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Research Article

Frameless LINAC Stereotactic Radiosurgery for Brain Metastasis using VMAT: A Review of 20 Cases and Institutional Experience

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Abstract

Background/Objectives: Brain metastases can be treated with Stereotactic Radiosurgery (SRS), a precise radiation therapy approach. This study aimed to review the feasibility and efficacy of frameless LINAC-based SRS using Volumetric Modulated Arc Therapy (VMAT) in a group of 20 patients.

Methods: Twenty patients diagnosed with brain metastases received VMAT SRS. Clinical characteristics such as demographics, gender, performance status, number of brain metastases, neurological symptoms, neurosurgical procedures, systemic status, prior treatments, lesion size, SRS dose, local control after SRS and toxicity profile were assessed.

Results: The median age of patients was 49.5 years (range 32-63), with 80% being female. Most patients (85%) had ECOG scores of 0-1. The median lesion size treated was 16 mm, with a median dose of 20 Gy for the first SRS (SRS1). After SRS1, 75% of patients achieved Local Control (LC), with a median duration of LC of 7.65 months. Six patients received a second SRS (SRS2) with a median dose of 20 Gy to a different location. Two out of six patients achieved LC after SRS2. Radiation necrosis occurred in 2 cases (10%). The median follow-up time from brain metastasis to the last follow-up was 20.31 months (range 0-50.43 months).

Conclusion: Frameless LINAC-based VMAT SRS appears to be a promising treatment option for brain metastases. Initial findings suggest favorable local control rates and further research is needed to optimize treatment strategies.

Keywords: Stereotactic Radiosurgery; Brain Metastasis; VMAT; LINAC; Local Control; Follow-up Duration

Introduction

Brain Metastasis (BMs) attracts a growing interest in medicine as it is a common complication related to cancer accounting for 10% - 40%, affecting the quality of life and increasing neurological mortality of patients [1-3]. Survival of these patients is typically poor [4]. Treatment modalities include neurosurgery-based resection, Stereotactic Radiosurgery (SRS), Whole-Brain External Beam Radiotherapy (WBRT) and best supportive care based on the anticipated prognosis [1].

Stereotactic Radiosurgery (SRS) refers to the delivery of a single or small number of radiation fractions with high dose per and high precision to relatively small targets. This is achieved by using multiple, non-parallel radiation beams that converge on the target lesion [5].

Modern LINAC-based radio-surgical systems now regularly employ online cone beam Computed Tomography (CT) scanning

for precision localization, which eliminates the need for skeletal fixation of the patient's head, motion is minimized by the application of an individualized frame or mask.

SRS local control reached up to 70% at first year as proven by controlled studies. Although traditionally used to treat a limited number of tumors, prospective nonrandomized data in patients with newly diagnosed brain metastases suggest that up to 10 tumors with a total cumulative volume ≤15 mL may be treated in a single session with similar efficacy and no increase in toxicity [6].

The most common delayed complication of SRS for treatment of brain metastases is radiation necrosis, which occurs in approximately 10 percent of treated tumors anywhere from six months to several years after treatment. Reported rates of radiation necrosis after postoperative SRS range from 4 to 18 percent [7].The two most important risk factors for radiation necrosis in patients with brain metastases are prior treatment with radiation to the same site and larger tumor size. For tumors treated with prior SRS, the risk of symptomatic adverse radiation effects may be as high as 20 percent within 12 months of retreatment [8]. Use of hypofractionated rather than single fraction SRS for tumors >2 cm may decrease the risk of radiation necrosis [9].

The long-term effects of SRS on neurocognition have not been well studied, but the available data are reassuring [10]. Moreover, in multiple randomized trials, SRS has been shown to be superior to traditional Whole Brain Radiotherapy (WBRT) in terms of cognitive outcomes [11].

In our current practice, if LINAC-based frameless treatment is used, the VMAT technique is always employed because the treatment planning and verification can be done in advance.

Feasibility and potential benefit of VMAT in SRS treatment of the 4-6 cm^3 size metastasis for normal tissue sparing and internal dose escalation has been demonstrated with VMAT optimization procedure, based on auxiliary inner volumes, for dose scaling [12].

This manuscript reviews the feasibility and institutional experience of frameless LINAC-based SRS using VMAT for the treatment of brain metastases.

Patient and Methods

A retrospective analysis of medical records from 2014 to 2021 was conducted, focusing on patients with brain metastases from biopsy-proven primary extra-cranial tumors, excluding certain histologies. The inclusion criteria encompassed patients with one to five metastases, each less than 3.5 cm in diameter. Eligible patients had minimal or stable extracranial metastases and a Karnofsky performance status of 70 or higher.

