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Tumor Control and Cranial Nerve Outcomes After Adjuvant Radiosurgery for Low-Grade Skull Base Meningiomas

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■ OBJECTIVE: **We evaluated the tumor control and cranial nerve (CN) outcomes after adjuvant stereotactic radiosurgery (SRS) for petroclival, cavernous sinus, and cerebellopontine angle meningiomas.**

■ METHODS: **From our prospectively maintained database of 2022 patients with meningioma who had undergone Leksell SRS during a 30-year interval, we found 43 patients with petroclival, 94 with cavernous sinus, and 13 patients with cerebellopontine angle meningiomas who had undergone adjuvant SRS after surgical resection of the meningioma. The patients included in the present report had had ≥1 CN deficit at the initial presentation and a minimum follow-up period of 12 months. The median age at SRS was 54 years (range, 22—81). SRS was performed for residual tumor in 104 patients (69%) and recurrent tumor in 46 patients (31%). The median tumor volume treated with SRS was 8.1 cm^3 (range, 0.3—42), and the median margin dose was 13 Gy (range, 10—20).**

■ RESULTS: **Tumor control was achieved in 135 patients (90%) at a median follow-up point of 75 months. The progression-free survival rate after SRS was 99.5% at 1 year, 98% at 3 years, 95% at 5 years, and 90% at 10 years. Overall, 29 of the 150 patients (19%) reported improvement in CN function. Deterioration in CN function after SRS developed in 15 patients (10%). The rate of deterioration was 3.5% at 1 year, 5.5% at 3 years, and 7% at 5 years.**

■ CONCLUSIONS: **Adjuvant SRS provides effective tumor control and a low rate of new or worsening CN deficits.**

INTRODUCTION

Meningiomas are the most common primary intracranial neoplasm, accounting for one third of all primary brain tumors.[1] Additionally, it has been estimated that almost one third of intracranial meningiomas arise from the skull base.[2] Surgery has generally been considered the primary management option, especially for symptomatic patients. However, the proximity of these tumors to critical vascular and cranial nerve (CN) structures makes complete surgical removal extremely difficult.

The success of stereotactic radiosurgery (SRS) in achieving tumor control has since altered the clinical paradigm in the management of skull base meningiomas, with reports demonstrating that partial tumor debulking, followed by adjuvant SRS, achieves high tumor control rates with a lower risk of postoperative complications.[3-5] The goal of SRS, whether used as primary therapy or adjuvant therapy after surgical resection, is to prevent tumor growth, forestall symptomatic brain stem compression, and maintain or improve CN function.

The goal of the present study was to determine tumor control and CN outcomes after adjuvant SRS for skull base meningiomas.

Key words
- Cranial nerve
- Meningioma
- Radiation
- Radiosurgery
- Skull base

Abbreviations and Acronyms
CN: Cranial nerve
CP: Cerebellopontine
GTR: Gross total resection
PFS: Progression-free survival
SRS: Stereotactic radiosurgery
STR: Subtotal resection
WHO: World Health Organization

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METHODS

Patient Population

We performed a retrospective analysis of an institutional review board—approved database of 2022 patients with intracranial meningioma who had undergone SRS during a 31-year interval. We identified a total of 659 patients with petroclival, cavernous sinus, and cerebellopontine (CP) angle meningiomas who had undergone adjuvant or salvage Leksell Gamma Knife (Elekta Instruments, Stockholm, Sweden) SRS at the University of Pittsburgh Medical Center. To be included in the current analysis, the following criteria had to have been met:

1. The presence of a CN deficit at SRS
2. A minimum of 12 months of clinical and radiological follow-up data available
3. Histologically proven World Health Organization (WHO) grade I meningiomas at the initial resection
4. A solitary meningioma, with no history of previous brain radiation therapy

A total of 150 patients met the inclusion criteria. Of the 150 patients, 43 had petroclival tumors, 94 had cavernous sinus tumors, and 13 had CP angle meningiomas. Petroclival meningiomas were defined as tumors with their maximal volume occupying the region between the upper two thirds of the clivus and the petrous apex.[6] CP angle meningiomas were defined as tumors with the maximal volume occupying the junction between the lateral cerebellum, pons, and internal auditory meatus.[7] Cavernous sinus meningiomas were defined as tumors with their maximal volume occupying the cavernous sinus.[8]

Of the 150 patients included in the present study, 43 were men and 107 were women. The age at symptom onset was 48 years (range, 21—78 years). The most common symptom in patients with cavernous sinus meningiomas was diplopia related to a new-onset CN VI deficit. The most common symptom in patients with petroclival meningiomas was trigeminal neuropathy. The most common presenting symptoms in patients with CP angle meningiomas were unilateral hearing loss and tinnitus.

The median duration from diagnosis to the first surgery was 12 months (range, 0—274). The median age at the initial surgical resection was 50 years (range, 21—78). Initial gross total resection (GTR) was achieved in 28 patients (19%).

The median duration from surgery until SRS was 18 months (range, 1—309). Adjuvant SRS was performed for residual tumor in 104 patients (69%), and salvage SRS was performed for recurrent tumor in 46 patients (31%). The median age at SRS was 54 years (range, 22—81). The patient demographic data in each group are presented in Table 1.

