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Original Research Article

Efficacy and Toxicity of Stereotactic Radiotherapy Using CyberKnife in Patients of Meningioma: A Single Institutional Study

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Abstract: *Meningiomas are among the most common primary intracranial tumors; while typically benign, management is challenging when lesions abut critical neurovascular structures. Stereotactic radiotherapy (SRT) with the CyberKnife® system provides a non-invasive, highly conformal alternative to surgery.* ***Objective:*** *To evaluate the efficacy and toxicity of CyberKnife-based stereotactic radiosurgery (SRS) and fractionated stereotactic radiotherapy (FSRT) for meningiomas treated at a single Pakistani institution.* ***Methods:*** *This observational descriptive study was conducted in the Department of Oncology, NORI, Islamabad, from December 2023 to December 2024 and enrolled 39 patients with WHO grade I–II or recurrent meningiomas. Treatment modality and dose were individualized by tumor size, grade, and proximity to organs at risk. SRS was delivered in a single fraction (13–18 Gy), and FSRT in 3–5 fractions (total 21.5–30 Gy), adhering to contemporary critical-structure constraints. Efficacy was assessed clinically (symptom change) and radiologically using Response Assessment in Neuro-Oncology (RANO) criteria on MRI at approximately 3, 6, and 12 months. Toxicities were recorded prospectively. Descriptive statistics (counts, percentages, medians) were used to summarize baseline characteristics, disease control, and adverse events.* ***Results:*** *The cohort consisted of 72.7% females, with a median age of 52 years. Common locations were parafalcine (25.6%) and cerebral convexity (20.5%). Thirteen patients received SRS and 26 received FSRT. At 6 months, radiologic disease control was achieved in 91% of patients, with stable disease in 91% and a minor radiographic response in 9%. No progressive disease was observed during follow-up. Symptomatic improvement occurred in 70% of patients with headaches and/or seizures and in 20% with focal neurological deficits. Treatment was well tolerated; transient headaches consistent with radiation-related edema were managed with short-course corticosteroids, and no clinically significant late toxicities were documented.* ***Conclusion:*** *CyberKnife-based SRS and FSRT provided high rates of radiologic stability and meaningful symptom relief with minimal toxicity in patients with meningioma at a Pakistani tertiary center. These findings support the effectiveness and safety of CyberKnife SRT as a practical option, including in resource-constrained settings.*

Keywords: Brain Edema; Meningioma; Neoplasm Recurrence, Local; Pakistan; Radiotherapy, Stereotactic; Treatment Outcome

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Introduction

Meningiomas, arising from the meninges, present a significant clinical challenge due to their variable behavior and potential for recurrence. Representing approximately 30% of all primary brain tumors, meningiomas are often benign but can exhibit aggressive characteristics depending on their location, size, and histological grading (1). Surgical resection is considered the gold standard for treatment; however, complete resection is not always achievable, particularly in cases where tumors are located near eloquent brain structures (2). In such scenarios, alternative therapeutic modalities, such as stereotactic radiosurgery (SRS) and stereotactic radiotherapy (SRT), have emerged as viable options. Notably, CyberKnife® radiosurgery has garnered attention due to its non-invasive nature, precision in targeting tumors, and reduced radiation exposure to surrounding healthy tissues (3).

Recent studies have shown that CyberKnife treatment can achieve impressive local control rates for meningiomas, particularly in patients with unresectable or recurrent tumors. Reportedly, local control rates can range from 92% to 100% at five years, demonstrating its efficacy when employed either as an initial therapy or as an adjunct to surgery (4). Furthermore, CyberKnife's ability to deliver high doses of radiation in a precise manner allows for effective tumor necrosis while minimizing the risk of significant radiological complications (5). Innovations such as real-time image guidance further enhance the safety and efficacy of CyberKnife, making it an ideal choice for treating meningiomas located in critical areas, such as the skull base (3).

