**Initial SRS for Patients with 5-15 Brain Metastases: Results of a Multi-Institutional Experience**

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**Purpose/Objective(s):** Several studies evaluating the use of stereotactic radiosurgery (SRS) for patients with >4 brain metastases (BM) have demonstrated similar outcomes after treatment of 1, 2-4, and 5-15 BM, while other reports have found clinically significant survival decrements in the latter group. In this multi-institutional retrospective review of eight North American academic centers, we aim to compare clinical outcomes of patients undergoing upfront SRS for 1, 2-4 and 5-15 BM.

**Materials/Methods:** A total of 2089 patients treated with upfront SRS for brain metastases at 8 institutions were included. Patients were stratified by number of lesions treated: 1, 2-4 and 5-15. Overall survival (OS) was estimated using the Kaplan-Meier method. Factors including age, gender, primary histology, number of metastases treated with SRS, SRS dose, systemic disease burden and extracranial disease status were evaluated as predictors of OS and DBF within the 5-15 BM group using stepwise multivariate Cox proportional hazards modeling.

**Results:** In total, 2089 patients with brain metastases from lung (46%), melanoma (19%), breast (14%), RCC (11%), and other (10%) were treated. Of these, 990 had 1 treated metastasis, 884 had 2-4 metastases, and 215 patients had 5-15 metastases treated. Median marginal dose was 18.5 Gy (IQR 17.5-20.3). Median OS for the 1, 2-4, and 5-15 BM groups was 14.6, 9.5, and 7.5 months, respectively (log-rank p<0.01). Cumulative incidence of DBF at 1 year was 30%, 41%, and 50% (Gray’s p<0.01) for these groups, respectively. Salvage WBRT was performed for 13% of patients with 1 BM, 16% of patients with 2-4 BM, and 19% of those with 5-15 BM (p=0.05). Subsequent SRS was utilized in 27%, 24%, and 20%, respectively (p=0.11). Median BMV was significantly higher in patients with 5-15 BM: 11.7 in the 5-15 group compared with 3.9 and 6.1 in the 1 and 2-4 BM groups, respectively (p<0.01). Multivariate analysis revealed melanoma primary to be associated with a higher hazard of death (HR 2.08), male gender (HR 1.76) and number of metastases (HR 1.15) were associated with an increased hazard of DBF and progressive systemic disease (HR 0.59) associated with a decreased hazard of DBF.

**Conclusion:** This multi-institutional experience represents one of the largest reported cohorts of patients treated with upfront SRS for 5-15 brain metastases. These patients exhibited shorter overall survival and a higher risk of DBF compared to patients with fewer BM. Salvage WBRT was more frequent and salvage SRS was less frequently utilized for the 5-15 BM group, though these did not reach statistical significance. Melanoma primary was associated with risk of death and male gender, number of BM, and progressive extracranial disease were associated with DBF. Further randomized trials regarding the optimal treatment paradigm for this cohort are warranted.