Gamma Knife radiosurgery for posterior fossa meningiomas: a multicenter study

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OBJECT Posterior fossa meningiomas represent a common yet challenging clinical entity. They are often associated with neurovascular structures and adjacent to the brainstem. Resection can be undertaken for posterior fossa meningiomas, but residual or recurrent tumor is frequent. Stereotactic radiosurgery (SRS) has been used to treat meningiomas, and this study evaluates the outcome of this approach for those located in the posterior fossa.

METHODS At 7 medical centers participating in the North American Gamma Knife Consortium, 675 patients undergoing SRS for a posterior fossa meningioma were identified, and clinical and radiological data were obtained for these cases. Females outnumbered males at a ratio of 3.8 to 1, and the median patient age was 57.6 years (range 12–89 years). Prior resection was performed in 43.3% of the patient sample. The mean tumor volume was 6.5 cm³, and a median margin dose of 13.6 Gy (range 8–40 Gy) was delivered to the tumor.

RESULTS At a mean follow-up of 60.1 months, tumor control was achieved in 91.2% of cases. Actuarial tumor control was 95%, 92%, and 81% at 3, 5, and 10 years after radiosurgery. Factors predictive of tumor progression included age greater than 65 years (hazard ratio [HR] 2.36, 95% CI 1.30–4.29, $p = 0.005$), prior history of radiotherapy (HR 5.19, 95% CI 1.69–15.94, $p = 0.004$), and increasing tumor volume (HR 1.05, 95% CI 1.01–1.08, $p = 0.005$). Clinical stability or improvement was achieved in 92.3% of patients. Increasing tumor volume (odds ratio [OR] 1.06, 95% CI 1.01–1.10, $p = 0.009$) and clival, petrous, or cerebellopontine angle location as compared with petroclival, tentorial, and foramen magnum location (OR 1.95, 95% CI 1.05–3.65, $p = 0.036$) were predictive of neurological decline after radiosurgery. After radiosurgery, ventriculoperitoneal shunt placement, resection, and radiation therapy were performed in 1.6%, 3.6%, and 1.5%, respectively.

CONCLUSIONS Stereotactic radiosurgery affords a high rate of tumor control and neurological preservation for patients with posterior fossa meningiomas. Those with a smaller tumor volume and no prior radiation therapy were more likely to have a favorable response after radiosurgery. Rarely, additional procedures may be required for hydrocephalus or tumor progression.

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KEY WORDS stereotactic radiosurgery; Gamma Knife surgery; meningioma; posterior fossa

ABBREVIATIONS CI = confidence interval; CN = cranial nerve; CPA = cerebellopontine angle; GKRS = Gamma Knife radiosurgery; HR = hazard ratio; OR = odds ratio; SRS = stereotactic radiosurgery.

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Of all intracranial meningiomas, approximately 7%–12% are located in the posterior fossa.^{13,16,56} Resection represents the upfront treatment for many patients with symptomatic or progressive posterior fossa meningiomas.⁵⁰ However, the extent of resection can be limited by the meningioma's proximity to critical vascular and neural structures. Gross-total resection rates reported in the literature for posterior fossa meningiomas vary significantly, from 40% to 96%, and resections are often associated with significant morbidity, mortality, and recurrence.^{1–5,7,9–12,15–17,20–22,24,27,28,31–33,36,38,41–43,45–48,51,54,56} Extent of resection and morbidity rates vary by location of the tumor in the posterior fossa. For instance, in a recent study, morbidity following resection of petroclival meningiomas and cerebellopontine angle (CPA) meningiomas varied from 20.3% to 47% and 10.4% to 35.7%, respectively.¹⁴ In that same study, extent of complete resection for petroclival meningiomas and CPA meningiomas was 0–48% and 82%–86.1%, respectively.¹⁴

Some neurosurgeons have recommended radical resection for recurrent meningiomas to prolong life in neurologically stable patients.⁵ Others have advocated for aggressive maximal resection of meningiomas at first presentation with the use of radiosurgery to treat recurrent or residual meningiomas.^{8,11,26,60} Stereotactic radiosurgery (SRS) has become an acceptable treatment option for recurrent/residual meningiomas as well as an upfront option.^{6,29,30}

The use of Gamma Knife radiosurgery (GKRS; Elekta AB) for intracranial meningiomas had been previously described in the literature. However, there are few large series for which meaningful statistical analysis can be performed. The posterior fossa has unique anatomical concerns in terms of mass effect, and radiosurgical constraints that differ from supratentorial meningiomas. In the current study, we evaluated the outcomes of patients with posterior fossa meningiomas treated with GKRS across a multiinstitutional experience spanning more than two decades.