Despite these advancements, the therapeutic landscape for meningiomas, particularly in low-resource settings, remains underexplored, particularly in Pakistan. The current literature emphasizes the necessity of tailored approaches based on the unique patient demographics and socio-economic contexts prevalent in such regions (6).

The application of CyberKnife techniques might not only improve treatment outcomes for meningioma patients but also provide substantial insights into its efficacy and toxicity profile. This variability in effectiveness may stem from differences in tumor biology, accessibility to healthcare facilities, and the patient's overall health status, thereby necessitating localized studies that comprehensively measure both efficacy and toxicity (7). Consequently, the goal of this research study is to evaluate the effectiveness and toxicity of CyberKnife in the treatment of meningiomas within a single institution in Pakistan, thereby adding invaluable data to the global body of literature.

Given the rising incidence of meningiomas and the evolving landscape of treatment options available, investigating CyberKnife's role within the specific context of Pakistani patients addresses a significant gap in regional oncological research. The insights gained could potentially refine treatment protocols and improve patient outcome metrics in under-resourced healthcare systems.

Methodology

This single-institution, observational descriptive study was conducted in the Department of Oncology at the Atomic Energy Cancer Hospital, NORI (Islamabad, Pakistan) between December 2023 and December

2024. The protocol received prior approval from the institutional ethics review committee, and all participants provided written informed consent before enrollment. Adults (≥18 years) with radiologically or histopathologically diagnosed intracranial meningioma were eligible if the maximum tumor diameter was <6 cm, Eastern Cooperative Oncology Group (ECOG) performance status was 0–1, and the tumor was WHO grade I or II; patients with recurrent disease after prior surgery were also eligible. Exclusion criteria were prior cranial re-irradiation, inability to tolerate supine positioning for the 30–40-minute treatment period due to comorbidities, and loss to follow-up. Thirty-nine consecutive patients meeting these criteria were included.

Pre-treatment evaluation consisted of a high-resolution, contrast-enhanced T1-weighted MRI of the brain (1-mm slices) for target definition and a non-contrast planning CT scan (vertex to C2; 1-mm slices), both acquired with a thermoplastic immobilization mask. Rigid image registration was performed to fuse the CT and MRI datasets for contouring. The gross tumor volume (GTV) encompassed the contrast-enhancing lesion on T1-weighted MRI. Organs at risk (OARs) including the brainstem and optic apparatus (optic nerves and chiasm) were delineated on the fused datasets. In accordance with stereotactic practice, a minimal margin (approximately 1 mm) was used when generating the planning target volume. Contours were transferred to the physics team for CyberKnife planning and inverse optimization.

Treatment selection and prescription were individualized based on tumor grade, size, site, and proximity to critical structures. Patients with lesions sufficiently distant from the optic pathway and brainstem were considered for single-fraction stereotactic radiosurgery (SRS); otherwise, fractionated stereotactic radiotherapy (FSRT) was favored. Typical prescriptions for grade I tumors were 13–15 Gy in a single fraction (SRS) or 21 Gy in 3 fractions (FSRT). For grade II tumors, prescriptions ranged from 14 to 21 Gy (SRS) or 24 Gy in 3 fractions (FSRT). Recurrent tumors commonly received 25–30 Gy in 5 fractions (FSRT). Across all plans, OAR dose constraints adhered to contemporary stereotactic consensus guidance (UK consensus, 2022) and the Timmerman stereotactic body radiotherapy tables (2021), to achieve target coverage while maintaining OAR doses at or below accepted tolerance thresholds. Final plans were reviewed jointly by radiation oncologists and medical physicists before delivery on the CyberKnife system.

