Clinic, Rochester, MN, USA, [13]McMaster University, Hamilton, ON, Canada, [14]University of Oklahoma, Oklahoma City, OK, USA, [15]Wayne State University, Detroit, MI, USA, [16]Vanderbilt University, Nashville, TN, USA

PURPOSE: RTOG 0933 demonstrated benefits to memory following HA-WBRT, supporting the hypothesis of hippocampal radiosensitivity and associated memory specificity. However, some patients demonstrated cognitive decline, suggesting mechanisms outside hippocampal radiosensitivity playing a role. WMI has been implicated in RT-induced cognitive decline. This secondary analysis explored the relationship between pre-treatment WMI and memory following HA-WBRT. METHODS AND MATERIALS: 113 patients received HA-WBRT. Standardized cognitive assessments were performed at baseline, 2, 4, and 6 months. The primary endpoint was Hopkins Verbal Learning Test Delayed Recall (HVLT-DR) at 4 mos. Secondary endpoints included HVLT Total Recall (HVLT-TR) and Recognition (HVLT-Recog). Of 113 patients, 34 underwent pre-treatment and 4-month post-treatment HVLT testing and pre-treatment post-contrast volumetric T1 and axial T2/FLAIR MRI. Volumetric analysis of metastatic disease burden and disease-unrelated WMI was conducted on the pre-treatment MRI. Correlational analyses were performed examining the relationship between pre-treatment WMI and HVLT outcomes following HA-WBRT. RESULTS: Correlation was found between larger volumes of pre-treatment WMI and decline in HVLT-Recog (r=.54, p< .05) and a correlational trend was observed between larger volume of pre-treatment WMI and decline in HVLT-DR (r=.31, p=.08). Patients with higher pre-treatment disease burden experienced a greater magnitude of stability or positive shift in HVLT-recall and –delayed recall following HA-WBRT. (r=-.36 and r=-.36, p's < .05), compared to the magnitude of stability/positive shift in those with lesser disease burden. CONCLUSION: In patients receiving HA-WBRT, pre-treatment-WMI predicts memory decline, suggesting white matter integrity pre-treatment contributes to the pathogenesis of post-WBRT cognitive toxicity independent of hippocampal stem cell radiosensitivity. Less decline or improvement in HVLT following HA-WBRT for patients with higher pre-treatment intracranial metastatic burden supports the importance of WBRT-induced intracranial control on cognition. These imaging biomarkers for cognitive toxicity will be further explored on NRG CC001 and CC003, phase III trials of WBRT with or without HA.

RADI-05. FRACTIONATED TREATMENT OF BRAIN METASTASES WITH GAMMA KNIFE ICON

Jameson Mendel, Ankur Patel, Toral Patel, Robert Timmerman, Tu Dan, Lucien Nedzi, and Zabi Wardak; UT Southwestern Medical Center, Dallas, TX, USA

PURPOSE/OBJECTIVE(S): Stereotactic radiosurgery with Gamma Knife is a common treatment modality for patients with brain metastasis. The Gamma Knife ICON allows for immobilization with an aquaplast mask, permitting fractionated treatments. We describe one of the first experiences utilizing this technique with brain metastasis and evaluate outcomes. MATERIALS/METHODS: From June 2017 to November 2018, 29 patients with 43 separate intracranial lesions were treated with fractionated stereotactic radiotherapy using the gamma knife ICON at a single institution. Patients received between 20–30 Gy in 3–5 fractions with no margin over the course of 5 to 23 days. Local control was physician assessed. Local failure over time was modeled using cumulative incidence; lesions were censored at last radiographic follow up. RESULTS: Median tumor volume and prescription isodose was 7.7 cm^3 (range 0.3–43.9) and 50% (range 40–65), respectively. Median radiographic follow-up was 7 months and median survival was 9 months. Radiation necrosis occurred in 3/3 patients treated with 27 Gy in 3 fractions, one requiring therapeutic resection. Incidence of local failure for all treated lesions was 9% at 1 year. Tumor volume >7 cm^3 was associated with local failure on univariate analysis (p=0.025). 100% (2/2) lesions treated with 20 Gy in 5 fractions developed local recurrence. CONCLUSION: Fractionated stereotactic radiotherapy with the Gamma Knife ICON provides excellent local control for small and large brain metastases with minimal toxicity. Tumors >7 cm^3 should receive at least 30 Gy in 5 fractions for optimal control. Treatment with 27 Gy in 3 fractions appears to have high rates of treatment related toxicity and should be avoided.

