Stereotactic radiosurgery for WHO grade I posterior fossa meningiomas: long-term outcomes with volumetric evaluation

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OBJECTIVE Research over the past 2 decades has been characterizing the role of stereotactic radiosurgery (SRS) in the treatment of benign intracranial tumors, including meningiomas. However, few studies have examined the long-term outcomes of SRS treatment for posterior fossa meningiomas (PFMs). Furthermore, previous studies have typically used single diameter measurements when reporting outcomes, which can yield misleading results. The authors describe the use of SRS in the treatment of benign WHO grade I PFMs and correlate volumetric analysis with long-term outcomes.

METHODS This study is a retrospective analysis of a prospectively maintained IRB-approved database. Inclusion criteria were a diagnosis of WHO grade I PFM with subsequent treatment via single-session SRS and a minimum of 3 follow-up MRI studies available. Volumetric analysis was performed on the radiosurgical scan and each subsequently available follow-up scan by using slice-by-slice area calculations of the meningioma and numerical integration with the trapezoid rule.

RESULTS The final cohort consisted of 120 patients, 76.6% (92) of whom were female, with a median age of 61 years (12–88 years). Stereotactic radiosurgery was the primary treatment for 65% (78) of the patients, whereas 28.3% (34) had 1 resection before SRS treatment and 6.7% (8) had 2 or more resections before SRS. One patient had prior radiotherapy. Tumor characteristics included a median volume of 4.0 cm³ (0.4–40.9 cm³) at treatment with a median margin dose of 15 Gy (8–20 Gy). The median clinical and imaging follow-ups were 79.5 (15–224) and 72 (6–213) months, respectively. For patients treated with a margin dose $\geq$ 16 Gy, actuarial progression-free survival rates during the period 2–10 years post-SRS were 100%. In patients treated with a margin dose of 13–15 Gy, the actuarial progression-free survival rates at 2, 4, 6, 8, and 10 years were 97.5%, 97.5%, 93.4%, 93.4%, and 93.4%, respectively. Those who were treated with $\leq$ 12 Gy had actuarial progression-free survival rates of 95.8%, 82.9%, 73.2%, 56.9%, and 56.9% at 2, 4, 6, 8, and 10 years, respectively. The overall tumor control rate was 89.2% (107 patients). Post-SRS improvement in neurological symptoms occurred in 23.3% (28 patients), whereas symptoms were stable in 70.8% (85 patients) and worsened in 5.8% (7 patients). Volumetric analysis demonstrated that a change in tumor volume at 3 years after SRS reliably predicted a volumetric change and tumor control at 5 years ($R^2 = 0.756$) with a $p < 0.001$ and at 10 years ($R^2 = 0.421$) with a $p = 0.001$. The authors also noted that the 1- to 5-year tumor response is predictive of the 5- to 10-year tumor response ($R^2 = 0.636$, $p < 0.001$).

CONCLUSIONS Stereotactic radiosurgery, as an either upfront or adjuvant treatment, is a durable therapeutic option for WHO grade I PFMs, with high tumor control and a low incidence of post-SRS neurological deficits compared with those obtained using alternate treatment modalities. Lesion volumetric response at the short-term follow-up of 3 years is predictive of the long-term response at 5 and 10 years.

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KEY WORDS meningioma; stereotactic radiosurgery; Gamma Knife; posterior fossa; cerebellopontine angle; petroclival; foramen magnum; tentorial; SRS

ABBREVIATIONS GKRS = Gamma Knife radiosurgery; PFM = posterior fossa meningioma; PFS = progression-free survival; SRS = stereotactic radiosurgery.

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MENINGIOMAS account for nearly a third of all primary intracranial tumors, making them one of the most common types of intracranial tumors.^{22,68} Posterior fossa meningiomas (PFMs) comprise about 7%–12% of intracranial meningiomas.^{18,69} Surgical treatment of skull base meningiomas has significantly improved through advances in microsurgical techniques, diagnostic and interventional radiology, anesthesia and postoperative management, and interdisciplinary care.⁶⁰ Thus, complete resection whenever possible remains preferable for many symptomatic or progressive lesions.⁶² However, a drawback of resection even via microsurgical techniques is the neurological impairment frequently associated with the surgical treatment of these challenging skull base lesions, and meningioma recurrence has been described even after complete resection.^{1,2,4–10,12,14,18,24,27–29,32,35,39,51,54,55,57–59,64}

Stereotactic radiosurgery (SRS) is increasingly used for both primary and adjuvant treatment of meningiomas. While this procedure has become widely applied in the treatment of skull base lesions, there have been few large studies describing its use for PFMs and even fewer with long-term follow-up.^{2,10,13,15,17,19–21,26,30,31,34,40,41,44,46–50,52,53,56,61,65–67,70,71} The posterior fossa has an especially unique anatomy with little room for mass effect, which in turn creates particular surgical and radiosurgical constraints.

