after retreatment was found in 5 patients, and only in one it was grade 2. Grade 1 ALT increase was found in 1 patients, and single patients experienced G1, and G2 increase of bilirubin level. The elevation of liver enzymes was related to the progression of the disease within and outside the liver.

Conclusions: High dose reirradiation with SBRT to the liver tumors is a safe option for patients with metastatic liver disease resulting with reasonable overall survival. Prospective studies are needed to establish accurate dose constraints and treatment guidelines.

Phase I-II Study of Stereotactic Radiotherapy for Low-Intermediate Risk Localized Prostate Cancer - A Preliminary Result

Osamu Suzuki, Yasuo Yoshioka, Keita Kurosu, Keisuke Otani, Shinichi Inoue, Iori Sumida, Motohide Uemura, Norio Nonomura and Kazuhiko Ogawa.

Objectives: The evidence suggesting that prostate cancer has low α/β ratio as low as 1.5 supports hypofractionated radiotherapy. We previously reported results of high dose rate interstitial brachytherapy with longer follow up of 8 years which showed good PSA relapse free survival even in the high risk patients. Our results of HDR indicate that the high risk patients also can be the candidate for the localized hypofractionated radiation therapy combined with hormonal therapy. Our present HDR treatment schema is 40 Gy /5 fr/ 3days. We launched phase I-II study for low-intermediate risk prostate cancer of stereotactic radiotherapy using CyberKnife to examine the recommended treatment dose (phase I) and the treatment feasibility (phase II). Here we present preliminary result of the trial.

Methods: The study was reviewed by the institutional review board in Osaka University Hospital and registered at UMIN (University hospital Medical information Network Center) clinical trials registry (UMIN 000014328). The key inclusion criteria is low-intermediate risk prostate cancer with biopsy proven adenocarcinoma. Age criteria is between 20 and 80 years old. Hormonal therapy within one year is allowed which is not done routinely for low or having one intermediate risk factor patients. The primary endpoints of the study is ratio of 2-year late adverse events \geq Grade 2. And the secondary endpoints are 2-year biochemical control rate and QOL questionnaire analysis. The dose level tested was three levels which starts from 7Gy x 5 fractions and increase 0.5Gy/fr up to 8Gy x 5 fractions delivered on consecutive days. Each dose levels contain 25 patients each. From Jun / 2014 to Feb / 2018, 75 patients were registered. Median age was 70 years old. Pretreatment PSA was 7.6 ng / ml (1.6-19.41), 18 and 57 patients were diagnosed histologically having GS 6 and 7 respectively. Nine patients were diagnosed as low risk and remaining 66 patients were diagnosed as intermediate risk according to the NCCN risk classification. CTV includes whole prostate and proximal seminal vesicles with 3mm margin except for rectal side (1mm). 2mm PTV margin was added. Treatment was delivered through consecutive five days.

Results: Median follow up period of the objective was 41, 30 and 14 months for 1st, 2nd and 3rd dose groups respectively. The shortest follow up period in each dose group is 33, 24 and 6 months respectively. About acute genitourinary (GU) toxicity, 20, 28, and 14% of patients in each group complained grade 2 symptoms which improved spontaneously. As far as gastrointestinal (GI) symptoms, 0, 8 and 8% of patients experienced toxicities \geq grade 2. GI symptoms were frequently observed in the higher dose groups. Compared with 35Gy group, G1 GI symptoms increased from 36% to 60-64% and G2 symptoms from 0% to 8-9% in the latter groups. PSA level decreased promptly in many patients, and no biochemical failure is observed so far. The primary endpoints of late toxicity rate at 2-year has been obtained in the 1st and 2nd dose groups. As for GU symptoms, G2 was observed in 8% and 44% of the patients in the 1st and 2nd dose groups respectively. The high incidence in the 2nd group is considered to be related to treatment dose, however the treatment outcomes in the 3rd group is not so severe so far. GI symptoms greater than G2 were observed only in the 2nd group and the proportion was 12%. GI symptoms were milder than the profile of GU symptoms. The immature results of 40 Gy in 5 fractions showed no increase in GI and GU profiled compared with 37.5Gy group.

Conclusions: Hypofractionated stereotactic radiotherapy with CyberKnife showed a tolerable toxicity profile in the acute and late period and favorable response. Continuous careful observation is needed in the higher dose treatment groups.

Reduced Rectal Dose Using Rectal Sparing Hydrogel Spacer for Prostate Cancer Patients Undergoing Robotic SBRT

Ruben Ter-Antonyan PhD, Faisal Siddiqui MD PhD, Michael Myers MD

Objectives: Stereotactic Body Radiation Therapy (SBRT) is now a recommended treatment option for patients with low risk and favorable intermediate risk prostate cancer. A self-absorbing hydrogel spacer, inserted between the rectum and prostate, has been increasingly used to reduce rectal toxicity during prostate radiotherapy. It has demonstrated benefits in clinical trials for both IMRT and SBRT. There is, however, little data on using hydrogel with Robotic Radiosurgery treatment that delivers non-isocentric and non-coplanar beams for conformal dose distribution. We present retrospective data on 24 prostate cancer patients with and without implanted hydrogel spacer, treated with robotic radiosurgery at our Cancer Center.

Methods: The hydrogel was placed between the prostate and rectum in the Denonvilliers' space at the time of fiducial marker placement. Patients returned the following week for treatment planning consisting of both a CT scan and MRI. RTOG 0938 protocol was used for prescription and treatment planning guidelines. Dosimetry data was compared between 12 patients with and 12 patients without the hydrogel spacer.

Results: RTOG 0938 dose constraints for rectum include Dmax, D3cc, D90%, D80%, and D50%. Compared to 12 patients treated without the hydrogel, patients with hydrogel had 9.8% less rectal Dmax ($P = 0.0003$), 19.3%, 21.6%, and 23.3% less rectal volumetric dose D3cc, D90%, D80%, correspondingly ($P = 0.0001$), and 15.2% less D50% ($P < 0.05$).

Conclusions: Our data indicate that using the hydrogel spacer for prostate cancer patients reduces rectal dose during SBRT treatments delivered with Robotic Radiosurgery.