RADI-06. SINGLE- VERSUS MULTI-FRACTION STEREOTACTIC RADIOSURGERY FOR BRAINSTEM METASTASES

Corbin Jacobs, Kehali Woldemichael, Hannah Williamson, Zhanerke Abisheva, Elizabeth Howell, Jihad Abdelgadir, Cosette Dechant, Scott Floyd, Peter Fecci, John Kirkpatrick, Justus Adamson, and Jordan Torok; Duke University Medical Center, Durham, NC, USA

BACKGROUND: For intracranial metastases with planning target volume (PTV) overlap of the brainstem (BSmet), the radiosurgical dose-fractionation that optimizes the therapeutic window is unknown. MATERIALS/METHODS: A retrospective review of brain metastases (BM) with/without BSmets treated with single-fraction stereotactic radiosurgery (SRS) or hypofractionated (2–5 fractions) radiosurgery (HF-SRS) between 2012–2016 was performed. Brainstem biologically effective doses (BED) and single-fraction equivalents of brainstem V10/V12 were calculated using $\alpha/\beta=3$. Characteristics were compared between patients with/without BSmet and between SRS/HF-SRS cohorts using Wilcoxon rank sum, chi-square, or Fisher's exact tests. Radiographic progression (RP) was assessed in patients with post-treatment contrasted MRI and defined as BSmet enlargement regardless of etiology (progression, radionecrosis, indeterminate). Kaplan-Meier estimates were compared between cohorts using log-rank test. RESULTS: 634 SRS/HF-SRS courses were identified, of which 59 (9.3%) treated ≥1 BSmet in 55 patients. BSmets occurred more commonly in patients with >4 BM (31% vs 10%, p< 0.001) and intracranial recurrence (39% vs 20%, p=0.003). BSmets were treated in 1 (22/59; 37%), 2 (1/59; 2%), or 5 (36/59; 61%) fractions. Age, KPS, and primary tumor site were balanced between SRS/HF-SRS cohorts. The HF-SRS cohort had significantly larger BSmet PTV (median 1.39cc vs 0.39cc, p=0.021), marginal dose (median 25Gy vs 15Gy, p< 0.001), brainstem V10 (median 1.60cc vs 0.47cc, p< 0.001), brainstem V12 (median 0.78cc vs 0.06cc, p< 0.001), and mean brainstem BED (median $9.27Gy_3$ vs $6.55Gy_3$, p=0.019). The SRS cohort was more likely to have prior whole brain radiotherapy (50% vs 14%, p=0.005) and restart steroids post-treatment (78% vs 41%, p=0.019). RP occurred in 6/17 vs 2/25 patients in the SRS vs HF-SRS cohorts, respectively (p=0.045). HF-SRS trended to higher freedom from RP (93% vs 74% @12mo; p=0.072). There was no overall survival difference (p=0.36). CONCLUSIONS: HF-SRS was associated with decreased RP and decreased likelihood of restarting steroids despite treating larger BSmets.

RADI-07. GAMMA KNIFE RADIOSURGERY FOR SMALL CELL LUNG CANCER: PROGNOSTIC FACTORS INCLUDING ADDITIONAL LESIONS IDENTIFIED ON THE DAY OF RADIOSURGERY

Kevin Chaung, Michael Kharouta, Stephen Shamp, Mitchell Machtay, Andrew Sloan, Aashish Bhatt, David Mansur, Tiffany Hodges, Yuxia Zhang, and Serah Choi; University Hospitals, Cleveland OH, USA

