Gamma Knife surgery for skull base meningiomas

Clinical article

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Object. Skull base meningiomas are challenging tumors owing in part to their close proximity to important neurovascular structures. Complete microsurgical resection can be associated with significant morbidity, and recurrence rates are not inconsequential. In this study, the authors evaluate the outcomes of skull base meningiomas treated with Gamma Knife surgery (GKS) both as an adjunct to microsurgery and as a primary treatment modality.

Methods. The authors performed a retrospective review of a prospectively compiled database detailing the outcomes in 255 patients with skull base meningiomas treated at the University of Virginia from 1989 to 2006. All patients had a minimum follow-up of 24 months. The group comprised 54 male and 201 female patients, with a median age of 55 years (range 19–85 years). One hundred nine patients were treated with upfront radiosurgery, and 146 patients were treated with GKS following resection. Patients were assessed clinically and radiographically at routine intervals following GKS. Factors predictive of new neurological deficit following GKS were assessed via univariate and multivariate analysis, and Kaplan-Meier analysis and Cox multivariate regression analysis were used to assess factors predictive of tumor progression.

Results. Meningiomas were centered over the cerebellopontine angle in 43 patients (17%), the clivus in 40 (16%), the petroclival region in 28 (11%), the petrous region in 6 (2%), and the parasellar region in 138 (54%). The median duration of follow-up was 6.5 years (range 2–18 years). The mean preradiosurgery tumor volume was 5.0 cm³ (range 0.3–54.8 cm³).

At most recent follow-up, 220 patients (86%) displayed either no change or a decrease in tumor volume, and 35 (14%) displayed an increase in volume. Actuarial progression-free survival at 3, 5, and 10 years was 99%, 96%, and 79%, respectively. In Cox multivariate analysis, pre-GKS covariates associated with tumor progression included age greater than 65 years (HR 3.41, 95% CI 1.63–7.13, p = 0.001) and decreasing dose to tumor margin (HR 0.90, 95% CI 0.80–1.00, p = 0.05).

At most recent clinical follow-up, 230 patients (90%) demonstrated no change or improvement in their neurological condition and the condition of 25 patients had deteriorated (10%). In multivariate analysis, the factors predictive of new or worsening symptoms were increasing duration of follow-up (OR 1.01, 95% CI 1.00–1.02, p = 0.015), tumor progression (OR 2.91, 95% CI 1.60–5.31, p < 0.001), decreasing maximum dose (OR 0.90, 95% CI 0.84–0.97, p = 0.007), and petrous or clival location versus parasellar, petroclival, and cerebellopontine angle location (OR 3.47, 95% CI 1.23–9.74, p = 0.018).

Conclusions. Stereotactic radiosurgery offers a high rate of tumor control and neurological preservation in patients with skull base meningiomas. After radiosurgery, better outcomes were observed for those receiving an optimal radiosurgery dose and harboring tumors located in a cerebellopontine angle, parasellar, or petroclival location.

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Key Words • stereotactic radiosurgery • Gamma Knife • meningioma • skull base • posterior fossa • clivus • petroclival • paracloind • cerebellopontine angle • sella • parasellar

Abbreviations used in this paper: FSRT = fractionated stereotactic radiotherapy; GKS = Gamma Knife surgery; SRS = stereotactic radiosurgery.

Moreover, resection has been associated with delayed recurrence.16,30,35,51,56,61,66

With early detection of meningiomas in the modern era, patients may present with small to moderate volume skull base meningiomas and have few to no symptoms associated with the tumor. Stereotactic radiosurgery may be an acceptable approach for patients with recurrent meningiomas after resection or even as an upfront treatment for others. In this study, we review our institutional experience using SRS for skull base meningiomas. We evaluate the long-term outcomes in patients with skull base meningiomas treated with GKS and assess factors predictive
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of new or worsening neurological signs or symptoms and tumor progression.

Methods

Patient Population

This is a retrospective analysis of a prospectively maintained, institutional review board–approved database. The database was assessed from 1989 to 2006 for patients with skull base meningiomas treated with GKS at the University of Virginia. The diagnosis was confirmed either by histopathological examination or characteristic findings for meningiomas on neuroimaging studies.17

Exclusion criteria included patients with multiple meningiomas, follow-up less than 24 months, or a confirmed tumor histological grade greater than WHO Grade I. All patients with tumor progression were included regardless of length of follow-up. Two hundred fifty-five patients with skull base meningiomas qualified for this study and were included in the analysis.

