systems in study documentation. Systematic evaluation of quality score adherence will allow us to identify common flaws in this field for enabling translation of models into clinical workflow.

## RADIATION

### RADI-01. CYSTIC BRAIN METASTASES MANAGED WITH RESERVOIR PLACEMENT AND STEREOTACTIC RADIOSURGERY

David Park, Michael Schulder; North Shore University Hospital, Manhasset, NY, USA

BACKGROUND: Stereotactic radiosurgery (SRS) has become a mainstay of treatment for patients with metastatic brain tumors. However, metastatic tumors with a large cystic component often exceed the size limit for safe and effective SRS. In such cases, surgical resection may not be the preferred first method of treatment, due to tumor location, patient co-morbidities, and patient preference. In such cases volume reduction by cyst aspiration followed by SRS may be a preferred option. METHODS: Seven patients were treated with this method. We performed reservoir insertion for the aspiration of cystic component in each patient and followed that with outpatient SRS. RESULTS: Mean overall volume reduction from this treatment method was 80% (range 46.5–94.9). Mean volume reduction from the cyst aspiration alone was 60.7% (range 3.5–90.9), and after SRS a further 71.6% (range 34.6–94.4), accounting for some cyst reaccumulation between the time of surgery and SRS. The interval between those two procedures were 24 days on average (range 11–58 days). Repeat reservoir aspiration was done a total of 10 times in 5 patients. CONCLUSION: Cyst aspiration with reservoir placement followed by SRS is a good option for patients with large cystic brain metastases. The reservoir allows for repeat aspiration if needed. Catheter placement at the center of the cyst, and SRS within 2–3 weeks of surgery, can maximize the likelihood of a successful outcome.

### RADI-02. HIPPOCAMPAL-SPARING WHOLE BRAIN VOLUMETRIC MODULATED ARC THERAPY (VMAT) PLANNING IN MONACO: A "HOW-TO" NOT PULL YOUR HAIR OUT.

Matthew Goss[1], Rochelle Rowles[1], Lisa Spanovich[1,2], Rodney Wegner[1], Shaakir Hasan[2], Zachary Horne[1]; [1]Allegheny Health Network Cancer Institute, Pittsburgh, PA, USA, [2]New York Proton Center, New York, NY, USA

PURPOSE: NRG-CC001 recently reported positive results on hippocampal-sparing IMRT (HS-IMRT) in conjunction with memantine for the reduction in cognitive decline compared to conventional whole brain radiation therapy. Herein, we report our experience in planning volumetric modulated arc therapy (VMAT) cases in Monaco® with the anticipation of increased utilization of the planning technique for delivery on Elekta linear accelerators. METHODS AND MATERIALS: Twelve patients previously treated with whole brain radiation therapy who would have been eligible for NRG-CC001 were replanned with VMAT HS-IMRT for to a dose of 30Gy/10fx using constraints from the trial. RESULTS: All twelve patients were able to be planned with VMAT and achieve NRG-CC001 dose constraints. Median maximum and D100% to the right and left hippocampi were: 13.37Gy and 13.43Gy, respectively and 8.76Gy and 8.86Gy, respectively. Median coverage of the brain minus the hippocampi with 30Gy was 96.53%. All cases passed quality assurance testing with 3%/3mm and 2%/2mm criterion. CONCLUSIONS: Hippocampal-sparing IMRT whole brain radiation therapy can be feasibly planned with VMAT technique in Monaco® and delivered on Elekta linear accelerators.

### RADI-03. A STRATEGY TO PERSONALIZE THE USE OF RADIATION IN PATIENTS WITH BRAIN METASTASIS BASED ON S100A9-MEDIATED RESISTANCE