Methods

Patient Population

Seven medical centers participating in the North American Gamma Knife Consortium obtained individual institutional review board approvals to participate in this study. A total of 675 patients were identified with posterior fossa meningiomas managed at least in part by GKRS (Table 1). At each center, retrospective clinical outcome analysis of patients with posterior fossa meningiomas who underwent GKRS was performed. The following centers contributed data for this study: the University of Pittsburgh (271 patients), Yale University (9 patients), Cleveland Clinic (12 patients), University of Sherbrooke (64 patients), Barrow Neurological Institute (118 patients), University of Pennsylvania (44 patients), and the University of Virginia (157 patients).

The records of patients with meningioma who underwent GKRS between 1988 and 2012 were evaluated by clinicians at each center for study inclusion. A database with selected variables was created and sent to all participating centers. Participating centers reviewed the

TABLE 1. Characteristics of 675 patients with posterior fossa meningiomas treated with GKRS

Characteristic	Total
Female sex (%)	535 (79.3)
Age (yrs)	
Median	57.6 ± 13.4
Range	12–89
Previous resection (%)	292 (43.3)
Prior radiotherapy (%)	11 (1.6)
Time from presentation to GKRS (mos)	
Mean ± SD	28.8 ± 47.0
Range	0–324
Initial presentation (%)	
Headache	227 (33.6)
Subjective dizziness	236 (35.0)
Subjective cognitive alteration	41 (6.1)
CN III/IV/VI	83 (13.1)
CN V	224 (33.3)
CN VII	54 (8.0)
CN VIII	193 (28.6)
CN IX/X	31 (4.6)
CN XI	3 (2.4)
CN XII	16 (2.4)
Cerebellar alteration/deficit	27 (4.0)
Body weakness	43 (6.4)
Change in body sensation	53 (7.9)
Location (%)	
Clival	48 (7.1)
Petroclival	254 (37.6)
Petrous	33 (4.9)
Tentorial	145 (21.5)
Cerebellopontine angle	177 (26.2)
Foramen magnum	18 (2.7)
Tumor volume (cm ³)	
Mean ± SD	6.5 ± 6.2
Range	0.15–41.8
Follow-up (mos)	
Mean ± SD	60.1 ± 45.4
Range	6–252

medical records of their patients, entered the data in the spreadsheet, and removed all patient identifiers from the database. Pooled and de-identified data were screened by an independent third party for errors. Any uncertainties or ambiguities in the data were addressed to the contributing center. Afterward, data were transmitted to the first author, who along with his coauthors developed this report.

Patients were included in the study if they had a histologically diagnosed WHO Grade I meningioma located within the posterior fossa. In addition, patients were included in this study if they had clinical and neuroimag-

ing features consistent with a benign meningioma of this neuroanatomical region. Clinical features would include a medical history absent of prior cancer and an intracranial tumor located in the posterior fossa with MRI and/or CT features most consistent with a meningioma. The neuroimaging features included an extraaxial location, contrast enhancement, dural attachment, and for some patients, tumor calcification. For inclusion, patients were required to have a minimum of 6 months of neuroimaging and clinical follow-up after GKRS.

Radiosurgical Technique

The Gamma Knife Models U, B, C, 4C, or Perfexion were used depending on the technology available at the time of treatment for the participating centers. The radiosurgery began with the application of the Leksell Model G stereotactic frame (Elekta AB) using local anesthetic supplemented by additional sedation as needed. After stereotactic frame placement, high-resolution stereotactic MRI was performed. In rare cases in which MRI was not feasible or when MRI distortion was a concern, a stereotactic CT scan was obtained. Thin-slice axial and/or coronal plane images were obtained after intravenous contrast administration. Radiosurgical dose planning was then performed by the neurosurgeon in conjunction with a radiation oncologist and medical physicist.

