

sible detriment in cognition post-radiation. We sought to compare the efficacy and safety between the surgical resection of brain metastases (BM) plus radiotherapy versus surgical resection alone. **MATERIALS AND METHODS:** We searched various biomedical databases from 1983 to 2019, for eligible randomized controlled trials (RCT). Outcomes studied were local recurrence (LR), overall survival (OS), and serious (Grade 3+) adverse events (AE). We used the random-effects model to pool outcomes. The methodological quality of each study was assessed using the Cochrane Risk of Bias tool. **RESULTS:** We included 5 RCTs comprising of 673 patients. The odds ratio (OR) for LR ranged from 0.06–0.34 with a pooled odds ratio of 0.26 (95% confidence interval (CI) 0.19–0.37,  $P < 0.001$ ), strongly favoring the patients who received postoperative radiation. The overall survival (OS) was only reported in 3 studies and did not show any significant difference. The hazard ratio (HR) ranged from 1.01–1.29 with a pooled HR of 1.1 (95% CI 0.90–1.34,  $P = 0.37$ ). The treatment-related toxicities were inconsistently reported to draw any meaningful conclusions. The risk of bias was predominantly due to the lack of blinding and was deemed to be high, affecting all outcomes. **CONCLUSION:** Our analysis confirms that postoperative radiation should be recommended after surgical resection of BM, for it significantly reduces the risk of local recurrence. However, we did not find any improvement in OS, suggesting that improvements in local control at the tumor bed alone may not impact survival. Balancing local control, and possible neuro-cognitive effects of whole-brain radiation, post-operative cavity radiation seems to be an attractive option.

#### RADI-11. EVALUATING THE TISSUE EFFECTS OF DOSE-ESCALATED PRE-OPERATIVE STEREOTACTIC RADIOTHERAPY FOR RESECTABLE BRAIN METASTASIS

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**BACKGROUND:** Although the classic radiobiologic principles of radiotherapy are well understood, the unique effects of the large fractional doses that characterize stereotactic radiotherapy (SRT), specifically in terms of antitumor immune cellular processes, vascular damage, tumor necrosis, and apoptosis on brain metastasis have yet to be adequately demonstrated. The objective of this study is to provide the first in-human evaluation of the biological effects of SRT in resected brain metastasis. **METHODS:** All paired primary tumors and metastases for patients who underwent dose-escalated preoperative SRT followed by resection were evaluated for tumor necrosis using hematoxylin-eosin staining. T cells (CD3+, CD4+, CD8+), natural killer cells (CD56+), vessel density (CD31+), and apoptotic factors (caspase-3) were determined by immunohistochemical analysis. **RESULTS:** Fifteen patients with brain metastases from solid tumors received a median preoperative SRT dose of 18 Gy (range: 15–18 Gy) in 1 fraction, with 2 patients receiving 27–30 Gy in 3–5 fractions, followed by resection within a median interval of 90 hours (Range: 17.1–260 hours). The rate of necrosis was found to be significantly higher in irradiated brain metastases than in non-irradiated primary tumor samples (mean paired difference: 30.47, SD: 29.28,  $p = 0.001$ ). A decrease in all immunomodulatory cell populations was found in irradiated metastasis: CD3 (mean paired difference -19.4, SD: 31.7,  $p = 0.03$ ), CD4 (-10.0, SD: 20,  $p = 0.01$ ), and CD8 (-17.4, SD: 22.1,  $p = 0.008$ ). While irradiated samples had numerically lower CD 31+, CD 56+, and caspase-3 scores, the difference was not statistically significant. Time interval from SRT to surgery had no effect on these parameters. **CONCLUSIONS:** There is complex interplay between tumor-associated cells and the unique radiobiological effects of SRT on tumor tissue. Although time interval from SRT to surgery was associated with increased tumor necrosis, differences in immunomodulatory factors may be multifactorial, including concurrent corticosteroids or the immunosuppressive effect of SRT.