OBJECTIVES: Prophylactic cranial irradiation (PCI) and whole brain radiation (WBRT) are standard of care for intracranial disease in small cell lung cancer (SCLC) patients. We sought to identify predictors of overall survival (OS) in SCLC patients treated with salvage Gamma Knife radiosurgery (GKRS) for brain metastases after prior WBRT or PCI. METHODS: Retrospective analyses were conducted on 26 SCLC patients treated with GKRS at one institution between May 2010 and June 2018. Factors predictive of OS were analyzed using Cox proportional hazards regression and Wilcoxon sum-rank testing. RESULTS: Median follow-up and median OS following GKRS was 6.6 mos (range 0.7–24.2 mos). Median OS was 21.4 mos from initial diagnosis (range 7.3–49.3 mos). Presence of extracranial metastases at the time of GKRS was not significantly associated with median OS after GKRS (5.8 mos for patients with extracranial metastases vs 7.2 mos for patients without, p=0.425). Mean number of lesions was 2.7 (range 1–10) on diagnostic brain MRIs and 4.1 (range 1–12) on GKRS planning MRIs. Eleven patients (42%) had the same number of lesions between diagnostic MRI and GKRS MRI, and 15 patients (58%) had additional lesions on the GKRS MRI. Number of lesions treated and total tumor volume were not associated with median OS. Patients who had additional lesions on GKRS MRI compared to diagnostic MRI had lower median OS from initial diagnosis of SCLC (29.9 mos vs 18.1 mos, p=0.0182) and a trend toward lower median OS from time of GKRS (7.3 mos vs 4.8 mos, p=0.0547) compared to patients who did not have additional lesions. CONCLUSIONS: Finding additional brain metastases on GKRS planning MRIs is associated with decreased OS in SCLC patients treated with salvage GKRS. Presence of extracranial metastases at the time of GKRS and number or total volume of brain metastases were not associated with OS.

RADI-08. A SURVEY BASED STUDY OF BRAIN METASTASES MANAGEMENT FOR PATIENTS WITH NON-SMALL CELL LUNG CANCERS OR MELANOMA

Chin Heng Fong[1], Natasha Leighl[1], Marcus Butler[1], Mark Doherty[1], Timothy Kruser[2], and David Shultz[1]; [1]University Health Network, Toronto, ON, Canada, [2]Northwestern University, Chicago, IL, USA

INTRODUCTION: The standard of care for 1–4 brain metastases (BrM) is stereotactic radiosurgery (SRS), whereas whole brain radiation remains the standard treatment for extensive BrM, and surgical resection is appropriate in certain scenarios. Some newer systemic therapies such as tyrosine kinase inhibitors and immunotherapy have impressive CNS activity and are used by some practitioners either alone or in combination with other modalities as first-line treatment for BrM. We conducted a survey to ascertain current real-world practices for the treatment of BrM from NSCLC and melanoma. OBJECTIVES: Our study aimed to assess practice patterns of oncologists who treat BrM from NSCLC or melanoma. We also investi-

gated the extent to which various clinical factors influence decision making. METHODOLOGY: We created 2 sets of surveys: one for Medical-/Clinical-/Neuro- oncologists and another for Radiation oncologists/Neurosurgeons. Surveys were conducted online or on-line. Following administration, data was tabulated and analyzed. Statistical analyses were performed using Fisher's exact test. RESULTS: Of 361 respondents, 250 were Radiation oncologists/Neurosurgeons, and 111 were Medical-/Clinical-/Neuro- oncologists. For patients with 1–3 brain lesions, all < 2cm, 34% of respondents recommended systemic therapy alone as first-line treatment. In contrast, only 15% recommend systemic therapy alone for >9 lesions, at least one > 2cm. Medical-/Clinical-/Neuro- oncologists were more likely to recommend systemic therapy alone compared to Radiation oncologists/ Neurosurgeons for 1–3 lesions, all < 2cm (53% vs. 28%, p< .0001). For patients with > 9 BrM, one >2cm diameter, Medical-/Clinical-/Neuro- oncologists were not significantly more likely to recommend systemic therapy alone (20% vs 13%, p=.11). DISCUSSION: Our results reveal that significant numbers of physicians recommend systemic therapy alone as first-line therapy in BrM and that management decisions correlate with a physician's type of practice. These findings underscore the need for prospective clinical trials to direct appropriate BrM management.

RADI-09. DEFINING PROGRESSION IN PATIENTS TREATED WITH TEN OR MORE BRAIN METASTASES FOLLOWING STEREOTACTIC RADIOSURGERY

Sirisha Devi Viswanatha[1], Zaker Rana[1], Matthew Ehrlich[2], Michael Schulder[2], and Anuj Goenka[1]; [1]Northwell Department of Radiation Medicine, Lake Success, NY, USA, [2]Zucker School of Medicine at Hofstra/Northwell, Lake Success, NY, USA

