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### Title

SURG-11. Surgery for control of brain metastases after prior checkpoint inhibitor immunotherapy: a single-center series

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### Authors

Morshed, Ramin

Chung, Jason

Sudhakar, Vivek

et al.

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group produced plasmonics-active gold nanostars (GNS) designed to preferentially accumulate within intracranial tumors and amplify the ablative capacity of LITT while better conforming to tumor boundaries and protecting surrounding tissue. **MATERIALS AND METHODS:** The 12nm GNS were synthesized using reduced HAuCl<sub>4</sub> with Na<sub>3</sub>C<sub>6</sub>H<sub>5</sub>O<sub>7</sub> seeds, mixed with AgNO<sub>3</sub>, C<sub>6</sub>H<sub>8</sub>O<sub>6</sub>, and HAuCl<sub>4</sub>, and coated with polyethylene glycol then functionalized with methoxy PEG thiol. CT-2A glioma cells were intracranially implanted into mice, followed 18 days later by IV injection of GNS. PET-CT was performed at 10-minutes, 24-, and 72-hours post-GNS administration, with autoradiography (AR) and histopathology (HP) on sacrifice after the last scan. To test the impact of GNS on LITT coverage capacity in appropriately sized *ex vivo* models, we utilized agarose gel-based phantoms incorporating control and GNS-infused central “tumors” in multiple shapes. LITT was administered with the NeuroBlate System. **RESULTS:** *In vivo*, GNS preferentially accumulated within intracranial tumors on PET-CT at the 24- and 72-hour timepoints. AR and HP confirmed high GNS accumulation within tumor. *Ex vivo*, in cuboid tumor phantoms, the GNS-infused phantom heated 5.5x faster than the control, rising 0.49°C per minute compared to 0.09°C. In a split-cylinder tumor phantom with half containing GNS, the GNS-infused border heated 2x faster and the surrounding area was exposed to 30% lower temperatures. In a GNS-infused star-shaped phantom, the heat spread contoured along phantom boundaries. **CONCLUSION:** Our results provide evidence for use of GNS to improve the specificity, efficiency, and potentially safety of LITT. The *in vivo* data support selective accumulation within intracranial tumors, and the GNS-infused phantom experiments demonstrate increased rates of heating within the tumor model, heat contouring to tumor borders, and decreased heating of surrounding regions representing normal structures.

#### **SURG-08. LASER INTERSTITIAL THERMAL THERAPY (LITT) VERSUS RESECTION IN THE TREATMENT OF LESIONS IN OR NEAR THE PRIMARY MOTOR CORTEX**

Ethan Srinivasan<sup>1</sup>, Emily Lerner<sup>1</sup>, Ryan Edwards<sup>1</sup>, David Huie<sup>2</sup>, Peter Fecci<sup>2</sup>; <sup>1</sup>Duke University School of Medicine, Durham, NC, USA, <sup>2</sup>Duke University Medical Center, Department of Neurosurgery, Durham, NC, USA

**INTRODUCTION:** Laser interstitial thermal therapy (LITT) is a minimally-invasive treatment option for radiographically-progressive (RP) brain metastases. This study compares the functional outcomes of LITT vs resection (RS) for lesions in or near the primary motor cortex (PMC). **METHODS:** Retrospective review was performed of patients treated for PMC lesions by LITT or RS. Functional outcomes were graded relative to pre-treatment symptoms and categorized as improved, stable, or worsened at 30, 90, and 180 days post-LITT/RS. **RESULTS:** 36 patients were identified with median follow-up of 194 days (IQR 72–503), age 64 years (57–72), and estimated baseline KPS 80 (80–90). 35 (98%) had pre-treatment weakness or motor seizure; 15 (42%) received LITT and 21 (58%) RS; all RS were performed with intra-operative motor mapping while LITT were not. All LITT patients were treated for RP lesions (radiation necrosis (RN) or disease progression) vs. 24% of RS patients (p<0.01). LITT patients trended towards smaller lesions (1.9 cm vs 2.7 cm, p=0.03) and were more likely to show RN (67% vs 5%, p<0.01) and be discharged home (87% vs 52%, p=0.04), with shorter ICU (0 vs 1 day, p<0.01) and hospital stays (1 vs. 2 days, p<0.01). At 30 days, 89% of surviving patients who received RS had stable or improved symptoms, compared to 46% of the LITT cohort (p=0.02). At 90 days, the difference was 88% to 50% (p=0.07), and at 180 days 100% to 80% (p=0.2941). **CONCLUSION:** In the short term (30 days), patients with PMC lesions have better functional outcomes when treated with RS compared to LITT, while those who survive to the 180-day timepoint experience similar outcomes. These differences are likely due to transient, expected post-LITT edema that subsides with time. Taken together, prognosis and patient priorities are important considerations in the decision between LITT and RS.

