RADI-11. Evaluating the Tissue Effects of Dose-escalated Pre-operative Stereotactic Radiotherapy for Resectable Brain Metastasis

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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 method 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 2 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 have a significant impact on study outcomes. CONCLUSION: 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 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 dose that characterizes 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+), vascular endothelial growth factor (VEGF), and apoptotic fragmented DNA (TUNEL) were determined by immunohistochemical analysis. RESULTS: Fifteen patients with brain metastases from solid tumors received a median preoperative SRT dose of 18 Gy (range: 15–20 Gy) in 1 fraction, with 2 patients receiving 27–30 Gy in 3–5 fractions. Necrosis observed by resection within a median interval of 90 hours (Range: 17.1–260 hours) post-SRT. 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 metastases: 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 3+ , CD 8+ , 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 SEGMENTATION 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 analysis involved the output contour from VBrain with the ground-truth 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: 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. Lesion contours were excluded from the analysis. The median (range) tumor size was 8.5 cm(3) (2.5 cm(3)–26.2 cm(3)), with a median (range) tumor thickness of 2.25 mm (0.44 mm–6.94 mm). Our analysis showed that SRS, if medically acceptable. 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 2 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 have a significant impact on study outcomes. CONCLUSION: 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 radiation seems to be an attractive option.

**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 metastases (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 ≥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 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 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
Triple-negative breast cancer (TNBC) is an aggressive forms of breast cancer. A two women with HER-2 positive breast cancer metastases metastasized to brain within 12 months, who were not statistically significant among groups (p=0.624). Similarly, mean T-cell count was significantly higher among patients with LN+ disease (p=0.001). Patterns of radiological responses differed at 6-month follow-ups, with rates of partial response significantly higher in the bevacizumab group (p=0.0001) and stable disease significantly higher in the LITT group (p=0.002). Survival rates were superior in the LITT cohort, and statistical significance was reached at 18 months (p=0.038, HR=0.737). Low rates of adverse events were reported in both groups (14.7% for bevacizumab and 12.2% for LITT). CONCLUSION: Bevacizumab and LITT can be safe and effective treatments for RN from brain metastases. Clinical and radiological outcomes are mostly comparable, but LITT may relate to superior survival benefits in select patients. Further studies are required to identify the best patient candidates for each treatment group.

RADI-15. RADIOTHERANOSTIC APPROACH IN BRAIN TUMOR
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PURPOSE: The aim of this study is feasibility and potential treatment of targeted radionuclide theranostic approach for patients with brain tumors. METHODS: For the period 2020–2021, 6 child and adult patients who had been diagnosed with brain tumors were treated using theranostic approach followed by refractory to conventional therapy. Two patients that were presented with HER-2 positive, ER and PR negative breast cancer and brain metastases as well as a history of several cycles of chemotherapy sessions and radiotherapy using gamma knife were treated with 177Lu-Trastuzumab (Herceptin). Three other patients with primary brain tumor underwent peptide receptor radionuclide therapy (PRRT) with 177Lu-DOTATATE. The last case was a patient with refractory primary cerebral lymphoma to standard therapy with confirmed CD20-positive B-cell lymphoma who underwent 177Lu-Rituximab. RESULTS: A two women with HER-2 positive breast cancer and brain metastasis underwent two cycles of 177Lu-trastuzumab. Post-therapy assessment showed some improvement. Next, a man with a high-grade glioma with no response to chemotherapy sessions and radiotherapy using gamma knife was treated with 177Lu-DOTATATE. She had a stable disease with some improvement in the clinical status. Also, a girl with an astrocytoma in suprasellar cistern underwent 2 cycles of 177Lu-DOTATATE. The complete response was des- signed. Finally, a patient with refractory primary cerebral lymphoma received 177Lu-Rituximab. CONCLUSION: Nuclear oncology in the field of neuro-oncology (neuoroaradotheranostics) has been toward a personalized approach, effective and safe therapy. These preliminary studies might demonstrate feasibility and therapeutic potential of theranostics in patients with primary, recurrent brain and metastasis brain tumors. Further studies are required to identify the best patient candidates for each treatment group.

