fluorothymidine (FLT) is a PET tracer which correlates with cellular proliferation and may improve response assessment. METHODS: A phase I trial of whole brain radiotherapy (WBRT)+sorafenib was conducted using a 3 + 3 design. Sorafenib was given daily at the start of WBRT for 21 days (dose levels: 200mg, 400mg, and 600mg). The primary endpoints were to determine a maximum tolerated dose (MTD) and to evaluate safety and toxicity. The secondary endpoint was CNS progression-free survival (CNS-PFS). Macdonald Criteria were used for response assessment. A correlative serial FLT-PET imaging study was conducted to assess radiographic changes among pts receiving WBRT +/- sorafenib, in parallel with MRI. RESULTS:13 pts in the dose escalation were evaluable for dose-limiting toxicity (DLT). DLTs were: Grade (G) 4 increased lipase at 200mg (1 pt) and G3 rash at 400mg (3 pts) level. MTD was 200mg. Six additional pts were treated in an expansion cohort without additional DLT. 14 pts were evaluable for response. The overall response rate was 71%: 4 complete + 6 partial responses. Median follow up was 14 months (range: 3–44). Median CNS-PFS was 12.8 months (95%CI: 6.7-NR). A total of 15 pts (10 WBRT+sorafenib and 5 WBRT) were enrolled in the FLT-PET study: all had baseline FLT-PET, 14 with follow up at 7–10 days post WBRT (FU1), and 9 with followup at 12 weeks post WBRT (FU2). 55 baseline lesions were observed and analyzed: 38 at FU1 and 15 at FU2. Decline in average SUVmax of ≥25% was seen in 9/10 (90%) of WBRT+sorafenib pts and 2/4 (50%) of WBRT only pts at FU1. CONCLUSIONS: Concurrent WBRT+sorafenib appears safe at 200mg daily dose with clinical activity. This combination should be considered for further efficacy evaluation. NCT01724606 and NCT01621906.

MLTI-03. FIRST-LINE STEREOTACTIC RADIOSURGERY COMBINED WITH SYSTEMIC TARGETED AND IMMUNE CHECKPOINT INHIBITOR THERAPY IN MELANOMA PATIENTS WITH NEWLY DIAGNOSED BRAIN METASTASES

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BACKGROUND: Of solid tumors, melanoma has the highest propensity for CNS spread with historic median survivals of 5–8 months following brain metastasis diagnosis. We evaluated the impact of systemic BRAF targeted and immune checkpoint inhibitor (ICI) therapies on survival outcomes in patients receiving stereotactic radiosurgery (SRS) for melanoma brain metastases (MBM) and assessed patient treatment burden associated with prolonged survival. METHODS: We retrospectively reviewed the demographics, disease characteristics, therapeutic regimens, overall survival, and first-year cumulative incidence of comorbid disease for patients with de novo MBM treated between 2013 and 2017 at a major melanoma referral center. RESULTS: Among 123 newly diagnosed MBM patients: 65% were male, 24% were 50 years old or less, 50% were BRAF mutated, 63% had multiple intracranial lesions at diagnosis. Locally, 73% received SRS as first-line treatment. Systemically, 73% received ICI, 46% received BRAF targeted therapy, and 12% received neither. With a median follow up of 11 months (mo), total cohort median OS was 13.2 mo. Median OS for first-line SRS combined with ICI and BRAF targeted therapy was 31.0 mo (47% 3-year OS), 17.5 mo (31% 3-year OS) with ICI monotherapy, and 6.1 mo (22% 3-yr OS) alone. SRS and BRAF targeted therapy were associated with improved OS. At one-year follow-up, comorbid conditions with the greatest cumulative incidence were fatigue, nausea, intracranial hemorrhage, deep vein thrombosis, major depressive disorder, and pneumonia. Patients averaged one inpatient visit every 4.5 mo (1 week average length of stay), and 2 advanced imaging studies (MR/CT/PET-CT) per month following MBM diagnosis. CONCLUSIONS: In one of the largest reported MBM series, survival has improved markedly for patients receiving first-line SRS combined with targeted and immunotherapies. Simultaneously, longer life expectancy comes with increasing incidences of comorbid conditions reflecting an evolving complexity of and need for coordination of care for patients with MBM.

