

# Stereotactic radiosurgery for brainstem metastases

**Brainstem metastases** (BSM) are associated with a poor **prognosis** and their **management** represents a therapeutic challenge. BSM are often **inoperable** and, in absence of **randomized trials**, the optimal **radiation therapy** of BSM remains to be defined.

## Systematic Review and Meta-analysis

Results showed that SRS for BSM was associated with effectiveness and safety and was comparable to SRS for nonbrainstem BM, suggesting that patients with BSM should be eligible for clinical trials of SRS. In this analysis, patients treated with SRS for BSM rarely died from BSM progression and often experienced symptomatic improvement. Given the apparent safety and efficacy of SRS for BSM in the context of acute morbidity or death from BSM growth, consideration of SRS at the time of enrollment on emerging trials of targeted therapy for BM should be considered <sup>1)</sup>.

## Case series

Nicosia et al. evaluated the **efficacy** and **toxicity** of **linear accelerator (linac)**-based **stereotactic radiosurgery** (SRS) and hypofractionated **stereotactic radiotherapy** (HSRT) in the treatment of BSM in a series of patients treated in different clinical **centers**.

They conducted a multicentric retrospective study of patients affected by 1-2 BSM from different histologies who underwent SRS/HSRT. Freedom from local progression (FLP), cancer-specific survival (CSS), overall survival (OS), and treatment-related toxicity were evaluated. In addition, predictors of treatment response and survivals were evaluated.

Between 2008 and 2021, 105 consecutive patients with 111 BMS who received SRS or HSRT for 1-2 BSM were evaluated. Median follow-up time was 10 months (range 3-130). One-year FLP rate was 90.4%. At the univariate analysis, tumor volume  $\leq 0.4$  cc, and concurrent targeted therapy were associated with longer FLP, with combined treatment that remained a significant independent predictor [0.058, HR 0.139 (95% CI 0.0182-1.064)]. Median OS and CSS were 11 months and 14.6 months, respectively. At multivariate analysis, concurrent targeted therapy administration was significantly associated with longer OS [HR 0.514 (95%CI 0.302-0.875);  $p = 0.01$ ]. Neurological death occurred in 30.4% of patients, although this was due to local progression in only 3 (2.8%) patients.

Linac-based SRS/HSRT offers excellent local control to patients with BSM, with low treatment-related **toxicity** and no apparent detrimental effects on OS. When treated with ablative intent, BSM are an uncommon cause of neurological death. The present results indicates that patients with BSM should not be excluded a priori from clinical trials <sup>2)</sup>.

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19 brainstem metastases from 14 patients who had follow-up brain imaging were identified. Median

tumor volume was 0.04 cc (range: 0.01-2.0 cc). Median prescribed dose was 17.5 Gy to the 50% isodose line (range: 14-22 Gy). Median survival after GK SRS treatment to brainstem lesion was 17.2 months (range: 2.8-45.6 months). The experience at Indiana University confirms the safety and efficacy of range of GK SRS prescription doses (14-22 Gy) to brainstem metastases <sup>3)</sup>.

Of 547 patients with 596 brainstem metastases treated with SRS, treatment of 7.4% of tumors resulted in severe SRS-induced toxicity (grade  $\geq 3$ , increased odds with increasing tumor volume, margin dose, and whole-brain irradiation). Local control at 12 months after SRS was 81.8% and was improved with increasing margin dose and maximum dose. Overall survival at 12 months after SRS was 32.7% and impacted by age, gender, number of metastases, tumor histology, and performance score.

The study provides additional evidence that SRS has become an option for patients with brainstem metastases, with an excellent benefit-to-risk ratio in the hands of experienced clinicians. Prior whole-brain irradiation increases the risk of severe toxicity in brainstem metastasis patients undergoing SRS <sup>4)</sup>.

<sup>1)</sup>

Chen WC, Baal UH, Baal JD, Pai JS, Boreta L, Braunstein SE, Raleigh DR. Efficacy and Safety of Stereotactic Radiosurgery for Brainstem Metastases: A Systematic Review and Meta-analysis. JAMA Oncol. 2021 Jul 1;7(7):1033-1040. doi: 10.1001/jamaoncol.2021.1262. PMID: 33983393; PMCID: PMC8120444.

<sup>2)</sup>

Nicosia L, Navarria P, Pinzi V, Giraffa M, Russo I, Tini P, Giaj-Levra N, Alongi F, Minniti G. Stereotactic radiosurgery for the treatment of brainstem metastases: a multicenter retrospective study. Radiat Oncol. 2022 Aug 9;17(1):140. doi: 10.1186/s13014-022-02111-5. PMID: 35945597.

<sup>3)</sup>

Patel A, Mohammadi H, Dong T, Shiue KR, Frye D, Le Y, Ansari S, Watson GA, Miller JC, Lautenschlaeger T. Brainstem metastases treated with Gamma Knife stereotactic radiosurgery: the Indiana University Health experience. CNS Oncol. 2018 Jan;7(1):15-23. doi: 10.2217/cns-2017-0029. Epub 2017 Dec 14. PMID: 29239214; PMCID: PMC6001560.

<sup>4)</sup>

Trifiletti DM, Lee CC, Kano H, Cohen J, Janopaul-Naylor J, Alonso-Basanta M, Lee JYK, Simonova G, Liscak R, Wolf A, Kvint S, Grills IS, Johnson M, Liu KD, Lin CJ, Mathieu D, Héroux F, Silva D, Sharma M, Cifarelli CP, Watson CN, Hack JD, Golfinos JG, Kondziolka D, Barnett G, Lunsford LD, Sheehan JP. Stereotactic Radiosurgery for Brainstem Metastases: An International Cooperative Study to Define Response and Toxicity. Int J Radiat Oncol Biol Phys. 2016 Oct 1;96(2):280-288. doi: 10.1016/j.ijrobp.2016.06.009. Epub 2016 Jun 15. PMID: 27478166; PMCID: PMC5014646.

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