Patients were considered for radiosurgery if they were not disabled by their tumor (Karnofsky Performance Scale score < 70). Patients were not candidates for primary surgical treatment based on their advanced age, the projected operative risks based on medical comorbidities, and/or refusal of microsurgical resection. Adjuvant radiosurgical treatment was carried out in patients with recurrence or regrowth of lesions following microsurgical excision or as part of multimodality treatment in cases in which the risks of complete resection outweighed the benefits of multimodality therapy.

Radiosurgical Technique

Our radiosurgical technique has been previously described.63,71 In brief, patients underwent placement of a stereotactic Leksell G-frame in the operating room. During frame placement, they received monitored anesthetic care. Stereotactic MR imaging was then obtained for the treatment planning. Thin slice (1-mm) axial and coronal MR sequences were obtained before and after administration of contrast medium. When an MR imaging could not be performed because of medical contraindications (for example, presence of a cardiac pacemaker), a thin-slice stereotactic CT scan was obtained with and without contrast medium. Radiosurgical dose plans were formulated under the direction of a neurosurgeon in conjunction with a medical physicist and radiation oncologist.64

The Leksell Gamma Unit Model U was used until July 2001, when use of Model C (Elekta Instruments, Inc.) was instituted. The Kula software was used for dose planning from 1989 to June 1994, and then Elekta’s GammaPlan software was used.

Clinical and Radiological Follow-Up

Patients were usually followed clinically and radiologically every 6 months for the 1st year, annually until Year 5 after radiosurgery, and then every 2 years thereafter. At each follow-up visit, a neurological examination was performed to evaluate for new neurological deficits, and neuroimaging studies were reviewed to assess tumor response. All follow-up was performed at the University of Virginia, unless the patient was unable to travel to our institution. In such cases, the referring physician performed the follow-up examinations and provided documentation of the patient’s neurological status as well as follow-up imaging.

All neuroimaging studies were reviewed by a neurosurgeon and a neuroradiologist at the University of Virginia. Lesions were categorized into the following locations defined by the presumed origin of maximum volume: sellar, cerebellopontine angle, petrous, clival, and petroclival.1–3,22,65,72 Petroclival meningiomas were defined as tumors whose maximal volume was centered over the region between the petrous apex and the upper two-thirds of the clivus.2,65 All parasellar lesions were in close proximity to the sella with cavernous sinus invasion.71

Imaging outcome was determined by the last available examination.60 A decrease or increase in tumor size was defined as a 15% or greater change in tumor volume compared with the volume at the time of GKS.60 To make this determination of tumor size, the tumor was outlined on radiographic images, and serial volumetric calculations were performed using ImageJ (NIH) in all patient imaging studies.60 Treatment was considered to have failed in any patient who had tumor progression of more than 15% even if the condition stabilized with further GKS or surgery.

Statistical Analysis

Data are presented as median or mean values and ranges for continuous variables and as frequency and percentage values for categorical variables. Statistical analyses of categorical variables were carried out using the chi-square test, the Fisher exact test, and the Mantel-Haenszel test for linear association, as appropriate. Statistical analysis of means was carried out using an unpaired Student t-test, both with and without equal variance (Levene test) as necessary and Wilcoxon rank sum tests when variables were not normally distributed. Analysis of variance followed by Bonferroni post hoc testing was used to assess means between 3 or more groups.

Kaplan-Meier plots of tumor progression were computed. The following factors were assessed for their ability to predict both tumor progression and new or worsening neurological function: age, sex, tumor location, tumor volume, maximum tumor diameter, brain-tumor interface (smooth versus irregular), time from presentation, length of follow-up, previous surgery, prior hydrocephalus, prior ventriculoperitoneal shunt placement, presentation, GKS planning modality (CT or MR imaging), number of isocenters, margin dose, maximum dose, percent isodose line, isodose volume, and conformity index (isodose volume/initial tumor volume). Factors predictive of tumor progression (p < 0.15) were entered into Cox regression analysis to assess hazard ratios. Additionally, clinical covariates predicting new or worsening neurological function with a univariate p value less than 0.15 were included in multivariable logistic regression analysis. Clinically significant variables and interaction expansion covariates were further assessed in both Cox and logistic multivari-
able analyses as deemed relevant. Probability values of 0.05 or less were considered statistically significant.

