MLTI-11. IMPLANTABLE POLYMERIC BCNU AS AN ADJUNCT TO SURGERY FOR METASTATIC INTRACRANIAL DISEASE
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SUMMARY: One hundred and thirty cases of craniotomy for tumor utilizing BCNU implantable chemotherapy were performed by the authors between including 23 cases for metastatic intracranial disease. The series included 12 woman and 11 men with an average age of 56.9 years. The diagnoses were as follows: non-small lung cancer (13), breast cancer (6), small-cell lung cancer (1), colon cancer (1), unknown primary (2). Patients undergoing resection plus implantable chemotherapy following whole brain radiotherapy (5 patients) or following stereotactic radiotherapy (5 patients) were the most common. Only patient oncologized possible local recurrence (3%). Complications included two cerebrospinal fluid leaks with associated complications requiring reoperations (11%) both following whole brain radiotherapy and 3 patients (17%) with thromboembolic episodes (3 deep venous thrombosis with a pulmonary embolus and subdural hematomas). In this challenging population, local implantable chemotherapy appears relatively safe and a reasonable consideration as a surgical adjunct.

MLTI-12. TIMING OF SYSTEMIC THERAPY ADMINISTRATION RELATIVE TO STEREOTACTIC RADIOSURGERY AND DEVELOPMENT OF RADIATION NECROSIS IN PATIENTS WITH BRAIN METASTASES
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PURPOSE: The mainstay of oncologic therapy for patients with brain metastases involves brain-directed radiation, increasingly given via stereotactic radiosurgery (SRS), and systemic therapy for extracranial disease control. We sought to investigate the association between the timing of systemic therapy and SRS administration on development of radiation necrosis among patients with brain metastases. METHODS: We retrospectively identified 429 patients treated at Brigham and Women’s Hospital/Dana-Farber Cancer Institute with SRS for newly-diagnosed brain metastases between 2001-2015. Systemic therapy was tiered into 4 categories: chemotherapy, immunotherapy, hormonal therapy, and targeted therapy. All images were manually reviewed by two radiation oncologists specializing in brain tumors to assess the presence versus absence of radiographic necrosis. Patients with radiographic necrosis who harbored associated neurologic symptoms or were managed with steroids/bevacizumab/resection were considered to have symptomatic radiation necrosis. Data were analyzed using univariable and multivariable Cox regression in SAS v9.4. The median follow-up in surviving patients was 1.79 years. RESULTS: In total, 252/429 and 361/429 patients received systemic therapy pre and/or post SRS, respectively. Patients receiving systemic therapy ≤5 days before SRS displayed higher rates of radiographic [HR 2.48, 95% CI 1.06–5.81, ps=.04] and symptomatic [HR 3.74, 95% CI 1.18–12.98, ps=.04] necrosis; a similar association was seen in patients receiving systemic therapy ≤5 days after SRS [HR 1.72, 95% CI 0.84–3.53, ps=.14 and HR 4.42, 95% CI 1.75–11.14, ps=.002, respectively]. Trends towards increased necrosis risk were noted when comparing systemic therapy administration 1–5 days versus 6–10 days before/after SRS. The above 4 associations were significant when restricting the cohort to patients receiving targeted systemic therapy (HR-range 3.57–21.49, p-range 0.01–0.04). CONCLUSION: Timing of systemic therapy may compromise outcome. Pseudoprogression is uncommon with immunotherapy alone; pseudoprogression rates were similar after SRS alone or in combination with immunotherapy or other systemic treatment.

MLTI-14. A SYSTEMATIC REVIEW OF TREATMENT PARADIGMS FOR PATIENTS WITH BREAST CANCER AND ONE OR MORE BRAIN METASTASES
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BACKGROUND: Upwards of 50% of patients with advanced breast cancer are diagnosed with brain metastases (BM). Treatment options for these patients have been rapidly evolving due to increased understanding of the tumor pathophysiology and its genetic underpinnings. This systematic review of randomized controlled trials (RCTs) aims to clarify the evidence guiding the treatment of brain metastases from breast cancer. METHODS: MEDLINE, EMBASE, Cochrane Controlled Register of Trials, ClinicalTrials.gov, and Web of Science were searched from inception to October 2018 for RCTs comparing treatments for breast cancer BM. We screened studies, extracted data, and assessed risk of bias independently and in duplicate. Outcomes assessed were overall survival (OS), progression-free survival (PFS), and adverse events (Grade 3+). RESULTS: Among 3188 abstracts, 30 RCTs (N=14212) meeting inclusion criteria were identified. The studies were phase II or III open-label parallel superiority trials. Inclusion criteria among these trials consisted of age >18 with radiologic evidence of ≥ 1 BM. Exclusion criteria consisted of prior radiation therapy, prior aromatase inhibitor use, and primary treatment (HR 0.52; 95%CI 0.332–0.816). No significant differences were found with PFS or rate of adverse events amongst treatment groups. CONCLUSION: Considering the high prevalence of breast cancer BM and our improved understanding of genomic/molecular features of these tumors, a greater number of RCTs dedicated to this disease are needed.