The unique architecture of the posterior fossa also results in complex potential growth patterns. Single-dimension diameter measurements for lesions in this location can thus yield misleading information. While many recommend volumetric measurement for follow-up, the technical constraints have as yet precluded its widespread use.^{16,25,33,63} In the current study, we describe the treatment of benign WHO grade I PFMs with single-session SRS as well as the long-term outcomes correlated with timing and volumetric changes in these lesions.

Methods

Patient Population

This study is a retrospective analysis of a prospectively maintained database with approval from the IRB at the University of Virginia. The database was searched for patients with a benign meningioma involving the posterior fossa region that had been treated with single-session SRS between 1991 and 2014. Inclusion criteria were clinical and radiological features consistent with a benign WHO grade I meningioma located in the posterior fossa of the skull base and a minimum of 3 available follow-up MRI scans post-SRS. Patients who had undergone SRS as a primary treatment lacked a definitive histological diagnosis. Radiological features consistent with benign meningioma included an extraaxial location, attachment to the dura (a dural tail), uniform contrast enhancement, and/or intratumoral calcification. Patients were excluded if they had a history of cancer, CT imaging alone, a WHO grade II or III meningioma, or multiple meningiomas suggestive of neurofibromatosis type 2 or other tumor-related genetic predispositions.

Radiosurgical Technique

Details of the Gamma Knife radiosurgery (GKRS)

technique employed at the University of Virginia have been described in a prior study.⁶⁵ In brief, the Leksell Gamma Knife model U was used until July 2001. Subsequently, the model C was instituted and used until September 2007. Since then, the Gamma Knife Perfexion model has been used. For dose planning, Kula software was used until June 1994, and GammaPlan software was used thereafter (both Elekta Instruments, AB). Dose plans and other radiosurgical parameters were formulated under the direction of the treating neurosurgeon in conjunction with a medical physicist and radiation oncologist.⁶¹ High-resolution stereotactic MRI was performed after stereotactic frame placement. Thin-slice axial and/or coronal plane images were obtained after intravenous contrast administration. The details of stereotactic imaging for radiosurgical planning varied over time, but planning generally included pre- and postcontrast, volumetrically acquired gradient-echo pulse sequences reconstructed into axial and coronal image stacks. Voxel sizes varied from (1 × 1 × 3 mm) to (1 × 1 × 1.3 mm).

The median dose to the tumor margin was 15 Gy (range 8–20 Gy) along a mean isodose of 50% (range 30%–60%; Table 1). A multi-isocentric approach was predominantly used with a mean of 10 isocenters (range 1–52 isocenters). An empirical algorithm was used for dose selection. Factors that influenced dose selection include tumor volume, lesion proximity to the brainstem and other critical neurovascular structures, any history of prior fractionated radiation therapy, and any previously existing neurological deficits.

Clinical and Radiological Follow-Up

After treatment with SRS, clinical evaluations with accompanying radiological scanning were performed approximately every 6 months for the first 2 years. Thereafter, if the patient showed no evidence of tumor growth on scans and did not experience deterioration or develop new neurological findings, follow-up intervals were increased to every 1–2 years. An attending neurosurgeon and neuroradiologist at the University of Virginia reviewed each neuroimaging study. The response of tumors, based on volumetric analysis, was considered to be stable if it was within 10% of the tumor volume at the time of treatment (original volume), increased if it was greater than 10% of the original volume, and decreased if it was at least 10% smaller than its original volume.^{17,63} Adverse radiation effects were defined as new or worsening perilesional hyperintensity noted on T2-weighted or FLAIR MRI sequences in the post-SRS follow-up. Radionecrosis was defined on the basis of neuroimaging studies (for example, PET, SPECT, and MR perfusion) or biopsy results that would be consistent with necrosis.

