

Primary Versus Salvage Stereotactic Radiosurgery for Patients With Olfactory Groove Meningiomas: A 35-Year Single-Institution Experience

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BACKGROUND AND OBJECTIVES: Stereotactic radiosurgery (SRS) is an important management strategy for patients with olfactory groove meningiomas (OGMs). This study aimed to compare outcomes after primary SRS vs salvage SRS postresection in our institution over the past 35 years.

METHODS: We reviewed the radiographic imaging of 2030 patients with meningiomas who underwent SRS between 1987 and 2022. Seventy-nine patients with OGM were identified. The median patient age at SRS was 62 years (range, 33–90 years). Forty-eight patients (60.76%) underwent primary SRS and 31 patients (39.24%) had previous resections. The median tumor volume was 4.30 cc (range, 0.19–26.90 cc), and the median margin dose prescribed at SRS was 13 Gy (range, 9–18 Gy). SRS protocol, neurological outcomes, overall survival, and local tumor control (LTC) were evaluated.

RESULTS: The overall survival for all OGM patients was 17 years (range, 0.8–24.3 years). No patient deaths were related to intracranial tumor progression. Among primary SRS in 48 patients, 4 (8.33%) had tumor progression at a median time of 9.2 years (range, 0.4–12.3 years). For patients who underwent salvage SRS, 7 patients (22.5%) had delayed tumor progression at a median time of 6.4 years (range, 0.4–15.2 years) after SRS. Previous resection was found to be associated with anosmia ($P < .01$) and decreased LTC ($P = .024$). After primary SRS, 73% of patients experienced symptom improvement change. After salvage SRS 23% of patients showed clinical improvement. In patients with peritumoral edema at SRS, the median percentage edema volume reduction was 82% after SRS.

CONCLUSION: SRS provided low risk long-term tumor control in OGM patients. Primary SRS provided superior LTC and preservation or improvement of olfactory function in most patients.

KEY WORDS: Olfactory groove meningioma, Stereotactic radiosurgery

Olfactory groove meningiomas (OGMs) represent 5% to 18% of all intracranial meningiomas.^{1–3} Although histologically benign, OGMs typically exhibit insidious growth that can lead to delayed diagnosis and late neurological deficits that impair the quality of life.⁴ Arising from the cribriform plate and frontosphenoid suture, larger volume OGMs are

associated with olfactory dysfunction, visual impairment, headaches, personality changes, and seizures.⁵

Many surgeons consider resection as the primary management for large OGMs. However, even meticulous microsurgical or endoscopic surgical resection may lead to new postoperative morbidity, cerebrospinal fluid leakage, and delayed tumor recurrence. Postoperative anosmia rates vary from 37.4% to 57.1% depending on the extent of tumor excision.⁵ Gamma Knife stereotactic radiosurgery (SRS) has been associated with durable rates of tumor control and low complication rates in the management of other skull base meningiomas.⁶ The aim of this study

ABBREVIATIONS: **AREs**, adverse radiation effects; **LTC**, local tumor control; **OGMs**, olfactory groove meningiomas; **OS**, overall survival; **SRS**, stereotactic radiosurgery.

was to retrospectively compare long-term clinical outcomes, including local tumor control (LTC) and neurological function, in patients with OGMs who underwent primary SRS vs those who underwent salvage SRS after surgical resection.

METHODS

Patient Inclusion Criteria

The authors retrospectively reviewed 2030 meningioma patients who underwent SRS at a single institution between 1987 and 2022. Seventy-nine OGM patients (65% female) had Gamma Knife® SRS and a minimum of 6 months follow-up. The patient characteristics are detailed in Table 1. Forty-one patients previously published by Gande et al¹ were included and updated in this study. Patients treated with primary SRS typically had tumors that were incidentally discovered, minimally symptomatic, or associated with medical comorbidities that made them suboptimal surgical candidates. In some cases, patients with symptomatic tumors opted for SRS over surgery based on preference. Conversely, patients in the salvage SRS group had previously undergone resection, often due to tumor size, mass effect, or progressive symptoms. We recognize the inherent selection bias in this retrospective, nonrandomized study design. This study was approved and patient consent was waived by the institutional review board.