Results

Patient, Tumor, and Treatment Attributes

In the 255 patients with skull base meningiomas, the median age was 55 years (range 19–85 years) (Table 1). There was a clear sex predilection, with 201 female patients (79%) and 54 male patients (21%). One hundred forty-six patients (57%) had prior resection with histological confirmation of WHO Grade I meningioma. The remaining patients displayed neuroimaging and clinical features consistent with benign meningioma. Meningiomas were centered over the cerebellopontine angle in 43 patients (17%), the clivus in 40 (16%), the petroclival region in 28 (11%), the petrous region in 6 (2%), and the parasellar region in 138 (54%).

The mean maximum dose to the tumor was 34 Gy (range 12–60 Gy), the mean tumor margin dose was 14 Gy (range 8–30 Gy), and the mean prescription isodose line was 41% (range 28%–80%) (Table 2). The median number of isocenters used was 8 (range 1–25).

Radiological Outcome

The mean preradiosurgery tumor volume was 5.0 cm³ (range 0.3–54.8 cm³). The median duration of follow-up was 6.5 years (range 2–18 years). At the most recent follow-up examination, 95 patients (37%) displayed no change in tumor size, 125 (49%) had a decrease in volume, and 35 (14%) displayed an increase in volume. The mean postradiosurgery tumor volume was 4.3 cm³ (range 0–61 cm³).

Kaplan-Meier analysis demonstrated radiological progression-free survival of 99%, 96%, and 79% at 3, 5, and 10 years, respectively (Fig. 1). Factors predictive of tumor progression in univariate analysis are summarized in Table 3. There was a trend toward a decreased rate of progression in patients with a history of pre-GKS resection (Fig. 2; p = 0.154). In Cox multivariate analysis, pre-GKS covariates associated with tumor progression included age greater then 65 years (HR 3.41, 95% CI 1.63–7.13, p = 0.001) and decreasing dose to the tumor margin (HR 0.90, 95% CI 0.80–1.00, p = 0.05).

Of those patients demonstrating tumor growth, 16 (41%) received a second treatment with GKS and 14 (36%) went on to resection. There was a trend for parasellar-based lesions to receive a second GKS (8% vs 3% for all other locations, p = 0.060) but not additional surgery (5% vs 5%) or further treatment (13% vs 8%, p = 0.16).

On follow-up imaging, 10 patients (3.5%) displayed new evidence of edema. In all cases, the edema was transient and could be managed with a short course of corticosteroids. Additionally, 3 patients required ventriculoperitoneal shunts for hydrocephalus. No radiosurgically induced tumor or malignant transformation of a tumor was observed in any of the patients.

Clinical Outcome

Two hundred eight (82%) of the 255 patients were symptomatic prior to GKS. At last clinical follow-up, 230 patients (90%) demonstrated no change or improvement in their neurological condition and the condition of 25 patients (10%) deteriorated. Neurological decline depended, in general, upon the location of the meningiomas and tumor progression; it most frequently involved new onset or progression of cranial neuropathies, which occurred in 22 patients (8.6%). Other neurological signs or symptoms after radiosurgery included decline in cognition or memory, cerebellar deficits, alterations in body sensation, and alterations in body strength; these occurred in an additional 6 patients (2%). Variables predictive of new or worsening symptoms in univariate analysis are shown in Table 4. In multivariate analysis, the factors predictive of new or worsening symptoms were increased duration of follow-up (OR 1.01, 95% CI 1.00–1.02, p = 0.015), tumor progression (OR 2.91, 95% CI 1.60–5.31, p < 0.001), decreasing maximum dose (OR 0.90, 95% CI 0.84–0.97, p = 0.007), and petrous or clival location versus parasellar, petroclival, and cerebellopontine angle location (OR 3.47, 95% CI 1.23–9.74, p = 0.018).