Table 1. Patient Demographic Data

Factor	Petroclival (n = 43)	Cavernous Sinus (n = 94)	CP Angle (n = 13)
Age (years)			
Median	55	54	49
Range	33—81	21—79	34—68
Sex (n)			
Male	14	29	0
Female	29	65	13
Resection (n)			
GTR	4	18	6
STR	39	76	7
Interval from surgery to SRS (months)			
Median	9	18	33
Range	1—120	1—309	5—235
CN involved (n)			
II	0	13	0
III, IV, VI	18	68	2
V	27	46	10
VII	6	15	7
VIII	13	15	16
IX—XII	8	4	2

CP, cerebellopontine; GTR, gross total resection; STR, subtotal resection; SRS, stereotactic radiosurgery; CN, cranial nerve.

Radiosurgery Technique

The Leksell Gamma Knife (Elekta Instruments) models U, B, C, 4C, Perfexion, or ICON were used, depending on the model available at the time of SRS. We began the procedure by applying a Leksell stereotactic head frame with the patient under conscious sedation and local anesthesia. After attachment of the fiducial system, the patients underwent high-definition intravenous contrast-enhanced magnetic resonance imaging or computed tomography studies. The images were uploaded to the dose planning software. A highly conformal and selective 3-dimensional plan was created to target the contrast-enhancing tumor volume in a single SRS procedure. Beam blocking was used to limit the dose delivery to adjacent critical structures. After the procedure, all the patients had received 20—40 mg of intravenous methylprednisolone, and all had been discharged within 24 hours of the procedure. The median tumor volume was 8.1 cm^3 (range, 0.3—42), the median margin dose was 13 Gy at the 50% isodose line (range, 10—20), the median maximum dose was 26 Gy (range, 20—40), and the median number of isocenters was 10 (range, 2—41). The median dose used for repeat SRS was 12 Gy (range, 10—14) at the 50% isodose line. The radiosurgical treatment parameters stratified by tumor location are presented in Table 2.

Follow-Up Protocol

The median follow-up period was 75 months (range, 12—312). Clinical and imaging follow-up evaluations were recommended every 6 months for the first year, annually for 2 years, and every 2—4 years thereafter. If a patient reported new or worsening

Table 2. Gamma Knife Treatment Parameters

Factor	Petroclival (n = 43)	Cavernous Sinus (n = 94)	CP Angle (n = 13)
Tumor volume (cm^3)			
Median	10.7	8.1	1.9
Range	0.5—42	0.3—37	0.5—11.3
Margin dose (Gy)			
Median	13	13	13
Range	10—18	11—20	12—16
Maximum dose (Gy)			
Median	26	26	26
Range	20—36	22—40	23.6—32
Isocenters (n)			
Median	12	9	8
Range	2—41	2—19	5—14
Isodose line (%)			
Median	50	50	50
Range	40—60	40—70	50—55

CP, cerebellopontine.

symptoms, earlier clinical and imaging follow-up evaluations were recommended. Magnetic resonance imaging was typically performed to evaluate for changes in tumor volume.

Improvement in a preexisting CN deficit was defined as improvement in the function of ≥1 CN deficit. Hearing status was evaluated by performing pre- and post-SRS audiograms and using the Gardner-Robertson hearing scale.[9] Hearing was considered improved if the audiogram had revealed a positive change in Gardner-Robertson grade after SRS. The Barrow International Institute pain intensity score[10] was used to assess trigeminal pain and to assess for changes in pain after the procedure. Trigeminal pain was considered improved if the patients had been classified into a more favorable Barrow International Institute pain intensity group. Facial nerve function was evaluated using the House-Brackmann scoring system.[11] Facial nerve function was considered improved if the patients had been classified into a more favorable House-Brackmann grade. Other determinants for symptom improvement were the patients' subjective sense of symptom change and the identification of any changes found on physical examination.

Tumor regression was defined as a ≥25% decrease in tumor volume. Tumor progression was considered present if a ≥25% increase in tumor volume was found compared with the volume at the SRS. The tumor volume at SRS was determined as the volume included in the tumor margin prescribed isodose. Marginal recurrence was defined as tumor progression occurring within 2 cm of the edge of the targeted tumor volume. In-field recurrence was defined as tumor progression within the targeted tumor volume. Stable tumor was defined as tumors with a <25% change in volume from SRS. The post-SRS tumor volume was calculated by multiplying the x, y, and z tumor parameters and dividing the total by 2.

Statistical Analysis

Kaplan-Meier plots were used to evaluate progression-free survival (PFS), improvement rate of CN deficits, and deterioration rates of CN deficits. A 2-sample t test was used to determine whether a difference in symptom duration, tumor volume, and age at SRS between the patients who had reported symptom improvement and those who had not. The χ^2 test was used to evaluate the effect of tumor location, radiation dose, and tumor response on the likelihood of improvement in CN deficits. A P value of <0.05 was set for statistical significance. Statistical analysis was performed using IBM SPSS Statistics, version 25 (IBM, Armonk, New York, USA).

RESULTS

Patient Survival and Tumor Control

At the data collection for the present study, 130 patients (87%) were alive and 20 had died. None of the patients had died of meningioma or complications of SRS. Imaging-defined overall tumor control was achieved in 135 patients (90%) at a median follow-up of 75 months. Tumor volume regression was seen in 83 patients (55%), the tumor volume was stable in 52 patients (35%), and delayed tumor progression was demonstrated in 15 patients (10%) at a median follow-up of 108 months (range, 20—288) after SRS. The actuarial PFS rate after SRS was 99.5% at 1 year, 98% at 3 years, 95% at 5 years, and 90% at 10 years. Tumor location, margin dose, duration from initial surgery to SRS, and tumor size were not associated with better or worse PFS.