Outcomes were defined a priori as efficacy and toxicity. Efficacy was assessed clinically by changes in presenting symptoms (e.g., headache intensity using a pain scale, seizure frequency, and focal neurological deficits) and radiographically on serial, contrast-enhanced brain MRIs at approximately 3, 6, and 12 months after SRS/FSRT. Radiologic response was classified using Response Assessment in Neuro-Oncology (RANO) criteria for meningioma. Acute and late adverse events were captured prospectively during treatment and at each follow-up visit; events were recorded in the clinical notes, with particular attention to treatment-related edema and visual/brainstem sequelae, and were managed per standard institutional practice (including short steroid courses when indicated).

Statistical analysis was descriptive, consistent with the study's observational design. Categorical variables were summarized as counts and percentages, while continuous variables were presented as means with standard deviations or medians with ranges, as appropriate. Analyses were performed using IBM SPSS Statistics; no formal hypothesis testing was prespecified.

Results

We identified a total of 39 cases in which females are affected in a greater proportion than men (72.7% versus 27.2% respectively). The median age was 52 years, and almost 61% patients were in the age group of 41-60years.

The majority of the lesions were located in the Parafalcine and cerebral convexity regions (25.6% and 20.5%, respectively). Histopathological diagnosis was present in almost 56.4% of patients, while the remaining 43.5% were diagnosed radiologically. Grade I meningiomas accounted for 33%, Grade II meningiomas for 23%, and recurrent meningiomas for 15.3%. It is important to note that among the recurrent tumors, most were grade I, while grade II tumors were only 33%.

The main symptoms were headache, seizures, and neurological deficit. The maximum and minimum tumor volumes were 77 cm^3 (in 4 cases) and 0.55 cm^3. The decision of SRS versus FSRT was made based on proximity to critical structures (e.g., brainstem, optic pathway). The dose range for SRS was 13-18Gy, while that of fractionated SRT was 21.5 – 30Gy in 3-5 fractions. For recurrent tumors, the dose was kept on the higher side—a total of 13 patients were treated with SRS, while the remaining 26 were treated with fractionated SRT. The doses to the critical organs at risk were kept below the optimal doses according to UK consensus guidelines updated in 2022 and Timmerman Tables updated in 2021.

The radiological response, assessed according to RANO criteria (13), showed that most patients had stable disease at 6 months. Still, it is worth noting that the size of the lesion remained the same. Still, the internal necrosis and decrease in contrast enhancement of the lesions (as shown in Figures 1 and 2) strongly support the symptomatic improvement. The main symptoms were headache, seizures, and neurological deficit. There was marked improvement in symptoms at three and six 6months—the intensity and frequency of headaches and seizures reduced in up to 70% of patients. However, the neurological deficit improved in only 20% patients.

There were no significant toxicities observed. Some patients experienced mildly increased headaches during radiation due to radiation-induced edema. Such side effects were alleviated by giving a higher dose of steroids during radiation, no long-term toxicities developed during the follow-up period.

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Table 1: Patient characteristics

Parameters	Percentage
Gender	
Male	27.2%
Female	72.7%
Performance status	
ECOG 0	5.5%
ECOG 1	94.5%
Age	
18-40years	17.9%
41-60years	61.5%
61 – 80years	20.5%
Symptoms	
Headache	68%
Neurological deficit	16%