Tumor Volumetric Assessment

The Gamma Knife planning software (GammaPlan) for the initial volumetric assessment on the planning stereotactic MR image or the NIH ImageJ software for all follow-up MR images was used for volume determinations, as previously described.^{25,63} Volumetric calculations for PFMs were performed longitudinally for each patient

TABLE 1. Summary characteristics for 120 patients with PFMs treated using GKRS

Characteristic	Value
Sex (M/F)	28/92
Median age in yrs (range)	61 (12–88)
Median pre-SRS tumor vol in cm ³ (range)	4.0 (0.4–40.9)
No. of tumors (no. [%])	
1	111 (92.5)
2	8 (6.7)
3	1 (0.8)
Tumor location (no. [%])	
Tentorium	28 (23.3)
CPA	38 (31.7)
Petroclival region	23 (19.2)
Petrous region	2 (1.7)
Foramen magnum	4 (3.3)
Clivus	24 (20.0)
Tentorium & CPA	1 (0.8)
Previous resection (no. [%])	
0	78 (65)
1	34 (28.3)
2	6 (5.0)
3	1 (0.8)
>4 times	1 (0.8)
Prior RT (no. [%])	1 (0.8)
Prior hydrocephalus status post-VP shunt (no. [%])	5 (4.2)
Median period btwn symptoms & GKRS in mos (range)	19 (0–324)
Median KPS score (range)	90 (0–100)
Median RPA (range)	1 (0–4)
GKRS parameters	
Median radiation vol (range)	3.6 (0.3–23.9)
Median margin dose in Gy (range)	15 (8–20)
Median max dose in Gy (range)	30 (20–60)
Mean isodose line in % (range)	50 (30–60)
Median conformal index (range)	1.2 (0.4–2.0)
Median clinical FU in mos (range)	79.5 (15–224)
Median imaging FU in mos (range)	72 (6–213)

CN = cranial nerve; CPA = cerebellopontine angle; FU = follow-up; KPS = Karnofsky Performance Status; RPA = recursive partitioning analysis; RT = radiotherapy; VP = ventriculoperitoneal.

for each available imaging data set by using postcontrast T1-weighted imaging for the contouring. Computations were done through slice-by-slice area calculations of the meningioma and numerical integration with the trapezoid rule.²⁵ For contouring and volume computations, ImageJ software was used.

Statistical Analysis

Statistical analysis was performed using a commercially available statistical package (IBM SPSS, version 20, IBM Corp.). Descriptive statistics were calculated for all

variables, including the mean, median, standard deviation, and frequency distributions, as appropriate. Univariate logistic regression was used to evaluate clinical covariates hypothesized to predict tumor control and post-GKRS improvement, including age, tumor volume at the time of GKRS, sex, radiation dose, and period between symptoms and GKRS. Kaplan-Meier analysis was performed for tumor control and post-GKRS improvement. All statistical tests were 2-sided unless indicated otherwise. A $p < 0.05$ was considered statistically significant. For the prediction of tumor volume changes, we attempted to correlate tumor volume changes (%) at the 3-year post-SRS follow-up and at the 5- and 10-year post-SRS follow-up by using linear regression. The R^2 , coefficient of determination, was also computed.

Results

Patient and Tumor Attributes

The final study cohort included 120 patients. Patient attributes and tumor characteristics are outlined in Tables 1 and 2. The final cohort consisted of 76.6% (92) female patients, and the cohort median age was 61 years (12–88 years). The most common neurological symptoms before SRS were dizziness or imbalance (44 patients [36.6%]), headache (44 patients [36.6%]), auditory dysfunction (30 patients [25%]), and facial numbness/hypesthesia (29 patients [24.2%]). The most common tumor location was the cerebellopontine angle (38 lesions [31.7%]), followed by the tentorium (28 [23.3%]), clivus (24 [20%]), petroclival region (23 [19.2%]), and other locations (7 [5.8%]). The median pre-SRS volume of the PFMs was 4.0 cm³ (range 0.4–40.9 cm³). The most common pre-SRS cranial nerve deficit was a trigeminal nerve deficit (47 patients [39.1%]), followed by vestibular nerve deficit (44 [36.6%]), cochlear nerve deficit (30 [25%]), and facial nerve palsy (10 [8.3%]). Stereotactic radiosurgery was the primary treatment for 65% of the patients (78), whereas 28.3% (34) had undergone only 1 resection before SRS, and 6.7% (8) had undergone 2 or more resections prior to SRS. The median time from the development of associated neurological symptoms to treatment with SRS was 19 months (range 0–324 months).