MLTI-04. EVOLUTION OF TREATMENT PARADIGMS FOR PATIENTS WITH ≥1 BRAIN METASTASES FROM PRIMARY NON-SMALL-CELL LUNG CANCER – A SYSTEMATIC REVIEW

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BACKGROUND: Brain metastases (BM) are common in non-small cell lung cancer (NSCLC), with approximately 10% of patients presenting with BM at the time of diagnosis. The aim of this systematic review was to critically evaluate the evolution of management paradigms for BM from NSCLC. METHODS: We searched MEDLINE, EMBASE, Web of Science, ClinicalTrials.gov, and CENTRAL for randomized controlled trials (RCTs) published until October 2018. Comparative RCTs based on > 50 patients were selected. The primary outcomes of interest were overall survival (OS) and progression-free survival (PFS). RESULTS: Among 3188 abstracts, 14 RCTs (2494 patients) met inclusion criteria. Median sample size was 97 (range 59–538). Most trials were open-label, parallel, superiority trials. All included patients aged >18 with histologically proven NSCLC and >1 BM proven on CT/MRI. The majority of trials (11/14) excluded patients with non-favorable performance status (ECOG, KPS, or WHO scales), prior SRS or WBRT, and/or leptomeningeal metastases. Interventions assessed included WBRT (11/14), SRS (3/14), targeted therapies (e.g. EGFR inhibitors, 5/14), and various chemotherapeutic regimens (12/14). Most trials (12/13) reported no significant difference in OS between interventions. 4/10 trials reported a difference in PFS, two of which only included patients with EGFR-mutant NSCLC; these showed a significant increase in PFS in patients managed with EGFR inhibitors. The other two trials reported longer PFS with sodium glycididazole + WBRT vs. WBRT alone (p=0.038) and temozolomide + SRS vs. SRS alone (p=0.003). The incidence of adverse events was consistent across most treatment groups. CONCLUSIONS: Most trials showed no significant improvement in OS; however, improvement in PFS was seen in several trials, most notably in EGFR-positive patients treated with EGFR inhibitors. Given the long-standing merit of radiation-based therapies for BM management, these data support the need for an in-depth meta-analysis assessing the comparative efficacy of current management paradigms for specific patient populations.

MLTI-05. IDENTIFYING BRAIN METASTATIC CASES FROM FREE TEXT CLINICAL NARRATIVES WITH REFINEMENT OF SEMANTIC HETEROGENEITY USING MACHINE LEARNING

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INTRODUCTION: Brain metastatic disease (BM) is ripe for discovery using computational tools like machine learning (ML) due to disease complexity and multidimensional critical data (imaging, genomics, primary disease, drug exposures)[1]. Leveraging real-world-evidence' (RWE) from routine health data to inform clinical management is hindered by fragmented unstructured data and semantic heterogeneity[2]. Clinical data in EHR and institutional registries are typically free text narratives absent common data elements (CDE). Curating existing data into CDE with machine learning (ML) may inform contemporary approaches (RWE, N-of-1 trials, and precision medicine) that are dependent on large high-quality datasets. Harvesting existing institutional registries may expand demographic representation, confirm benchmarks of established treatments, and provide test environment for prospective ML applications. METHOD: An R-based deep convoluted neural network (DNN) using keras and an API for Tensorflow python was trained on physician narratives of 2000 BM cases and 8000 other CNS conditions labeled by diagnosis spanning 17 years[3,4]. The ML model was tested with 405 non-labeled narratives to: A) Identify BM from other CNS conditions (i.e. glioma, meningioma, non-tumor). B) Evaluate word embedding using GLoVe[5] to standardize abbreviations and misspellings by assigning terms to CDE by training the model to plot "mets", "metastases" and "spine" with the 20 most similar contextual words. RESULTS: DNN architecture achieved 97% accuracy in distinguishing BM (n=178) for others (n=227). "Mets" and "metastasis" have a connected contextual network suggesting shared meaning, whereas spine did not share a network. CONCLUSIONS: ML can identify BM cases in free-text registries which can serve as a quality control measure and aid data aggregation. Standardizing shorthand terminology to CDE with DNN trained in word embedding can possibly address semantic heterogeneity and facilitate data automation. Solutions are needed to compile and automate quality BM data across institutions to achieve the volume and complexity required for contemporary analysis using ML.

