treatment of brain metastases (BMs) with minimal toxicity and less systemic therapy interruption. Here we assessed clinical outcomes in BC patients who received upfront stereotactic radiosurgery (SRS). METHODS: We identified 216 patients who received upfront SRS for BM from metastatic BC from 06/2007 to 05/2018. Twenty-four patients who received SRS for surgical cavity were excluded for analysis. Overall survival (OS) and salvage radiation-free survival (SRSFs) were estimated using Kaplan-Meier analysis. Cox proportional hazard regression was used to identify prognostic factors. RESULTS: At a median follow-up time of 15.4 months (range, 0.8–119.6), the estimated median OS was 18.5 mo (95% CI, 14.9–21). Factors associated with OS on multivariate analysis (MVA) were subtype (12.2% of triple-negative vs 3.3% of HER2+ vs 11.8% of HR+/HER2+ patients, p = 0.015), receipt of chemotherapy (p = 0.016) or anti-HER2 therapy (p = 0.029) after diagnosis of BM, and type of salvage radiation (p = 0.0001). OS was comparable in patients who received upfront SRS to less or more than 4 lesions (19.3 months for ≤4 vs 16.2 months for ≥5). The 12-month salvage RT rate was 25% for WBRT and 24.6% for SRS. The median SRSF was 7.4 months (95% CI, 6.3–8.3). Factors associated with SRSFs on MVA were subtype (p = 0.002), KPS (p = 0.011), and receipt of hormone therapy after diagnosis of BM (p = 0.031). CONCLUSIONS: The median OS for BC patients who developed BM is over 15 months. Molecular subtypes (HER2+ and HR+/HER2+), good KPS and anti-HER2 or hormone therapy predicted better OS and SRSF. Prospective studies are needed to verify these results and refine the best treatment strategies for these patients.

RADI-19. THE INCIDENCE OF NEW BRAIN METASTASES IN PATIENTS WITH NON- SMALL CELL LUNG CANCER FOLLOWING DISCONTINUATION OF SYSTEMIC THERAPY

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PURPOSE: Patients with non-small cell lung cancer (NSCLC) metastatic to the brain increasingly are living longer due to improvements in systemic therapy and local modalities. The risk of new brain metastases when these patients stop systemic therapy is unknown. Recognizing patterns of new tumor occurrence is necessary to determine the frequency of follow-up and the need for further treatment. METHODS: We included patients in a prospective registry who had non-small cell lung cancer (NSCLC) brain metastases, discontinued systemic therapy for at least 90 days, and underwent active surveillance. 63 patients with 73 off-periods were studied. The risk factors for the development of new tumors were determined using Cox regression and multi-state Markov modeling. RESULTS: The median time to new brain metastases off systemic therapy was 16.0 months. The probability of developing an additional new tumor at 6, 12, and 18 months was 26%, 40%, and 53%, respectively. There were no additional new tumors 22 months after stopping therapy. Patients who discontinued therapy due to intolerance or progression of the disease and those with mutations in RAS or receptor tyrosine kinase pathways (e.g. KRAS, EGFR) were more likely to develop a new brain metastasis (HR: 2.21, 95% CI on presentation. The benefits of Gamma Knife Surgery (GKS) have been shown for BMs10, but there is no consensus on the upper limit where GKS is no longer beneficial. We hypothesized that selected patients with ≤20 BM may benefit by replacing WBRT with GKS to preserve neurofunction without compromising intracerebral tumor control and overall survival, with additional treatments as needed. Methodology: This is retrospective analysis of 31 patients with ≤20 BM who underwent single-session GKS between 2016–2021. Twenty-two patients had ECOG of 0 at the time of GKS. Median number of BM at GKS was 30 (20–79) with median total tumour volume 4cm3 (2–28 cm3). Median marginal dose was 20Gy (10-25Gy). RESULTS: Median overall survival following GKS was 14-months (95%CI 4-24months), justifying GKS in this population. 11/12 patients that died succumbed due to extracranial disease, while 1 patient, who was treated with WBRT before GKS, succumbed to intracranial tumor progression. Local tumor control achieved was achieved for 63% of patients at 2-years and distal tumor control in 24% of patients at 1.5-years without additional radiation treatment. Salvage GKS was given in seven patients and salvage WBRT in three. One local recurrence was surgically resected. Systemic treatment given to most patients probably contributed to intracranial tumor control. No patients developed significant neurocognitive deficits attributable to GKS during the follow-up period of median 7-months (Q1-Q3: 1-11.2 months). CONCLUSIONS: Most patients treated with GKS for ≤20 BM have sufficient time to benefit from the treatment. Local and distal recurrences can be managed with systemic treatment, salvage GKS, or WBRT, resulting in intracerebral tumor control in vast majority of cases.