Discussion

Patients with WHO Grade I meningiomas of the skull base are generally expected to live with a high degree of function and do so for many years following treatment of their tumor. Historically, resection has been the primary
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Fig. 1. Kaplan-Meier progression-free survival.

Natural History of Skull Base Meningiomas

Data on the natural history of untreated skull base meningiomas are limited. In a retrospective study of 40 patients, Bindal et al. reported on the natural history of untreated meningiomas located in the cavernous sinus, petroclival region, or anterior clinoid. Clinically, 28 patients (70%) presented with partial cranial nerve deficits, and 11 (27.5%) were asymptomatic, having lesions that were discovered incidentally. Radiologically, brainstem compression was initially seen in 23 patients (57.5%), carotid artery encasement in 21 (52.5%), and carotid artery occlusion in 3 (7.5%). The mean duration of clinical follow-up was 83 months, and 11 patients (27.5%) experienced new or worsening cranial nerve deficits that were mostly mild and did not negatively impact their daily functioning. The mean duration of imaging follow-up was 76 months, and 7 patients (17.5%) had lesions demonstrating growth. The authors state that there was a poor correlation between clinical and radiographic findings, noting that 6 (54.5%) of the 11 patients with neurological progression did not have any changes on neuroimaging and only 3 patients (27.2%) had neurological progression and imaging progression that occurred at the same time. Although a number of patients developed tumor progression and new neurological deficits, it was difficult to predict which patients were likely to have disease progression.

Van Havenbergh et al. reported on a series of 21 untreated petroclival meningiomas. Initially, 13 patients (61.9%) presented with cranial nerve deficits, and 5 (23.8%) presented with cerebellar signs or gait disturbance. The mean duration of follow-up was 82 months, and, at the most recent assessment, 17 patients (81.0%) exhibited cranial nerve deficits, and 9 patients (42.9%) had cerebellar signs. Fifty percent of initially asymptomatic patients developed cranial nerve deficits, and 20% of already affected patients had involvement of new cranial nerves. Additionally, 2 patients (9.5%) had mild functional deterioration (10-point decrease in Karnofsky Performance Scale score), 4 patients (19.0%) had moderate deterioration (20-point decrease), and 4 (19.0%) had severe deterioration. Eleven patients (52.4%) had no change in functioning. Sixteen tumors (76.2%) demonstrated growth on neuroimaging, and 10 (62.5%) of these growing tumors were associated with functional deterioration. Again, a number of lesions will demonstrate growth and

TABLE 3: Factors predictive of tumor progression

<table>
<thead>
<tr>
<th>Pre-GKS Variables</th>
<th>HR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>predictive in univariate analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>parasellar/clival/petrous</td>
<td>1.8</td>
<td>0.94–3.48</td>
<td>0.76</td>
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<td>petroclival, CPA</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
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<td>age &gt;65 yrs</td>
<td>3.5</td>
<td>1.72–6.93</td>
<td>0.001</td>
</tr>
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<td>decreasing margin dose</td>
<td>0.91</td>
<td>0.82–1.01</td>
<td>0.081</td>
</tr>
<tr>
<td>decreasing max dose</td>
<td>0.97</td>
<td>0.93–1.01</td>
<td>0.136</td>
</tr>
<tr>
<td>previous surgery</td>
<td>0.60</td>
<td>0.31–1.21</td>
<td>0.154</td>
</tr>
<tr>
<td>predictive in multivariate analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>age &gt;65 yrs</td>
<td>3.41</td>
<td>1.63–7.13</td>
<td>0.001</td>
</tr>
<tr>
<td>decreasing margin dose</td>
<td>0.90</td>
<td>0.80–1.00</td>
<td>0.05</td>
</tr>
</tbody>
</table>

* Median duration of follow-up was 6.5 years (range 2–18 years). Abbreviation: CPA = cerebellopontine angle.
TABLE 4: Factors predictive of new or worsening symptoms*

