JBUON 2013; 18(3): 717-722
ISSN: 1107-0625, online ISSN: 2241-6293 • www.jbuon.com
E-mail: editorial_office@jbuon.com

ORIGINAL ARTICLE

Evaluation of linear accelerator-based stereotactic radiosurgery in the management of meningiomas: a single center experience

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Summary

Purpose: *Stereotactic radiosurgery (SRS) has emerged as a viable alternative to surgery in the management of meningioma through exploiting the advantage of being minimally invasive with few complications and acceptable local control rates. The aim of this study was to evaluate the efficiency of linear accelerator (LINAC)-based SRS in the management of meningiomas and to report our experience using this sophisticated technique.*

Methods: *Between July 1998 and March 2012, 79 patients (42 female, 37 male) were treated using LINAC-based SRS in the Department of Radiation Oncology, Gulhane Military Medical Academy. Median dose was 13 Gy (range 10-16) prescribed to the 80-95% isodose line encompassing the target.*

Results: *Median follow-up time was 53 months (range 9-112). Median tumor volume was 3.43 cc (range 0.3-14.1). Local tumor control was 89.7% in the 68 patients with adequate follow-up.*

Conclusion: *LINAC-based SRS offers a safe and effective treatment alternative to surgery in intracranial meningiomas with high local control rates and low morbidity.*

Key words: *linear accelerator, meningioma, stereotactic radiosurgery*

Introduction

Meningiomas arise from the arachnoid cap cells and account for 30% of all central nervous system tumors [1-3]. In World Health Organization (WHO) classification, meningiomas are classified as benign (WHO grade I), atypical (WHO grade II), and anaplastic or malignant (WHO grade III) meningiomas regarding their features including mitosis, hypercellularity, loss of architecture, spontaneous necrosis and brain invasion [4,5]. Meningiomas are usually well-circumscribed, homogeneous lesions which are easily diagnosed with non-invasive imaging methods [6]. Based on the study of Simpson et al. in 1957, gross total resection of meningiomas with involved dura and bone is suggested [7], however, for lesions such as skull base meningiomas, the close proximity of the tumor to critical structures including cranial nerves or the optic pathways usually preclude complete surgical resection despite advances in microsurgery [8,9]. It is estimated that complete surgical resection is not possible in 20-30% of the patients [10]. In addition, some patients are poor candidates for surgical approach considering their comorbidities which increase the risk of surgical resection. Even in case of gross total resection, recurrence rates have been reported to be in the range of 4-14% and 18-25% at 5 and 10 years, respectively [10,11] notwithstanding the gold standard still being complete surgical removal in suitable patients [10,12,13].

Radiotherapy may be used in both the adjuvant and definitive setting for meningiomas. Fractionated external radiotherapy is effectively used as adjuvant therapy in partially resected cases while it may also be used in unresectable meningiomas resulting in high local control rates of 70-80% at 10 years [14,15]. External beam radiotherapy has been shown to reduce postoperative

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Received: 24/01/2013; Accepted: 11/02/2013

recurrences, however it may have long-term detrimental effects due to excess exposure of optic pathways and hypophysis in addition to potential cognitive function impairment [16,17].

With recent advances in the discipline of radiation oncology such as intensity modulated radiation therapy (IMRT), stereotactic radiosurgery (SRS), and fractionated stereotactic radiation therapy (FSRT) allowing more precise treatments, improved local control with lower toxicity profile is achieved. SRS offers an alternative treatment option for the management of patients deemed unsuitable for surgery, and confers 5 and 10 year tumor control rates comparable to surgery, particularly in skull base meningiomas [18]. Utilization of SRS in the management of meningiomas since 1990s for both the primary and adjuvant settings has conferred satisfactory control rates ranging between 86 and 100% [19-29]. In this study, we evaluated the efficiency of LINAC-based SRS in the management of meningiomas.