Patients who had undergone SRS for residual tumor after previous subtotal resection (STR) demonstrated significantly better PFS compared with patients who had undergone salvage SRS for recurrent tumor after GTR (P = 0.02; **Figure 1**). The interval between the last surgery and SRS was significantly longer for the patients who had undergone initial GTR (77 months) compared with patients who had undergone STR (30 months; P < 0.001). No statistically significant differences in tumor volume or margin dose were found between the patients who had undergone STR and those who had undergone GTR. None of the patients developed radiation-induced malignant transformation of the tumor.

CN Outcomes

Improvement in CN Deficits. At the final follow-up evaluation, 29 patients (19%) reported improvement, 106 (71%) demonstrated no change, and 15 patients (10%) reported delayed onset of either a new CN deficit or exacerbation of a preexisting CN deficit. From the Kaplan-Meier analysis, the improvement rate was 10% at 1 year, 13% at 3 years, and 18% at 5 years (**Figure 2**). Although patients with tumor volume regression were more likely to report symptom improvement, this finding just missed statistical significance (P = 0.057).

Improvement was reported in 16% of patients with cavernous sinus meningiomas, 23% of patients with petroclival meningiomas, and 31% of patients with CP angle meningiomas. Tumor location did not affect the likelihood of symptom improvement.

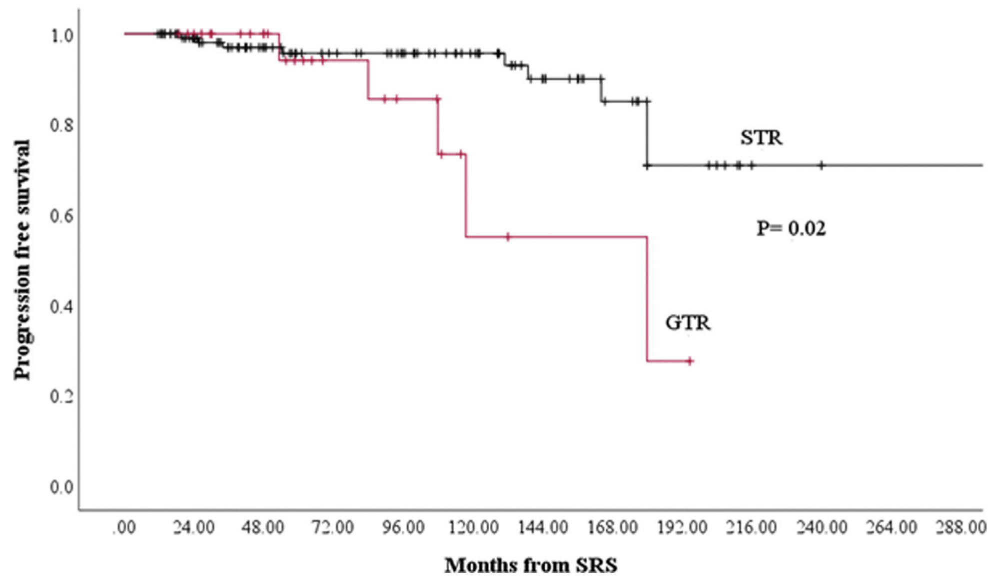

Figure 1. Graph showing progression-free survival after stereotactic radiosurgery (SRS) stratified by surgical resection. GTR, gross total resection; STR, subtotal resection.

Other factors, such as tumor volume, interval between the last surgery and SRS, symptom duration, margin dose, degree of resection, and patient age at SRS, did not significantly affect the likelihood of improvement of a CN deficit. The CN outcomes stratified by tumor location are presented in Table 3.

The most common presenting symptom was diplopia. Of the 87 patients with diplopia, 16 patients (18%) reported improvement at a median of 91 months after SRS. From the Kaplan-Meier analysis, the improvement rate of diplopia was 17% at 3 years and 17% at 5 years (Figure 3). Tumor location did not affect the improvement rate of diplopia ($P = 0.35$).

Of the 83 patients with trigeminal neuropathy or neuralgia, 15 (18%) reported symptom improvement at a median duration of 60 months. The Kaplan-Meier analysis revealed an improvement rate

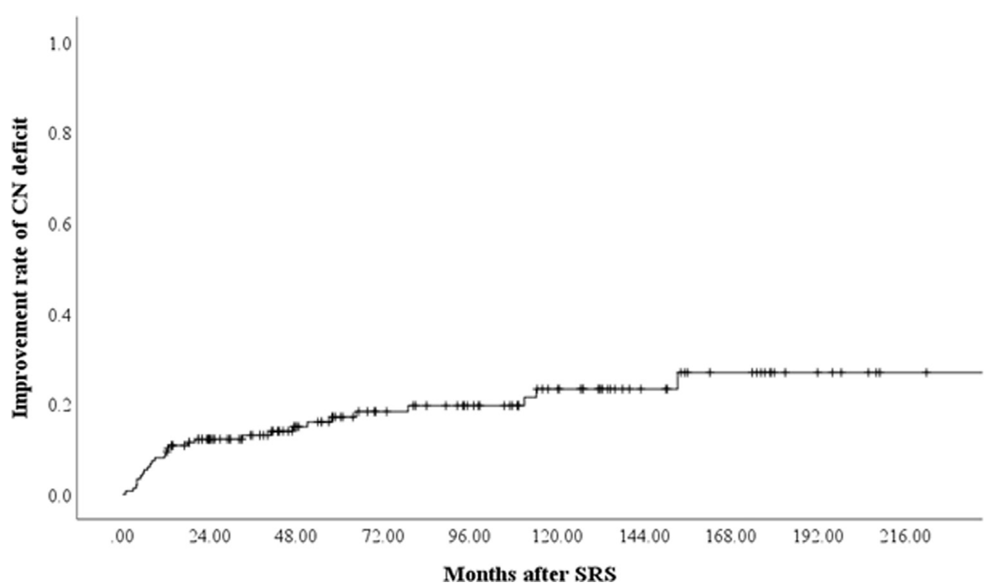

Figure 2. Graph showing improvement rate of cranial nerve (CN) deficit after stereotactic radiosurgery.