Tumor Control

Specific parameters of tumor control are outlined in Table 3. The overall tumor control rate was 89.2% (107 patients), with a median clinical and imaging follow-up of 79.5 (15–224) and 72 (6–213) months, respectively. Eighty-six patients (71.7%) demonstrated tumor volume regression (volume decrease by 10% or more) and 21 (17.5%) demonstrated tumor volume stability (change in volume < 10%). Tumor progression was noted in 13 patients (10.8%) at the last follow-up. Tumor progression occurred as an in-field recurrence in 9 patients (7.5%) and as an outfield recurrence in 4 (3.3%). Overall 2-, 4-, 6-, 8-, and 10-year actuarial progression-free survival (PFS) rates were 97.5%, 94.4%, 89.5%, 85.8%, and 85.8%, respectively (Fig. 1). Adverse radiation effects were documented in 9 patients (7.5%). We did not observe imaging features or histological confirmation of radionecrosis following resection in this series.

TABLE 2. Neurological signs and CN deficits in 120 patients pre- and post-GKRS

Signs & Deficits	Before GKRS		After GKRS	
	Intact	Impaired	Non-Deterioration	Deterioration
Neurological symptom				
Headache	76	44	114	4
Cerebellar sign including ataxia	108	12	118	2
Cognition/orientation/memory	108	12	120	0
Face sensation				
Facial numbness/hypesthesia	91	29	117	3
Facial pain	104	16	119	1
Facial paresthesia	118	2	119	1
Masseter weakness	119	1	120	0
Facial weakness	111	9	119	1
Facial spasm/twitch	119	1	119	1
Auditory dysfunction	90	30	118	2
Dizziness/imbalance	76	44	120	0
Dysphagia	119	1	119	1
Body sensation				
Numbness/hypesthesia	115	5	119	1
Pain	119	1	120	0
Paresthesia/tingling	118	2	120	0
Body weakness	108	12	119	1
Impaired shoulder shrug	119	1	120	0
Tongue deviation	118	2	120	0
CN deficit				
Trigeminal nerve	73	47	116	4
Abducens nerve	120	0	120	0
Facial nerve	110	10	119	1
Cochlear nerve	90	30	118	2
Vestibular nerve	76	44	120	0
Glossopharyngeal nerve	119	1	119	1
Vagus nerve	119	1	119	1
Accessory nerve	119	1	120	0
Hypoglossal nerve	118	2	120	0

Overall post-GKRS neurological improvement: 23.3% (28 patients) improved, 70.8% (85 patients) remained stable, and 5.8% (7 patients) deteriorated.

Clinical and Neurological Outcomes

The most common post-SRS neurological symptoms were headache (4 patients [3.3%]), followed by facial numbness/hypesthesia (3 patients [2.5%]), cerebellar ataxia (2 patients [1.6%]), auditory dysfunction (2 patients [1.6%]), trigeminal neuralgia (1 patient [0.8%]), facial weakness (1 patient [0.8%]), facial spasm (1 patient [0.8%]), dysphagia (1 patient [0.8%]), body numbness (1 patient [0.8%]), and hemiparesis (1 patient [0.8%]; Table 2). Improvement in neurological function after SRS was observed in 28 patients (23.3%), whereas symptoms remained stable in 85 (70.8%) and deteriorated (new or worsened deficit) in 7 (5.8%). We evaluated the impact of tumor progression on the development of new or worsening neurological deficits at the last follow-up from SRS, but the relation was not statistically significant ($p = 0.874$, logistic regression).

Pre-SRS Factors Influencing Tumor Progression

Cox regression was used to evaluate for any pre-SRS characteristics that predicted local failure. Through multivariate analysis, we found that a low margin dose is the only predictor of tumor progression ($p = 0.007$; Table 4). For patients treated with a margin dose ≥ 16 Gy, actuarial PFS rates were 100%. For patients treated with a margin dose of 13–15 Gy, the actuarial PFS rates at 2, 4, 6, 8, and 10 years were 97.5%, 97.5%, 93.4%, 93.4%, and 93.4%, respectively. Those who were treated with ≤ 12 Gy had actuarial PFS rates of 95.8%, 82.9%, 73.2%, 56.9%, and 56.9% at 2, 4, 6, 8, and 10 years, respectively (Fig. 2).