Exclusion criteria comprised lesions abutting or within critical neurological structures, as well as contraindications to imaging or radiation.

For the patient positioning, a 1 mm slice thickness non-contrast-enhanced CT simulation scan was acquired in the supine position, using a thermoplastic mask for immobilization. For planning purposes, image co-registration with a 1 mm contrast enhanced T1 weighted brain MRI used for Gross Tumor Volume (GTV) delineation. The GTV was defined as the entire lesion volume as visualized on the T1 MRI series fusion; the Planning Target Volume (PTV) created by adding 0-2 mm to GTV to account for any image uncertainty, patient internal movement and setup errors. Organs at risk including eyes, lenses, optic pathway, normal brain tissue, brain stem, cervical cord, cochleae were contoured. Before each fraction, daily cone beam CT was performed for the setup verification. The number of fractions, dose per fraction were chosen based on previously approved clinical trials and guidelines [13,14]. Treatment planning was carried out using multi arc non coplanar VMAT with a single isocentre to produce high quality plans with less treatment time (Fig. 1,2).

Patients' data were recorded in treatment charts including patients' demographics and treatment details, toxicity profile and follow up visits. Follow up examination was reordered including contrasted MRI within 2 months post treatment. Subsequent visits with diagnostic imaging were scheduled every 3 months.

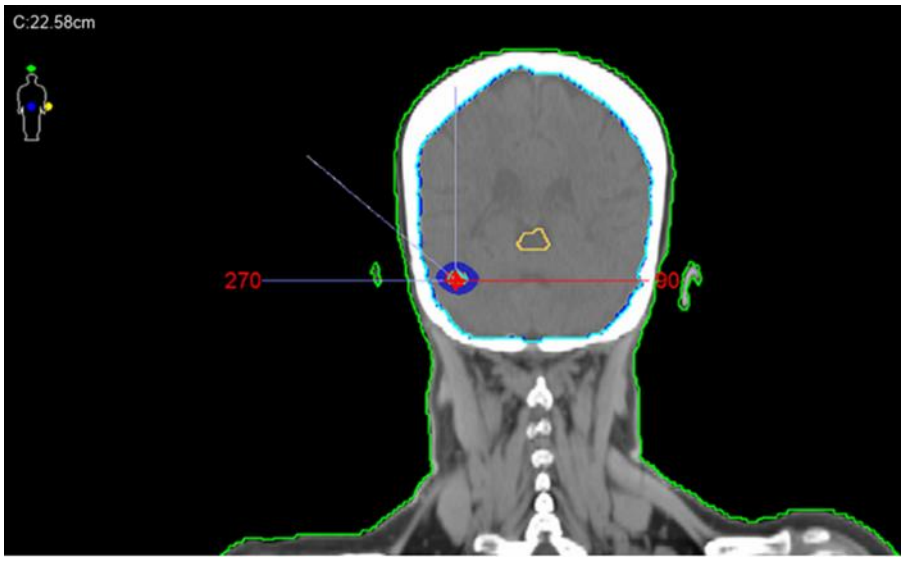

Figure 1: Multi arc non coplanar VMAT with a single isocentre.

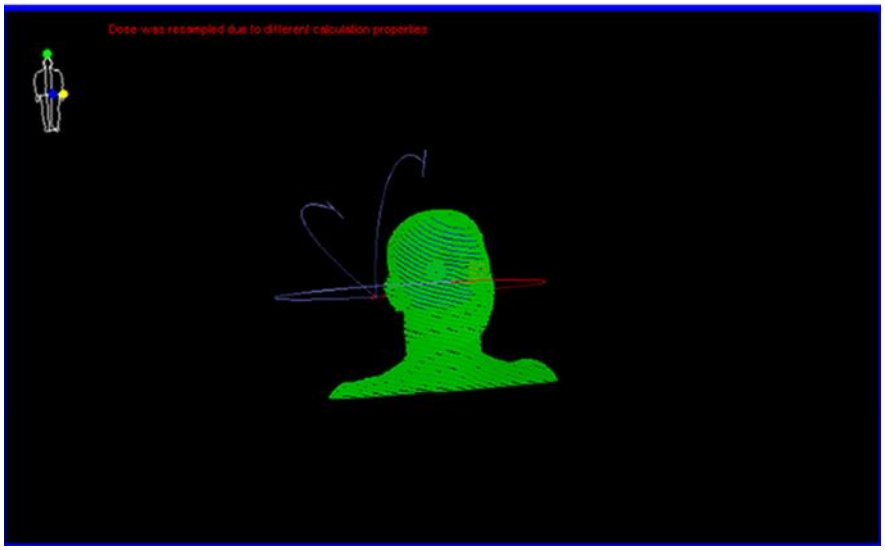

Figure 2: 3D view of multi arc non coplanar VMAT with a single isocentre.