#### RADI-12. DEEP LEARNING FOR AUTOMATIC DETECTION AND CONTOURING OF METASTATIC BRAIN TUMORS IN STEREOTACTIC RADIOSURGERY: A RETROSPECTIVE ANALYSIS WITH AN FDA-CLEARED SOFTWARE ALGORITHM

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**INTRODUCTION:** Artificial intelligence-based tools can significantly impact detection and segmentation of brain metastases for stereotactic

radiosurgery (SRS). VBrain is a deep learning algorithm, recently FDA-cleared, to assist in brain tumor contouring. In this study, we aimed to further validate this tool in patients treated with SRS for brain metastases at Stanford Cancer Center. **METHODS:** We included randomly selected patients with brain metastases treated with SRS from 2008 to 2020. Computed tomography (CT) and axial T1-weighted post-contrast magnetic resonance (MR) image data were extracted for each patient and uploaded to VBrain. Subsequent analyses compared the output contours from VBrain with the physician-defined contours used for SRS. A brain metastasis was considered “detected” when the VBrain “predicted” contours overlapped with the corresponding physician contours (“ground-truth” contours). We evaluated performance against ground-truth contours using the following metrics: lesion-wise Dice similarity coefficient (DSC), lesion-wise average Hausdorff distance (AVD), false positive count (FP), and lesion-wise sensitivity (%). **RESULTS:** We analyzed 60 patients with 321 intact brain metastases treated over 70 SRS courses. Resection cavities were excluded from the analysis. The median (range) tumor size was 132 mm<sup>3</sup> (7 to 24,765). Input CT scan slice thickness was 1.250 mm, and median (range) pixel resolution was 0.547 mm (0.457 to 0.977). Input MR scan median (range) slice thickness was 1.000 mm (0.940 to 2.000), and median (range) pixel resolution was 0.469 mm (0.469 to 1.094). In assessing VBrain performance, we found mean lesion-wise DSC to be 0.70, mean lesion-wise AVD to be 9.40% of lesion size (0.805 mm), mean FP to be 0.657 tumors per case, and lesion-wise sensitivity to be 84.5%. **CONCLUSION:** Retrospective analysis of our brain metastases cohort using a deep learning algorithm yielded promising results. Integration of VBrain into the clinical workflow can provide further clinical and research insights.

#### RADI-13. SYSTEMIC THERAPY TYPE AND TIMING EFFECTS ON RADIATION NECROSIS RISK IN HER2+ BREAST CANCER BRAIN METASTASES PATIENTS TREATED WITH STEREOTACTIC RADIOSURGERY

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**BACKGROUND:** Current standard of care options for HER2+ breast cancer brain metastasis (BCBrM) include radiation therapy, brain permeable systemic therapies, and in select cases, neurosurgical resection. There is a concern that HER2-directed systemic therapies when administered concurrently with stereotactic radiosurgery (SRS) may increase the risk of radiation necrosis (RN). This study explores the impact of timing and type of systemic therapies on the development of RN in patients treated with SRS for HER2+ BCBrM. **METHODS:** This was a single-institution, retrospective study including patients  $\geq 18$  years of age with HER2+ BCBrM who received SRS between 2013 and 2018 with at least 12-month post-SRS follow-up. Presence of RN was determined at one-year post-SRS. Demographics, radiotherapy parameters, and timing (“during” defined as four weeks before/after SRS) and type of systemic therapy were evaluated. **RESULTS:** Among 46 patients with HER2+ BCBrM who received SRS, 28 (60.9%) developed RN and 18 (39.1%) did not. Age (mean 53.3 vs 50.4 years, respectively), radiotherapy parameters (dose, fraction, CTV, GTV, CI, V12Gy, all  $p > 0.05$ ), and receipt of any type of systemic therapy during SRS (60.7% vs 55.6%,  $p = 0.97$ ) did not differ between patients who did or did not develop RN. However, patients who developed RN more commonly received more than one line of HER2-directed therapy independent of SRS timing compared to those who did not develop RN (75.0% vs 44.4%,  $p = 0.08$ ). In fact, a significantly higher proportion of those who developed RN received more than one line of HER2-directed therapy during a given SRS treatment compared to those who did not develop RN (35.7% vs 5.6%,  $p < 0.05$ ). **CONCLUSIONS:** Patients with HER2+ BCBrM who receive multiple lines of HER2-directed therapy during SRS for BCBrM may be at higher risk of RN. Collectively, this data supports a practice of holding HER2-directed therapy during treatment with SRS if medically acceptable.

#### RADI-14. BEVACIZUMAB VS LASER INTERSTITIAL THERMAL THERAPY IN RADIATION NECROSIS FROM BRAIN METASTASES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**OBJECTIVE:** Radiation necrosis (RN) represents a serious post-radiotherapy complication in patients with brain metastases. Bevacizumab