Early Volume Changes as a Predictor of Long-Term Response

Volumetric analysis data are shown in Fig. 3. Tumor volume changes through the follow-up period for each

TABLE 3. Outcome of GKRS treatments in patients with PFM

Parameter	No. (%)
Tumor response	
Regression: vol decrease $\geq 10\%$	86 (71.7)
Stable: vol change $< 10\%$	21 (17.5)
Progression: vol increase $> 10\%$	13 (10.8)
Infield recurrence	9 (7.5)
Outfield recurrence	4 (3.3)
Complication	
None	111 (92.5)
AREs	9 (7.5)
Radiation necrosis	0 (0)
Further intervention	
Resection	2 (1.7)
Repeated GKRS	2 (1.7)
For same tumor, infield recurrence	1 (0.8)
For new tumor, outfield recurrence	1 (0.8)

ARE = adverse radiation effect.

patient are shown relative to the volume at the time of initial treatment, which was defined as 100%. The linear regression model is also shown in Fig. 3. Tumor volume measurements at the early follow-up of 3 years after SRS appear predictive of the 5- and 10-year tumor volumetric response after SRS. Figures 4 and 5 show that tumor volume change at the early follow-up at 3 years predicts the

long-term tumor volume change at 5 years with good reliability ($R^2 = 0.756$) with a $p < 0.001$ and at 10 years with less reliability ($R^2 = 0.421$) with a $p = 0.001$. We also determined that the 1- to 5-year tumor response is predictive of the 5- to 10-year response ($R^2 = 0.636$, $p < 0.001$; Fig. 6).

Management of Tumor Progression

There were a total of 13 tumor progressions either infield (9 patients) or outfield (4 patients). Of these patients, 4 underwent additional treatment including resection (2 patients [1.7%]) or repeated radiosurgery (2 patients [1.7%]; Table 5). Resection was performed for 2 patients who developed new focal neurological deficits (dysphagia, hemiparesis and facial weakness, spasms). The remaining 9 patients were followed conservatively. Those with progression (either infield or out of field) demonstrated the progression at times ranging from 52 to 84 months after SRS. The interval for progression in these cases emphasizes the need for long-term follow-up even in tumors that show an initially favorable response.

Discussion

Posterior fossa meningioma is a challenging clinical entity for neurosurgeons given its location along the skull base, which presents significant potential morbidities from the surgical approach. It is also challenging due to its frequent vascularity, firm consistency, and proximity to the brainstem, cranial nerves, and other critical neurovascular structures.^{1-10,12,14,18,24,27-29,32,35,39,51,54,55,57-59,64} In addition to the high rates of morbidity and mortality as-

FIG. 1. Kaplan-Meier curve representing overall actuarial PFS.

TABLE 4. Prognostic factors associated with local failure

Factor	No. of Patients	Univariate			Multivariate		
		p Value	HR*	95% CI	p Value	HR*	95% CI
Age		0.296					
≤65 yrs	78		Ref				
>65 yrs	42		0.446	0.098–2.027			
Sex		0.452					
M	28		Ref				
F	92		1.785	0.395–8.069			
No. of tumors		0.111			0.067		
Single	111		Ref			Ref	
Multiple	9		3.422	0.753–15.554		4.355	0.904–20.966
Previous op		0.410					
Yes	78		Ref				
No	42		0.608	0.186–1.985			
Lesion location		0.907					
Tentorium	28	0.650	1.769	0.150–20.815			
CPA	38	1.000	0.000	0.000–0.000			
Petroclival	23	0.269	3.485	0.382–31.832			
Petrous	2	0.975	1.045	0.062–17.765			
Foramen magnum	4	0.999	0.000	0.000–0.000			
Clivus	24	0.999	0.000	0.000–0.000			
Tentorium & CPA	1	0.999	0.000	0.000–0.000			
Tumor vol at GKRS		0.988					
<4 cm ³	60		Ref				
4–10 cm ³	43	0.880	0.919	0.971–2.961			
>10 cm ³	17	0.977	0.000	0.000			
Margin dose		0.011			0.007		
≤12 Gy	24		Ref			Ref	
13–15 Gy	80	0.003	0.179	0.058–0.553	0.002	0.159	0.050–0.501
≥16 Gy	16	0.977	0.000	0.000	0.978	0.000	0.000
Max dose		0.364					
≤30 Gy	68		Ref				
31–39 Gy	30	0.398	1.640	0.520–5.170			
≥40 Gy	22	0.356	0.373	0.046–3.035			
Period btwn symptoms & GKRS	120	0.943	1.000	0.990–1.009			