The mean volume of the posterior fossa meningiomas was 6.5 cm³ (range 0.15–41.8 cm³; Table 1). The median prescription dose delivered to the tumor margin was 13.6 Gy (range 8–40 Gy). The mean prescription isodose line was 48.5% (range 25%–65%; Table 2). Most of the dose plans involved a multiisocentric approach; a mean of 11 isocenters (range 1–59) were used. Dose selection was based on an empirical algorithm that included considerations related to tumor volume, proximity to critical structures such as the brainstem, preexisting neurological deficits, and history of previous treatment with fractionated radiation therapy.

Clinical and Neuroimaging Follow-Up

Clinical and neuroimaging evaluations were generally performed at follow-up intervals of 6 months for the first 2 years after radiosurgery. In patients who demonstrated no evidence of tumor growth and absence of new neurological findings, follow-up intervals were later increased to every 1–2 years. Whenever feasible, patients underwent follow-up neurological examination and neuroimaging at the respective treating center. However, because participating institutions represent tertiary referral centers, some patients underwent follow-up evaluations by their local physicians. For such patients, clinical notes and actual neuroimaging studies (i.e., not just the radiological reports) were received and reviewed by the treating clinicians who performed the GKRS. The follow-up images were compared with the images obtained at the time of GKRS. Tumor dimensions were assessed in the axial, sagittal, and coronal planes and compared with the comparable measurements on the Gamma Knife neuroimaging studies. Tumor growth, as defined by an increase in 1 of these measurements beyond the tomographic margin of

TABLE 2. Gamma Knife radiosurgery parameters

Characteristic	Value $\pm$ SD	Range
Median margin dose (Gy)	13.6 $\pm$ 2.2	8–40
Mean maximum dose (Gy)	28.6 $\pm$ 5.6	12–80
Mean isodose line (%)	48.5 $\pm$ 5.3	25–65
Mean no. of isocenters	11.0 $\pm$ 7.4	1–59

uncertainty within the planned treatment volume or adjacent to it, was considered tumor progression.

Statistical Analysis

Data are presented as median or mean and range for continuous variables, and as frequency and percentage for categorical variables. Calculations of normality were performed by ladder of powers and assessed graphically. Statistical analyses of categorical variables were performed using chi-square, Fisher's exact, and Mantel-Haenszel tests for linear association as appropriate. Statistics of means were conducted using the unpaired Student t-test, both with and without equal variance (Levene's test) as necessary and Wilcoxon rank-sum tests when variables were not normally distributed. The following dependent variables were assessed in univariate and multivariate analysis: tumor-free progression, worsening or new decline in neurological function, and favorable outcome (no tumor progression or worsening or new decline in neurological function). Kaplan-Meier risk of tumor progression was calculated. Factors predictive of tumor progression ($p < 0.15$) were entered into multivariate Cox regression analyses to assess hazard ratios (HRs). Clinical covariates predicting new or worsening neurological function with a univariate p value < 0.15 were included in multivariable logistic regression analyses. Additionally, clinical covariates predicting unfavorable outcome with a univariate p value < 0.15 were included in multivariable logistic regression analyses. Clinically significant variables and interaction expansion covariates were further assessed in both Cox and logistic multivariable analyses as deemed relevant. Those p values ≤ 0.05 were considered statistically significant.

Results

Patient and Tumor Attributes

Of the 675 patients, the median patient age was 57.6 years (range 12–89 years; Table 1). There was a clear sex predilection in the series, with 535 (79.3%) female patients and only 140 (20.7%) male patients. Two hundred and ninety-two patients (43.3%) had previously undergone resection with histologically confirmed WHO Grade I meningiomas. The remaining patients displayed neuroimaging and clinical features consistent with a benign meningioma. Prior fractionated radiation therapy had been used in 1.6% of patients. The most common presenting symptoms were headaches and dizziness in 33.6% and 35% of patients, respectively. Deficits were observed most frequently in cranial nerves (CNs) V (33.3%) and VIII (28.6%).