Seizures	23%

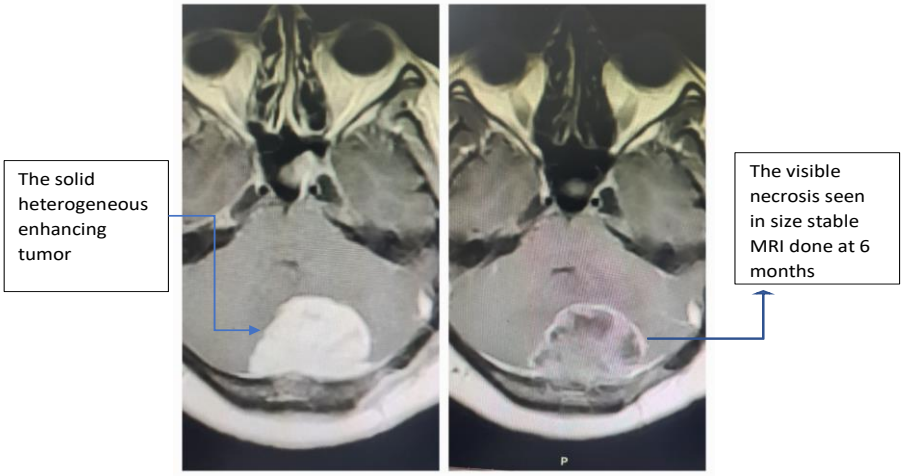

Figure 1 : Pre-treatment and post-treatment images

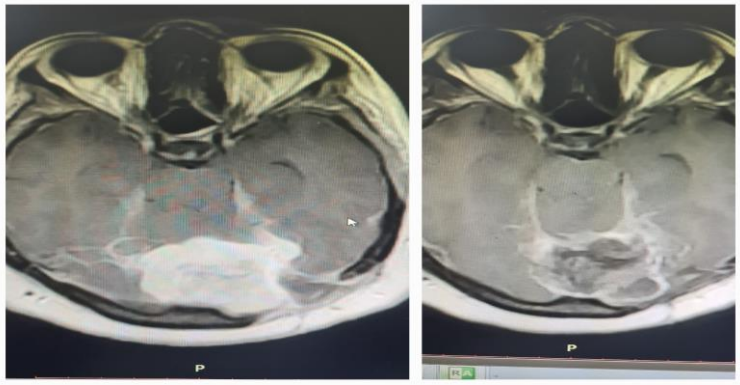

Figure 2: Pre and post-treatment images of recurrent grade II tumor

Table 1: Disease features

Site	Percentage
Parafalcine	25.6%
Along the Cerebral Convexity	20.5%
CP(Cerebellopontine) angle	15.4%
Sphenoid wing	12.8%
Parasagittal	7.6%
Optic nerve meningioma	5.1%
Others	13%
Diagnosis	
Histopathological	56.4%
Radiological	43.5%
Grade	
I	33%
II	23%
Recurrent	15.3%
Treatment volume (ml)	
Minimum volume	0.55cm^3
Maximum volume	77cm^3

Table 2: Treatment and follow-up characteristics

Parameter	Percentage	Dose (range)
No of SRS	28%	13-15Gy
No of FSRT	71.7%	21.5—30Gy (3-5frcations)

	Maximum Dose (D_{max})		Dose Range		
Tumor dose	140% (SRS) 124 %(FSRT)				
Brainstem* (0.035cc)	22.9Gy FSRT		(0.04-22.9) Gy—FSRT		
Optic apparatus * (0.035cc)	22.2Gy FSRT		(0.01—22.2) Gy---FSRT		
Radiological Response (RANO Criteria)					
Months	Complete Response	Partial Response	Minor Response	Stable Response	Progressive Disease
3 months	None	None	none	100%	None
6 months	None	None	9%	91%	None
12 months	None	None	21%	79%	None
*While considering SRS, the first requirement was the location. Hence, all patients who were given SRS had lesions well away from the brainstem and optic apparatus. Thus, the metric dose for the brainstem and optic pathways is written for FSRT cases only.					

Discussion

The findings from our study indicate a significant female predominance in meningioma incidence, with female patients comprising 72.7% of our sample. This aligns with existing literature that consistently reports a higher prevalence of meningiomas in females compared to males. For instance, Ihwan et al. noted a female-to-male ratio of 4.2:1 within their cohort, indicating a similar trend of higher female involvement (8). Likewise, Walsh et al. emphasized that this trend is observed across different demographics and outlined the impact of age and race on the incidence of grade-specific meningiomas [9]. In our study, the median age of 52 years supports previous findings by Smitha and Sivaraman, who reported that the incidence is higher among older adults, particularly those over 40 years of age (10).

