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Stereotactic Radiosurgery in Brain Metastases Treatment Outcomes and Patterns of Failure

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Abstract
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Abstract

Objective: Brain metastases are the most common intracranial malignancy in adults and an important cause of morbidity and mortality. Management options depend on patients and tumor characteristics. External beam radiotherapy is almost always the standard treatment of brain metastasis. Stereotactic radiosurgery (SRS) has become a preferred treatment option in the initial management of patients with limited brain metastases. Randomized trials have demonstrated that SRS provides equivalent survival and better neurocognition compared to whole-brain radiotherapy (WBRT) in both initial management (stand-alone) or post-operative adjuvant settings. In this single-institution retrospective study, we investigated local control (LC), distant intracranial tumor control (DC), leptomeningeal control, overall survival (OS), and radiation necrosis rate in patients undergoing SRS for brain metastases. We also aimed to identify the patient, tumor, and treatment-related factors that predict failure, survival, and radiation necrosis (RN) after SRS.

Methods: We conducted an IRB-approved retrospective cohort study including all patients with brain metastases with treated SRS. We retrospectively reviewed the electronic medical records of all consecutive patients with brain metastases. In general, the institutional philosophy for use of salvage SRS vs WBRT was to postpone the use of WBRT for as long as possible and to treat with salvage SRS when feasible. After undergoing SRS, patients underwent follow-up with clinical and radiographic surveillance per institutional standards. Data were collected primary diagnosis, age, Karnofsky Performance Status (KPS), number of brain metastases, lesion locations in the brain, dose- fractions, treatment date, extracranial disease status, prior brain metastasis surgery or WBRT/PCI, neurological status, time until first CNS progression after SRS, type of first CNS progression (local, distant, leptomeningeal), cause of death and duration of follow-up. All local recurrences and radiation necroses were defined by an experienced radiologist with a contrast-enhanced MRI and additional perfusion MRI in the neurooncological tumor board. DC was defined as any new brain metastasis that developed outside of the prior SRS treatment volume. MRI evidence of new nodular enhancement of the dura or diffuse leptomeningeal enhancement or positive cerebrospinal fluid cytology were all considered a leptomeningeal failure. Overall survival was defined as the time from SRS to death.

Results: December 2016-April 2020 148 consecutive patients, a total of 444 lesions were analyzed. Patient and tumor characteristics are listed in Table 1. The median follow-up was 14.8 months (range 6-51). The median age was 57 (26-85 range). Median Karnofski performans score (KPS) 90 (50-90 range). Median 2 (1-16) lesions were treated. At the time of analyses, 72.3% of the patients were alive, 41 patients were dead and 36 patients were alive without disease. 71 patients were alive with disease progression. Presence of initial neurological deficit (HR; 2.71 (1.07-6.9); p=0.036) and prior RT (WBRT and PCI) (HR; 2,55 (1,28-5,09); p= 0.008) is associated with overall survival in multivariate analyses. The local recurrence rate was 11.5 %. The median time to local recurrence was 9.6 months (between 2,8- 45,7). No significant prognostic factors were associated with local control. Distant brain recurrence rate was 53,4 %. Median distal brain metastasis number was 2 (1-50). Median time to DBM 6.4 months (between 0.3-73). In multivariate analysis brainstem located lesions (HR:7,96 (1,02-62,28) p: 0,048) and age (HR: 1,02 (1-1,05) p: 0,021) were independent parameters for DBR.
Leptomeningeal metastasis was seen in 11 patients (7.4%). The median time to LMD was 14.8 months (between 1.5- 27.4). No significant prognostic factors were associated with LMD. Symptomatic radiation necrosis was seen in 19 patients (12.8 %). Median follow up was longer in patients with RN 13.4 vs 17.1 (p= 0.015). Median time to RN development after SRS was 12.7 months (between 4.8-39.6). There were less extracranial metastasis in RN group (68.4% vs 31.6%; p: 0,031) but more bone metastasis (83.3 % vs 40.3 %; p: 0,040). Maximal tumor diameter was bigger in patients with radiation necrosis (13 vs 23 mm; p= 0.034). Cavity radisurgery is assosicate with more RN (63,2 % vs 36,8%; p: 0,004).

Conclusion: With advances in systemic treatments, longer survival in metastatic disease can be achieved.

For this reason, local disease control and side effects become more important. Distant brain metastasis is the main cause of CNS recurrences after SRS. Strict follow-up with brain MRI after SRS may be possible to detect these recurrences and salvage treatments. Radiation necrosis is more common in post-surgical cavity SRS applications. Routine metastasectomy should not be recommended except in selected cases requiring immediate palliation, causing mass effect, large lesions, mass effects, and need for pathological diagnosis.