<table>
<thead>
<tr>
<th>Pre-GKS Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
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<tr>
<td>predictive in univariate analysis</td>
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<tr>
<td>location</td>
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<td></td>
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<tr>
<td>petrous/clival</td>
<td>2.5</td>
<td>1.01–6.10</td>
<td>0.045</td>
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<td>petroclival, CPA</td>
<td>1.00</td>
<td></td>
<td></td>
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<td>increasing vol</td>
<td>1.1</td>
<td>1.01–1.11</td>
<td>0.023</td>
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<tr>
<td>decreasing max dose</td>
<td>0.92</td>
<td>0.86–0.98</td>
<td>0.012</td>
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<tr>
<td>decreasing peripheral dose</td>
<td>0.83</td>
<td>0.71–0.98</td>
<td>0.030</td>
</tr>
<tr>
<td>increasing FU duration</td>
<td>1.01</td>
<td>1.00–1.02</td>
<td>0.004</td>
</tr>
<tr>
<td>tumor progression</td>
<td>2.60</td>
<td>1.52–4.50</td>
<td>0.001</td>
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<tr>
<td>predictive in multivariate analysis</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>location</td>
<td></td>
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<tr>
<td>petrous/clival</td>
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<td>petroclival, CPA</td>
<td>1.00</td>
<td></td>
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<tr>
<td>decreasing max dose</td>
<td>0.90</td>
<td>0.84–0.97</td>
<td>0.007</td>
</tr>
<tr>
<td>increasing FU duration†</td>
<td>1.01</td>
<td>1.00–1.02</td>
<td>0.015</td>
</tr>
<tr>
<td>tumor progression</td>
<td>2.91</td>
<td>1.60–5.31</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Median duration of follow-up was 7 years (range 0–16 years). There were new or worsening symptoms in 25 patients (10%); 230 patients (90%) had either no change or improvement in their symptoms. In multivariable analysis there was a trend toward clinical deterioration in patients with increased length of follow-up (p = 0.06).

cause symptomatic decline, but it is difficult to determine which lesions will progress. As these lesions are in close proximity to key structures, further growth often makes resection or GKS more difficult. Our results suggest that results following GKS compare favorably with the natural history of untreated skull base meningiomas.

Particularly with the advent of CT and MR imaging, which have facilitated improved targeting and early detection, SRS has been used with increased frequency to treat patients with skull base meningiomas. In our series, follow-up imaging demonstrated tumor control in 86% of patients at a median follow-up of 6.5 years. The necessary long follow-up of this type of study was further demonstrated by our radiological progression-free survival of 99% at 3 years, 96% at 5 years, and 79% at 10 years. Similar time-dependent drop-offs of disease control are reported throughout the SRS literature. 

The combination of microsurgery and SRS appears to attain higher long-term tumor control rates of above 80% and even above 90% in most series. Ichinose et al. reported a long-term tumor control rate of 98.1% in their skull base meningioma case series involving 27 patients who were treated with SRS after radical tumor resection. The results of multimodality treatment also appear durable. Davidson et al. reported 100% local tumor control at 5 years and a persistently high rate of 94.7% at 10 years in 36 patients who all received postoperative GKS. Conversely, Pollock and Stafford found tumor control rates of 85% and 80% at 3 and 5 years, respectively, in 49 patients who received only primary GKS. Within a much larger study of all intracranial tumors at the University of Pittsburgh, there were no significant differences in long-term tumor control rates of those 384 patients who underwent postoperative SRS compared to 488 patients treated with primary SRS. Growing acceptance of the efficacy and safety, as well as increased availability of radiosurgery at many institutions, permits neurosurgeons to plan for cytoreductive, neurologically preserving resections followed by SRS.