MLTI-06. BEVACIZUMAB VERSUS SURGICAL INTERVENTION FOR RADIATION NECROSIS IN PREVIOUSLY IRRADIATED BRAIN METASTASES

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INTRODUCTION: Both medical management with bevacizumab and surgical management via craniotomy or more recently with laser interstitial thermal ablation (LITT) have been shown to be efficacious in the management of radiation necrosis (RN) after radiosurgery for brain metastases (BM). Indications for how to choose medical versus surgical management however remains unclear. METHODS: Single-institution chart review was performed of all patients with biopsy or radiographically confirmed RN after radiosurgery for BM between 2011 and 2017. Progression-free survival (PFS) and overall survival (OS) were compared between those treated using bevacizumab versus surgical intervention. RESULTS: 15 patients underwent craniotomy, 18 patients underwent LITT, and 18 patients were treated with bevacizumab. Those treated with bevacizumab had significantly higher number of re-

growing lesions (n >1) at time of intervention (50.0%) versus those treated with surgery (15.2%) (p< 0.05). Likewise, pre-treatment KPS was lower in the bevacizumab cohort (median: 60) vs the surgery cohort (median: 90) (p< 0.05). Patients treated with bevacizumab demonstrated significantly decreased PFS (%PFS at 1-year 16.7% vs 86.7% and 87.8% for craniotomy and LITT, respectively; %PFS at 2-years 0% vs 86.7% and 73.2% for craniotomy and LITT, respectively, p < 0.05). Similar results were observed for OS (%OS at 1-year for bevacizumab 33.3% vs 93.3% and 73.8% for craniotomy and LITT, respectively; %OS at 2-years for bevacizumab 11.1% vs 64.6% and 63.2% for craniotomy and LITT, respectively, p< 0.05). CONCLUSIONS: Preliminary analysis shows that bevacizumab therapy in our institution is being chosen for patients with lower KPS and multiple regrowing lesions while surgical intervention is being chosen for patients with good KPS and single, symptomatic regrowing lesions. While the comparative outcomes after bevacizumab appear to be significantly worse than surgical management, it remains unknown if the difference is more related to its true efficacy or the significant discrepancy between the comparison groups.

MLTI-07. PREOPERATIVE VERSUS POSTOPERATIVE STEREOTACTIC RADIOSURGERY FOR LARGE BRAIN METASTASES: AN INTERNATIONAL META-ANALYSIS

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PURPOSE: Preoperative stereotactic radiosurgery (SRS) for symptomatic brain metastases has arisen as a therapeutic option for patients with brain lesions, potentially reducing radionecrosis risk, leptomeningeal disease risk, as well as delays in systemic therapy after craniotomy. The purpose of our work is to analyze the current evidence regarding 1-year local control (LC) and RN rates in the preoperative and postoperative settings. METHODS AND MATERIALS: Population, Intervention, Control, Outcomes, Study Design/Preferred Reporting Items for Systematic Reviews and Meta-analyses and Meta-analysis of Observational Studies in Epidemiology guidelines were used to select articles in which patients had "large" brain metastases (>4 cm3 or >2 cm in diameter) solely treated with preoperative or postoperative SRS and 1-year LC and/or rates of RN reported. Radiosurgery was stratified by timing: preoperatively or postoperatively. Random effects meta-analyses using timing of SRS relative to surgery as covariates were conducted. Meta-regression and Wald-type tests were used to determine the effect of increasing tumor size on the summary estimate, where the null hypothesis was rejected for p < 0.05. RESULTS: Fifteen studies were included (of 314 screened), published between 2012 and 2018 with 854 brain metastases. Preoperative SRS was delivered in 229 lesions. The 1-year LC random effects estimate was 79.1% (95% confidence interval [CI]: 55.9–95.0%; *I2* = 80%) for preoperative SRS and 80.5% (95% CI: 66.3–91.5%; *I2* = 93%) for postoperative SRS (p=0.9). Radionecrosis incidence random effects estimate was 2.1% (95% CI: 0.1–8.6%; *I2* = 36%) for preoperative SRS and 6.3% (95% CI: 1.1–15.4%; *I2* = 90%) for postoperative SRS (p=0.52). CONCLUSIONS: Rates of 1-year LC and RN incidence are similar after preoperative SRS as compared to postoperative SRS for large brain metastases. Results from ongoing prospective clinical trials studying preoperative SRS are important to further investigate these two techniques.