MLTI-15. A CASE SERIES OF PRE-OPERATIVE GAMMA-KNIFE RADIOSURGERY FOR RESECTABLE BRAIN METASTASES
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Recent advances in the systemic treatment of various cancers have resulted in longer survival and higher incidence of brain metastases. Phase 3 trials in North America and in Japan have demonstrated that stereotactic radiosurgery will be a standard adjuvant modality following surgery for resectable brain metastases. However, we don’t know the optimal sequence of this combination therapy. We hypothesized that pre-operative stereotactic radiosurgery for resectable brain metastases provides favorable rates of local response.
control, overall survival, leptomeningeal dissemination and symptomatic radiation necrosis. We have experienced 4 cases of resected brain metastases within 1-7 days after Gamma-knife surgery (median margin dose 22 Gy) and have been following their clinical course. We will show the repressive cases.

**MLTI-16. SYSTEMIC THERAPY FOLLOWING CRANIOTOMY IN PATIENTS WITH A SOLITARY BRAIN CANCER BRAIN METASTASIS**

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**INTRODUCTION:** Between 15–50% of patients with metastatic breast cancer will develop brain metastases, with the frequency more common in patients with HER2-positive or triple-negative subtypes. Surgical resection is often indicated for diagnostic and/or therapeutic intent for patients presenting with a solitary lesion and/or symptomatic lesion(s) with mass effect. Practice patterns and patient outcomes with respect to the use of postoperative systemic therapy (ST) after resection of a solitary breast cancer brain metastasis (BCBM) have not been previously well-described, particularly in the modern era. METHODS: A multi-institutional retrospective review of 44 patients was performed to assess the impact of types of ST on site of recurrence, progression-free survival (PFS) and overall survival (OS). Determination of solitary BCBM. RESULTS: Stratified estimated survival was 15, 24 and 23 months for patients with triple negative, estrogen receptor positive (ER+), and human epidermal growth factor receptor 2 positive (HER2+) BCBMs. Patients receiving postoperative ST had a longer median PFS (8 versus 4 months) and OS (32 versus 15 months). Nine patients (20%) had extracranial progression, 23 (52%) had intracranial progression, three (8%) had both, and nine (20%) did not experience progression at last follow-up. Multivariate analysis showed that postoperative hormonal therapy was associated with longer OS in estrogen receptor (ER) positive patients (HR = 0.26; CI = 0.08 - 0.89; p = 0.03), but not with longer PFS. Postoperative human epidermal growth factor receptor 2 (HER2)-targeted therapy was not associated with longer PFS or OS in HER2+ patients. CONCLUSIONS: Disease progression occurred extracranially more often in PFS and OS patients, postoperative hormonal therapy was associated with longer OS. Postoperative HER2-targeted therapy did not show survival benefits in HER2+ patients. These results should be validated in larger cohorts.

**MLTI-17. DIFFERENTIATION OF RADIATION INJURY FROM RECURRENT BRAIN METASTASIS USING COMBINED FET PET/ MRI RADIOMICS**

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**BACKGROUND:** The aim of this study was to investigate the potential of combined radiomics textural feature analysis of contrast-enhanced MRI (CE MRI) and static O-[18F]fluoroethyl-L-tyrosine (FET) PET for the differentiation of recurrent brain metastasis from radiation injury. METHODS: Fifty-two patients with newly diagnosed or progressive contrast-enhancing brain lesions on MRI after radiotherapy (predominantly radiosurgery, 84% of patients) of brain metastases were additionally investigated using FET PET. Based on histology (n=19) or clinicoradiological follow-up (n=33), local recurrent brain metastases were diagnosed in 21 patients (40%) and radiation injury in 31 patients (60%). Forty textural features (shape-based, first and second order features) were calculated on both unfiltered and filtered CE MRI and summed FET PET images (20–40 min p.i.). After feature selection, logistic regression models using a maximum of five features to avoid overfitting were calculated for each imaging modality separately and for the combined FET PET/MRI features. The resulting models were validated using cross-validation. Diagnostic accuracies were calculated for each imaging modality separately as well as for the combined model. RESULTS: For differentiation between radiation injury and brain metastases recurrence, textural features extracted from CE MRI had a diagnostic accuracy of 81%. FET PET textural features revealed a slightly higher diagnostic accuracy of 83%. However, the highest diagnostic accuracy was obtained when combining CE MRI and FET PET features (accuracy 89%). CONCLUSION: Our findings suggest that combined FET PET/MRI radiomics using textural feature analysis offers a great potential to contribute significantly to the management of patients with brain metastases. SUPPORT: This work was supported by the Wilhelm-Sander Stiftung, Germany.