RADI-16. EFFICACY OF WBRT AMONG THE SUB-TYPES OF METASTATIC BREAST CANCER
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OBJECTIVES: To understand the effect of Whole Brain Radiation (WBRT) in terms of Age, Neurological performance, Radiological Improve- ment and the Overall Survival. METHODS: 34 Patients [Median Age: 45 years (31- 65)] with Metastatic Breast Carcinoma who presented with Brain metastasis to the Department of Radiation Oncology at Kidwai Me- morial Institute Of Oncology and subjected to Whole Brain Radiotherapy. Focal RT were taken into the study. The efficacy of WBRT was assessed among the four subtypes of MBC. RESULTS: 39% of the patients belonged to Luminial A, 25%, 22% and 14% belonged to Luminial B, Her2 amplified and Basal respectively. Patients under Luminial A, presented with brain me- tastases by 25 months after the diagnosis of the primary. 60% presented with single lesion, amenable to resection and 58% underwent surgery followed by WBRT and OS fared better as compared to patients with WBRT alone with no distant recurrences on imaging and improvement in KPS. Patients with Luminal B, Her2 amplified and Basal had predominantly oligometastatic lesions (65%), presented with brain metastases at 15 months after diag- nosis of Carcinoma Breast,18% received Herceptin and Lapatinib and 33% and 22% received Herceptin and Lapatinib alone. OS was superior over WBRT alone with exagerated radiation necrosis in 5 patients. Further studies preferentially biological therapy and RT in patients with Basal subtype,75% had multiple metastatic brain lesions, presented with symptoms by 10 months of diagnosis of the primary with poor KPS and OS remained poor despite WBRT. CONCLUSIONS: Lessons be amenable for surgery, focal RT to post op cavity alone may be considered in patients with Luminal A. WBRT plus boost for those unfit for surgery. Addition of TKI +/- oral chemo for all patients with Luminal B and HER 2 amplified to Focal RT or WBRT. Triple Negative patients present with poor KPS can be considered for SCS/WBRT on case basis.

RADI-17. OUTCOMES FOR PATIENTS WITH TRIPLE NEGATIVE BREAST CANCER TREATED WITH UPTOTON STEREOTACTIC RADIOSURGERY BRAIN METASTASES
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BACKGROUND: Triple-negative breast cancer (TNBC) is an aggressive subtype with high propensity of developing brain metastases (BM); Clinical outcomes and prognostic factors after metastasis radiosurgery (SRS) for BM were not well defined. METHODS: We identified 57 consecutive TNBC pa- tients (pts) treated with single fraction SRS for BM during 05/2008-04/2018. Overall survival (OS) from BM diagnosis and freedom from BM progression (FFMBP) after initial SRS were evaluated. BM progression was defined as local and/or distant brain failure (LDF, DBF) after SRS. Kaplan-Meier analyses and Cox proportional hazard regression were used to estimate survival outcomes and identify prognostic factors. RESULTS: The median time to BM develop- ment from TNBC diagnosis was 23.7 months (range 0.7-271.1). Me- dian OS was 13.1 mo (95%CI 8.0-19.5). On univariate analysis, Karnofsky performance score (KPS) >70 (p=0.03), number of BMs <3 (p=0.016), and BM among the first metastatic sites (p=0.04) were associated with longer OS. On multivariate analysis, KPS >70 was associated with higher risk of death (HR 3.0, p=0.03). BMs with adequate imaging follow-up, 29 (63%) had intracranial progression with a median FFMBP of 7.4 mo (95% CI 5.7-12.7). At 12 mo the estimated cumulative DBF rate was 61.1% (95% CI 40.8– 74.4%) and LDF rate was 17.8% (95% CI 2%-31%). Number of BMs (≥3 vs <3) and BM progression (p=0.01) were associated with worse OS. For patients with BM progression, additional radiotherapy (RT) (vs. no RT) was associated with improved survival (21.7 vs. 7.0 mo, p<0.0001). CONCLUSIONS: TNBC pts with BM treated with SRS had an OS of 13.1 mo and FFMBP of 7.4 mo. Good KPS was an independent prognostic factor for OS. Further studies with more pts or conducted prospectively are needed to better understand and to improve treatment outcomes in this pt population.

RADI-18. SURVIVAL AND DISEASE CONTROL AFTER UPTOTON STEREOTACTIC RADIOSURGERY BRAIN METASTASES FROM BREAST CANCER
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BACKGROUND: As systemic therapy for metastatic breast cancer (BC) improves, the survival benefit from hormonal and targeted therapy urges