Lauritz Miarka[1], Catia Moteiro[1], Celine Dalmasso[2], Coral Fustero-Torre[3], Natalia Yebra[1], Aisling Hegarty[4], Stephen Keelan[4], Yvonne Goy[5], Malte Mohme[6], Eduardo Caleiras[7], Vareslija Damir[4], Leonie Young[4], Riccardo Soffietti[8], Jose Fernández- Alén[9], Guillermo Blasco[9], Lucia Alcazar[9], Juan Manuel Sepúlveda[10], Angel Perez[11], Aurelio Lain[12], Aurore Siegfried[13], Harriet Wikman[14], Elisabeth Cohen-Jonathan Moyal[2], Manuel Valiente[1]; [1]Brain Metastasis Group, CNIO, Madrid, Spain, [2]Radiation Oncology Department, Institut Claudius Regaud, IUCT-Oncopole, Toulouse, France, [3]Bioinformatics Unit, CNIO, Madrid, Spain, [4]Endocrine Oncology Research Group, RCSI University of Medicine and Health Sciences, Dublin, Ireland, [5]Radiation Oncology Department, UKE, Hamburg, Germany, [6]Neurosurgery Department, UKE, Hamburg, Germany, [7]Histopathology Unit, CNIO, Madrid, Spain, [8]Department of Neuro-Oncology, University and City of Health and Science Hospital, Turin, Italy, [9]Department of Neurosurgery, Hospital La Princesa, Madrid, Spain, [10]Neuro-Oncology Unit, Hospital Universitario [12] de Octubre, Madrid, Spain, [11]Neurosurgery Unit, Hospital Universitario [12] de Octubre, Madrid, Spain, [12]Neuropathology Unit, Hospital Universitario [12] de Octubre, Madrid, Spain, [13]Anatomopathology Department, CHU Toulouse, IUCT-Oncopole, Toulouse, France, [14]Department of Tumor Biology, UKE, Hamburg, Germany

Finding effective treatment options for patients with brain metastasis remains an unmet need. Given the limitations imposed by the blood-brain-barrier for systemic approaches, radiotherapy offers a superior ability to access the brain. While clinical practice recently adapted the use of stereotactic radiosurgery (SRS), Whole-Brain-Radiotherapy (WBRT) continuous to be an important treatment option, since many patients present with multifocal lesions or bad performance scores, rendering them ineligible for SRS. Unfortunately, overall survival of patients remains unaffected by radiotherapy. Despite this clinical data, the molecular mechanisms that allow metastatic cells to resist radiotherapy in the brain is unknown. We have applied WBRT to experimental brain metastasis from lung and breast adenocarcinoma and validated their resistance *in vivo*. An unbiased search to identify potential mediators of resistance identified the S100A9-RAGE-NFkB-JunB pathway. Targeting this pathway genetically reverts the resistance to radiotherapy and increases therapeutic benefits *in vivo*. In two independent cohorts of brain metastasis from lung and breast adenocarcinoma patients, levels of S100A9 correlate with the response to radiotherapy, offering a novel approach to stratify patients according to their expected benefit. In order to make this biomarker also available for brain metastasis patients receiving palliative WBRT without preceding surgery, we complemented our tumor-specimen based approach with the less invasive detection of S100A9 from liquid biopsies. Here, serum S100A9 also correlated with a worse response to WBRT in brain metastasis patients. Furthermore, we have validated the use of a blood-brain-barrier permeable RAGE inhibitor to restore radio-sensitivity in experimental brain metastasis models *in vivo* and in patient-derived organotypic cultures of radio-resistant brain metastasis *ex vivo*. In conclusion, we identified S100A9 as a major mediator of radio-resistance in brain metastasis and offer the molecular framework to personalize radiotherapy by exploiting it as a biomarker and as a therapeutic target, thus maximizing the benefits for the patient.

### RADI-04. STEREOTACTIC RADIOSURGERY IN ALVEOLAR SOFT PART SARCOMA BRAIN METASTASIS

Jia Xu Lim[1], Bengt Karlsson[2], Angela Pang[3], Vellayappan Balamurugan[3], Vincent Nga[3]; [1]National Neuroscience Institute, Singapore. [2]National University of Singapore, Singapore, [3]National University Hospital, Singapore

