

STEREOTACTIC RADIOSURGERY AND RADIOTHERAPY OF MENINGIOMAS

Clinical White Paper

Meningiomas are estimated to constitute 13 to 26% of all intracranial tumors¹. Most meningiomas are slow-growing, benign neoplasms, deriving from arachnoid cap cells, and are classified as grade I according to the World Health Organization histopathologic classification². Atypical grade II meningiomas are reported in 5 to 7% of all cases, whereas the incidence of malignant grade III meningiomas affects 0.17 out of 100,000 people per year³.

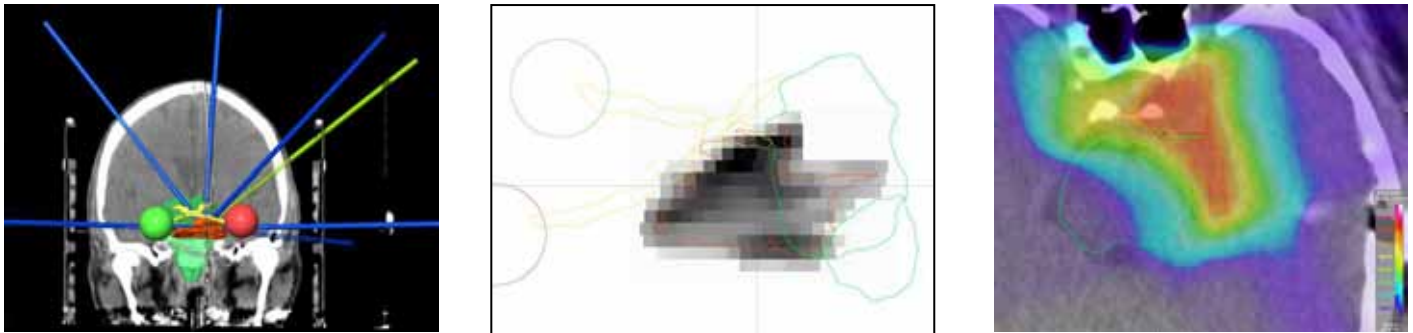


Figure: Details of a typical meningioma treatment plan

Incidences of meningiomas increase with age and are most common in the sixth and seventh decade of life. In adults, there is a marked female bias. Meningiomas are predominantly found in the brain, most frequently in the parasagittal area⁴, and the cavernous sinus⁵. Spinal meningiomas account for less than 10% of all meningiomas and are most often situated in the thoracic spine⁶.

Most meningiomas have good long-term prognosis. In population-based cancer registry series of patients, the overall five year relative survival following diagnosis exceeds 80%⁷. The large majority of meningiomas can be cured by surgery⁸. The primary goal of surgery is complete removal of the tumor, limiting possible recurrence and increasing the chance for a cure. Because most meningiomas are histologically benign, a less than optimal functional outcome after treatment may not be acceptable.

Notwithstanding substantial improvements in microsurgical techniques, surgery of meningiomas has a high rate of significant complications, dependent on the location of the lesion⁹. Mortality rates are reportedly up to 10%¹⁰. These considerations motivate the application of single fraction stereotactic radiosurgery (SRS) and fractionated radiotherapy (SRT) as minimally invasive treatment options.

Both SRS and SRT can be used as an effective adjuvant therapy for partially resected meningiomas, as well as the primary treatment modality for inoperable tumors in close vicinity to organs at risk¹¹⁻¹⁶.

SRS and SRT should not be compared, since both modalities are used in different clinical scenarios and should be available to complement each other, providing safer treatment options for patients.

Small, spherically shaped meningiomas with a maximum dimension less than 3 mm are commonly selected for SRS, while SRT is usually employed for large, irregularly shaped lesions^{12,17}. The radiobiologic benefits of dose fractionation allow the surrounding healthy tissue to recover from the large SRT doses¹⁸.

An overview of some dedicated studies of SRS and SRT treatments of benign meningiomas is presented in the table below. The treatment outcomes are expressed in terms of local control and tumor response, since slow-growing, benign meningiomas are notorious for prolonged intervals between treatment and tumor regression¹³. The tumor response can be quantified by comparing the gross tumor volume contrast-enhanced margins in the three standard MRI dimensions before and after treatment. The tumor response is in general defined as a measurable reduction of the tumor size in any dimension.

The mean prescribed SRS dose is situated between 14 and 16 Gy in order to minimize long-term toxicity while maintaining efficacy. This dose is typically delivered by multiple noncoplanar arcs using a set of conical collimators, ensuring steep dose fall-off in the close proximity of organs at risk.