Table 3. Cranial Nerve Outcomes After Stereotactic Radiosurgery

Factor	Petroclival (n = 43)	Cavernous Sinus (n = 94)	CP Angle (n = 13)
Improved	10 (23)	15 (16)	4 (31)
Unchanged	29 (67)	68 (72)	9 (69)
New-onset or worsening preexisting deficit	4 (4)	11 (12)	0 (0)

Data presented as n (%).
CP, cerebellopontine.

of trigeminal findings of 7% at 1 year, 12% at 3 years, and 18% at 5 years. Of the 26 patients with trigeminal symptoms secondary to petroclival meningioma, 7 (27%) reported symptom improvement at a median of 63 months. Of the 13 patients with trigeminal symptoms secondary to CP angle meningioma, 4 (31%) reported symptom improvement at a median of 43 months. In contrast, only 4 of 44 patients (10%) with trigeminal neuropathy related to cavernous sinus meningiomas reported symptom improvement at a median follow-up of 73 months. Patients with trigeminal neuropathy secondary to cavernous sinus meningioma were significantly less likely to report neuropathy improvement compared with patients with petroclival and CP angle meningiomas ($P = 0.02$). Additionally, the improvement rate of trigeminal symptoms was significantly lower in patients with cavernous sinus meningiomas ($P = 0.03$).

Of the 44 patients with hearing loss related to vestibulocochlear nerve involvement, 7 (16%) reported symptom improvement at a median of 53 months after the procedure. The Kaplan-Meier analysis showed that the improvement rate was 3% at 1 year, 6% at 3 years, and 13% at 5 years. Tumor location did not affect the possibility of hearing improvement ($P = 0.1$).

Of the 28 patients with facial weakness, 5 (18%) reported symptom improvement at a median of 50 months after SRS. The improvement rate was 4% at 1 year, 5% at 3 years, and 17% at 5 years. The tumor location did not affect the likelihood of improvement in facial weakness ($P = 0.7$).

New-Onset or Worsening CN Deficit. Of the 150 patients, 15 (10%) developed new or worsening CN deficits, most of whom (12 patients) also had imaging evidence of tumor progression. Patients with tumor progression were more likely to report new or worsening CN deficits ($P \leq 0.01$). In 2 patients without evidence of tumor progression, symptom worsening was attributed to adverse radiation effects. Six patients (40%) reported new or worsening symptoms within 1 year after the procedure. Of the 15 patients, 7 developed worsening trigeminal nerve symptoms, 3 reported worsening facial weakness, 3 reported worsening diplopia, and 2 patients reported worsening hearing. The Kaplan-Meier analysis revealed that the rate of new or worsening CN function was 3.5% at 1 year, 5.5% at 3 years, and 7% at 5 years (Figure 4). Tumor location and margin dose did not significantly affect the likelihood of new-onset or worsening symptoms, likely because of the relatively small number of patients with such complications.

Additional Management

Fifteen patients with demonstrated tumor growth on imaging required additional management. Thirteen patients with marginal tumor recurrence underwent a second SRS at a median of 108 months (range, 25–288) after the initial procedure. Two patients

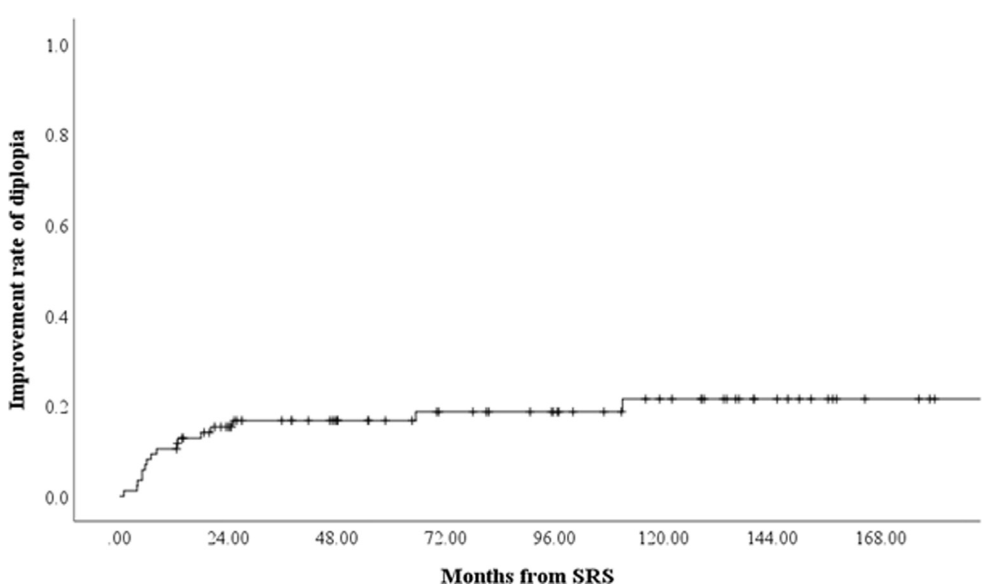

Figure 3. Graph showing improvement rate of diplopia after stereotactic radiosurgery (SRS).