BACKGROUND: Alveolar soft part sarcoma (ASPS), although rare, has the highest incidence of brain metastasis amongst all sarcomas. Stereotactic radiosurgery (SRS) has been shown to be a well tolerated and effective treatment of intracranial sarcomatous metastasis. However, there is a paucity of published literature that guides radiation therapy in this condition. METHODS: This is a single centre retrospective review of all ASPS patients with intraparenchymal brain metastasis in our centre treated with stereotactic radiosurgery (SRS). SRS dosing is dichotomised into high and low dose (≥25 Gy and <25 Gy respectively) and outcomes such as local recurrence (LR) and radiation effects are noted. Successful treatment was defined as a lesion that regressed, is stable, or has less than 25% increase in tumour volume. Local recurrence (LR) was defined as increase in tumour volume by more than 25% during follow up. RESULTS: There were three patients with 11 ASPS metastatic brain lesions, one of which underwent retreatment. Each lesion was followed up for a mean duration of 12 months (range: 5 – 22 months). Five lesions treated with a high dose regime and six lesions were given low dose. Lesions treated with high dose SRS experienced significantly less LR (20% vs 83.3%, OR 20.0 [95%CI 0.93 – 430), p = 0.036) with no increase in undue symptomatic radiation effects. Retreatment of lesions with LR after initial SRS using a low dose regime was successful, albeit only in the single recurrent lesion. CONCLUSIONS: We conclude that SRS can be used as a first line treatment for ASPS brain metastasis that are not surgically accessible and that using a high dose for treatment is effective and safe. Multicentre collaborative studies can be performed to validate this claim.

### RADI-05. METASTATIC NEOPLASM VOLUME KINETICS FOLLOWING TWO-STAGED STEREOTACTIC RADIOSURGERY

Ethan Damron[1], Antonio Dono[1], Hatim Chafi[2], Magda Martir[2], Tse-Kuan Yu[3,2], Shariq Khwaja[1,2], Mark Amsbaugh[1,2], Nitin Tandon[1,2], Yoshua Esquenazi[1,2], Angel Blanco[1,2]; [1]Vivian L. Smith Department of Neurosurgery, McGovern Medical School, the University of Texas Health Science Center at Houston, Houston, TX, USA, [2]Memorial Hermann Hospital – Texas Medical Center, Houston, TX, USA, [3]Oncology Consultants, Houston, TX, USA

INTRODUCTION: Multisession staged stereotactic radiosurgery (2-SSRS) represents an alternative approach for management of large brain metastases (LBMs), with potential theoretical advantages over fractionated SRS and rep-

resents an alternative to surgery in poor surgical candidates. We aimed to investigate the clinical efficacy and safety of 2-SSRS in patients with LBMs. METHODS: LBMs of patients treated with 2-SSRS between 2014 and 2020 were evaluated. Demographic, clinical, and radiologic information was obtained. Volumetric measurements at first SSRS, second SSRS, and follow-up imaging studies were obtained. RESULTS: Twenty-six patients with 28 LBMs were included in the study. Fifteen patients (58%) were male. Median age at 2-SSRS was 61 years (range: 31–84). Median marginal doses for first and second SSRS were 15 Gy (range: 12–18 Gy) and 15 Gy (range: 12–16 Gy), respectively. Median duration between sessions was 32 days. Two patients (8%) failed to receive their second SSRS due to local progression. Median tumor volumes at first SSRS, second SSRS, 3-month follow-up, and 6-month follow-up were 8.7 $cm^3$ (range: 1.5–34.7 $cm^3$), 3.3 $cm^3$ (range: 0.8–26.1 $cm^3$), 1.7 $cm^3$ (range: 0.2–10.1 $cm^3$), and 1.4 $cm^3$ (range: .04–20.7 $cm^3$), respectively. The median absolute and relative decrement between S-SRS sessions was 3.7 $cm^3$ (range: 2.8–16.5 cm3) and 49.5% (range: 17.1- 87.1%), respectively. Overall, 26 of the 28 lesions (93%) demonstrated early local control following the first SSRS with 18 lesions (69%) demonstrating a decrease in volume of >30% and 3 lesions (12%) remaining stable. Six lesions (23%) showed disease progression. There were no grade 3 adverse events. CONCLUSIONS: Our study supports the effectiveness and safety of 2-SSRS as a treatment modality for patients with large, symptomatic brain metastases, especially in non-surgical candidates. The local failure rate and low occurrence of adverse effects are comparable to other staged radiosurgery series.