Surgical Resection

The mystique of skull base surgery has long attracted neurosurgeons to attempt resection of meningiomas. Before the widespread availability of CT and MR imaging, many of these lesions were diagnosed late in their course. The very size of the lesion required relief of mass effect, and resection accomplished that task, as well as permit-
diotherapy for skull base meningiomas using 50–55 Gy delivered in 30–33 fractions range between 75% and 95% at both 5 and 10 years posttreatment.7,12,20,42,47 Overall actuarial control rates for the combined results of 5 studies were 90% and 83% at 5 and 10 years, respectively.7,12,20,42,47 Neurological deficits are reported to improve or stabilize in up to 69%–100% of cases after conventional radiotherapy.38,43,44 Accompanying these positive outcomes are complication rates with radiotherapy ranging from 0% to 24%.44 Injury to nearby cranial nerves is one of the most commonly reported complications. The rate of radiation injury to the optic apparatus is reported to be between 0% and 3%, with similar rates of dysfunction after radiotherapy reported for other cranial nerves.44 Newer techniques such as intensity-modulated radiotherapy and fractionated stereotactic radiotherapy (FSRT) that use image guidance and smaller treatment-volume principles similar to radiosurgery may offer more favorable outcomes with regard to neurological preservation in patients with skull base meningiomas. The results of several studies directly comparing the outcomes of FSRT and SRS suggest that both are safe and fairly effective techniques in the treatment of skull base meningiomas, affording comparable satisfactory long-term tumor control.38,43,44,68 Local tumor control rates with FSRT and SRS were reported to be 93%–97% and 90%–94%, respectively.38,43,68 The rates of permanent morbidity were also similar—between 0% and 2.6% for both FSRT and SRS.38,43 Minniti et al.44 suggested the major criteria for selecting between FSRT and SRS were the average diameter of the meningioma and the close proximity to radiation-sensitive structures. While SRS was favored in cases with tumors less than 3 cm and more than 3–5 mm away from radiosensitive structures, FSRT was used for all tumors that were not deemed amenable to SRS. Intuitively, smaller treatment volume and lower overall integral dose to the normal tissues of the intracranial space seem appealing to neurosurgeons and radiation oncologists alike.

Stereotactic Radiosurgery

Tumors of the skull base effectively treated with SRS are often benign lesions, such as meningiomas, schwannomas, and craniopharyngiomas. Since 1990, Gamma Knife or linear accelerator therapy has been used in the radiosurgical treatment of skull base meningiomas. Now more than 20 years after the introduction of these technologies, we are able to observe their long-term tumor control and morbidity profiles. Based on a better understanding of the natural history of meningiomas and expected longevity of most patients in this population, recently published series have identified the need to report results in terms of 5- and 10-year actuarial control rates. Such long-term actuarial control rates have become available for SRS but are less frequently found in microsurgical series. A summary of large published case series involving patients with skull base meningiomas treated with radiosurgery is presented in Table 5.

In a large series of 972 patients with meningiomas in diverse locations who underwent GKS at the University of Pittsburgh, the reported actuarial tumor control rates were 93% at 5 years and 87% at 10 and 15 years.34 The median dose to the tumor margin in this series was 13 Gy. These results confirmed the findings of an earlier study of 159 patients from the same institution in which tumor volumes decreased in 3%, remained stable in 60%, and increased in 6% of patients.46 In a review article, Minniti et al. compiled data from 18 studies including a total of 2919 skull base meningiomas treated with GKS.44 They reported a 5-year actuarial control of 91%. Seven of these studies (including 1626 skull base meningiomas) reported an averaged 10-year actuarial control of 87.6%. When summarizing the recent large case series that all included more than 100 patients, 5- and 10-year local control rates ranged from 86.2% to 98.5% and 73% to 97%, respectively.11,23,28,32,35,36,46,62,67 Minniti et al.44 noted that the rate of tumor shrinkage ranged widely from 16% to 69% in different series. Neurological improvements rate have been reported at between 8% and 66% for most large series that have included more than 100 patients.14,15,23,25,28,32,34,36,46,62,67 Our own series found comparable local tumor control and neurological improvement rates with the extended follow-up period.

While microsurgery and radiotherapy have evolved, SRS has also improved. The goal of current dosing regimes is to minimize long-term toxicity while maintaining efficacy. With this aim, lower radiosurgical doses to meningiomas have been used in the last decade than at the onset of GKS at the University of Virginia in 1989. Moreover, radiosurgical conformity and dose fall-off have been enhanced with routine use of multiple, composite-isocenter treatments. In a review of 7 series, Minniti et al. reported that 5-year actuarial tumor control rates did not drop from the respectable range of 90%–95% when the median dose was lowered to 12–14 Gy.9,15,19,28,32,49,67 Dosing must also be specific for the region and potential nearby structures. Current practice aims to avoid irradiating the optic apparatus beyond point doses of 8–10 Gy. The use of multiple isocenters of different size and configurations, differential weighting of the individual isocenters, and selective beam blocking enables dose plans to closely conform to the irregular shape of most skull base meningiomas.33 The present study with a median margin dose of 14 Gy was consistent with the dosing regimes and the associated low rate of toxicity reported in the literature from other busy centers.

