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Pre-Operative Fractionated Stereotactic Radiosurgery for Brain Metastases: Results of a Single Institution Phase II Protocol

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Abstract

Purpose: Brain metastases are a common occurrence in patients with advanced malignancy. Treatment ranges from surgical resection, stereotactic radiosurgery (SRS), whole brain radiation therapy (WBRT), or some combination thereof. Traditionally SRS has followed surgical resection to help reduce risk of local recurrence. In recent years interest has arisen in treating these patients in the preoperative setting to help reduce risk of leptomeningeal disease and radiation necrosis while preserving rates of local control. This phase II protocol investigated the use of 3 fraction pre operative SRS on the Gamma Knife (GK) Icon with the goal of examining those outcomes.

Methodology: Patients with symptomatic and limited brain metastases amenable to surgical resection were prospectively enrolled on this study. Patients had to have a biopsy proven extracranial malignancy. Patients were treated with fractionated SRS on the GK Icon to 24-27 Gy in 3 fractions followed by surgical resection within 2 weeks. Post operative MRIs were obtained to assess extent of resection. Patients were then followed with standard of care MRIs every three months for the first two years. Rates of local control, distant brain failure, LMD, and delivery of WBRT were recorded in follow up.

Results: Twenty patients were prospectively enrolled on the phase II trial and an additional 11 were treated off study using 1-3 fractions between April 2021 and June 2024. The median age was 64 (31-81) and 55% were females. Primary malignancies were mainly non small cell lung cancer, melanoma, and esophageal cancer. The median prescription dose was 27 Gy (15-27 Gy) in 3 (1-3) fractions. Surgery was done at a median of 1 day post-SRS (0-11). All available post operative MRIs showed gross total resection. Median follow up was 9 months. One patient experienced a local failure yielding a 1 year local control rate of 95%. The rate of distant brain failure at 6 and 12 months was 38% at each time point. Three patients (9.6%) developed LMD in follow up. Six patients ultimately received WBRT, yielding a one year WBRT-free survival of 78%. Overall survival at one year was 52%. There were no predictors of overall survival, local failure, or distant brain failure on Cox regression. Two patients experienced short term toxicity including grade 2 intracranial swelling and one grade 5 hemorrhagic stroke related to uncontrolled blood pressure in the post operative setting. There was no recorded radionecrosis in follow up.

Conclusions: Fractionated pre operative SRS appears to be safe and effective with high rates of local control and low rates of LMD and radionecrosis. Results of ongoing phase III studies directly comparing pre operative to post operative SRS will help further define the appropriate sequencing of therapies.