Meningioma location was classified by the participating centers based upon the location of the majority (i.e., maximum volume) of the tumor. Locations were categorized based upon commonly used neuroanatomical regions of the skull base.^{2,3,5,27,55,59} Meningioma locations included 7.1% clival, 37.6% petroclival, 4.9% petrous, 21.5% tentorial, 26.2% CPA, and 2.7% foramen magnum. Mean tumor volume was 6.5 cm³. Mean follow up was 60.1 months (range 6–252 months). Preradiosurgical patient characteristics, presentations, and tumor characteristics are detailed in Table 1.

Radiological Outcome

The mean follow-up duration was 60.1 ± 45.4 months (range 6–252 months). Following radiosurgery, tumor volume decreased by a mean of 1.6 cm³ to a mean posttreatment volume of 4.9 ± 5.9 cm³ (range 0–33 cm³; Table 3). At the last follow-up evaluation, 59 patients (8.8%) had an increase in tumor size, 275 (41.0%) had a decrease in tumor size, and 336 (50.2%) displayed no change in tumor size. Thus, the overall rate of tumor control (i.e., stable or decreased tumor) was 91.2%.

Kaplan-Meier analysis demonstrated radiological progression-free survival at 3, 5, 10, and 12 years to be 95%, 92%, 81%, and 77% respectively (Fig. 1). Factors predictive of tumor progression in univariate analysis are displayed in Table 4. Patients with a history of prior resection were not more likely to have tumor progression (HR 1.10, 95% CI 0.65–1.85, *p* = 0.719; Fig. 2 upper). Progression-free tumor survival according to mean volume is presented in Fig. 2 lower. There was no statistically significant difference in progression-free survival according to tumor location (Fig. 3).

In Cox multivariate analysis, pre-GKRS covariates predictive of tumor progression included age greater than 65 years (HR 2.36, 95% CI 1.30–4.29, *p* = 0.005), prior history of conventional radiotherapy (HR 5.19, 95% CI 1.69–15.94, *p* = 0.004), and increasing tumor volume (HR 1.05, 95% CI 1.01–1.08, *p* = 0.005; Table 4). There was a trend toward tumor progression with increasing time from symptom onset to GKRS in multivariate analysis (HR 1.01, 95% CI 1.00–1.01, *p* = 0.065). An absence of pre-GKRS resection was not predictive of tumor progression in multivariate analysis when controlling for other covariates or when assessing for interaction between potential relevant covariates. Patients with tumor progression after radiosurgery were 5.16 times more likely to have new or worsening neurological function (95% CI 2.58–10.31, *p* < 0.001).

Clinical Outcomes

At last clinical follow-up, 424 patients (64.9%) demonstrated no change in clinical outcome, 179 (27.4%) had improvement in clinical outcome, and 50 (7.7%) had new or worsening neurological function (Table 3). Specific alterations in clinical signs and symptoms following GKRS are detailed in Table 5. Following GKRS, new or worsening CN dysfunction was observed most commonly in CN V followed by aggregate dysfunction of CNs III/IV/VI and least commonly in lower cranial nerves including

TABLE 3. Overall clinical and tumor outcomes

Characteristic	Outcome
Pre-GKRS tumor volume (cm ³)	
Mean ± SD	6.5 ± 6.2
Range	0.15–41.8
Post-GKRS tumor volume (cm ³)	
Mean ± SD	4.9 ± 5.9
Range	0–33
Tumor volume (%)	
Decrease	336 (50.2)
No change	275 (41.0)
Increase	59 (8.8)
Clinical outcome (%)	
No change	424 (64.9)
Improvement	179 (27.4)
New or worsening neurological function	50 (7.7)
Overall outcome (%)	
Favorable	557 (85.8)
Unfavorable	92 (14.2)
Post-GKRS (%)	
Hydrocephalus	14 (2.1)
Ventriculoperitoneal shunt placement	11 (1.7)
Radiotherapy	10 (1.5)
Resection	24 (3.6)

CN IX through XII (Table 5). Following radiosurgery, 24 patients (3.6%) required resection and 10 (1.5%) underwent radiation therapy to treat tumor progression. Of the 653 patients with reliable clinical follow-up information, 14 patients (2.1%) developed hydrocephalus apparent on radiological imaging, and 11 (1.7%) required ventriculoperitoneal shunt placement.