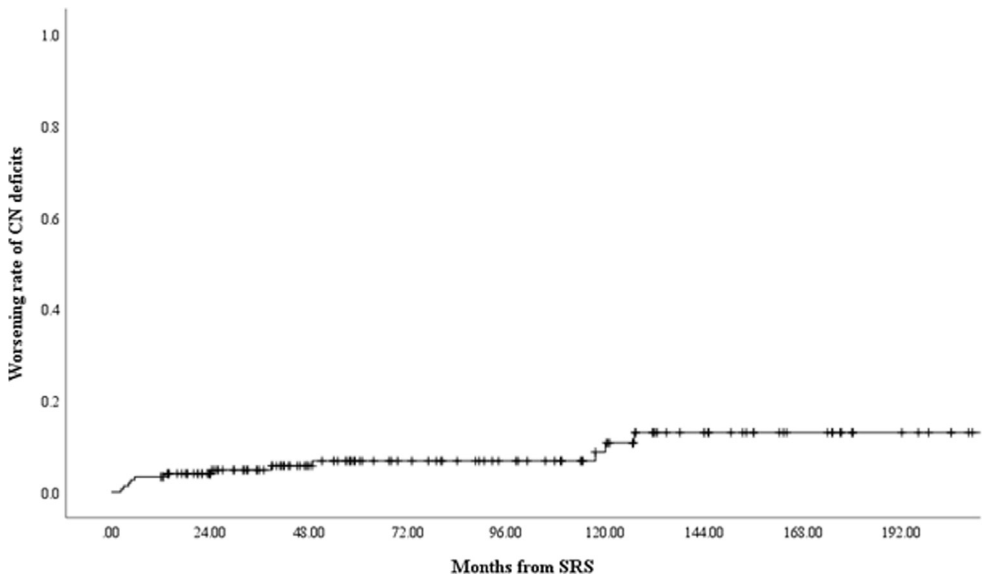

Figure 4. Graph showing worsening rate of cranial nerve (CN) deficits after stereotactic radiosurgery (SRS).

underwent delayed surgical resection at 20 and 34 months after SRS.

After SRS, 2 patients (1 with CP angle meningioma and 1 with petroclival meningioma) had developed hydrocephalus found on follow-up imaging. The patient with a CP angle meningioma was asymptomatic and required no cerebrospinal fluid diversion procedure. In addition, the hydrocephalus improved as the tumor demonstrated regression on the follow-up imaging studies. The patient with a petroclival meningioma presented with worsening balance and underwent ventriculoperitoneal shunt placement 12 months after SRS. However, the tumor volume in that patient was stable.

DISCUSSION

The options available for the management of skull base meningiomas include observation with serial imaging studies, SRS, and surgical resection. For patients with small, asymptomatic tumors, observation can be considered.[12] However, owing to the proximity of these tumors to critical CN and vascular structures, tumor growth will often be associated with neurological deficits.[13] Surgery has often been considered the treatment of choice for meningiomas, in particular, when complete surgical resection can be achieved. For skull base meningiomas, however, surgical cure can be associated with high mortality and morbidity.[14-16] In addition, even with GTR, the tumor recurrence rates have been as high as 19%.[17] In their report on the surgical outcomes of 48 patients with petroclival meningiomas, Natarajan et al.[18] reported that tumor progression was observed in 15% of patients who had reportedly undergone complete tumor resection. Tumor debulking, followed by SRS, has been used more frequently to avoid the high complication rates associated with attempting complete tumor resection.[3,19] SRS is a minimally invasive alternative to surgery, especially for patients with minimal symptoms and those with tumors encasing or in proximity to critical CN and vascular structures. Since its introduction in 1987, multiple studies have demonstrated the success of SRS in achieving high tumor control rates with low complication rates as either primary therapy or as adjunct treatment after incomplete surgical resection.[20-22] Sughrue et al.[23] conducted a meta-analysis of the predictors of outcomes after treatment of patients with cavernous sinus meningiomas. In their series of 2065 patients, those who had undergone primary SRS demonstrated greater tumor control rates compared with patients who had undergone either complete or partial resection. In addition, the rate of postoperative CN deficits was greater in the patients with previous resection compared with primary SRS.[23]

Tumor Control

In the present study, tumor control was achieved in 135 patients (90%) at a median follow-up period of 75 months. In 85 patients (55%), tumor volume regression was observed. Recent studies related to SRS for skull base meningiomas have reported tumor control rates ranging from 90% to 100%.[20-22,24-28] Tumor progression was observed in 15 patients (10%) and was detected at a median of 108 months after SRS. The actuarial PFS rate was 99.5% at 1 year, 98% at 3 years, 95% at 5 years, and 90% at 10 years. The 10-year PFS rate was similar to the recurrence rate after Simpson grade I resection of low-grade meningiomas.[29] Tumor location was not predictive of tumor control. However, we found that patients with previous STR had better PFS rates than patients with reported GTR. The duration between surgery and adjuvant SRS for the patients who had undergone STR was significantly shorter than that of patients who had undergone GTR. In the present experience, the difference in the interval between surgery and either adjuvant or salvage SRS did not significantly affect the tumor control rates. In contrast, a recently reported study of the outcomes of SRS for subtotal resection of pituitary adenomas demonstrated that patients who had undergone SRS within 6 months of surgery had a significantly lower risk of radiological tumor progression compared with the patients who had undergone SRS >6 months after surgery.[30]

