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Safety and Feasibility of Stereotactic Radiation Therapy For Patients with 15 or More Brain Metastases

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Abstract
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Abstract

Objectives:

With prolonged survival of cancer patients and availability of better imaging, incidence of brain metastases (BM) has been increasing. Stereotactic radiotherapy (SRT) is associated with excellent local tumor control with minimal side-effects and is the standard of care in management of patients with limited BMs. Recent studies have suggested that the volume, and not the number, of BMs may be the driver in determining the outcomes, but patients with 15 or more BMs continue to be treated with whole brain radiation therapy (WBRT), despite poor neurocognitive outcomes. We analyzed our experience of treating patients with 15 or more BMs with SRT with the aim of further broadening the use of SRS in this group of patients.

Methods:

A single-institutional retrospective review of patients treated with SRT from January 2014 to April 2022 was performed. We included patients who received SRT for 15 or more BMs in single or multi-fractions with a dose of at least 5 Gy per fraction given in 5 fractions or fewer. Patients were typically treated with a single isocenter multi-target VMAT technique (SIMT) which has been previously described. Our primary endpoint was grade 3 or higher toxicity, while the secondary end points were overall survival (OS) and intracranial progression free survival (PFS). All statistical analyses were performed using SPSS v23.0.

Results:

From January 2014 to April 2022, a total of 104 patients underwent 110 courses of Linac-based SRT treating 15 or more lesions per course. The mean and median number of lesions treated per patient was 24.2 and 19.5 respectively (range 15 – 94). Median age of patients at RT was 61.6 years (IQR 51.4 – 69.5), and 58.2% patients were males. Most common primary tumor location was lungs (48.2%) followed by melanoma (21.8%) and breast (15.5%). Median RT dose used was 24 Gy (range 18 – 27 Gy) with 92.7% patients receiving the total radiation dose in 3 daily fractions. About 45.5% of patients had brain metastases at diagnoses, while 29.1% patients had no or controlled systemic disease at the time of SRT. About 51.8% patients had a KPS of 70-80 and 44.6% had a KPS of 90-100. At the time of current SRT course, 20% patients had received prior WBRT and 25.4% had received prior SRT course(s). 23.6% patients also underwent surgery for 1 or more BMs (9.1% pre-op RT and 14.5% post-op RT); while 90% patients received systemic therapy after SRT. The treatment was safe, with rates of any grade radiation necrosis (RN) of 15.5% and grade 3 or higher RN of 3.6%. New onset seizures were seen in 2.7% patients, alopecia in 2.7% and subjective cognitive decline in 4.5% patients.
At last follow-up, 20% patients were alive. The cumulative incidence of distant intracranial failure at 12 months was 79.2%, while local progression was 3.6%. A total of 7.3% patients had leptomeningeal disease progression and 21.8% patients required salvage whole brain radiation. Median OS after SRT was 6.1 months (95% CI 4.4m – 7.8m), while 12 month survival was 29.1%. Median intracranial PFS after RT was 4.2 months (95% CI 2.2m – 6.2m). At 12 months, freedom from neurological deaths, leptomeningeal disease and salvage WBRT were 81.1%, 84.9% and 66.5% respectively. On univariate analysis, presence of brain metastases at diagnoses, higher KPS at RT, systemic therapy after RT and RN after RT predicted for improved OS, while none of the factors were significant predictors of PFS.

Conclusion(s):

SRT is safe and feasible for patients with 15 or more BMs and can help prevent neurological deaths and leptomeningeal failure. Our cohort of patients had similar OS and PFS compared to historical cohorts of patients receiving upfront WBRT. Further randomized studies comparing SRT and hippocampal avoidance WBRT in this group of patients is warranted.