Statistical Analysis

The baseline characteristics of the patients were collected using descriptive statistics. Survival estimates were performed with the Kaplan-Meier method. All the statistical analyses were carried out using the SPSS software (IBM SPSS version 22.0).

Results

The study included 20 patients diagnosed with brain metastases who underwent frameless LINAC-based Stereotactic Radiosurgery (SRS) using Volumetric Modulated Arc Therapy (VMAT). The clinical characteristics of the patients are summarized in Table 1.

The median age of the patients was 49.5 years (range 32-63), with 80% being female. Most patients (85%) had ECOG scores of 0-1.

The median lesion size treated was 16 mm and the median dose for the first SRS (SRS1) was 20 Gray. Seventy-five percent of patients achieved Local Control (LC) after SRS1, with a median duration of LC of 7.65 months.
Six patients received a second SRS (SRS2) to a different location, with a median dose of 20 Gray. Two of these patients achieved local control after SRS2.

Radiation necrosis was observed in 2 cases (10%) during the follow-up period. This aligns with reported rates of radiation necrosis after stereotactic radiosurgery for brain metastases.

The median follow-up time from brain metastasis to the last follow-up was 20.31 months (range 0-50.43 months) with overall survival of 75% at one year and 45% at 2 years (Fig. 3).

Demographics	**N**	**Median**	**Mean**
Age (in years) *	20	49.5 (32-63)	47.75
		n	%
Total		20	100
Gender	Male	4	20
	Female	16	80
ECOG*	0-1	17	85
	4-Feb	3	15
Number of Brain Mets*	2-Jan	15	75
	>2	5	25
Neurological Symptoms*	Yes	18	90
	No	2	10
Neurosurgical Procedures	No	14	70
	Biopsy	0	0
	Resection	6	30
Systemic Status*	No other sites	1	5
	Controlled	9	45
	Uncontrolled	4	20
	Untreated	6	30
Initial Radiotherapy	No	0	0
	WBI alone	3	15
	SRS alone	8	40
	SRS & WBI	9	45
Whole Brain 1st treatment	Yes	14	70
	No	6	30
Whole brain Dose*	30 Gy/10F	6	42.9
	20 Gy/5 F	8	57.1
SRS	Yes	20	100
	No	0	0
No of SRS courses	1	15	75
	>2	5	25
Size of treated lesion in mm			
	Mean	20 (8-42)	
	Median	16	

	Mean	19.67Gy	
SRS 1 Dose	Median	20 Gy	
	Range	10-27.5 Gy	
No of Fractions SRS1	1 #	14	70
	2 #	1	5
	5 #	5	25
Local Control after SRS1	Yes	15	75
	No	5	25
	Treatment effect	0	0
Duration of LC in months after SRS1	N	Median	Mean
	20	7.65	11.74
	Range	(1-47.9)	
SRS 2 Dose	N	Median	Mean
	6	20 Gy	21 Gy
	Range	(15-25 Gy)	
Local Control after SRS 2	N	Yes	No unknown
	6	2	2 2
Radiation Necrosis	N	Yes	No %
	20	2	18 10%
Follow up from BM to death or last F/U in days	N	Median	Mean
	20	618	631
	Range	(0-1534 Days)	

Table 1: Clinical characteristics of the studied patients (N = 20).