Standard fractionated external beam radiation therapy and, more recently, multisession (or fractionated) SRS have also been used as an alternative to SRS. Chung et al.[31] analyzed the outcomes of both treatment modalities and found that both had similar tumor control rates, symptomatic improvement, and complication rates. The rates of tumor regression were greater for the patients who had undergone SRS. Depending on the SRS technique, for certain patients, fractionated SRS might reduce the risk of optic neuropathy in patients whose tumors are adjacent to the optic apparatus.[25]

CN Outcomes

Improvement in pre-existing CN deficits was documented in 19% of patients, and the symptoms were unchanged in 71% of the patients. Patients with tumor volume regression found on imaging studies were more likely to have reported symptom improvement. Flannery et al.[32] argued that the pressure relief associated with tumor regression was 1 possible mechanism explaining the observed improvements.

Overall, tumor location did not significantly affect the likelihood of improvement in CN deficits. The factors affecting the likelihood of symptom improvement after SRS include previous surgical resection, previous radiation therapy, symptom duration before SRS, and tumor location.[25,33,34] In our previous report on CN outcomes after primary SRS for skull base meningiomas, we found that 46.5% of patients reported symptom improvement.[33] In addition, patients who had undergone SRS within 12 months of the onset of symptoms and those with cavernous sinus and petroclival meningiomas were more likely to report improvement at the final follow-up evaluation.[33] Kano et al.[25] reported that patients with cavernous sinus meningiomas who had not undergone previous surgical resection were significantly more likely to report symptom improvement. In the present report, we found no statistically significant difference in improvement according to the type of CN deficit. Diplopia was the most common symptom, with 18% reporting improvement of preexisting diplopia. Moreover, trigeminal symptoms improved in 18% of patients, hearing improved in 16% of patients, and 18% experienced improvement in preexisting facial weakness.

Fifteen patients (16%) with cavernous sinus meningioma reported symptom improvement. The most common presenting symptoms was diplopia related to CN VI deficit. Nicolato et al.[27] reported that 60.5% of their patient population who had undergone adjuvant SRS reported improvements in CN deficits. Hasegawa et al.[35] reported symptom improvement in 34% of their patients who had undergone adjuvant SRS. Using linear accelerator-based radiosurgery, Spiegelmann et al.[36] reported that 19% of patients reported improvement after adjuvant linear accelerator SRS. In addition, they found that patients who had undergone SRS <1 year from the onset of symptoms were more likely to report symptom improvement.[36]

Ten patients (23%) with petroclival meningioma reported improvement of preexisting CN deficits. The most common presenting symptom was related to trigeminal nerve deficit. Flannery et al.[32] reported that 27% of patients in their cohort who had undergone adjuvant SRS for petroclival meningiomas reported symptom improvement at a median of 72 months. Kim et al.[24] reported the outcomes of 89 patients who had undergone SRS for petroclival meningiomas. The most common symptom was related to trigeminal nerve dysfunction. CN improvement was documented in 30.3% of patients at a mean follow-up of 74 months. Starke et al.[22] conducted a multicenter study of the outcomes of SRS in 254 patients with petroclival meningiomas. At a mean follow-up period of 71 months, 27.1% of patients had reported improvement of CN symptoms. However, in the previous 2 reports, the CN outcomes were reported for a heterogeneous patient population composed of patients who had undergone primary SRS and some who had undergone adjuvant SRS.

Four patients (31%) with CP angle meningiomas reported symptom improvement. Ding et al.[20] reported that 57.4% of patients reported symptom improvement after SRS for CP angle meningiomas. Park et al.[7] reported neurological improvement in 31% of their patients. Both studies reported the outcomes for patients who had undergone primary SRS and adjuvant SRS; thus, making any outcome comparisons inaccurate. Details from recent radiosurgical series of adjuvant SRS for skull base meningiomas are listed in Table 4.

Complications

Overall, 10% of patients reported new-onset or worsening preexisting symptoms. The Kaplan-Meier analysis, the deterioration rate was 3.5% at 1 year, 5.5% at 3 years, and 7% at 5 years. The incidence of delayed CN dysfunction after SRS has ranged from 0% to 25%.[22,25,32,34,37,38] Patients with tumor progression found on imaging studies were more likely to report worsening symptoms. Most patients (40%) reported symptom worsening within 1 year of the procedure, with trigeminal nerve symptoms the most commonly reported. In 2 patients, worsening symptoms was attributed to the development of adverse radiation effects, and in 1 patient, the exact cause was unknown.

Management of Skull Base Meningiomas

Complete surgical resection can be difficult and, even if achieved, has been associated with significant mortality and morbidity. The success of SRS in achieving tumor control is well-established in reported studies. In addition, multiple reports have since demonstrated significant rates of improvement in CN deficits over time, especially after primary SRS. Using adjuvant SRS after incomplete tumor resection allows the operating surgeon the opportunity to partially resect moderate to large meningiomas, knowing that residual tumor can be successfully controlled using SRS.