RADI-20. BRAIN METASTASIS TREATMENT WITH HIGH ENERGY RADIOTherapy AND CHERenkov RADIation-ACTivated PHOTOTHERAPY

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Radiation therapy is a mainstay in the treatment of brain metastases, yet some patients are resistant, and elsewhere brain recurrence outside the radiation field is common. Phototherapy using UV light-activated compounds can both kill cancer cells directly and trigger an immune response to extend the reach of the radiation beyond the tumor. Here we report our experience in using a high-energy laser-based phototherapy system and an organotypic brain slice platform to test this phenomenon to enhance radiation therapy for brain metastases. We first tested UV-activated psoralen derivatives in combination with UV light in vitro for activity against murine 4T1 breast cancer cells, and then we irradiated a murine brain slice with/without surgery for BMs from metastatic BC from 06/2007 to 05/2018. Twenty-four patients who received SRS for surgical cavity were excluded for analysis. Overall survival (OS) and salvage radiation-free survival (SRSFs) were estimated using Kaplan-Meier analysis. Cox proportional hazard regression was used to identify prognostic factors. RESULTS: At a median follow-up time of 15.4 months (range, 0.8–119.6), the estimated median OS was 18.5 mo (95% CI, 14.9–21). Factors associated with OS on multivariate analysis (MVA) were subtype (12.2% of triple-negative vs 3.3% of HER2+ vs 11.8% of HR+/HER2+ patients, p = 0.015), receipt of chemotherapy (p = 0.016) or anti-HER2 therapy (p = 0.029) after diagnosis of BM, and type of salvage radiation (p = 0.0001). OS was comparable in patients who received upfront SRS to less or more than 4 lesions (19.3 months for ≤4 vs 16.2 months for ≥5). The 12-month salvage RT rate was 25% for WBRT and 24.6% for SRS. The median SRSF was 7.4 months (95% CI, 6.3–8.3). Factors associated with SRSFs on MVA were subtype (p = 0.002), KPS (p = 0.011), and receipt of hormone therapy after diagnosis of BM (p = 0.031). CONCLUSIONS: The median OS for BC patients who developed BM is over 15 months. Molecular subtypes (HER2+ and HR+/HER2+), good KPS and anti-HER2 or hormone therapy predicted better OS and SRSF. Prospective studies are needed to verify these results and refine the best treatment strategies for these patients.

RADI-21. FEASIBILITY OF GAMMA KNIFE SURGERY FOR PATIENTS WITH 20 OR MORE BRAIN METASTASES

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BACKGROUND: The current standard-of-care treatment for brain metastases (BM)>20 is Whole Brain Radiotherapy (WBRT), which can cause neurocognitive decline detrimental to patients’ quality of life, especially if their pre-morbid status is good on presentation. The benefits of Gamma Knife Surgery (GKS) have been shown for BMs10, but there is no consensus on the upper limit where GKS is no longer beneficial. We hypothesized that selected patients with ≤20 BM may benefit by replacing WBRT with GKS to preserve neurofunction without compromising intracerebral tumor control and overall survival, with additional treatments as needed. Methodology: This is retrospective analysis of 31 patients with ≤20 BM who underwent single-session GKS between 2016–2021. Twenty-two patients had ECOG of 0 at the time of GKS. Median number of BM at GKS was 30 (20–79) with median total tumour volume 4cm3 (2–28 cm3). Median marginal dose was 20Gy (10-25Gy). RESULTS: Median overall survival following GKS was 14-months (95%CI 4-24months), justifying GKS in this population. 11/12 patients that died succumbed due to extracranial disease, while 1 patient, who was treated with WBRT before GKS, succumbed to intracranial tumor progression. Local tumor control achieved was achieved for 63% of patients at 2-years and distal tumor control in 24% of patients at 1.5-years without additional radiation treatment. Salvage GKS was given in seven patients and salvage WBRT in three. One local recurrence was surgically resected. Systemic treatment given to most patients probably contributed to intracranial tumor control. No patients developed significant neurocognitive deficits attributable to GKS during the follow-up period of median 7-months (Q1-Q3: 1-11.2 months). CONCLUSIONS: Most patients treated with GKS for ≤20 BM have sufficient time to benefit from the treatment. Local and distal recurrences can be managed with systemic treatment, salvage GKS, or WBRT, resulting in intracerebral tumor control in vast majority of cases.
abstracts