The median age at OGM diagnosis for primary SRS patients was 58 years (range, 36-90 years). The median time between meningioma diagnosis and SRS was 4.5 months (range, 0-179 months). Two patients had a history of fractionated childhood radiation therapy for pediatric cancers. The median age at SRS was 62 years (range, 33-90 years). For salvage SRS patients, the median age at diagnosis was 54 years (range, 30-46 years) and the median age was 62 years (range, 33-82 years). Forty-eight patients underwent primary SRS and 31 patients underwent salvage SRS for delayed tumor recurrence despite craniotomy (21 patients) or endoscopic transphenoidal resections (10 patients). Sixteen patients had previous gross total resection. The median Ki-67 was 3% (n = 16, range, 1%-10%). Twenty-nine patients had pathology-confirmed WHO Grade I meningiomas. Two patients had WHO Grade II tumors. The median time from resection to SRS was 3.25 years (range, 0.2-14.1 years). The most common presenting symptoms were anosmia, headache, and seizures.

SRS Technique

The details of the SRS procedure have been documented in previous publications.^{1,7,8} The procedure started with the application of a Leksell stereotactic head frame under intravenous sedation and local scalp anesthetic administration. From 1987 through 1990, SRS was guided by computed tomographic imaging. Since 1991, high-resolution contrast-enhanced T1-weighted axial imaging (1.5 mm) with a T2-volumetric axial study (1 mm) was obtained for SRS dose planning.

SRS procedure parameters are documented in Table 2. A median margin dose of 13 Gy (range, 9-18 Gy) was prescribed at a median of 50% isodose line (range, 40%-70%). The median maximum dose received by primary SRS patients was 26 Gy (range, 18-36 Gy). The median tumor volume was 4.3 cc (range, 0.19-26.90 cc). The median total 12 Gy volume was 5.55 cc (range, 0.25-26.90 cc). Sixteen patients presented with peritumoral edema at the time of SRS. The median volume of peritumoral edema was 26.7 cc (range, 4.4-107.9 cc). All patients

underwent single-session SRS. No significant statistical difference was observed between primary SRS and salvage SRS for all parameters.

Follow up Protocol

After SRS, patients were followed at 6-month intervals for the first year and then every 1 to 2 years if no tumor progression was detected. The follow-up imaging findings were compared with previous images. Local failure was defined as $\geq 20\%$ enlargement of tumor volume after SRS. The follow-up MRI scans were loaded into the GammaPlan system and superimposed with the original SRS treatment plan. The follow-up tumor volume was contoured in GammaPlan for precise measurement. The tumor volume reduction percentage was calculated as: $[(\text{SRS treatment day tumor volume} - \text{follow-up tumor volume}) / \text{SRS treatment day tumor volume}] \times 100$. Adverse radiation effects (AREs) were defined as the development of increased peritumoral edema, intratumoral cyst formation, or biopsy-proven ARE. Indeterminate contrast enhancement (ARE vs tumor recurrence) was followed with serial imaging until progressive tumor growth or ARE were differentiated.

Outcome Parameters

Overall survival (OS), LTC, neurological outcomes, risk of ARE, tumor volume change, and need for additional management were determined through clinical and radiographic follow-up. LTC and OS were calculated from the initial SRS date to the date of local tumor progression, death, or last clinical follow-up.

Statistical Methods

Patient demographics, primary tumor characteristics, SRS treatment data, and patient outcomes data were analyzed using Excel version 2021 (Microsoft). OS and LTC were plotted using Kaplan-Meier survival curves on Prism version 9 (GraphPad). Data are presented in the tables as median (range). Log-rank tests and Cox regressions were performed separately on unresected and WHO Grade I tumor patient subsets of our study population using SPSS Statistics 29.0.1.0 (IBM). A *P*-value $< .05$ indicated statistical significance. Significant prognostic variables identified by univariate analysis were incorporated into a multivariate model as confirmation.