#### **SURG-09. BENEFITS OF LASER INTERSTITIAL THERMAL THERAPY IN THE TREATMENT OF BIOPSY-PROVEN RADIATION NECROSIS**

Emily Lerner<sup>1</sup>, Ethan Srinivasan<sup>1</sup>, Eric Sankey<sup>1</sup>, Matthew Grabowski<sup>2</sup>, Andrew Griffin<sup>1</sup>, Elizabeth Howell<sup>1</sup>, Balint Otvos<sup>1</sup>, Vadim Tsvankin<sup>1</sup>, Ahmet Akit<sup>2</sup>, Krishna Joshi<sup>2</sup>, Gene Barnett<sup>2</sup>, Peter Fecci<sup>1</sup>, Alireza Mohammadi<sup>2</sup>; <sup>1</sup>Duke University School of Medicine, Durham, NC, USA, <sup>2</sup>The Cleveland Clinic Lerner College of Medicine, Cleveland, OH, USA

**INTRODUCTION:** Laser interstitial thermal therapy (LITT) is a minimally-invasive treatment option often used for patients with deep-seated intracranial lesions. It has been implemented as a definitive treatment for radiation necrosis (RN), which occurs in 9–14% of patients after stereotactic radiosurgery (SRS) for brain metastases (BM). Medical management (MM)

with steroids is a common first-line therapy, with variable response and numerous side effects, especially regarding immunotherapy. **METHODS:** Patients with biopsy-proven RN after SRS for BM who received LITT or MM at two academic centers were retrospectively reviewed. Treatment failure was defined as radiographic progression that necessitated a change in management. Measurements of total (TLV) and contrast-enhancing lesion volume (ceLV) were obtained from MRI by semi-automated analysis using the BrainLab iPlan Cranial 3.0 software. **RESULTS:** Seventy-two patients were followed for 10.0 (4.2–25.1) months and 57 (79%) received LITT. Steroid cessation occurred at a median of 37 days post-LITT compared to 245 days after MM (p<0.01). On Kaplan-Meier analyses, there was no significant difference between the two groups in overall survival (LITT median of 15.2 months vs 11.6 months, p = 0.60) or freedom from local progression (13.6 months vs. 7.06 months), though LITT trended to show a benefit in both metrics. When controlled for follow-up duration, patients treated with LITT were three times more likely to be weaned off steroids prior to the study endpoint compared to those who were medically managed (p=0.003). The LITT cohort demonstrated a general radiographic trend of initially increased CeLV followed by contraction, with significant decreases from pre-operative at 10–12 months (p<0.01). The MM group did not demonstrate any statistically significant radiographic trends. **CONCLUSION:** These results suggest that LITT for RN significantly reduces the time to steroid cessation and characterize a stereotyped radiographic response to LITT. Future prospective studies will be important to their validation.