Our analysis opens more discussion on the clinical outcome of 18 patients treated with stereotactic radiosurgery (SRS). Two hundred patients were included: 100 controls and 100 patients who received radiation therapy. This collaborative institutional experience support efficacy and value of early initial surveillance MRI scans in patients with brain metastases undergoing stereotactic radiosurgery (SRS), as this imaging modality is low cost and patient stressor. METHODS: We identified a retrospective cohort of patients with brain metastases treated with SRS and followed at a single institution with scheduled 6-week or 12-week initial surveillance MRI. Imaging interval was based on policy of different providers. Outcome measures included new/progressive lesions, salvage treatment, detection of new lesions before symptoms, and use of surgical resection. RESULTS: Two hundred patients were included: 100 consecutive patients scanned with 6-week and 12-week imaging. Eighty-seven and 74 patients, respectively, had available follow-up imaging every three months from the time to MRI was 6.7 weeks and 13.3 (p<0.001). No difference in primary site, prior SRS, number of treated brain metastases, or use of targeted therapy/immune checkpoint inhibitors was detected. A lower percentage of patients with 6-week MRI had controlled extracranial disease at initial treatment (30% vs 47%, p<0.003). Twenty-eight percent with 6-week MRI had findings concerning for new/progressive disease, compared to 47% with 3-month MRI (p=0.01). Fifteen percent (10/87) with 6-week MRI underwent intervention (i.e., SRS, whole brain radiotherapy, or surgery) compared to 34% (27/74) with 12-week MRI (p=0.004). Of patients receiving SRS, a higher percentage had new/worsening neurologic symptoms (45% vs 30%) at follow-up although a lower percentage had new lesions >1cm (20% vs 50%) when discovered. One patient in each group underwent surgical salvage. CONCLUSION: While shorter 6-week interval MRI surveillance post-SRS may detect new/progressive disease less frequently than 12-week MRI surveillance intervals, short interval MRI may be more likely to detect new/progressive lesions before symptoms develop. Surgical salvage was uncommon with either schedule. Further study is needed to identify a high-risk subgroup who would benefit from early surveillance.

Surgery

SURG. 3. THE EFFECT OF SURGERY ON RADIATION NECROSIS IN IRRADIATED BRAIN METASTASES: EXTENT OF RESECTION AND LONG-TERM CLINICAL AND RADIOGRAPHIC OUTCOMES

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INTRODUCTION: To treat a solitary metastasis in the brain, surgical resection and/or radiotherapy are the standard treatments of care. However, the clinical scenarios in which to use these techniques alone or in combination are controversial. While a course of stereotactic radiotherapy is often administered to a patient who presents with multiple metastases, surgical resection is often considered against a large solitary brain metastasis, but irradiating the resection bed. The management of a smaller solitary tumor (diameter less than 4 cm) is less clear. Accordingly, our meta-analysis assembled studies that focused on patients with a solitary tumor less than 4 cm in diameter. METHODS: Following PRISMA guidelines (PROSPERO ID: CRD42021242343), we searched PubMed, Web of Knowledge, and Cochrane Library databases for randomized controlled trials (RCT) and observational studies comparing surgery to radiotherapy for solitary metastatic brain tumors less than 4 cm in diameter. From 498 total records, we included 9 studies for meta-analysis. Analysis was performed on R. RESULTS: 2 RCTs and 7 observational studies were identified. 431 patients underwent surgical intervention, and 349 patients exclusively underwent radiotherapy. The surgical treatment cohort did not exhibit a difference in progression-free survival (p=0.095, 95% CI [0.868–1.249]). The median survival with either schedule was 12 (1.7 [0.843–3.428]) years, or overall survival (1.8 [0.598–3.327]). However, the surgical treatment group demonstrated greater local tumor recurrence after 1-year (3.975 [1.979–7.987]) and overall local recurrence (3.045 [1.276–7.268]). There was no difference between the overall rates of distant recurrence (0.365 [0.218–1.466]). CONCLUSIONS: Our analysis opens more discussion on the management of solitary brain metastasis. Patient selection is paramount in achieving better local control. Stereotactic radiotherapy should be considered for treatment of solitary brain metastasis less than 4 cm in diameter in selected patients. Future randomized control trials for small solitary masses are recommended.