Univariate predictors of new or worsening neurological function after GKRS are displayed in Table 6. These predictors of new or worsening neurological function after GKRS within the univariate analysis were male sex; clival, petrous, and CPA location; prior conventional radiotherapy; symptomatic presentation other than headache; peripheral and maximal dose; and increasing tumor volume (Table 6). In multivariate analysis, increasing tumor volume (OR 1.06, 95% CI 1.01–1.10, *p* = 0.009) and clival, petrous, or CPA location versus petroclival, tentorial, and foramen magnum location (OR 1.95, 95% CI 1.05–3.65, *p* = 0.036) were predictive of new or worsening neurological function after radiosurgery.

Favorable Outcome After SRS

A favorable outcome, defined as tumor control along with neurological stability or improvement, was achieved in 557 (85.8%) of 649 patients. An unfavorable outcome (i.e., tumor progression and/or new or worsening neurological function) was found in 92 patients (14.2%). Univariate predictors of overall outcome are demonstrated in Table 7. Multivariate predictors of an unfavorable out-

FIG. 1. Kaplan-Meier plot of progression-free survival after SRS for all 675 patients with posterior fossa meningiomas. Numbers in parentheses represent the number of patients reaching each significant timeline milestone.

come included increasing tumor volume (OR 3.24, 95% CI 1.12–9.37, $p = 0.001$) and a history of prior conventional radiotherapy (OR 13.46, 95% CI 2.4–75.22, $p = 0.003$).

Other Serious Adverse Effects

In the current study, there was no evidence of radiation-induced tumor formation or malignant transformation of an existing meningioma.

Discussion

Posterior Fossa Location and Resection

Meningiomas involving the posterior fossa comprise approximately 7%–12% of all meningiomas.^{13,16,56} Posterior fossa meningiomas present a unique set of challenges as compared with those involving the supratentorial region. Posterior fossa meningiomas are often closely associated with critical arteries, venous sinuses, cranial nerves, and the brainstem, and such proximity to critical structures makes resection more challenging. Also, their resulting growth can lead to mass effect that is less tolerated than their supratentorial counterparts. In instances of appreciable mass effect, hydrocephalus, or significant histological uncertainty, resection remains a valuable approach. Nevertheless, complete resection rates for posterior fossa meningiomas vary substantially, with rates ranging from 40% to 96%.^{1–5,7,9–12,15–17,20–22,24,27,28,31–33,36,38,41–43,45–48,51,54,56}

Although some continue to advocate for aggressive resection, others have instead proposed a more conservative approach involving subtotal resection that is guided by relief of mass effect and preservation of neurological

function.^{6,9,34,60} In published series, this contemporary approach has led to morbidity and mortality rates of 0%–13% and 13%–40%, respectively. Recurrence rates after an initial resection vary from 12% to 91%.^{1–5,7,9–12,15–17,20–22,24,27,28,31–33,36,38,41–43,45–48,51,54,56} Such recurrences depend upon the length of follow-up, characteristics of the tumor, and the extent of the initial resection. Although repeat resection is feasible, repeat resection is associated with increased morbidity and mortality due to difficult resection planes.^{5,7,22,24,60}

TABLE 4. Factors predictive of tumor progression in univariate and multivariate analyses*

Analysis	Pre-GKRS Variables	HR (95% CI)	p Value
Univariate			
	Age >65 years	1.95 (1.13–3.34)	0.016
	Increasing time from symptom onset	1.01 (1.00–1.01)	0.011
	Prior radiotherapy	6.87 (3.22–14.67)	<0.001
	Increasing tumor volume	1.04 (1.01–1.08)	0.010
Multivariate			
	Age >65 years	2.36 (1.30–4.29)	0.005
	Increasing tumor volume	1.05 (1.01–1.08)	0.005
	Prior radiotherapy	5.19 (1.69–15.94)	0.004

* Factors predictive of tumor recurrence ($p < 0.15$). There was a trend toward increased tumor progression with increasing time from symptom onset in multivariate analysis (HR 1.01, 95% CI 1.00–1.01, $p = 0.065$).