MLTI-08. AN EXCEPTIONAL INTRACRANIAL RESPONSE TO REPEAT RADIATION AND IMMUNOTHERAPY IN A PATIENT WITH METASTATIC, POORLY DIFFERENTIATED ADENOCARCINOMA OF THE LUNG

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We report an unusual case of a long-term survivor of metastatic, poorly differentiated adenocarcinoma of the lung (EGFR- ALK-) who developed intracranial disease after definitive treatment of a stage IIIB lung cancer. He received a complex course of RT which began with SRS to his intracranial disease in 2012 and included: brainstem (pontine) mass, left parietal mass, left frontal, left lateral temporal, and left insular lesions. The left temporal mass progressed and was resected. Subsequently, SRS was given to a right anterior frontal lesion. Additional SRS was given to progressive right superior frontal mass & left temporal tumor bed was given fractionated RT to the left temporal tumor bed. Later, he developed bilateral cerebellar masses and right-sided progression. More SRS was given to right frontal area, and then to bilateral cerebellar lesions. Surprisingly, he did well neurologically until seizures developed. His repeat biopsy was sent for NGS and noted to be PDL1+, APC mutated, and KRAS mutated. This gentleman was started on pembrolizumab in May 2016. Due to colitis, his therapy stopped in January 2017. His colitis progressed such that immunotherapy could not be restarted. Now, after observation only for the past 2.5 years. his disease has disappeared. He is doing well neurologically. We propose that the use of radiation and immunotherapy worked to produce an exceptional, durable response.

MLTI-09. UNDERWEIGHT AND WEIGHT LOSS ARE PREDICTORS OF POOR OUTCOME IN PATIENTS WITH BRAIN METASTASIS

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BACKGROUND: Despite increased risk of comorbidities, overweight may be associated with improved outcome in patients with metastatic cancer. Conversely, tumor cachexia has been identified as a negative predictor of outcome in patients with brain metastasis (BM) from lung cancer. Here we evaluate the association of abnormal body mass index (BMI) and weight change with outcome in patients with BM from different primary tumors. METHODS: Patients with a diagnosis of BM diagnosed and treated at the University Hospital Zurich (n=703) were assessed for associations of BMI, weight change, comorbidities and survival. RESULTS: Compared with patients with normal BMI of 18.5–24.9 kg/m2 who experienced a median overall survival (OS) of 9 months (95% confidence interval (CI) 7.5–10.5), OS was inferior in patients with BMI< 18.5 kg/m2 (OS 6 months, 95% CI 1.6–10.3, p=0.04), but superior in patients with BMI >25 kg/m2 (OS 13 months, 95% CI 11.0–15.0; p=0.033). For patients with documented weight course (n=173 of 703), we report a median relative weight loss of 5% within the first 6 months of BM diagnosis (95% CI 3.3–6.5). Reduction above the median was associated with an unfavorable outcome in this subgroup (weight loss ≧5% 22.0 months, 95% CI 19.2–24.8; weight loss < 5% 14.0 months, 95% CI 11.9–16.). CONCLUSIONS: Despite being associated with a worse cardiovascular risk profile, high BMI is associated with preferable and underweight with poor outcome in BM patients. Conversely, weight loss above median may be a predictor of poor outcome. Future studies need to address the question whether vigorous treatment of tumor cachexia, e.g. by specific nutrition management, might improve outcome of BM patients. In contrast, regimens that are associated with weight loss such as ketogenic diet may be detrimental.

MLTI-10. ESTABLISHMENT OF A MULTIDISCIPLINARY BRAIN METASTASIS CLINIC TO FACILITATE PATIENT-CENTERED CARE AND COORDINATED RESEARCH

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BACKGROUND: ~30% cancer patients develop brain metastases (BM), reflected by ~1600 BM patients treated at MD Anderson Cancer Center annually. With advances in systemic therapy and extracranial disease control, BM is a growing challenge. Multi-disciplinary BM management is critical and complex requiring coordination of multiple oncology sub-specialties. There is limited data on pragmatic clinic models to streamline and advance care. METHODS: Recognizing deficiency in BM treatment and research, a steering committee was formed at MDACC to establish an interdisciplinary BM clinic (BMC), with a multi-disciplinary BM research retreat held in 2016. The goal of BMC was to centralize patient referrals, improve patient outcomes and experience, and advance research by developing clinical trials and biomarker discovery programs. Meetings were held to address BMC format, workflow, EMR integration, data collection infrastructure, and staffing model. RESULTS: MDACC BMC clinic opened in 01/2019 with two half-day clinics staffed by neurosurgery, neuro-radiation oncology, neuro-radiology and medical/neuro oncology. A dedicated advanced practice provider screens the referrals according to a well-developed algorithm. A multidisciplinary conference is held immediately before each clinic where patient images are reviewed, cases are discussed and consensus recommendations are developed. The treatment plan and follow up appointments are arranged at the completion of the clinic visit to expedite care.