Our study population demonstrated a trend toward a decreased rate of progression in patients who underwent resection prior to initial GKS (Fig. 2; p = 0.154). Resection affords a smaller tumor volume to target with radiosurgery and may permit greater clearance for dose fall-off to surrounding, radiation-sensitive structures. Pre-GKS covariates associated with tumor progression in our series include age greater than 65 years and decreasing peripheral dose. As reported in the literature, factors associated with worse long-term local control include larger tumor volume (> 10 cm³), inadequate conformity index, and treatment for recurrent tumor.11,27,34 Most published series report that sex, site of meningioma, and presenting neurological status do not significantly affect radiosurgical outcomes.11,27,34 Our overall factors predictive of new or worsening symptoms were increasing duration of

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follow-up, decreasing maximum dose, tumor progression, and petrous or clival versus parasellar, cerebellopontine angle, or paraclival location. Another series of 98 cases reported by Han et al.21 similarly supports the importance of tumor location. The authors found that cranial neuropathies caused by meningiomas of the cavernous sinus are more likely to improve with GKS than are other skull base meningiomas. Furthermore, most series demonstrate that the factors predicting local tumor control do not significantly differ between patients treated with primary SRS and those treated with postoperative SRS.44

Overall postradiosurgical complication rates are reported in 3%—40% of cases, with most series reporting around an 8% rate of neurological complications, with the rate of transient complications being approximately 3% and the rate of permanent complications being approximately 5%.45 Infrequent early and generally minor complications include headache, nausea, and pin-site infections. Long-term complications include cranial nerve dysfunction and neurologic deficits associated with adverse radiation effects (such as edema and necrosis). Among published series involving 100 patients or more, rates of these significant long-term complications ranged from 0% to 16% in centers utilizing median doses of 12–15 Gy.11,14,15,23,25,32,34–36,46,67

The much talked about but seldom seen risk of radiosurgical neoplasia was not observed in our series of cases of skull base meningiomas. Radiosurgery-induced neoplasia has a reported incidence of between 0 and 3 cases per 200,000 patients, and this does not appear to be above the natural incidence of cancer in the general population.48,52 Among the few cases of radiation-induced tumors, most are glioblastomas.19,39,53,57,73 While the risk of radiosurgery-induced secondary tumor is very low, it still must be weighed in the treatment of patients with benign tumors and a long life expectancy, particularly for those young patients presenting with skull base meningiomas.

Finally, for those patients demonstrating tumor growth after SRS, repeat resection or SRS represent viable options to gain tumor control.16,24,28,45 In general, it has been the experience of the senior author (J.P.S.) that the rare skull base tumor that grows can often be managed conservatively particularly in those patients over the age of 65 years. In those patients in whom resection is required, resection after radiosurgery is not markedly more difficult. On occasion, a second radiosurgery may be attempted for elderly patients demonstrating meningioma growth and for whom an open resection or watchful waiting would not be deemed prudent. It is quite likely that any prior attempt that fails makes a subsequent attempt at treatment of a skull base meningioma slightly more challenging particularly as the tumor has grown and necessitated another operation.
Radiosurgery of skull base meningiomas

Study Limitations

As the data presented are the result of a single-institution experience, limitations include patient selection bias and treatment bias. Furthermore, the retrospective nature of the study and lack of an untreated control group restrict our ability to assess the full benefit of GKS as well as complications arising after GKS.

Conclusions

Stereotactic radiosurgery offers an acceptable rate of tumor control for skull base meningiomas. After radiosurgery, neurological preservation or improvement in patients with skull base meningiomas was more commonly observed in patients with lesions arising from petroclival, parasellar, and cerebellopontine angle locations.

Disclosure

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 to the study and manuscript preparation include the following. Conception and design: Starke, Williams, Sheehan. Acquisition of data: all authors. Analysis and interpretation of data: Starke, Williams, Sheehan. Drafting the article: Starke, Williams, Hiles, Sheehan. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Starke.


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