When analyzing the distribution of lesion locations, our findings revealed that 25.6% of tumors were located in the para-falcine region, followed by 20.5% in the cerebral convexity, consistent with the anatomical tendencies observed by Gunadi et al. and Hosainey et al., who also reported the falx and convexity as standard locations for meningiomas (11, 12). These similarities suggest that the anatomical risk factors involved in meningioma growth may be universally applicable, supporting a broader understanding of pathological behavior across different populations.

Histopathological analysis demonstrated that 33% of identified tumors were Grade I and 23% were Grade II. These findings are consistent with data presented in recent studies, such as Naeem et al., who reported a predominance of Grade I meningiomas among non-recurrent cases (13). However, it is noteworthy that recurrent tumors in our study mainly consisted of Grade I (15.3%), which deviates from earlier assertions that recurrent tumors are typically higher in grade (14). This raises questions about tumor biology and treatment effectiveness in our specific cohort, suggesting that local treatment protocols might play a significant role in recurrence rates.

Symptoms presented by patients indicated a clear impact on quality of life, with headaches reported by 68% of patients and neurological deficits in 16%. Similar prevalence rates have been observed in other studies; for instance, Cao et al. highlighted headaches as a common symptom, affecting a significant portion of patients (14). Headache symptomatology correlated strongly with tumor dimensions, where a maximum volume of 77 cm^3 was noted in our patients, mirroring indications by Wu et al. that larger tumors contribute to increased symptom severity (14).

The therapeutic implications from our findings show a preference for Fractionated Stereotactic Radiotherapy (FSRT) in 71.7% of cases, reflecting a contemporary approach that balances efficacy with minimization of damage to surrounding critical structures. This strategy aligns with current guidelines for dose constraints in meningioma management [15]. Our treatment doses ranged from 13 to 18 Gy for Stereotactic Radiosurgery (SRS) and from 21.5 to 30 Gy for FSRT. This supports previous findings by Wafa et al., who confirmed that carefully modeled treatment regimens can yield favorable outcomes with acceptable toxicity profiles (16).

The response rates evaluated using RANO criteria indicated that most patients had stable disease at 6 months, with noted symptomatic improvement, particularly regarding headaches and seizures. This outcome is paralleled by Behling et al., who reported a high stability rate in similar treatment protocols (17). Moreover, while some patients experienced radiation-induced edema leading to transient increases in headache severity, our low incidence of significant toxicities is consistent with existing literature advocating for the feasibility of SRS and SRT in meningioma management without substantial adverse effects (10, 14).

Thus, while our study reflects expected trends in the epidemiology and clinical management of meningiomas, it highlights the need for further localized studies that scrutinize the interplay between gender, age, and treatment regimens in the Pakistani context. Understanding these dynamics could enhance personalized treatment approaches and improve outcomes for meningioma patients in resource-limited settings.

A limitation of our study is the time duration, as we included low-grade meningiomas, which are slow-growing tumors that generally take months to years to show a significant reduction in size on MRI images.

A second limitation is the histopathological diagnosis, as we had 43.5% image-based diagnoses. In a study by Flickinger et al., the actuarial rate of having a diagnosis other than meningioma was found to be 2.3% at both 5 and 10 years following the initial radiotherapy. Consequently, for patients with medically inoperable meningiomas or those with operable tumors who decline surgical intervention and biopsy, clinicians often must proceed under the assumption that the tumor is benign.

Conclusion

CyberKnife stereotactic radiotherapy provided effective local control and symptomatic improvement in meningioma patients, with minimal short-term toxicities and no serious late effects, making it a valuable treatment option for tumors in critical brain locations.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-23)

Consent for publication

Approved

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Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

SMS
Manuscript drafting, Study Design,
Review of Literature, Data entry, Data analysis, and drafting an article.
HM
Conception of Study, Development of Research Methodology Design, Study Design, manuscript review, and critical input.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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