Hypofractionated Stereotactic Radiosurgery and Radiotherapy to Large Resection Cavity of Metastatic Brain Tumors

Leonardo conrado S. Lima[1,2], Justin Sharim[3], Rebecca Levin-Epstein[1], Stephen Tenn[1], Alisson R. Teles[4,5], Tania Kaprealian[1], Nader Pouratian[1,3,6,7]

■ OBJECTIVE: **To evaluate the efficacy of postoperative fractionated stereotactic radiosurgery (FSRS) and hypofractionated stereotactic radiotherapy (SRT) to large surgical cavities after gross total resection of brain metastases.**

■ METHODS: **A retrospective analysis of 41 patients who had received tumor-bed FSRS (5 fractions) or SRT (10 fractions) after resection of brain metastasis between 2005 and 2015 was performed. All resection cavities were treated with a frameless linear accelerator-based system. Patients who underwent subtotal resection, single-dose SRS to the resection cavity, or were treated with a fractionation schedule other than 5 or 10 fractions, were excluded.**

■ RESULTS: **Twenty-six patients were treated with 5 fractions and 15 patients with 10 fractions. The median planning target volume was 19.78 cm^3 (12.3–28 cm^3) to the 5-fraction group and 29.79 cm^3 (26.3–47.6 cm^3) to the 10-fraction group ($P = 0.020$). The 1-year and 2-year local control rates for all patients were 89.4% and 77.1%, respectively, and 89.6% and 78.6% were free from distant intracranial progression, respectively. No difference was observed in local control or freedom from distant intracranial progression between the 5-fraction or 10-fraction groups. The median overall survival was 28.27 months (95% confidence interval, 19.42–37.12) for all patients. No patient developed necrosis at the resection cavity.**

■ CONCLUSIONS: **Fractionation offers the potential to exploit the different biological responses between neoplastic and normal tissues to ionizing radiation. The use of 5 daily doses of 5–6 Gy or 10 daily doses of 3 Gy is a good strategy to have a reasonable local control and avoid neurotoxicity.**

INTRODUCTION

Brain metastases are the most common tumors of the central nervous system (CNS), affecting up to 40% of patients with cancer.[1] About 25% of patients who die of extracranial oncologic disease have CNS metastases detected at autopsy.[2] Despite the recent advances in neuro-oncology, the optimal management of these patients is still controversial.

In 1998, Patchell et al.[3] showed that the recurrence rate of tumor anywhere in the brain was significantly less with postoperative whole-brain radiotherapy (WBRT) (18%) compared with observation alone (70%). However, WBRT is not harmless and can cause short-term and long-term sequelae, particularly impairment of cognitive function, in particular verbal memory, executive functioning, and processing speed.[4,5]

Stereotactic radiosurgery (SRS) to the surgical cavity has been proposed as an alternative approach to treatment after primary resection of brain metastases. SRS delivers a single large cytotoxic dose of radiation to a target with high precision, thus minimizing the radiation dose to the surrounding normal tissue.[6] Several studies have evaluated the usefulness of single-dose SRS to metastatic resection cavities, reporting no increase in local recurrence or decrease in overall survival compared with WBRT.[4,7-9]

Key words
- Brain metastasis
- Stereotactic radiosurgery
- Stereotactic radiotherapy

Abbreviations and Acronyms
CI: Confidence interval
CNS: Central nervous system
FSRS: Fractionated stereotactic radiosurgery
LMD: Leptomeningeal dissemination
MRI: Magnetic resonance imaging
PTV: Planning target volume
SRS: Stereotactic radiosurgery
SRT: Stereotactic radiotherapy
WBRT: Whole-brain radiotherapy

From the Departments of [1]Radiation Oncology and [3]Neurosurgery, [6]Brain Research Institute, and [7]Neuroscience Interdepartmental Program, David Geffen School of Medicine at UCLA, Los Angeles, California, USA; [2]Department of Neurosurgery, Sao Rafael Hospital, Salvador, Brazil; [4]Department of Neurosurgery, Montreal Neurological Institute, McGill University, Montreal, Canada; [5]Laboratory of Clinical Studies and Basic Models of Spinal Disorders, University of Caxias do Sul, Caxias do Sul, Brazil

To whom correspondence should be addressed: Nader Pouratian, M.D., Ph.D. [E-mail: npouratian@mednet.ucla.edu]