Cox regression was used to evaluate local failure. Boldface type indicates statistical significance.

* The higher the hazard ratio, the higher the relative risk to local treatment failure.

sociated with resection, delayed recurrence after partial or even complete resection has been noted and suggests the need for other management techniques for these unique lesions.^{1–10,12,14,18,24,27–29,32,35,39,51,54,55,57–59,64} Rates of complete resection for PFMs vary considerably, ranging from 40% to 96%, and recurrence rates after upfront resection range from 12% to 91%.^{1,2,4–10,12,14,18,24,27–29,32,35,39,51,54,61} Furthermore, resection planes during repeat resections pose added difficulty associated with increased morbidity and mortality.^{6,7,29,71} Resection remains valuable for patients with appreciable mass effect from a tumor or when tissue diagnosis is required. Regarding the extent of resection, many have recently proposed conservative subtotal resection prioritizing the relief of mass effect and avoiding neurological injury, while others had previously supported

aggressive resection. Even with conservative resection tactics, however, recent studies in patients undergoing resection of PFMs have still reported morbidity and mortality rates of 13%–40% and 0%–13%, respectively.^{8,43,71}

Radisurgery for PFMs

Meningiomas are increasingly found at earlier stages because of the increased accessibility and cost-utility of radiological imaging. Consequently, they are increasingly asymptomatic or associated with minimal symptoms. The meningioma control rates reported following SRS have been high.^{2,10,11,13,15,17,19–21,26,30,31,34,40,41,44–50,52,53,56,61,65–67,70,71} Progression-free survival rates greater than 90% have been reported for adjuvant SRS (postresection) at a minimum 5-year follow-up.^{11,23,25,38,42,45,61,65} Similar rates

FIG. 2. Kaplan-Meier curve representing tumor margin dose-based actuarial PFS. Obs = observed.

FIG. 3. Individual patients' volumetric data indicating changes (%) in tumor volume during the follow-up period. The change is depicted as a line by using linear regression ($R^2 = 0.0737$, $y = -0.0023x + 0.9826$), showing overall tumor control. Figure is available in color online only.

FIG. 4. The correlation between tumor volume changes (%) at the 3-year post-SRS follow-up and at the 5-year post-SRS follow-up. A strong linear correlation is shown ($R^2 = 0.756$)

FIG. 5. The correlation between tumor volume changes (%) at the 3-year post-SRS follow-up and at the 10-year post-SRS follow-up. A moderate linear correlation is shown ($R^2 = 0.421$).

have also been reported after SRS as the primary treatment.^{11,23,36–38,42,45,61,65}

Table 6 outlines radiosurgical studies in the literature that specifically focused on PFMs.^{26,45,53,61,65–67,72} The follow-up period among these studies ranges from 28.7 to 84 months. Additional characteristics include overall tumor control rates from 87% to 100%, rates of preserved neurological function from 85% to 100%, and complication rates from 0% to 9%. Prognostic factors for tumor advancement included age greater than 65 years, prior history of radiotherapy, and increasing tumor volume.^{26,53,61,65–67} In the current study, we found that a margin dose < 16 Gy portended a lower chance of long-term volumetric control. In the literature, factors predictive of neurological deterioration after SRS included increasing tumor volume and a tumor location in the clivus, petrous portion, or cerebellopontine angle (as opposed to the foramen magnum, tentorium, or petroclival region),^{26,53,61,65–67} but these factors did not show any statistically significant relation in the present study, probably secondary to the lower number of complications.

