

STEREOTACTIC RADIOSURGERY AND RADIOTHERAPY OF BRAIN METASTASES

Clinical White Paper

Brain metastases are a common manifestation of systemic cancer constituting as much as 30% of all intracranial malignant tumors¹. Each year, 15 to 30% of cancer patients develop brain metastases, yielding an incidence of over 100,000 patients in the US². Development of brain metastases leads directly to the patient's death in the majority of cases³.

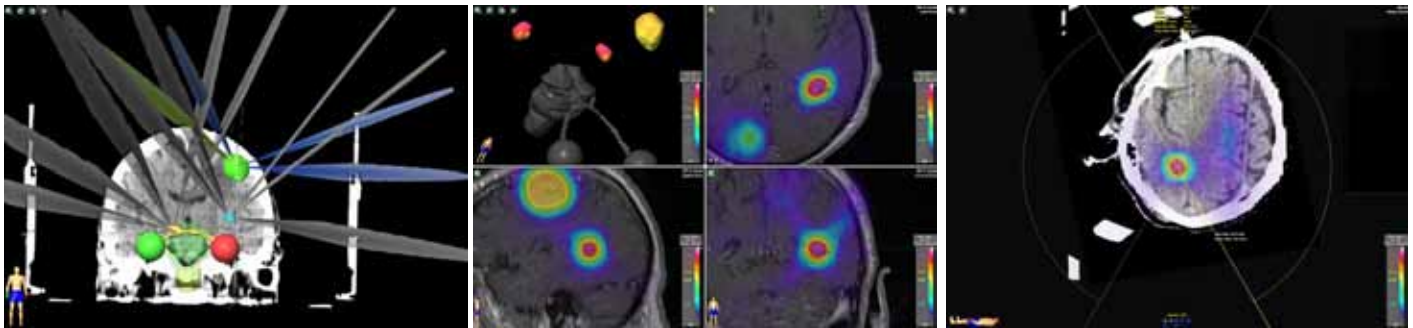


Figure: Details of a typical brain metastases treatment plan

Historical studies suggest that the median survival time for patients with untreated brain metastases is approximately one month⁴. The use of corticosteroids has been shown to double survival time, while the addition of whole brain radiotherapy (WBRT) can further palliate symptoms and prolong survival to six months^{5,6}.

Because the whole brain can be seeded with metastases, WBRT was long considered the standard treatment⁷. However, long-term neurotoxicity has been the major reason to replace WBRT by more focal treatments⁸⁻¹⁴.

For lesions that are accessible and symptomatic requiring urgent decompression, surgery is the treatment of choice for rapid debulking and associated symptom relief. It has been shown that the addition of WBRT to the surgical resection of brain metastases decreases death from neurologic causes¹⁵ and results in increased overall survival compared with WBRT alone¹⁶.

For patients with limited life expectancies, the development of radiation-induced neurologic deficits after WBRT is an important clinical outcome and a significant drawback. A current alternative to WBRT is stereotactic radiosurgery (SRS). With SRS, a single high dose of focused radiation can be delivered to the lesion, while sparing adjacent tissue and thereby lowering complication rates¹⁷.

Minimally invasive SRS can be used as an exclusive treatment or in combination with surgery and WBRT. The dose can also be delivered in several fractions in order to exploit the different biologic responses and repair mechanisms between the tumor and normal tissues to ionizing radiation. This enables dose escalation, which makes fractionated stereotactic radiotherapy (SRT) the ideal treatment modality for large volume metastases.

The treatment of brain metastases represents one of the leading uses of SRS and SRT worldwide. A summary of some recent studies on SRS and SRT treatment of brain metastases is presented in the table below⁸⁻¹⁴.

A significant number of brain metastases patients present with either a solitary lesion or fewer than three total¹⁸. The mean dose and the number of fractions depend on the size and location of the metastases, as well as the choice for possible adjuvant WBRT.

The dose is typically delivered by multiple non-coplanar arcs and the choice for either conical or high-resolution multi-leaf collimators relies on the lesion shape. The overall survival is expressed as a Kaplan-Meier estimate and as the time passed from the last day of treatment to the last clinical visit or death, which is characteristic for brain metastases studies.

Prior to treatment, patients are either fixated with a frame or a thermoplastic, frameless, rigid mask. The latter technique is completely non-invasive and minimizes the patient's discomfort and much of the anxiety related to the procedure.

Frameless treatments also allow for greater flexibility in scheduling personnel and resources. Because the frameless and frame-based patient positioning accuracy was found to be comparable^{19,21}, the former is specifically preferred for the implementation of SRT.

The literature overview in the table below clearly demonstrates that SRS and SRT, either as an exclusive treatment or in combination with WBRT, achieve significantly high tumor control rates ranging from 47 to 80% at one year after treatment.

This translates in a sustained overall survival of 9 to 17 months combined with a low incidence of radiation-induced toxicity, which establishes SRS and SRT as the ideal candidate for the treatment of brain metastases.

Overview of the recent clinical literature on SRS and SRT for brain metastases

Author	Institution	Year	# Patients / # Lesions	Mean Dose (Gy)	# Fractions	% IDL covering PTV	% WBRT	% Local Control	% Overall Survival	Overall Survival (months)	% Toxicity
Manning ⁸	Virginia Commonwealth, Richmond	2000	32 / 57	27	3	80 - 90	100	90 at 6 months	44 at 1 year	12	18
Chitapanarux ¹¹	Chiang Mai University, Chiang Mai	2003	41 / 77	18	1	90	29	68 at 12 months	48 at 1 year 28 at 2 years	10	22
Ernst-Stecken ¹⁴	Novalis Surgery Center, Erlangen	2006	51 / 72	32	5	90	57	76 at 12 months	57 at 1 year	11	NA
Samlowski ⁹	Huntman Cancer Institute, Salt Lake City	2007	44 / 156	18	1	80	48	47 at 12 months	48 at 1 year 18 at 2 years	9	NA
Fahrig ¹⁰	Novalis Surgery Center, Erlangen	2007	150 / 228	35 - 40	5 - 10	90	61	72 at 28 months	66 at 1 year	16	10
Do ¹²	UCI School of Medicine, Irvine	2009	30 / 53	16	1	80 - 90	47	82 at 12 months	51 at 1 year	12	27
Breneman ¹³	Brain Tumor Center, University of Cincinnati	2009	53 / 168	18	1	NA	60	80 at 12 months	44 at 1 year	10	10

The period of overall survival is in general expressed as the time passed from the last day of treatment to the last clinical visit or death.

References

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