FIG. 2. Kaplan-Meier plot of progression-free survival after SRS for patients with and without a prior resection (upper), and for patients with tumors < 6.5 cm³ versus those with tumors ≥ 6.5 cm³ (lower). Numbers in parentheses represent the number of patients reaching each significant timeline milestone.

Radiation Therapy

Radiation therapy has been used for some patients with intracranial meningiomas, including ones involving the posterior fossa. Progression-free survival rates at 5 and 10 years after conventional radiotherapy range from 73% to 92% and 61% to 83%, respectively.^{23,25,26,35,40,57} More contemporary techniques such as intensity-modulated radiation therapy and proton therapy offer increased conformality and more sparing of critical structures compared with conventional techniques.^{44,58} The lower integral dose and higher conformality that are touted as the advantages of intensity-modulated radiation therapy and proton beam

over conventional radiotherapy techniques for meningiomas have been longstanding features of radiosurgery. While radiotherapy has been used for large volume or poorly delineated posterior fossa meningiomas, its role for smaller to moderately sized and well-demarcated meningiomas involving the posterior fossa has largely been displaced by SRS.

Stereotactic Radiosurgery

Radiosurgery has proven to be an important tool in the treatment of meningiomas, with most large radiosurgical

FIG. 3. Kaplan-Meier plot of progression-free survival after SRS for meningiomas in a specific location in the posterior fossa. Figure is available in color online only.

series demonstrating tumor control rates of 85% or higher for patients with Grade I meningiomas.⁴⁹ Following radiosurgery, tumor control has generally been accompanied by neurological preservation or improvement in the majority of patients.⁴⁹ However, most radiosurgical series have looked broadly at meningiomas of various locations, and few have focused on the challenges associated with meningiomas of the posterior fossa.

In the published literature, there are only a few radiosurgical series that focus exclusively on posterior fossa meningiomas (Table 8). In an earlier series by the University of Pittsburgh team, Subach and colleagues reported on their experience with 62 patients exhibiting petroclival meningiomas. Of these 62 patients, 39 (63%) had at least 1 prior resection. With a median follow-up of 37 months, tumor control was achieved in 92% of patients, and neurological status improved in 21% and remained stable in 66% of patients.⁵⁵ In a later series by that same group, tumor control and neurological preservation were achieved in 90% and 85%, respectively, of 168 patients with petroclival meningiomas who underwent GKRS.¹⁸ In another study by the group in Verona, Italy, Nicolato and colleagues³⁹ used GKRS to treat 57 patients with 62 posterior fossa meningiomas. With a median follow-up of 28.7 months, tumor regression was observed in 55% of cases and stability in another 40%.³⁹ Transient side effects due to radiosurgically induced edema were noted in 6.5%, but there were no instances of permanent morbidity associated with GKRS in this series.³⁹ More recently from the University of Virginia, a series of 152 patients with posterior fossa meningiomas were evaluated after GKRS. With a median follow-up of 84 months, tumor control and neurological preservation were achieved in 87% and 91% of patients, respectively.⁵² Smaller radiosurgical series confirm the efficacy and safety of radiosurgery for patients

with posterior fossa meningiomas, even of the foramen magnum.^{53,61}

The current series represents the largest one to date for posterior fossa meningiomas treated with radiosurgery (Table 8). This series has sufficient statistical power to permit subgroup analysis to evaluate the effect of tumor location, and the study also gives a broader assessment of neurological complications associated with GKRS. In the current series, tumor control was achieved in 91.2% of patients at last follow-up. Just if not more importantly, neurological preservation was accomplished in 92.3% of