From our 30-year experience at the University of Pittsburgh Medical Center, we would advocate the use of SRS as a primary management option for small to moderate size skull base meningiomas when the tumor has demonstrated growth after observation or when it is causing neurological deficits owing to

Table 4. Recent Radiosurgical Series for Adjuvant Stereotactic Radiosurgery for Skull Base Meningiomas

Investigator	Patients (*n*)	Location	Adjuvant SRS (%)	Overall Tumor Control (%)	Improvement After Adjuvant SRS (%)	Overall New or Worsening CN Deficit (%)
Nicolato et al.,[27] 2002	122	CS	52	97.5	60.5	1
Hasegawa et al.,[35] 2007	115	CS	57	88	34	12
Flannery et al.,[32] 2010	163	PC	44.5	93	18	2
Starke et al.,[22] 2014	254	PC	45	91	NA	6.4
Park et al.,[7] 2014	74	CP	19	97	31*	10.8
Ding et al.,[20] 2014	177	CP	29.9	92	57.4*	9
Kim et al.,[24] 2017	89	PC	35	94.4	31*	9
Azar et al.,[34] 2017	177	CS	29.9	92.1	40.4*	10.8
Present study	150	CS, PC, CP	100	90	16, 23, 31	10

SRS, stereotactic radiosurgery; CN, cranial nerve; CS, cavernous sinus; PC, petroclival; CP, cerebellopontine angle.
*Overall rate of CN improvement (adjuvant and primary SRS).

compression on adjacent CNs. In some cases in which the tumor is large and is causing significant compression symptoms, partial tumor resection to relieve the compression followed by SRS is a strategy that can achieve long-term tumor control and has been associated with lower rates of morbidity and mortality.

Study Limitations

The retrospective nature of the present study and the referral bias were the main limitations. In addition, improvement or worsening of symptoms were often dictated by the patients' subjective sense of symptom change. In some cases, the patients could have had the symptoms for an extended period and, thus, might have adapted to their presence, with minor changes considered improvement. In some cases, the CN deficit might have been a direct surgical injury, rather than a tumor deficit, thus making recovery of such a deficit less likely.

Another limitation was related to the use of the ever-changing WHO grading system in patient selection. Considering that the present study included a long-term analysis of outcomes spanning from 1987 to 2017, the limitation relating to the use of WHO grading system could not be avoided. The tumor volume on the follow-up images was calculated using the X, Y, and Z diameters, with the assumption that the tumor was a sphere. This results in a rough estimate of the tumor volume and was a limitation of the findings of the present study. The present report, however, was enhanced by the long-term follow-up period. In addition, our report was unique in that it specifically reported on the outcomes after adjuvant SRS.

CONCLUSION

SRS was associated with a high tumor control rate at long-term imaging follow-up evaluations. In addition, despite the low improvement rates, only a few patients developed morbidity after SRS. Adjuvant SRS is a highly effective and safe option for patients with residual tumor after partial surgical resection.

REFERENCES

1. Ostrom QT, Gittleman H, Liao P, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2010-2014. *Neuro Oncol*. 2017;19(suppl 5):v1-v88.

2. Magill ST, Lee DS, Yen AJ, et al. Surgical outcomes after reoperation for recurrent skull base meningiomas [e-pub ahead of print]. *J Neurosurg*. 2018:1-9. https://doi.org/10.3171/2018.6.

3. Bambakidis NC, Kakarla UK, Kim LJ, et al. Evolution of surgical approaches in the treatment of petroclival meningiomas: a retrospective review. *Neurosurgery*. 2008;62(suppl 3):1182-1191.

4. Nanda A, Javalkar V, Banerjee AD. Petroclival meningiomas: study on outcomes, complications and recurrence rates. *J Neurosurg*. 2011;114:1268-1277.

5. Morisako H, Goto T, Ohata K. Petroclival meningiomas resected via a combined transpetrosal approach: surgical outcomes in 60 cases and a new scoring system for clinical evaluation. *J Neurosurg*. 2015;122:373-380.

6. Al-Mefty O, Fox JL, Smith RR. Petrosal approach for petroclival meningiomas. *Neurosurgery*. 1988;22:510-517.

7. Park SH, Kano H, Niranjan A, Flickinger JC, Lunsford LD. Stereotactic radiosurgery for cerebellopontine angle meningiomas. *J Neurosurg*. 2014;120:708-715.

8. Lee JY, Niranjan A, McInerney J, Kondziolka D, Flickinger JC, Lunsford LD. Stereotactic radiosurgery providing long-term tumor control of cavernous sinus meningiomas. *J Neurosurg*. 2002;97:65-72.

9. Gardner G, Robertson JH. Hearing preservation in unilateral acoustic neuroma surgery. *Ann Otol Rhinol Laryngol*. 1988;97:55-66.

10. Rogers CL, Shetter AG, Fiedler JA, Smith KA, Han PP, Speiser BL. Gamma knife radiosurgery for trigeminal neuralgia: the initial experience of the Barrow Neurological Institute. *Int J Radiat Oncol Biol Phys*. 2000;47:1013-1019.

11. House JW, Brackmann DE. Facial nerve grading system. *Otolaryngol Head Neck Surg*. 1985;93:146-147.

12. Bindal R, Goodman JM, Kawasaki A, Purvin V, Kuzma B. The natural history of untreated skull base meningiomas. *Surg Neurol*. 2003;59:87-92 [discussion: 92].