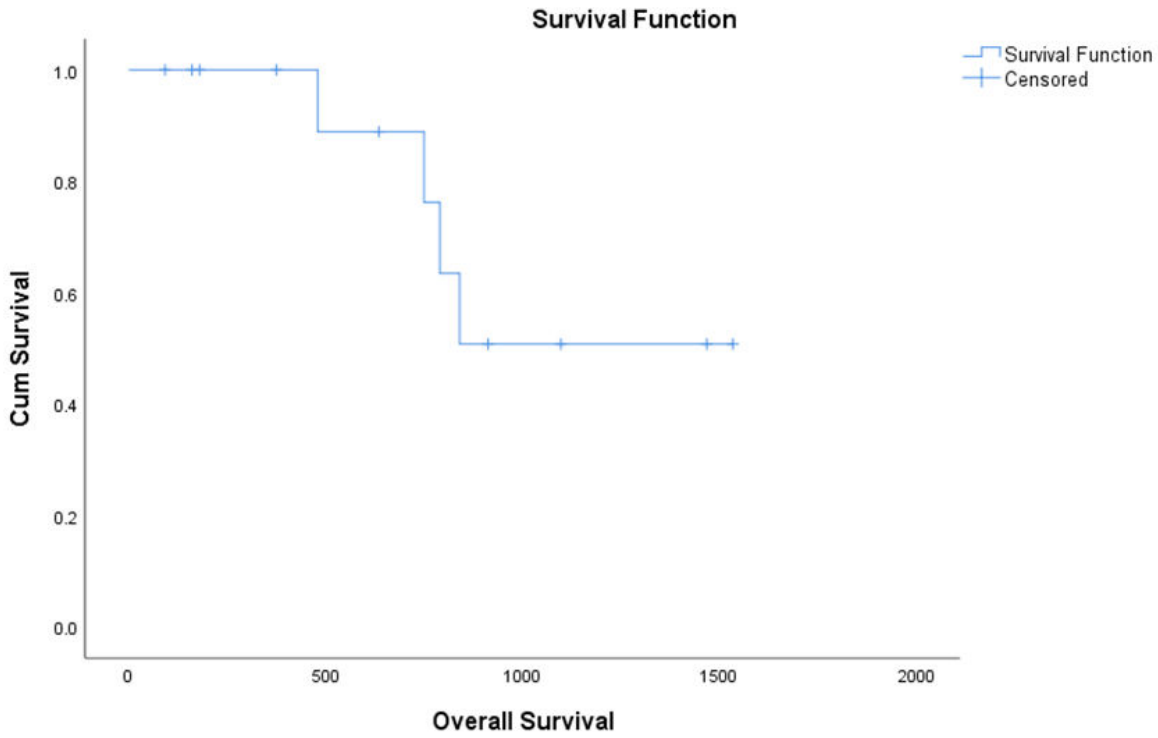

Figure 3: Overall survival curve. *At Time of Brain Metastasis Diagnosis.

Discussion

The use of stereotactic radiotherapy for treating brain metastases is becoming more popular as it offers a more effective alternative to conventional whole brain radiotherapy. This treatment option can provide an improved local control with minimal incidence of neurotoxicity and can be used in combination with new systemic therapies [6].

The results of this study support the feasibility and efficacy of frameless LINAC-based SRS using VMAT for the treatment of brain metastases. These findings align with previous studies highlighting the precision and effectiveness of SRS in treating brain lesions [5,6]. The use of VMAT in SRS has shown promise in terms of treatment planning and verification, as demonstrated by Perez-Calatayud, et al., [12]. VMAT allows a superior normal tissue sparing plus conformity and dose scaling using the auxiliary volumes [12,15].

The observed local control rate of 75% after the first SRS session is consistent with reported rates in the literature [6,16]. The study also noted that larger tumor volumes treated with prior SRS may be associated with an increased risk of adverse radiation effects, emphasizing the importance of individualized treatment strategies [8]. The data on the second SRS session contribute to the ongoing discussion on the optimal management of recurrent lesions [18].

In our study we followed the international guidelines as regard critical structures dose constraints which reduced risk of neurotoxicity. The incidence of radiation necrosis in 10% of treated cases falls within the reported range. The identified risk factors, such as prior radiation to the same lesion and larger tumor volumes, underscore the need for careful consideration in retreatment decisions [8,9,17].

The median follow-up time provides valuable information on the duration of the treatment effect. While the study did not find significant radiation-induced neurocognitive effects, the long-term impact of SRS on neurocognition warrants further investigation [11].

Our study results are like recently published literature indicating that the use of VMAT-SRS for BM was feasible, effective and associated with low treatment-related toxicity rates. Thus, treatment with VMAT is a safe technique to plan to achieve local control without toxicity [18,19].

Limitations and Future Directions

Acknowledging the retrospective nature and the relatively small sample size of this study, future research endeavours should aim to validate these findings in larger cohorts. Exploring potential predictors of treatment response, as highlighted in studies like the one by Bilger et al., will further enhance our understanding and guide the optimization of treatment strategies [16].

Conclusion

In conclusion, our findings underscore the promise of frameless LINAC-based VMAT SRS in treating brain metastases, demonstrating favourable local control rates and an acceptable toxicity profile. These results contribute substantively to the existing body of evidence supporting the efficacy of SRS and underscore the imperative for continued refinement of treatment strategies.

Conflict of Interests

Authors declare that there is no conflict of interest for this paper.

Ethics Approval and Consent to Participate

Approval from King Faisal Specialist Hospital and Research Centre, Jeddah, Institutional Review Board was obtained after approval from all concerned departments.

Consent for Publication

Not applicable

Availability of Data and Materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests
None

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Authors' Contributions
AA PI, research idea, IRB preparation, data collection, statistical analysis, abstract and manuscript writing.
HM CoPI, research idea, IRB review, data sheet preparation, abstract and manuscript review and editing.
ZM IRB review, data collection, discussion and review abstract and manuscript.
HI data collection, discussion and review of abstract and manuscript.
AAH data collection, discussion and review of abstract manuscript.

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