TABLE 5. Specific alterations in clinical signs and symptoms following GKRS

Characteristic	Presentation (%)	New or Worsening Function (%)
Subjective dizziness	236 (35.0)	34 (5.1)
Subjective cognitive alteration	41 (6.1)	15 (2.2)
CN III/IV/VI	83 (13.1)	21 (3.3)
CN V	224 (33.3)	28 (4.2)
CN VII	54 (8.0)	8 (1.2)
CN VIII	193 (28.6)	12 (1.8)
CN IX/X	31 (4.6)	6 (0.9)
CN XI	3 (2.4)	1 (0.2)
CN XII	16 (2.4)	3 (0.5)
Ataxia	4 (12.4)	14 (2.1)
Other cerebellar alteration/deficit	27 (4.0)	27 (4.0)
Body weakness	43 (6.4)	10 (1.5)
Change body sensation	53 (7.9)	8 (1.2)

TABLE 6. Factors predictive of new or worsening symptoms following radiosurgery in univariate and multivariate analyses*

Analysis	Pre-GKRS Variables	OR (95% CI)	p Value
Univariate			
	Male sex	2.62 (0.84–3.09)	0.148
	Location		
	Clival, petrous, CPA	1.61 (0.90–2.87)	0.106
	Petroclival, tentorium, foramen magnum	1	
	Prior radiotherapy	5.43 (1.36–21.67)	0.017
	Symptomatic presentation other than headache	2.35 (0.92–6.05)	0.076
	Increasing peripheral dose	0.83 (0.69–0.99)	0.034
	Increasing maximal dose	0.95 (0.89–1.01)	0.147
	Isodose volume	1.06 (1.01–1.10)	0.008
	Increasing volume	1.05 (1.01–1.09)	0.024
Multivariate			
	Location		
	Clival, petrous, CPA	1.95 (1.05–3.65)	0.036
	Petroclival, tentorium, foramen magnum	1	
	Increasing tumor volume	1.06 (1.01–1.10)	0.009

* Factors predictive of tumor recurrence ($p < 0.15$).

patients. Thus, based upon the high chance of tumor control and neurological preservation observed in the current series, those with small to moderately sized posterior fossa meningiomas for whom relief of mass effect is not required would appear well served by GKRS. Those with a smaller tumor volume and no prior radiation therapy were more likely to achieve both tumor control and a favorable neurological outcome after radiosurgery of their posterior fossa meningiomas. The benefit of a smaller tumor volume at the time of radiosurgery does underscore the benefits of a cytoreductive but neurologically preserving surgery

for those patients who have larger tumors at initial presentation. In terms of prior radiotherapy, patients in whom radiation therapy was unsuccessful likely exhibit a more aggressive tumor. Also, prior radiotherapy can require a reduction in the radiosurgical dose below that which might be optimal. Thus, the radiosurgical cohort that had unsuccessful prior radiotherapy is an inherently more challenging one to manage, and the prescription dose lower than what would likely have been given in the absence of prior ionizing radiation makes tumor control less likely.

Cranial nerve dysfunction after GKRS varied depending upon the nerve. Cranial nerve V and aggregate CN III, IV, and VI dysfunction were most common whereas lower CN dysfunction was exceedingly rare (Table 4). The risk factors for CN palsy after GKRS are likely multifactorial. Variability of the CNs to ionizing radiation may be due in part to the functionality (e.g., special sensory, visceral sensory, visceral motor, and somatic motor), relative radioresistance, vascular supply to the nerve, and irradiated length of a particular nerve. In particular, CN V can routinely tolerate a maximum dose of 80 Gy in cases of trigeminal neuralgia when such a dose is delivered to a small volume of the nerve. While the doses used in this series to treat meningiomas were substantially lower than 80 Gy, the length of nerve irradiated and the integrated dose to the nerve have been shown to be related to and affect the probability of trigeminal nerve dysfunction after GKRS, and these parameters were likely responsible for some of the CN V dysfunction.³⁴ Tumor location (e.g., petrous vs petroclival) also affected the likelihood of new or worsening neurological symptoms following radiosurgery. In cases in which the tumor may have a broader interface with the brainstem or traversing cranial nerves, neurological dysfunction may occur with a higher probability after radiosurgery.