### RADI-06. GAMMA KNIFE SURGERY FOR BRAIN STEM METASTASES

Choo Heng Tan[1,2], Bengt Karlsson[1], Shilin Wang[1], John J.Y. Zhang[1], Yvonne Ang[1], balamurugan Vellayappan[3], Kejia Teo[1], Vincent D.W Nga[1], Sein Lwin[1], Tseng Tsai Yeo[1]; [1]National University Hospital, Singapore. [2]National Neuroscience Institute, Singapore. [3]National Institute of Cancer, Singapore

INTRODUCTION: Gamma Knife Surgery (GKS) is widely used for treatment of brainstem metastases (BSMs) with or without whole bran radiation therapy (WBRT). We hypothesized that BSMs treated with GKS using lower doses and omitting WBRT result in acceptable tumor control rates and low complication rates. METHODS: A retrospective single center study was performed to investigate the outcome following GKS of BSMs. All 33 patients with follow-up information treated with GKS for 39 metastases located in the cerebral peduncle, midbrain, pons or medulla oblongata were included in the study. The median treatment dose, defined as the lowest dose to 95% of the tumor volume, was 18 Gy. The tumor control rate as well as the survival time were related to a number of patients, tumor and treatment parameters. RESULTS: The local tumor control rate was 100% at one year and 89% at five years, and the overall median survival was 17 months. A good performance status and a treatable extracranial disease were favorably related to survival time. Two complications were observed, one lethal hemorrhage at the day of the treatment and one transient complication three months following GKS, resulting in a 6% complication rate at five years. Four of the 10 patient with symptomatic BSM improved clinically after GKS, while six remained unchanged. CONCLUSIONS: High local control and a low complication rates can be achieved using GKS for BSMs using lower doses as compared to brain metastases in other locations.

### RADI-07. INDIVIDUALIZED NOMOGRAM FOR PREDICTING SURVIVAL OF PATIENTS WITH BRAIN METASTASES AFTER STEREOTACTIC RADIOSURGERY

Lei Wen, Changguo Shan, Mingyao Lai, Zhaoming Zhou, Linbo Cai; Guangdong Sanjiu Brain Hospital, Guangzhou, China

BACKGROUND: Given the increasing use of *stereotactic radiosurgery* (SRS) for brain metastases (BM), there is an emerging need for more precise assessment of survival outcomes after SRS, especially in the modern targeted therapy era. METHODS: Patients with BM and treated by SRS were eligible in this study. Primary endpoint was overall survival (OS). Cox models were used to identify independent prognostic factors. Survival predictive nomogram was developed and evaluated by Concordance-index (C-index), area under the curve (AUC) and calibration curve. RESULTS: From January 2016 to December 2019, a total of 356 BM patients were eligible. Median OS was 17.7 months (95%CI 15.5–19.9) and actual OS at 1- and 2-year measured 63.2% and 37.6%, respectively. Nomogram for OS was developed by incorporating four independent prognostic factors: *Karnofsky Performance Score*, cumulative tumor volume, driver gene mutation status and serum *lactate dehydrogenase*. The nomogram was validated in a separate cohort demonstrated a well calibration and good discriminative ability (C-index=0.780, AUC=0.784). The prognostic accuracy of the nomogram (0.792) was considerably enhanced compared with classical prognostic indices, i.e., GPA (0.708), RPA (0.587) and SIR (0.536). Kaplan-Meier curves showed significant difference of OS among stratified low-, median- and high-risk groups ($P$ < .001). CONCLUSION: In conclusion, we developed and validated an individualized prognostic nomogram by integrating physiological, volumetric, clinical chemistry and molecular biological surrogates. This nomogram, should be validated by independent external study, has a potential to facilitate more precise risk-stratifications to guide personalized treatment for BM.