#### **SURG-10. THE EVOLVING ROLE OF NEUROSURGERY FOR CENTRAL NERVOUS SYSTEM METASTASES IN THE ERA OF PERSONALIZED MEDICINE**

Philipp Karschnia<sup>1</sup>, Emilie Le Rhun<sup>2</sup>, Stefan J. Grau<sup>3</sup>, Matthias Preusser<sup>4</sup>, Riccardo Soffietti<sup>5</sup>, Martin van den Bent<sup>6</sup>, Michael Vogelbaum<sup>7</sup>, Louisa von Baumgarten<sup>1</sup>, Manfred Westphal<sup>8</sup>, Michael Weller<sup>2</sup>, Joerg-Christian Tonn<sup>1</sup>; <sup>1</sup>Ludwig-Maximilians-University, Munich, Germany, <sup>2</sup>University Hospital and University of Zurich, Zurich, Switzerland, <sup>3</sup>University Hospital of Cologne, Cologne, Germany, <sup>4</sup>Medical University of Vienna, Vienna, Austria, <sup>5</sup>University and City of Health and Science Hospital, Turin, Italy, <sup>6</sup>Erasmus MC Cancer Institute, Rotterdam, Netherlands, <sup>7</sup>Moffitt Cancer Center, Tampa, FL, USA, <sup>8</sup>University Hospital Hamburg, Hamburg, Germany

**BACKGROUND:** Novel therapies translating into improved survival of patients with advanced cancer have emerged. The number of metastases in the central nervous system is therefore seen to increase. Neurosurgery assumes an expanding role within multi-disciplinary care structures for such patients. **METHODS:** We performed a comprehensive literature review on the current status of neurosurgery for brain metastases patients. Based on the extracted data, we developed a review from experts in the field on the role of brain metastasis surgery in the era of personalized medicine. **RESULTS:** Traditionally, three metastases were considered the cutoff to offer surgical resection. With respect to the clinical status, the resection of a symptomatic mass may nowadays be considered even in presence of multiple tumors in a multimodal setting: surgical resection of brain metastasis provides immediate relief from mass effect-related symptoms and histology in case of unknown primary tumor; surgery may help stabilizing the disease, thus enabling further therapy; and in situations where immunotherapy is considered and non-surgical management would require long-term steroid administration, surgery may also provide expeditious relief of edema and reduction of needs for steroids. In patients with multiple brain metastasis and mixed response to non-surgical therapy, tumor resampling may allow tissue analysis for expression of molecular tumor targets. In patients with leptomeningeal dissemination and consecutive hydrocephalus, ventriculo-peritoneal shunting improves quality of life but also allows for time to administer more therapy thus prolonging survival. Addressing the limited efficacy of many oncological drugs for brain metastases, clinical trial protocols in which surgical specimens are analyzed for pre-surgically administered agents may offer pharmacodynamic insights. **CONCLUSION:** Comprehensive neurosurgical care will have to be an integral element of multi-disciplinary oncological centres providing care to patients with brain metastases to improve on therapy and tumour biology research.

#### **SURG-11. SURGERY FOR CONTROL OF BRAIN METASTASES AFTER PRIOR CHECKPOINT INHIBITOR IMMUNOTHERAPY: A SINGLE-CENTER SERIES**

Ramin Morshed<sup>1</sup>, Jason Chung<sup>1</sup>, Vivek Sudhakar<sup>2</sup>, Daniel Cummins<sup>1</sup>, Jacob Young<sup>1</sup>, Shawn Hervey-Jumper<sup>1</sup>, Philip Theodosopoulos<sup>1</sup>, Manish Aghi<sup>1</sup>; <sup>1</sup>UCSF, San Francisco, CA, USA, <sup>2</sup>UPMC, Pittsburgh, PA, USA