Methods

Between July 1998 and March 2012, patients with meningiomas were treated using LINAC-based single-dose SRS in the Department of Radiation Oncology, Gulhane Military Medical Academy. Informed consent of all patients was taken before the SRS treatment. Details of the SRS procedure were published previously [30-33]. For the first 10 years (1998-2008), cone-based SRS planning was performed with XKnife-3 (Radionics, Boston, MA, USA) and treatment was delivered by LINAC SL-25 with circular cones (Elekta, UK). In 2008, Xknife-3 radiosurgery planning system was replaced with ERGO ++ (CMS, Elekta, UK) planning system allowing Volumetric Modulated Arc Radiosurgery, and treatments were started to be delivered by LINAC Synergy (Elekta, UK) with 3 mm thickness head-on micro multileaf collimator (mMLC). On the day of treatment, a stereotactic frame (Leksell frame or Brown-Roberts-Wells frame) was affixed with 4 pins to the patient's skull under local anesthesia. Contrast-enhanced CT images with 1.25 mm slice thickness were acquired by computed tomography (CT)-simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK). Acquired images were sent to the workstation (SimMD, GE, UK) for contouring of target volume and critical structures. CT images were fused with T1 contrast-enhanced volumetric MRI images, which were acquired 1 day before the treatment day. With the help of fusion, we took advantage of both CT and MRI modalities to better localize the target and critical structures. Coronal and sagittal images were used in addition to axial images to improve target and organ-at-risk (OAR) delineation accuracy. After completion of contouring, structure sets including the target volume and OARs were transferred to the treatment planning system (ERGO++ planning system, Elekta or XKnife-3, Radionics) to perform radiosurgery planning. SRS treatment planning was done with 6 MV photons with either a mMLC of 3 mm-thick leaves or SRS circular cone collimators. In the mMLC-based intensity modulated SRS planning using the volumetric-modulated arc therapy (VMAT) technique, arc modulation optimization algorithm (AMOA) was used to avoid exceeding OAR (i.e optic nerves, optic chiasm, brainstem) dose constraints and to improve dose homogeneity within the target volume. Figure 1 shows axial, coronal, and sagittal treatment planning images of a patient with meningioma in ERGO planning system. Figure 2 shows a pre-SRS axial MR images of the patient in Figure 1. Figure 3 shows a post-SRS 3rd year follow-up axial MR images of the same patient.

In the planning, either a single 360-degree arc, double 360-degree arcs, or five 180-degree arcs were used to optimize OAR sparing. Median marginal dose was 13 Gy (range 10-16) prescribed to the 80-95% isodose line encompassing the target volume. Isocenters of all patients undergoing mMLC-based SRS were checked by image guided radiation therapy (IGRT) techniques including kV-CBCT (kilovoltage Cone Beam CT) and X-ray Volumetric Imaging (XVI, Elekta, UK) system. Eight mg intravenous dexamethasone with H2-antihistamines were used immediately after SRS. After completion of the SRS procedure, follow-up visits were scheduled for every patient routinely at 3-month intervals for the first year, at 6-month intervals for the second year, and annually thereafter including clinical examination with neurological evaluation and neuroimaging with contrast-enhanced MRI. Follow-up tumor sizes measured for each patient were compared with pre-SRS measurements to assess local tumor control which was defined as no tumor enlargement or presence of tumor downsizing on follow-up imaging. Patients were requested to inform the treating physician about any unexpected neurological worsening regardless of the follow-up schedule.

Results

A total of 79 patients referred to our department between July 1998 and March 2012 received LINAC-based SRS. The median patient follow-up time was 53 months (range 9-112). Forty-two patients (53.2%) were female and 37 (46.8%) male. Median age was 41.1 years (range 23-74). Thirty out of the total 79 patients (37.9%) underwent surgery or biopsy before SRS; of these 30 patients, the type of operation was total resection in 10 (12.6%) patients, subtotal resection in 12 (15.2%), and biopsy in 8 (10.1%). Indication for post-surgery SRS was the presence of recurrent tumor in all 10 patients undergoing total resection, and the presence of residual tumor in the remaining