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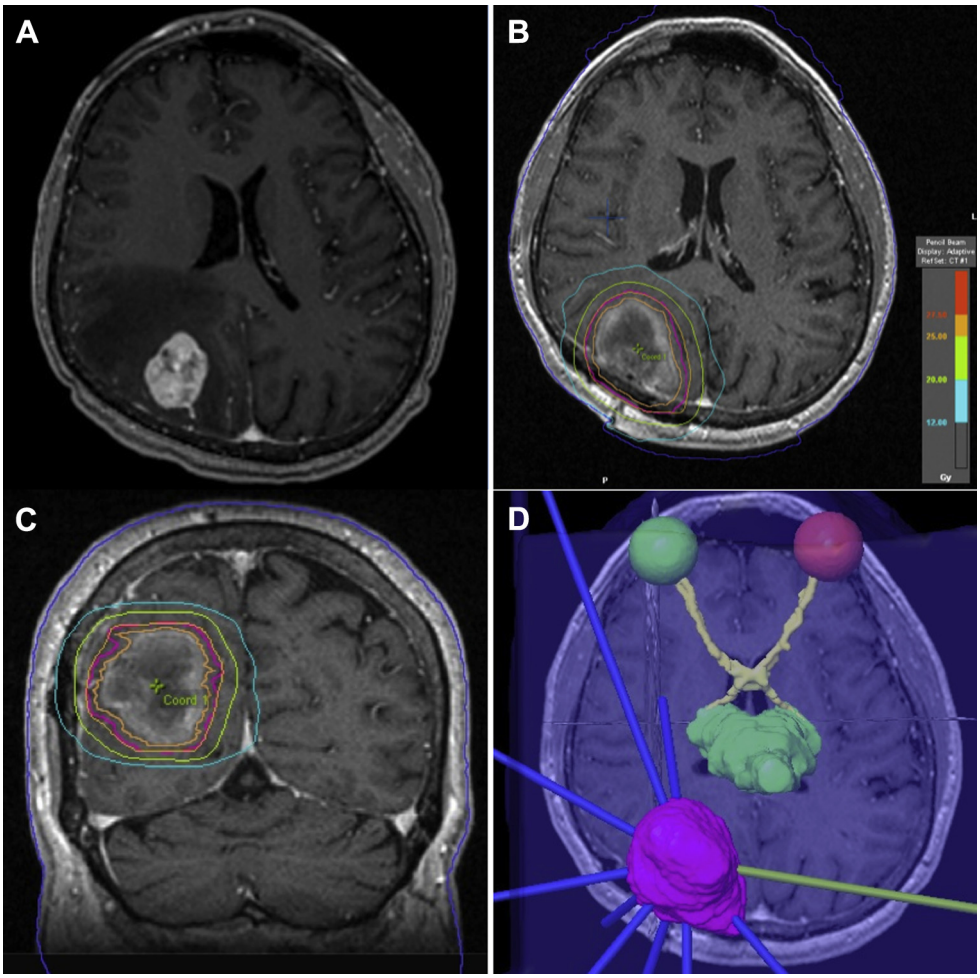

Figure 1. (**A**) Right occipital metastasis of thyroid cancer. (**B**, **C**) The patient was submitted to craniotomy and after 4 weeks the resection cavity (planning target volume, 48.3 cm^3) was treated with 5 fractions of 5 Gy. (**D**) Three-dimensional reconstruction showing multiple radiation beams delivering radiation to the cavity with high precision, minimizing the radiation dose to the surrounding normal tissue.

Moreover, Chang et al.[10] reported that memory is more likely to be preserved with initial SRS alone than with SRS plus WBRT. Given good local control and better neurocognitive outcomes with SRS, the role of WBRT might be reconsidered.

Although several studies[4,7,8,11,12] have assessed the role of single-fraction SRS to metastatic resection cavities, some resection cavities are too large to be treated with single-dose SRS because of radiation toxicity concerns.[13,14] This factor is increasingly important because surgery is generally reserved for larger, symptomatic tumors. Yet, there have been limited reports assessing the role of hypofractionated radiotherapy to large resection cavities.[15-20] Studies have been carried out using 3 fractions,[16] but this still seems to be associated with radiation injury.

According to the terminology guidelines of the International Leksell Gamma Knife Society, FSRS implies that the repeated treatment is directed to the same target and with the same dose distribution.[21] In semantic terms, the difference between FSRS and stereotactic radiotherapy (SRT) is an arbitrary limit of 5 sessions.[21] We investigated the use of FSRS and SRT to the resection bed of metastatic tumors as an alternative to WBRT in a select group of patients.

METHODS

Patient Selection

We retrospectively reviewed the records of all consecutive patients with brain metastasis who underwent craniotomy followed by FSRS or hypofractionated SRT to the resection cavity from 2005 to 2015. All patients were treated at Ronald Reagan UCLA Medical Center.