**MLTI-18. PRECISION IMAGING OF METASTATIC AND PRIMARY BRAIN TUMORS AFTER RADIATION WITH [18F]F-FDOPA PET/MRI IS FEASIBLE AND COST EFFECTIVE**

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**PURPOSE:** Post-radiation changes in the brain can mimic tumor recurrence on MRI, requiring multiple short term follow-ups to differentiate tumor progression from radiation necrosis. We propose combining functional and anatomic imaging with [18F]F-FDOPA PET tracer in hybrid PET/MRI to improve detection of tumor recurrence. MATERIALS AND METHODS: Seventeen adult patients treated with radiotherapy were identified - four with metastatic disease from breast and lung cancer and thirteen with primary brain glioma (11 IDH wildtype glioblastoma and 2 astrocytoma). Patients were scanned on hybrid PET-MRI (GE Healthcare) with clinical MRI brain sequences and dynamic FDG PET/CT uptake. Dynamic FDG PET/CT uptake within these tumors over 45 minutes after tracer injection was analyzed compared to ADC histogram analysis. RESULTS: The patients, clinical multi sequence gadolinium enhanced MRI and dynamic PET imaging for up to 45 minutes with [18F]F-FDOPA amino acid tracer was obtained. The total cost savings of scanning 17 patients in groups was 51.4% ($28,321, as opposed to the cost of individual radiosynthesis performed for each study. Quantitative analysis of tracer uptake in striatum, internal carotid artery, and superior sagittal sinus were performed with appropriate accumulation and subsequent washout of tracer respectively. Successful dynamic FDOPA uptake within the tumor was seen in all patients and ratio of tumor to contralateral ROI were found to range from 1.8–4.5. While raw SUV values did not differentiate between recurrent tumor and radiation changes, TIC SUVmax ratios were elevated to 4.5 in recurrent glioblastoma, 2.5 in 18F-fluoroethyl tyrosine treated glioblastoma, and 1.8 in non-recurrent metastatic breast cancer after gamma knife treatment. CONCLUSION: Batch imaging of patients with [18F]F-FDOPA PET/MRI is feasible and cost effective. Understanding radiomucule synthesis process is critical for increasing accessibility of novel PET tracers to patients and results in significant cost savings.

**MLTI-19. VENOUS THROMBOEMBOLOMBIC EVENTS IN PATIENTS WITH BRAIN METASTASES: THE PICOS SCORE**

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**BACKGROUND:** Venous thromboembolic events are significant complications in patients and possibly associated with an unfavorable outcome. Embolus risk is poorly defined for patients with brain metastases, and available risk calculation scores are not validated for these patients. METHODS: We identified 811 patients with brain metastases followed at our institution and screened electronic charts retrospectively for the occurrence of venous thromboembolic events, along with candidate risk factors. Risk factors were tested in uni- and multivariate analyses and finally integrated in a score model for risk prediction. RESULTS: Venous thromboembolic events were documented in 97 of 811 patients (12.0%). Primary tumors with high thrombogenicity (p=0.02, odds ratio 1.7, 95% CI 1.1–2.8), dexamethasone (p=0.001, odds ratio 2.27, 95% CI 1.5–4.5), chemotherapy (p=0.005, odds ratio 3.4, 95% CI 1.6–7.5), BMI > 35 kg/m2 (p=0.002, odds ratio 3.4, 95% CI 1.6–7.5) and immobilization (p=0.003, odds ratio 2.4, 95% CI 1.3–4.3) were confirmed as independent predictors of VTE. We derived a score model for venous thromboembolic event prediction, the PICOS (thrombogenic Primary, Immobilization, Chemotherapy, Obesity, Steroids) score (0–7 points). Receiver Operating Characteristic Curve Analysis demonstrated its prognostic accuracy (AUC=0.71, 95% CI 0.64–0.77), and its predictive capability was superior to the other scores proposed for the evaluation of venous thromboembolic event risk such as the Khorana (AUC=0.51) or CONKO (AUC=0.52) scores. CONCLUSIONS: We report a rate of venous thrombotic events of 12.0% in our cohort of 811 patients with brain metastases. We define a risk model for prediction of venous thrombotic events in patients with BM, the PICOS score. It may become a valuable tool for the identification of brain metastasis patients at high risk for venous thromboembolic events and be helpful for guidance of clinicians towards decision making to start thrombosis prophylaxis. Further, the PICOS score might be used for stratification in controlled studies.