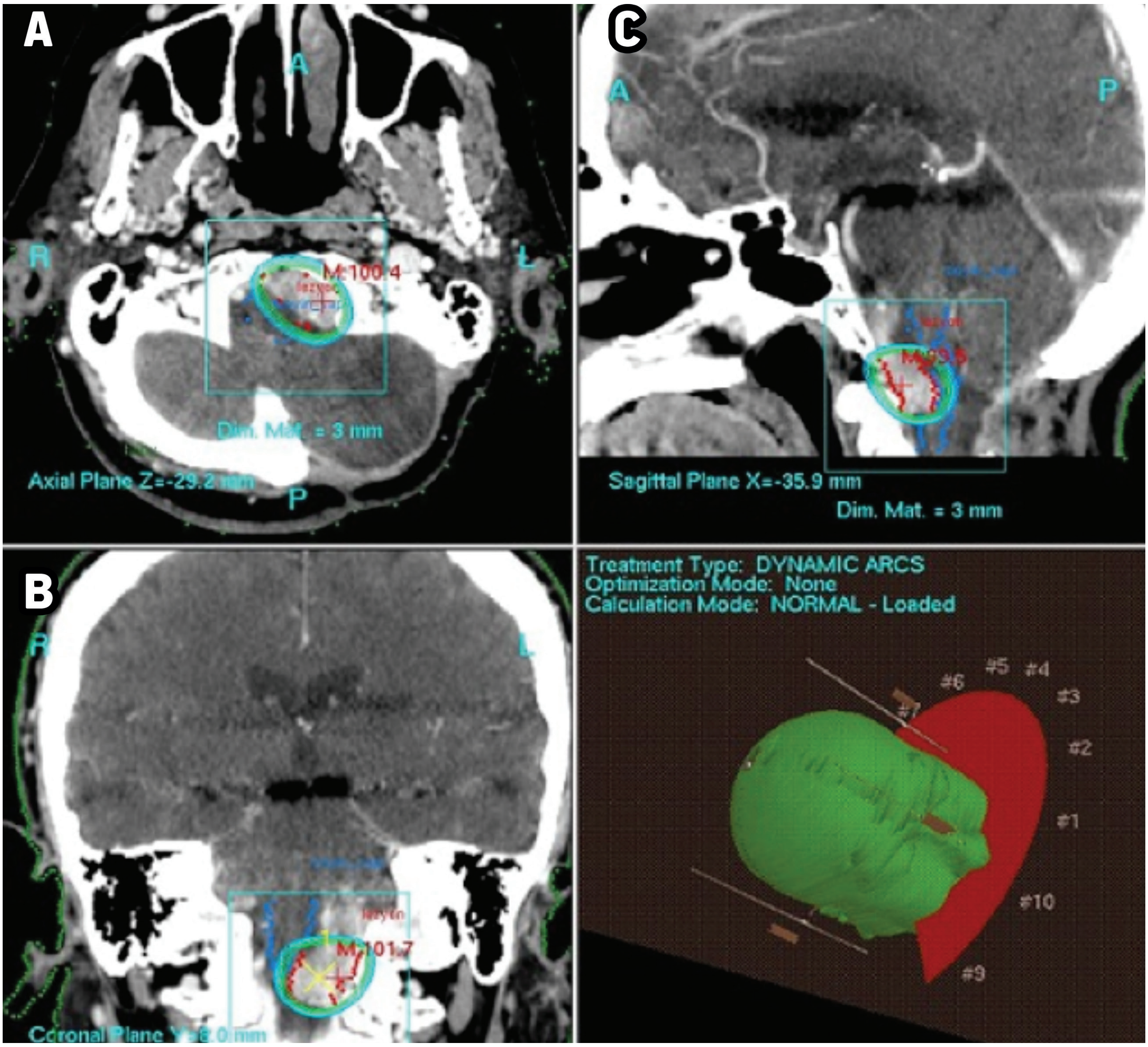

Figure 1. Axial (**A**), coronal (**B**), and sagittal (**C**) treatment planning images of a patient with meningioma in ERGO planning system.

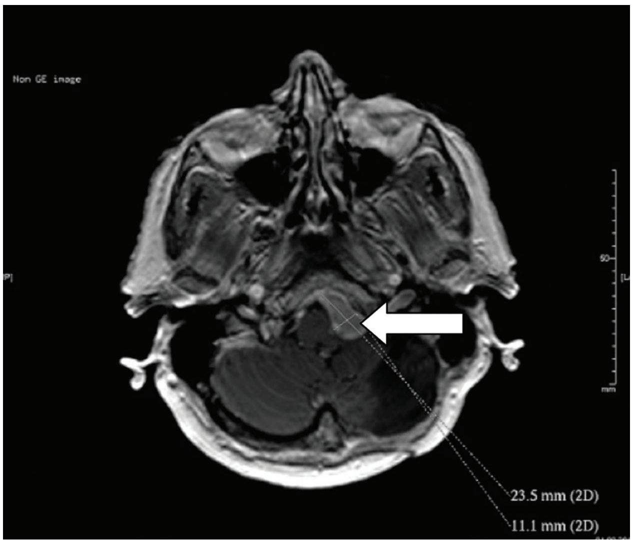

Figure 2. Pre-SRS axial MR images of the patient in Figure 1 showing the meningioma (arrow).