BACKGROUND: An increasing trend has been to elect for Stereotactic Radiosurgery (SRS) for the treatment of brain metastases. Progression following treatment is typically defined as a 20% increase in the initial lesion volume treated. Challenges in defining progression can arise as the reported incidence of pseudoprogression or radiation necrosis following treatment ranges from 5%-30%. The purpose of this study was to assess patterns of failure in patients treated with 10 or more brain metastases. METHODS: From March 2014 to April 2018, fifty-five patients with 10 or more total brain metastases were retrospectively reviewed following frame-based radiosurgery to a dose of 12–20 Gy. Post-treatment MRI scans were used to assess tumor response in 3 month intervals. Tumor control was defined as tumor volume ≤ 1.2 times the baseline tumor volume at each measured interval. RESULTS: Fifty-five patients received 75 total radiosurgery treatments to 692 tumors. Forty patients received synchronous treatment, while 15 received metachronous treatment. 20 patients (36%) and 72 tumors (10%) experienced progression following treatment. 46 tumors were larger after first MRI in 15 patients (28%). Of these 15 patients, eight had complete resolution in 15 tumors on subsequent scan. Of the eight patients who had resolution, six patients received immunotherapy during and after treatment and all but one patient saw an initial increase >100% of their initial tumor volume. Median overall survival was 11 months. Univariate analysis revealed an association between larger brain volumes irradiated with 12 Gy and decreased overall survival ($p < 0.05$). CONCLUSION: It is important to consider tumor growth velocity and concurrent therapy when assessing true progression after SRS treatment of brain metastases.

RADI-10. THERAPEUTIC EFFECTS OF FSRS IN 44 CASES OF BRAIN METASTASES OF NSCLC WITH A MAXIMUM DIAMETER ≥ 4CM AND ANALYSIS OF ITS PROGNOSTIC FACTORS

Lai Mingyao, Junjie Zhen, Juan Li, Jiangfen Zhou, Qingjun Hu, Minting Ye, Shaoqun Li, Xiao Xiao, and Lichao Wang; Guangdong Sanjiu Brain Hospital, Guangzhou, China

OBJECTIVE: To analyze the therapeutic effects of fSRS on brain metastases of NSCLC with a maximum diameter ≥ 4 cm, and explore the prognostic factors. METHODS: A retrospective analysis was conducted on the clinical data of 44 cases of brain metastases of NSCLC with a maximum diameter ≥ 4 cm in Guangdong Sanjiu Brain Hospital from January 2006 to December 2016. RANO criteria were adopted for imaging evaluation at 3 months after completion of radiotherapy. One- and 2-year survival rates were calculated and the differences in survival rates between groups were analyzed with Log-rank test. Kaplan-Meier method was used in univariate analysis to investigate the effects of KPS, RPA classification, number of metastases, total lesion volume, systemic treatment and surgery on prognosis; and Cox regression model in multivariate analysis. RESULTS: The postoperative imaging evaluation showed that there were 5 cases of CR, 20 of PR, 12 of SD and 7 of PD. The median PFS, OS, 1- and 2-year survival rates were 6 months, 16 months, 65.9% and 20.5%, respectively. KPS, RPA classification, number of metastases and surgery had no significant correlations with prognosis. However, systemic treatment and the maximum lesion volume <28.3cc were considered as favorable factors related to prognosis (P=0.046, 0.027). Moreover, the maximum lesion volume <28.3cc was found to be the independent prognostic factor for the survival (P=0.035). CONCLUSION: Treatment of brain metastases of NSCLC with a maximal diameter ≥4 cm with fSRS is proved to be feasible. The maximum lesion volume is related to prognosis. Systemic treatment (chemotherapy, TKI treatment, etc.) may improve prognosis, but more cases are needed to investigate the prognostic significance.

RADI-11. NRG ONCOLOGY CC001: A PHASE III TRIAL OF HIPPOCAMPAL AVOIDANCE IN ADDITION TO WHOLE-BRAIN RADIOTHERAPY (WBRT) PLUS MEMANTINE TO PRESERVE NEUROCOGNITIVE FUNCTION IN PATIENTS WITH BRAIN METASTASES (BM)

