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Multi-Institutional Datasets Validate the Recursive Partitioning Analysis for Overall Survival in Patients Undergoing Spine Radiosurgery for Spine Metastasis

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implant is proposed. The contouring algorithm utilizes the surgical cavity (well-seen on MRI), LDR seeds (well-seen on CT) and simple Boolean operations, resulting in a straightforward and reproducible CTV structure. The corresponding dose statistics (D90%, D95%, min, and max) proved to be useful metrics for dose review. The proposed standardized formalism for contouring CTV and its use in dose evaluation will be further tested to determine its utility in minimizing interobserver variability to evaluate the dosimetry of collagen tile BT implants in brain.

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De Ritis Ratio as a Novel Prognostic Biomarker in Atypical Meningiomas: A Multi-Institutional Study

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Purpose/Objective(s): To investigate the impact of prognostic serum biomarkers in newly diagnosed surgically resected intracranial atypical meningiomas.

Materials/Methods: This multi-institutional study included 523 grade 2 (according to the 4th edition of WHO Classification of Tumors of the Central Nervous System) patients who underwent resection between 1998−2018. The baseline characteristics and serum laboratory data within one week after surgery were obtained for analyses investigating the association with progression/recurrence (P/R) rate or progression-free survival (PFS). Optimal cut-offs were calculated for each serum marker using the maxstat package of R. Nomograms were developed based on the multivariate analyses of statistically significant prognosticators.

Results: Among 523 patients, 454 patients were included in the multivariate analysis for P/R rate excluding patients with incomplete histopathologic or laboratory data. On multivariable analysis, tumor size >5 cm (HR, 2.18; 95% CI, 1.49−3.19) and subtotal resection (HR, 3.60; 95% CI, 2.37-5.47) were associated with higher P/R rate, whereas adjuvant radiotherapy (HR, 0.32; 95% CI, 0.20-0.53) and postoperative platelet $>137 \times 10^3/\mu L$ (HR, 0.58; 95% CI, 0.39-0.86) were associated with lower P/R rate. Interestingly, postoperative De Ritis Ratio (aspartate aminotransferase/alanine aminotransferase) >2 proved to be an adverse prognosticator (HR, 1.87; 95% CI, 1.15-3.05). Similarly, patients with De Ritis ratio >2 showed inferior PFS (HR, 1.87; 95% CI, 1.23-2.84). In the subgroup of patients who received adjuvant radiotherapy, tumor size >5 cm and postoperative neutrophil-to-lymphocyte ratio >21 were the only prognosticators and were associated with higher P/R rate. On the other hand, postoperative De Ritis ratio >2 remained to be an adverse prognosticator in patients who did not receive radiotherapy.

Conclusion: Postoperative De Ritis Ratio was unrevealed as a novel serum prognosticator in newly diagnosed atypical meningiomas. Further studies are warranted to validate its clinical significance and biological background.

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Planning for the Impact of SC.24 on Spine Stereotactic Body Radiotherapy (SBRT) Utilization at a Tertiary Cancer Center

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Purpose/Objective(s): CCTG SC.24 was a recently reported randomized phase 2/3 trial that demonstrated superior complete response rates for pain following spine stereotactic body radiotherapy (SBRT; 24 Gy in 2 daily fractions) compared to conventional radiotherapy (CRT; 20 Gy in 5 fractions). These findings support a practice-changing paradigm shift whereby a subset of eligible patients with painful spine metastases may be offered upfront spine SBRT over CRT. At many institutions, this would mark an increase in spine SBRT cases. Therefore, we sought to assess the potential real-world impact of this study on spine SBRT utilization by estimating the proportion of patients treated with CRT who would have been eligible for spine SBRT per SC.24 inclusion criteria.

Materials/Methods: All patients who received palliative spine radiation at our institution between August to October 2020 were reviewed retrospectively. Data extracted included eligibility criteria of the SC.24 study, provider-reported pain response, and overall survival. Descriptive statistics and survival analyses were performed.

Results: Of the 73 patients reviewed, 24 (33%) patients met eligibility criteria for SC.24. The most common exclusion factors included irradiation of more than 3 consecutive spinal segments (n=32, 44%), ECOG greater than 2 (n=17, 23%), symptomatic spinal cord compression (n=13, 18%), and frank mechanical instability (n=12, 16%) as measured using the Spinal Instability in Neoplasia Score (SINS). SINS was indeterminable in 7 cases (10%) of epidural-only disease, which also renders a patient ineligible; otherwise, the median SINS was 9 (IQR: 7−10). Four (5%) patients had prior surgery and 8 (11%) patients had prior overlapping radiation to the area, also rendering them ineligible. Of eligible patients, the mean age was 68.92 years (SD 13.84), median SINS was 8 (IQR: 7−9) and median ECOG was 2 (IQR: 1−2). The most common primary cancer types among eligible patients were lung (n=10) and breast (n=4). The median dose delivered to eligible patients was 20 Gy in 5 fractions (IQR: 8−20 Gy). Fifteen (63%) eligible patients had additional radiation to a site other than the spine at the same time. The median survival of eligible patients was 10 months (95% CI: 4 months−not reached) with 58% surviving longer than 3 months. 75% of patients had pain response documented and of these, 54% had at least some response after CRT.

Conclusion: Around 1/3 of patients who received palliative CRT to the spine met eligibility criteria for SC.24. This possible expanded indication for spine SBRT can have a substantial impact on resource utilization. In addition to increased MR simulation utilization, there can also be higher demand on contouring, planning and quality assurance resources. These data may be useful in guiding resource and workforce planning at institutions looking to commence or expand a spine SBRT program.