**BACKGROUND:** Despite the promising results for treating metastatic cancer with checkpoint inhibitor immunotherapies, there are limited data on surgical outcomes for brain metastases (BMs) that have progressed after

prior checkpoint inhibitor treatment. The objective of this study was to identify factors associated with local progression, leptomeningeal disease, and survival for patients undergoing surgical resection of a BM in patients previously treated with checkpoint inhibitor immunotherapy. **METHODS:** A retrospective, single-center cohort study was conducted with inclusion of adult patients undergoing surgical resection of a BM in the setting of progression after prior checkpoint inhibitor treatment. Univariate and multivariate analyses were performed to identify factors associated with outcomes of interest. **RESULTS:** Over an 8-year period, 26 patients who underwent resection of 30 BMs met inclusion criteria. Median patient age at surgery was 63.9 years, and median clinical follow-up was 6.9 months (range 0.1–52.9). Extracranial disease was present at the time of surgery in 73.3% of cases. There were 6 postoperative complication events (20% of cases) by 30-days. By last follow-up, 65.4% of the cohort had died with a median censored survival of 7.6 months from surgery. Eight patients (30.8%) died within 3 months of surgery. On multivariate analysis, postoperative complications were associated with worse survival (HR 5.33, 95% CI 1.15–24.77,  $p=0.03$ ). Four BMs had local progression (13.3%), and 60% of procedures were associated with distant progression within a median time of 3.6 months. Leptomeningeal disease developed in 32% of cases. On multivariate analysis, increased time from BM diagnosis to surgery was associated with a greater risk of leptomeningeal disease (OR 1.2, 95% CI 1.00–1.43,  $p=0.021$ ). **CONCLUSION:** Patients who require BM resection after prior checkpoint inhibitor treatment have an overall poor prognosis. Although local control rates are acceptable, these patients are at high risk for developing leptomeningeal disease postoperatively.

#### **SURG-12. MALIGNANT BREAST NEOPLASM AND BRAIN METASTASES: SERIES OF CASES AND MAIN APPROACHES IN A HOSPITAL COMPLEX IN BRAZIL**

Frederico Tavares de Lima, Nataly Regina Medeiros, Luiz Domingues Vasconcelos Filho, Bruno Leimig, Walter Matias, Joacil Carlos Silva, José Roberto Vieira de Mello; Pernambuco Cancer Hospital, Recife/Pernambuco, Brazil

**INTRODUCTION:** With the advancement of clinical and surgical oncology, patients with breast cancer had an increase in survival. In this context, up to 30% of patients affected with metastases from this site will develop brain tumors. The latter is an important impacting factor for life quality and expectancy, therefore, its clinical and surgical management is essential in public health. We present some rare cases and their outcomes. **METHODS:** We describe a case series of 07 patients with breast cancer metastases to the brain, involving large portions of the dura, bone or skin. There were 64 surgical interventions of the disease in the period, but only those with more exuberant and atypical presentations were selected. The interventions were carried out in a hospital oncology complex in northeastern Brazil between 2016 and 2020. The diagnosis was based on the clinical description, laboratory and image exams, histopathology and surgical performance of the patients. **RESULTS:** The mean age of the patients was 49.7 years, with all patients being female. Rare presentations were observed, such as bone and skin meninges. Clinical presentations demonstrated advanced stages of the disease with a large tumor volume. Extra axial involvement was verified. All patients underwent neurosurgery for tumor removal and decompression. Biopsies were submitted to anatomopathological and immunohistochemistry examination. Corticotherapy was instituted in the immediate postoperative period and some cases had genetic analysis due to an important family history. There was a reduction in symptoms in most cases. **CONCLUSION:** Although brain metastases are still a challenge for medical practice, their proper management can prolong and improve patients' lives. Metastatic breast cancers seem to have a predilection for the central nervous system and their detection and intervention, even in an advanced clinical stage, sound as determinant for the control and severity of symptoms.