TABLE 7. Factors predictive of an unfavorable outcome in univariate and multivariate analyses*

Analysis	Variables	OR (95% CI)	p Value
Univariate			
	Increasing tumor volume	1.06 (1.02–1.09)	0.001
	Symptomatic other than headache	1.79 (0.95–3.40)	0.074
	Prior radiotherapy	26.38 (5.50–126.35)	<0.001
	Increasing time from symptom onset	1.01 (1.0–1.01)	0.046
	Margin dose	0.88 (0.77–1.00)	0.051
	Isodose line	0.96 (0.92–0.99)	0.013
Multivariate			
	Increasing tumor volume	3.24 (1.12–9.37)	0.001
	Prior radiotherapy	13.46 (2.4–75.22)	0.003

* Favorable outcome defined as no tumor progression or new or worsening neurological function. Factors predictive of tumor recurrence ($p < 0.15$).

TABLE 8. Major radiosurgical series for posterior fossa meningiomas

Authors & Year	No. of Patients	Median or Mean Follow-Up (mos)	Tumor Control (%)	Neurological Preservation (%)	Complications (%)
Subach et al., 1998	62	37	92	87	8
Nicolato et al., 2001	57	28.7	95	100	6.5
Flannery et al., 2010	168	72	90	85	8
Starke et al., 2010	5	60	100	100	0
Starke et al., 2011	152	84	87	91	9
Zenonos et al., 2012	24	47	100	100	0
Current series	675	60	91	92.3	7.7

Similarly to patients undergoing resection, radiation therapy, or no treatment, longitudinal follow-up of patients after radiosurgery is required. In the current series, 2.1% of patients with posterior fossa meningiomas developed hydrocephalus following radiosurgery. The incidence of postradiosurgical hydrocephalus compares favorably with the 16% incidence noted in a recent surgical series of posterior fossa meningiomas by Nanda et al.³⁷ Cerebrospinal fluid malabsorption from a high protein level has been postulated to be the cause of postradiosurgical hydrocephalus.¹⁹ Such patients require CSF diversion, typically with a shunt as was the case in 1.6% of patients in the current series. Tumor progression in the current series was rare, but 5.1% of patients in the current series required additional intervention for their meningioma. Close surveillance with neuroimaging and clinical assessments will allow detection of problems and timely intervention when necessary for radiosurgical patients.

Study Limitations

The current study represents the largest radiosurgical one to date on this particular indication. Nevertheless, the study has limitations worth noting. The participating centers use a common radiosurgical platform and dose planning software. The outcomes, both favorable and unfavorable, may not be representative of other commercially available systems. Also, radiosurgery comprises a significant portion of the practice of the contributing clinicians in this study. We did not examine the learning curve for this indication nor did we examine the number of cases required to maintain proficiency. In addition, the radiosurgical techniques for planning, treatment, and delivery have evolved over the time span of this study. We do not account for the evolution of the field in assessing outcomes with posterior fossa meningiomas.

The study suffers from inherent biases of a retrospective study. These include selection bias and a lack of a control arm to the study. In particular, selection criteria varied from center to center and as a function of time as the field of radiosurgery has evolved over the past two decades. Also, not all of the tumors were histologically confirmed to be a meningioma. Thus, it is possible that some other benign skull-based lesions were included in this study. However, any patient with histology inconsistent with a WHO Grade I meningioma was excluded from the study. This is true of preradiosurgical histology and histology obtained at the time of resection following failed radiosurgery.

Conclusions

Gamma Knife radiosurgery affords tumor control and neurological preservation in the vast majority of patients with posterior fossa meningiomas. While resection continues to be of value for relief of mass effect and histological confirmation in ambiguous cases, radiosurgery either as an upfront treatment or an adjuvant one after prior resection represents a valuable neurosurgical tool for treatment of patients with posterior fossa meningiomas.

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