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Multi-Institutional Datasets Validate the Recursive Partitioning Analysis for Overall Survival in Patients Undergoing Spine Radiosurgery for Spine Metastasis

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Purpose/Objective(s): The recently published spine radiosurgery (sSRS) recursive partitioning analysis (RPA) for overall survival (OS) separated patients into 3 distinct prognostic groups. We sought to externally validate this RPA using a multi-institutional dataset.

Materials/Methods: A total of 444 patients were utilized to develop the recently published sSRS RPA predictive of OS in patients with spine metastases. The RPA identified three distinct prognostic classes. RPA Class 1 was defined as KPS >70 and controlled systemic disease (n=142); RPA Class 2 was defined as KPS>70 with uncontrolled systemic disease or KPS ≤70, age ≥54 and absence of visceral metastases (n=207); RPA Class 3 was defined as KPS ≤70 and age <54 years or KPS≤70, age ≥54 years and presence of visceral metastases (n=95). We utilized data from large tertiary care centers to validate this RPA. A total of 749 patients were in the validation cohort and were divided based on their RPA Class. Kaplan-Meier method was used to estimate OS and log-rank test was used to compare OS between RPA classes.

Results: In the validation cohort (749 patients), the median OS was 11.0 months. One-hundred-thirteen (15.1%) patients were in RPA Class 1, 432 (57.7%) patients in RPA Class 2 and 204 (27.2%) patients in RPA Class 3. The median OS in the validation cohort based on RPA Class was 27.1 months for Class 1, 13.0 months for Class 2 and 3.5 months for Class 3. Patients in RPA Class 1 had a significantly better OS compared to those in Class 2 of the validation cohort (p<0.01). Similarly, patients in RPA Class 2 had a significantly better OS compared to those in Class 3 (p<0.01).

Conclusion: The external datasets from two large centers validated the spine SRS RPA successfully for RPA for OS for patients undergoing sSRS for spinal metastases. This is the first RPA for OS to have been externally validated using a large dataset. Based on this validation, upfront spine SRS is strongly supported for patients in RPA Class 1. Upfront SRS is also supported for RPA Class 2 patients. Patients in RPA Class 3 would benefit most from upfront conventional radiotherapy given their poor expected survival. Given successful external validation, this RPA helps guide physicians to identify those patients with spinal metastases who most benefit from sSRS.

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Use of Anti-Resorptive Medications prior to Stereotactic Body Radiotherapy for Spinal Metastasis Reduced the Incidence of Vertebral Body Compression Fracture

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Purpose/Objective(s): Stereotactic body radiotherapy (SBRT) is frequently utilized for pain relief and tumor control in patients with spinal metastases. A common adverse effect of SBRT is vertebral body compression fracture (VCF), which can be associated with pain and disability. Anti-resorptive (AR) drugs are often given to patients with bone metastases to minimize this risk, but minimal data exist regarding optimal regimens. This study examines the association between peri-SBRT AR drug use and VCF incidence. We hypothesized that patients taking AR drugs prior to SBRT will have lower VCF incidence than those taking them afterward.

Materials/Methods: Patients treated with SBRT for spinal metastases at a single institution from 2009-2020 were retroactively reviewed. Those with primary site multiple myeloma, hemangioma or radiation-level vertebral hardware were excluded. Statistical analysis was performed and p<0.05 was considered significant. Kaplan-Meier survival analysis was used to compare the cumulative incidence of VCF for subgroups including no AR drugs, AR drugs after SBRT only, and AR drugs before SBRT. Cox proportional hazards and Fine-Gray competing risk models were used to separately analyze those taking bisphosphonates (BPs) and those taking denosumab. Model covariates included AR duration, AR cumulative dose, radiation dose and fractionation, BMI, radiotherapy (RT) naivety and total SINS score. Fine-Gray model competing risks were local progression and death.

Results: Of the 234 patients (410 vertebrae) analyzed, 366 (89%) were RT naive. 79 (19.3%) patients were taking BPs alone, 79 (19.3%) were taking denosumab alone, and 49 (12.0%) were taking both. For those taking pre-SBRT AR drugs, the median interval between the last dose of BPs or denosumab and SBRT was 378.3 and 396.3 days. Kaplan-Meier analysis revealed a lower VCF incidence for patients initiating AR drugs before SBRT compared to no AR drugs (6-month 4% vs. 8%, 1-year 4% vs. 12%, 2-year 4% vs 23%, p=0.008). In multivariable analysis, those initiating denosumab prior to SBRT were 81% less likely to develop VCF versus after SBRT (SHR: 0.19, 95% CI [0.04-0.98], p=0.047). There was a trend towards reduced risk of VCF in those initiating BPs prior to SBRT versus after SBRT (SHR: 0.27 [0.06-1.36], p=0.114). Denosumab duration (SHR: 0.99 [0.99-1.01], p=0.45) and cumulative dose (SHR: 1.00 [0.99-1.00], p=0.69) did not affect VCF incidence. BP duration (SHR: 1.14 [1.05-1.24], p=0.003) and cumulative dose (SHR: 0.99 [0.98-0.99], p=0.02) had small statistically significant effects.

Conclusion: These data suggest that denosumab use prior to SBRT may reduce the risk of treatment-induced VCF. AR drugs are underutilized in patients with spine metastases and may represent a useful intervention to improve long-term outcomes. Confirmation of these findings using multi-institution datasets and prospective trials will be important.

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Safety and Efficacy of Dose-Escalated Radiotherapy with a Simultaneous Integrated Boost for the Treatment of Spinal Metastases

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