**Keywords:** Brain Neoplasms, Neoplasm Metastasis, Breast Neoplasms

#### **SURG-13. MULTIPLICITY DOES NOT AFFECT OUTCOMES IN PATIENTS WITH SURGICALLY TREATED BRAIN METASTASES**

Kaiyun Yang, Enrique Gutierrez, Alexander Landry, Aristotelis Kalyvas, Jessica Weiss, David Shultz, Paul Kongkham; University of Toronto, ON, Canada

**BACKGROUND:** Having multiple brain lesions has been considered a negative prognostic factor in patients with brain metastases. The role of surgery in the management of these patients remains a matter of debate. **METHODS:** We retrospectively reviewed our patients who underwent surgical resection of brain metastases from January 2018 to December 2019, and examined outcomes including overall survival (OS), progression free survival (PFS) and rates of local failure. **RESULTS:** We identified 130 patients who underwent surgical resection as the primary treatment modality of brain metastases. At the time of surgery, 117 patients harbored 1–3 lesions, 13 had more than 3 lesions. Overall survival at two years for our entire cohort was 46%. The difference in OS between patients with > 3 metastases (21%) and 1–3 metastases (49%) was not statistically significant (HR=1.34, 95% CI: 0.67–2.68,  $p=0.41$ ). Similarly, 27% of patients had PFS at two years, with 25% in the multiple metastases group and 28% in the comparison group (HR=1.19, 95% CI: 0.63–2.23,  $p=0.59$ ). Additionally, 32% of patients overall experienced local failure at two years and there was no significant difference between patients with >3 metastases (15%) and those with fewer (33%) (HR=0.68, 95% CI: 0.21–2.19,  $p=0.52$ ). A multivariate regression model examining multiple preoperative features revealed large tumor volume to be the only independent predictor of limited OS ( $p = 0.017$ ) and PFS ( $p = 0.023$ ), and local failure ( $p = 0.031$ ). **CONCLUSIONS:** In carefully selected patients, surgical resection is a reasonable management option for patients with multiple brain metastases.

#### **SURG-14. LASER ABLATION FOR BRAIN METASTASES: RISK FACTORS FOR NEUROLOGIC COMPLICATION**

Jacob Pawloski<sup>1</sup>, Hassan Fadel<sup>1</sup>, Sam Haider<sup>1</sup>, Lisa Rogers<sup>1,2</sup>, Ian Lee<sup>1,2</sup>, Adam Robin<sup>1,2</sup>; <sup>1</sup>Henry Ford Hospital, Detroit, MI, USA, <sup>2</sup>Hermelin Brain Tumor Center, Detroit, MI, USA

**INTRODUCTION:** Laser interstitial thermal therapy (LITT) is a routinely used in treatment of recurrent brain metastases following SRS or open craniotomy. While considered safer than craniotomy, patients do experience neurologic decline following LITT. Identifying which patients are at risk for neurologic deterioration can help better advise patients on the most appropriate treatment options for their tumor. **OBJECTIVE:** The objective of the present study was to assess the frequency and identify risk factors for neurologic decline following LITT. **METHODS:** Data was gathered on patients who underwent LITT for ablation of metastatic brain tumors at our institution between 2014–2019. These cases were analyzed retrospectively and data was collected on patient demographics, tumor characteristics, procedural details, and post-operative complications and outcomes. Pre-operative neurologic function was compared to neurologic status at the 6–12 week post-op visit. **RESULTS:** 16 patients underwent LITT of a total of 18 metastatic lesions during the study time period and were included in the analysis. 7/16 patients demonstrated reduced KPS or worse neurologic function at 6–12 week follow up. 4 patients (25%) demonstrated neurologic deficits that were attributable to the laser ablation procedure, and each of these 4 patients had lesions in eloquent areas. Comparatively, none of the other 12 patients analyzed had eloquent lesions ( $p = 0.002$ ). The presence of a pre-op neurologic deficit was not predictive of worsening neurologic function following LITT ( $p = 0.35$ ). Average lesion size in patients who experienced neurologic deficit was 5.69cm<sup>3</sup> compared to 3.15cm<sup>3</sup> in those that did not ( $p = 0.1$ ). **CONCLUSION:** Our complications rate is similar to other published case series (15–44%). LITT, while better tolerated than standard craniotomy, can lead to neurologic decline in patients with brain metastases regardless of lesion size or pre-operative functional status. Eloquence is a significant predictor of neurologic complications following laser ablation.