Wolfgang Tomé[1], Snehal Deshmukh[2], Vinai Gondi[3], Paul Brown[4], Jeffery Wefel[5], Terri Armstrong[6], Deborah Bruner[7], Joseph Bovi[8], Clifford Robinson[9], Deepak Khuntia[10], David Grosshans[5], Andre Konski[12], David Roberge[13], Vijayananda Kundapur[14], Kiran Devisetty[15], Sunjay Shah[16], Kenneth Usuki[17], Bethany Marie Anderson[18], Minesh Mehta[19], and Lisa Kachnic[20]; [1]Albert Einstein College of Medicine, Bronx, NY, USA, [2]NRG Oncology, Philadelphia, PA, USA, [3]Northwestern Medicine Cancer Institute, Warrenville, IL, USA, [4]Mayo Clinic, Rochester, MN, USA, [5]UT MD Anderson Cancer Center, Houston, TX, USA, [6]National Cancer Institute, Bethesda, MD, USA, [7]Emory University, Atlanta, GA, USA, [8]Medical College of Wisconsin, Milwaukee, WI, USA, [9]Washington University, St. Louis, MO, USA, [10]Sutter Health, Sacramento, CA, USA, [12]Univerrsity of Pennsylvania, Philadelphia, PA, USA, [13]University of Montreal - CHUM, Montreal, QC, Canada, [14]University of Saskatchewan, Saskatoon, SK, Canada, [15]Wayne State University, Detroit, MI, USA, [16]Christiana Care Health System, Newark, DE, USA, [17]University of Rochester, Rochester, NY, USA, [18]University of Wisconsin, Madison, WI, USA, [19]Miami Cancer Institute, Miami, FL, USA, [20]Vanderbilt University, Nashville, TN, USA

BACKGROUND: NRG CC001, a phase III trial of WBRT+memantine (WBRT+M) with or without Hippocampal Avoidance (HA), sought to assess the neuro-protective effects of lowering the radiation dose received by the hippocampus. METHODS: Patients (pts) with brain metastases were stratified by RPA class and prior radiosurgery/surgery and randomized to either WBRT+M or HA-WBRT+M (30Gy/10 fractions). Standardized neurocognitive function (NCF) tests were performed at baseline, 2, 4, 6, and 12 months (mos.). The primary endpoint was NCF failure, defined as decline using the reliable change index on Hopkins Verbal Learning Test-Revised, Trail Making Test, or Controlled Oral Word Association. Cumulative incidence estimated NCF failure (death without NCF failure was competing risk); between-arms differences tested using Gray's test. Deterioration at each collection time point was tested using a chi-square test. Patient-reported symptoms were assessed using the MD Anderson Symptom Inventory with Brain Tumor module and analyzed using mixed effects models and t-tests. RESULTS: From 7/2016 to 3/2018, 518 patients were randomized. Median follow-up was 7.9 mos. HA-WBRT+M was associated with lower NCF failure risk (adjusted HR=0.74, p=0.02) due to lower risk of deterioration in executive function at 4 mos. (p=0.01); and encoding (p=0.049) and consolidation (p=0.02) at 6 mos. Age≤61 predicted for lower NCF failure risk (HR=0.60, p=0.0002); non-significant test for interaction indicated independent effects of HA and age. Patient-reported fatigue (p=0.036); difficulty speaking (p=0.049); and problems remembering things (p=0.013) at 6 mos. favored the HA-WBRT+M arm. Imputation models accounting for missing data also favored the HA-WBRT+M arm for patient-reported cognition (p=0.011) and symptom interference (p=0.008) at 6 mos. Treatment arms did not significantly differ in toxicity; intracranial progression or overall survival. CONCLUSIONS: While achieving similar intracranial control and survival; Hippocampal Avoidance during WBRT+M for brain metastases better preserves NCF and patient-reported symptoms. Supported by UG1CA189867 (NCORP) and DCP from the NCI.

RADI-12. LEPTOMENINGEAL FAILURE AFTER PREOPERATIVE VERSUS POSTOPERATIVE RADIOSURGERY

John Fiveash, Kristen Riley, James Markert, Bart Guthrie, Paul Foreman, Richard Popple, Sam Marcrom, Scott Strickler, Christopher Willey, Andrew McDonald, Evan Thomas, John Stewart, and Markus Bredel; University of Alabama at Birmingham, Birmingham, AL, USA

INTRODUCTION: Postoperative stereotactic radiosurgery (postop SRS) is potentially complicated by difficulty defining the target volume and the risk of leptomeningeal seeding at the time of surgery. It is hypothesized that preop SRS may render cells less viable to disseminate in the leptomeningeal space. This retrospective study compares the leptomeningeal dissemination (LMD) rate for preop versus postop radiosurgery METHODS: We identified 140 patients with brain metastases who underwent resection and radiosurgery at the University of Alabama at Birmingham including 91 postop patients (2005–2015) and 49 preop patients (2011–2018). The preop group included 19 patients enrolled in a phase I trial of preoperative