We did not find a statistically significant factor that predicted neurological decline in our patient cohort with PFMs. In particular, we did not find a significant association between tumor progression and neurological decline ($p = 0.874$, OR 1.121, 95% CI 0.875–1.682). This is proba-

bly attributable to the modest statistical power and low incidence of neurological deficits following radiosurgery in our series. However, in a larger multicenter study of SRS for PFMs including 675 patients, tumor progression was a significant predictor of neurological decline after SRS.⁶¹ However, this finding may have been an artifact of selection bias and the fact that most of the patients in that study demonstrated either neurological improvement or stability at the last follow-up.

Our results largely substantiate those from other studies with a similar follow-up (median clinical follow-up of 79.5 months and radiological follow-up of 72 months) and uniquely demonstrate predictability with tumor volumetric change. Importantly, the tumor volumetric change at the short-term follow-up of 3 years reliably predicted the long-term follow-up at 5 years and reasonably predicted the long-term follow-up at 10 years. We noted higher tumor control rates when PFMs were treated with a margin dose ≥ 16 Gy. Therefore, a favorable volumetric response at 3 years serves as an early predictor of a durable and probably successful response for the long-term radiological outcome (Figs. 4 and 5).

Study Limitations

This study is inherently limited by its retrospective data

TABLE 5. Management when patients had PFM enlargement

Second Treatment	TV at GKRS (cm ³)	TV at Recurrence (cm ³)	Increment (%)	Interval (mos)
Craniotomy (n = 2)	1.0, 17.0	5.0, 30.2	500%, 178%	52, 72
Repeated GKRS (n = 2)	3.9, 8.4	5.4, 11.8	139%, 141%	54, 84

Interval = time interval between GKRS and the observation of recurrence; TV = tumor volume.

Data are presented as case 1, case 2.

FIG. 6. The correlation between tumor volume changes (%) at the 1- to 5-year post-SRS follow-up and at the 5- to 10-year post-SRS follow-up. A strong linear correlation is shown ($R^2 = 0.636$)

collection and analysis. Patients who underwent SRS as a primary treatment had a presumed diagnosis of a benign WHO grade I meningioma but lacked a definitive histological diagnosis. The posterior fossa contains numerous sublocations, and meningiomas within each specific location can reasonably differ with respect to behavior, natural history, and SRS response. Selection bias may have affected the use of upfront radiosurgery, resection, radiation therapy, and salvage radiosurgery. Further limitations include those inherent to a single-center study. There may be patient selection bias within the treatment algorithms of our center. Patients who developed complications post-SRS may be overrepresented as it is likely that they were followed up more frequently and with more evaluations. While the considerable long-term follow-up is a strength of our study, the extensive period of time over which SRS was performed includes changes in the Gamma Knife

unit, the Gamma Knife software, and imaging. Lastly, the results of this single-center analysis may not be completely generalizable and reflect data from a tertiary care center with appreciable experience with SRS.

Conclusions

Stereotactic radiosurgery, as an either upfront or adjuvant treatment, is a durable therapeutic option in appropriate candidates with benign PFM, with high rates of tumor control and suitably low incidences of post-SRS neurological deficits compared with those following alternate treatment modalities. Doses of 13–16 Gy seem to afford reasonable tumor control and neurological preservation for the majority of PFM patients. Lesion volumetric response at the short-term follow-up of 3 years is predictive of the long-term response at 5 and 10 years.

TABLE 6. Literature review of major radiosurgical studies on PFMs

Authors & Year	No. of Cases	FU (median/mean)	% Tumor Control	Volumetry	% Neurological Preservation	% Neurological Complications
Subach et al., 1998	62	37	92	No	87	8
Nicolato et al., 2001	57	28.7	95	No	100	6.5
Flannery et al., 2010	168	72	90	No	85	8
Starke et al., 2011	152	84	87	No	91	9
Zenonos et al., 2012	24	47	100	No	100	0
Sheehan et al., 2015	675	60	91	No	92.3	7.7
Current study	120	79.5	89.2	Yes	94.2	5.8

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Sheehan, Patibandla. Acquisition of data: Patibandla, Addagada. Analysis and interpretation of data: Sheehan, Patibandla, Lee. Drafting the article: Sheehan, Patibandla, Tata, Addagada. Critically revising the article: Sheehan, Patibandla. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Sheehan. Statistical analysis: Lee. Administrative/technical/material support: Sheehan. Study supervision: Sheehan.

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