The mean prescribed SRT dose ranges from 48 to 54 Gy, delivered in 26 to 30 daily fractions of 1.8 to 2 Gy. All SRT studies utilize a micro-multi-leaf collimator for field shaping, which enables versatile treatment delivery options like static conformal beams¹²⁻¹⁴, dynamic conformal arcs¹⁵ and intensity-modulated radiotherapy¹⁶.

The mean follow-up for the patients in the described studies ranges from 17 to 45 months. The tumor growth control rates for both SRS and SRT treatments are higher than 92% for all studies presented.

A reduction of the tumor volume, defined as the tumor response, was observed in 30 to 70% of all cases. The treatment was well tolerated, with an incidence of late toxicity less than 9%.

It is therefore concluded that both SRS and SRT, delivered as primary treatment or adjuvant to conservative resection, have improved the management of intracranial benign meningiomas and are highly effective and safe treatment options.

Overview of the recent clinical literature on SRS and SRT for meningiomas

Author	Institution	Year	# of Lesions	% Prior Surgery	Mean Volume (cm ³)	Mean Dose (Gy)	# of Fractions	% IDL covering PTV	% Local Control	% Tumor Response	% Late Toxicity
Villavicencio ¹¹	Brigham and Women's Hospital, Boston	2001	56	64	0.06	15	1	100	95 at 26 months	41	9
Spiegelmann ⁵	The Chaim Sheba Medical Center, Tel Hashomer	2002	42	26	8.20	14	1	72	98 at 36 months	60	7
Torres ¹²	UCLA School of Medicine, Los Angeles	2003	63	66	12.7	16	1	67	92 at 41 months	35	5
Torres ¹²	UCLA School of Medicine, Los Angeles	2003	72	66	16.1	48	26	89	97 at 24 months	34	5
Selch ¹³	David Geffen School of Medicine, Los Angeles	2004	45	64	14.5	50	28	90	97 at 36 months	18	0
Candish ¹⁴	BC Cancer Agency, Vancouver	2006	36	28	8.90	50	28	90	100 at 26 months	NA	6
Hamm ¹⁵	Helios Klinikum, Erfurt	2006	65	69	18.9	54	30	90	100 at 45 months	54	3
Yenice ¹⁶	Memorial Sloan-Kettering Cancer Center, New York	2006	7	57	7.80	54	30	100	100 at 17 months	71	0

The tumor response can be quantified by comparing the gross tumor volume contrast-enhanced margins in the three standard MRI dimensions before and after treatment. A complete response is defined as the absence of contrast-enhancing tumor on follow-up MRI studies. For the majority of studies, a partial response is defined as a measurable reduction of the tumor size in any dimension. However, Selch et al. define a partial response as a reduction of at least 50% in the largest tumor dimension.

References

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| <p>[1] Marosi C. et al., Crit Rev Oncol Hemat 67, 153, 2008
 [2] Louis D.N. et al., IARC Press, 176, 2000
 [3] Rohringer M. et al., J Neurosurg 71, 665, 1989
 [4] Girvigian M.R. et al., Neurosurg 62, A19, 2008
 [5] Spiegelmann R. et al., Neurosurg 51, 1373, 2002
 [6] De Salles A.A.F. et al., J Neurosurg 101, 435, 2004
 [7] Talback M. et al., Eur J Cancer 40, 1361, 2004
 [8] McCutcheon I.E., J Neurooncol 29, 207, 1996
 [9] Cusimano M.D. et al., Neurosurg 37, 1, 1995</p> | <p>[10] De Jesús O. et al., Neurosurg 39, 915, 1996
 [11] Villavicencio A.T. et al., Acta Neurochir 143, 1141, 2001
 [12] Torres R.C. et al., Neurosurg Focus 14(5), E5, 2003
 [13] Selch M.T. et al., Int J Radiat Oncol Biol Phys 59(1), 101, 2004
 [14] Candish C.C. et al., Int J Radiat Oncol Biol Phys 66(4), S3, 2006
 [15] Hamm K.D. et al., Int J Radiat Oncol Biol Phys 66(4), S7, 2006
 [16] Yenice K.M. et al., Int J Radiat Oncol Biol Phys 66(4), S95, 2006
 [17] Minniti G. et al., Radiat Oncol 4, 42, 2009
 [18] Tome W.A. et al., Technol Cancer Res Treat 1, 153, 2002</p> |
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