13. Couldwell WT, Heros R, Dolenc V. Skull base meningiomas. *Neurosurg Focus*. 2011;30, 1p prior to E1.

14. Reinert M, Babey M, Curschmann J, Vajtai I, Seiler RW, Mariani L. Morbidity in 201 patients with small sized meningioma treated by microsurgery. *Acta Neurochir (Wien)*. 2006;148:1257-1265 [discussion: 1266].

15. Tahara A, de Santana PA Jr, Calfat Maldaun MV, et al. Petroclival meningiomas: surgical management and common complications. *J Clin Neurosci*. 2009;16:655-659.

16. O'Sullivan MG, van Loveren HR, Tew JM Jr. The surgical resectability of meningiomas of the cavernous sinus. *Neurosurgery*. 1997;40:238-244 [discussion: 245, 237].

17. De Jesus O, Sekhar LN, Parikh HK, Wright DC, Wagner DP. Long-term follow-up of patients with meningiomas involving the cavernous sinus: recurrence, progression, and quality of life. *Neurosurgery*. 1996;39:915-919 [discussion: 919-920].

18. Natarajan SK, Sekhar LN, Schessel D, Morita A. Petroclival meningiomas: multimodality treatment and outcomes at long-term follow-up. *Neurosurgery*. 2007;60:965-979 [discussion: 979-981].

19. Zentner J, Meyer B, Vieweg U, Herberhold C, Schramm J. Petroclival meningiomas: is radical resection always the best option? *J Neurol Neurosurg Psychiatry*. 1997;62:341-345.

20. Ding D, Starke RM, Kano H, et al. Gamma knife radiosurgery for cerebellopontine angle meningiomas: a multicenter study. *Neurosurgery*. 2014;75:398-408 [quiz: 408].

21. Sheehan JP, Starke RM, Kano H, et al. Gamma Knife radiosurgery for posterior fossa meningiomas: a multicenter study. *J Neurosurg*. 2015;122:1479-1489.

22. Starke R, Kano H, Ding D, et al. Stereotactic radiosurgery of petroclival meningiomas: a multicenter study. *J Neurooncol*. 2014;119:169-176.

23. Sughrue ME, Rutkowski MJ, Aranda D, Barani IJ, McDermott MW, Parsa AT. Factors affecting outcome following treatment of patients with cavernous sinus meningiomas. *J Neurosurg*. 2010;113:1087-1092.

24. Kim JW, Kim DG, Se YB, et al. Gamma knife radiosurgery for petroclival meningioma: long-term outcome and failure pattern. *Stereotact Funct Neurosurg*. 2017;95:209-215.

25. Kano H, Park KJ, Kondziolka D, et al. Does prior microsurgery improve or worsen the outcomes of stereotactic radiosurgery for cavernous sinus meningiomas? *Neurosurgery*. 2013;73:401-410.

26. Morita A, Coffey RJ, Foote RL, Schiff D, Gorman D. Risk of injury to cranial nerves after gamma knife radiosurgery for skull base meningiomas: experience in 88 patients. *J Neurosurg*. 1999;90:42-49.

27. Nicolato A, Foroni R, Alessandrini F, Bricolo A, Gerosa M. Radiosurgical treatment of cavernous sinus meningiomas: experience with 122 treated patients. *Neurosurgery*. 2002;51:1153-1159 [discussion: 1159-1161].

28. Pollock BE, Stafford SL. Results of stereotactic radiosurgery for patients with imaging defined cavernous sinus meningiomas. *Int J Radiat Oncol Biol Phys*. 2005;62:1427-1431.

29. Simpson D. The recurrence of intracranial meningiomas after surgical treatment. *J Neurol Neurosurg Psychiatry*. 1957;20:22-39.

30. Pomeraniec IJ, Kano H, Xu Z, et al. Early versus late Gamma Knife radiosurgery following transsphenoidal surgery for nonfunctioning pituitary macroadenomas: a multicenter matched-cohort study. *J Neurosurg*. 2018;129:648-657.

31. Chung LK, Mathur I, Lagman C, et al. Stereotactic radiosurgery versus fractionated stereotactic radiotherapy in benign meningioma. *J Clin Neurosci*. 2017;36:1-5.

32. Flannery TJ, Kano H, Lunsford LD, et al. Long-term control of petroclival meningiomas through radiosurgery. *J Neurosurg*. 2010;112:957-964.

33. Faramand A, Kano H, Niranjan A, et al. Cranial nerve outcomes after primary stereotactic radiosurgery for symptomatic skull base meningiomas. *J Neurooncol*. 2018;139:341-348.

34. Azar M, Kazemi F, Jahanbakhshi A, et al. Gamma Knife radiosurgery for cavernous sinus meningiomas: analysis of outcome in 166 patients. *Stereotact Funct Neurosurg*. 2017;95:259-267.

35. Hasegawa T, Kida Y, Yoshimoto M, Koike J, Iizuka H, Ishii D. Long-term outcomes of Gamma Knife surgery for cavernous sinus meningioma. *J Neurosurg*. 2007;107:745-751.

36. Spiegelmann R, Cohen ZR, Nissim O, Alezra D, Pfeffer R. Cavernous sinus meningiomas: a large LINAC radiosurgery series. *J Neurooncol*. 2010;98:195-202.

37. Cusimano MD, Sekhar LN, Sen CN, et al. The results of surgery for benign tumors of the cavernous sinus. *Neurosurgery*. 1995;37:1-9 [discussion: 9-10].

38. DeMonte F, Smith HK, al-Mefty O. Outcome of aggressive removal of cavernous sinus meningiomas. *J Neurosurg*. 1994;81:245-251.

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