### RADI-08. ELUCIDATING THE ELECTROPHYSIOLOGY OF INTRAOPERATIVE RADIOTHERAPY – EXPERIENCE FROM TWO CASES

Ugur Sener, Aman Dabir, Christopher Cifarelli; West Virginia University, Morgantown, WV, USA

Brain metastases require multimodality treatment, often combining surgical resection, radiation therapy, and individualized systemic pharmacotherapy based on oncogenic drivers. Intraoperative radiation therapy (IORT) is an emerging treatment option where radiation is delivered directly to the resection cavity at the time of surgery. We present two patients who underwent electrocorticography (ECoG) during IORT, providing information regarding electrophysiologic safety and tolerability of the technique. In the first case, a 65-year-old woman underwent resection of a hemorrhagic right occipital metastasis from non-small cell lung cancer. IORT was administered over sixteen minutes for a surface dose of 30 Gy. In the second case, a 73-year-old man with underwent resection of a right posterior frontal metastasis from non-small cell lung cancer. IORT was delivered over eleven minutes for a surface dose of 30 Gy. In both cases, a 1x6 contact array of subdural electrodes was placed adjacent to the planned field of radiation. Electrocortigraphy (HFF 70 Hz, TC 0.3 sec, sensitivity 150uV/mm) was obtained from the array two minutes prior to initiation of therapy, during therapy, and two minutes after completion of therapy in both cases. We found that IORT did not induce electrophysiological change in the tissue surrounding it in both cases with no epileptiform or ictal discharges during 20 minutes of ECoG recording around the time radiation therapy, nor did the patients have episodes suggestive of epileptic seizures in the acute post-operative period. One of the patients (case 1) experienced a single epileptic seizure 4 months after IORT, but this was temporally related to a new intraparenchymal hemorrhage and unlikely due to radiation therapy. These two cases illustrate the relative safety of IORT with respect to induction of immediate epileptiform changes within the brain parenchyma.

### RADI-09. CLINICAL FACTORS ASSOCIATED WITH DEATH AFTER RADIOTHERAPY FOR BRAIN METASTASES

Divya Natesan, David Carpenter, William Giles, Taofik Oyekunle, Donna Niedzwiecki, Zachary Reitman, John Kirkpatrick, Scott Floyd; Duke University Medical Center, Durham, NC, USA

INTRODUCTION: It can be challenging to accurately identify patients with brain metastases who have very poor prognosis and are unlikely to benefit from radiation (RT). We characterized factors of patients who died within 30 days of receiving RT for brain metastases. METHODS: Patients who received whole brain RT (WBRT) or stereotactic radiosurgery (SRS) for brain metastases between 1/1/2017–9/30/2020 at a single institution were identified. Patient, tumor, treatment, and death variables were collected. Characteristics between those who did and did not die within 30 days were compared using the Wilcoxon Rank-Sum or Chi-Square test. Survival was estimated with Kaplan-Meier method. RESULTS: 636 patients received WBRT (n=117) or SRS (n=519). Median age was 61. Median survival was 6 months (95% CI 5–7 months). 75 (12%) died within 30 days of RT. Patients who died within 30 days had worse median KPS (50 vs 80, p<0.001). A higher proportion who died within 30 days had innumerable intracranial metastases (45% vs 11%, p<0.001), leptomeningeal disease (16% vs 5%, p<0.001), and higher burden of neurologic symptoms at presentation (seizures (12% vs 4%, p=0.003); cranial neuropathies (32% vs 9%, p<0.001); motor/sensory deficits (51% vs 29%, p<0.001); altered mentation (60% vs 26%, p<0.001); headaches (48% vs 30%, p<0.001); steroid use (68% vs 48%, p<0.001)). Patients who died within 30 days had progressive extracranial disease (intrathoracic: 87% vs 50%; spinal: 57% vs 18%; liver/adrenal: 60% vs 24%), p<0.001. More patients who died within 30 days received inpatient RT (39% vs 4%, <0.001) and did not complete RT (24% vs 1%, p<0.001). DISCUSSION: Patients who died within 30 days of RT had worse KPS, intracranial/extracranial disease burden, and neurologic symptoms. Future analyses will assess whether these factors can inform a prognostic model to identify patients with poor prognosis who may be appropriate for supportive care alone.

### RADI-10. IS THERE ANY BENEFIT FOR POST-OPERATIVE RADIATION IN BRAIN METASTASES? A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Nagarjun Bolem, Yu Yang Soon, Sreyes Ravi, Kejia Teo, Vincent Diong Weng Nga, Sein Lwin, Tseng Tsai Yeo, Balamurugan Vellayappan; National University Hospital, Singapore

PURPOSE: The benefits of adding upfront post-operative radiation (either whole-brain or cavity radiation) have been debated, particularly due to the pos-