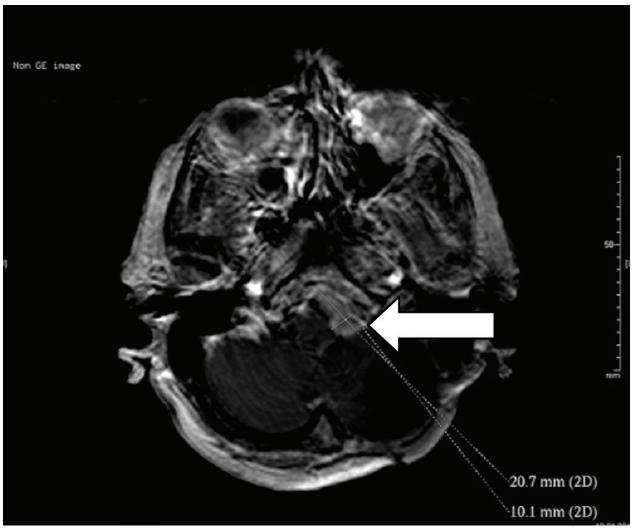

Figure 3. Post-SRS 3rd year follow-up axial MR images of the patient in Figure 1 showing lesion downsizing (arrow).

Table 1. Patient characteristics

Characteristics	*N*	*%*
Number of lesions	79	100
Median age, years (range)	41.1 (23-74)	
Gender		
Male	37	46.8
Female	42	53.2
Surgery before SRS		
Subtotal	12	15.2
Gross total	10	12.6
Biopsy	8	10.1
None	49	62.1
Diagnosis		
By imaging	49	62.1
Histopathologically	30	37.9
WHO grade		
I	22	27.8
II	8	10.1
Previous radiotherapy	None	-
Presenting symptoms		
Headache	26	33
Seizure	17	21.5
Cranial nerve deficit	6	8
Dizziness	5	6
Motor deficit	5	6
Hearing loss	4	5
Sensory deficit	2	2.5
Other	3	4
None	11	14
Tumor localization		
Parasagittal/falx	27	34.2
Convexity	18	22.8
Cavernous sinus	11	13.9
Petroclival	6	7.6
Cerebellopontine angle	5	6.3
Other	12	15.2
Median RT dose (range)	13 Gy (10-16)	
Median tumor volume, cc (range)	3.43 (0.3-14.1)	
Local tumor control (%)	89.7	
Symptoms after SRS		
Clin. improvement	32	47.1
No change	29	42.6
Deterioration	7	10.3
Morbidities		
Peritumoral edema	4	5.9
Necrosis	1	1.5

SRS: stereotactic radiosurgery, RT: radiotherapy

20 patients. Median tumor volume for the total 79 patients was 3.43 cc (range 0.3-14.1). Out of the total 79 patients undergoing SRS, 46 patients (58.2%) were treated using cone collimators in the first 10 years (1998-2008) and 33 patients (41.8%) received mMLC-based SRS between 2008 and 2012. Of the total 79 patients 49 (62.1%) were diagnosed radiologically whereas 30 (37.9%) had histopathologically verified diagnosis. Of the 30 patients with histopathological diagnosis 22 had WHO grade I and 8 WHO grade II meningiona. Periodical follow-up with serial MRI for at least 4 years was available in 68 of 79 patients (86%). Assessment of 68 patients with periodical follow-up MRI revealed unchanged tumor size in 38 patients (55.9%), tumor downsizing in 23 (33.8%), and tumor upsizing in 7 (10.3%). Thus, the predefined local tumor control rate was 89.7% in the 68 patients with periodical follow-up neuroimaging. Of the 7 patients with tumor upsizing, enlargement of tumor after SRS occurred within 24 months in 3 of them, and later than 36 months in 4. Of these 7 patients with tumor upsizing, 5 underwent surgery, one patient underwent a second SRS session and one patient underwent external radiotherapy. Five out of 68 patients (7.4%) with adequate follow-up experienced morbidities (peritumoral edema in 4 and radiation necrosis in 1 patient) following SRS which resolved after medical treatment. Of the 68 patients having symptoms before SRS, 32 patients (47.1%) experienced clinical improvement, 29 (42.6%) had no change in symptoms and 7 (10.3%) had deterioration of the symptoms at follow-up. Out of the 32 patients with clinical improvement in preSRS symptoms, 19 patients suffered from headaches, 10 had seizures, 1 had diplopia, 1 had numbness in the face and 1 leg weakness, all of whom had alleviated symptoms in the postSRS follow-up period. Patient characteristics are shown in Table 1.

Discussion

In this study, using LINAC-based SRS, we observed alleviation in preSRS symptoms including headache, seizures, diplopia, facial numbness, leg weakness and high local control of the meningioma lesions. In the management of surgically accessible intracranial meningiomas, gross total resection remains the mainstay of treatment. Extent of surgical resection is associated with long-term local control. In the study by Mirimanoff et al., rates of freedom from recurrence for totally resected lesions were 93, 80, and 68% at 5, 10, and 15 years, respectively, whereas these rates were 63, 45, and 9% in the setting of subtotal resection [10]. Total surgical removal of meningiomas is achieved in 26-86% of the cases, and local recurrence rates are as high as 25% despite gross total resection [10]. Convexity meningiomas are frequently totally resected, however complete resection is rarely achievable in parasellar and sphenoidal meningiomas, resulting in high rates of recurrence. Recurrence rates may reach 100% after subtotal resection with prolonged follow-up [34].

Significant developments in radiation techniques enable improved critical organ sparing with more homogeneous dose distributions. These developments in the technique improve local control and decrease morbidity. SRS is considered to be an effective treatment modality since it is minimally invasive compared to surgery with few complications and acceptable local control rates. In the studies by Kondziolka and Flickinger; Gamma Knife radiosurgery achieved a local control rate of 93% in the management of patients with meningioma [18,35]. Pollock et al. compared upfront SRS with surgery in the management of small and medium-sized meningiomas in all locations, and found equivalent tumor control rates with SRS compared to Simpson grade 1 resection at 3 and 7 years [36] . SRS conferred superior progression free survival (PFS) than surgery in the setting of less complete resections (Simpson grade 2-4) at 3 and 7 years [36] .

Including the "dural tail" in the treatment field for SRS is controversial due to the irradiation of larger fields and less conformal treatment plannings which led us to exclude dural tail in our treatment fields. However, some studies reported higher disease free survival (DFS) rates by including the dural tail in the treatment field. In the study by Dibiase et al., 5-year DFS was superior in patients with dural tail included in treatment field (96.0 vs 77.9% , p=0.038) [22]. However, in our study we found local tumor control comparable with many studies as 89.7% [20-29].

Tumor volume has been shown to be a predictor for success with radiosurgery. DiBiase and colleagues reported 5-year disease-free intervals of 91.9% for patients with tumors of 10 cc or smaller vs 68% for larger tumors [22]. Kondziolka et al. similarly reported a decreased control rate for larger tumors [37]. In our study, of the 7 patients with local failure, 5 had tumors larger than 10 cc.

FSRT is a viable treatment modality to treat lesions larger than 3 cm and in close proximity to critical structures. Han et al. reported no significant difference in the radiographic and clinical response in patients with skull base meningiomas treated with either SRS or FSRT [38].

SRS is not devoid of complications. Morbidities including radiation necrosis, peritumoral edema, cranial nerve deficits, delayed hydrocephalus may occur despite the low risk of complications at the time of the treatment. Zada et al. rewieved their experience using SRS in the management of meningiomas with an overall complication rate of 8% [39]. In our study, symptomatic peritumoral edema was observed in 4 patients and radiation necrosis in one patient. These 5 patients benefited from steroid treatment.

Conclusion

LINAC-based SRS offers a safe and effective alternative treatment modality to surgery in intracranial benign meningiomas with high local control rates and low morbidity. Its efficiency in particularly inaccessible lesions around critical regions at risk makes it an invaluable non-invasive modality for patients suffering from meningioma.

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