RESULTS

Local Tumor Control

Overall, 68 patients (86.1%) had documented controlled tumor at the last clinical follow-up. The 5-, 10-, and 15- year LTC rates were 94.0%, 77.6%, and 64.5%, respectively. The median time of tumor progression was 6.9 years (range, 0.4-15.2 years) after SRS. For the tumor that were successfully controlled, the median tumor volume reduction percentage was 51.9% (range 5.2%-89.0%). Among the 48 primary SRS patients, 44 patients had tumor successfully controlled. The median time of tumor progression was 9.2 years (range, 0.4-12.3 years) after SRS. Two patients underwent repeat SRS, 1 patient had surgical resection, and 1 patient (25%) declined additional management. Seven patients out of 31 patients who underwent salvage SRS had delayed tumor progression at a median time of 6.4 years (range, 0.4-15.2 years). Three patients underwent repeat SRS and achieved long term tumor control. Three patients required

TABLE 1. Patient Demographics and Presenting Clinical Characteristics

Characteristics	Value			P-value
	Overall cohort	Primary SRS	Salvage SRS	
Total number of patients	79	48 (60.76%)	31 (39.24%)	—
Sex				.461
Male	25 (31.65%)	17 (35.42%)	8 (25.81%)	
Female	54 (68.35%)	31 (64.58%)	23 (74.19%)	
Age at diagnosis, y	56 (30-90)	58 (36-90)	54 (30-46)	.148
Age at SRS, y	62 (33-90)	61.5 (39-90)	62 (33-82)	.687
Time between diagnosis and SRS, mo	20 (0-230)	4.5 (0-179)	57 (1-230)	<.001 ^a
KPS score at SRS	80 (70-100)	80 (80-100)	80 (70-100)	.452
Previous radiation therapy	3 (3.79%)	2 (4.17%)	1 (3.23%)	—
Pre-SRS resection	31 (39.42%)		31 (100%)	—
Degree of resection				
Gross total			16 (51.61%)	
Subtotal			10 (32.26%)	
NR			5 (16.13%)	
Ki-67 (%), (n = 16)			3 (1-10)	
Time from resection to SRS, y			3.25 (0.2-14.1)	
SRS indication				
Primary SRS	48 (60.76%)	48 (100%)	—	
Salvage, at time of recurrence	20 (25.32%)	—	20 (64.52%)	
Boost for residual after resection	11 (13.92%)	—	11 (35.48%)	—
Total no. of meningiomas (%)				—
1	66 (83.54%)	41 (85.42%)	25 (80.65%)	
2	9 (11.39%)	5 (10.42%)	4 (12.90%)	
3	3 (3.80%)	2 (4.17%)	1 (3.22%)	
4	1 (1.27%)	0 (0%)	1 (3.22%)	
Initial presentation, no. of patients				
Asymptomatic	14	9	5	
Total anosmia	16	3	13	
Partial anosmia	10	7	3	
Headache	33	26	7	
Changes in behavior	3	3	0	
Visual dysfunction	15	6	9	
Ocular motion dysfunction	4	2	2	
Seizures	12	6	6	—

KPS Karnofsky Performance Status; NR, No Records; SRS, stereotactic radiosurgery.

^aP < .05.

Data reported as number of patients (%) or median (range).

TABLE 2. SRS Treatment Characteristics

Characteristic	Value			
	Overall cohort	Primary SRS	Salvage SRS	P-value
Margin dose, Gy	13 (9-18)	13 (9-18)	13 (10-16)	.852
Maximum dose, Gy	26 (18-36)	26 (18-36)	25 (20-32)	.149
Percent isodose, %	50 (40-70)	50 (40-70)	50 (50-70)	.06
Maximum tumor diameter, mm	23.20 (9.10-43.90)	23.20 (3.50-36.20)	19.90 (9.10-43.90)	.957
Tumor volume, cc	4.30 (0.19-26.90)	4.39 (0.56-23.40)	3.40 (0.19-26.90)	.331
V12 treatment volume, cc	5.55 (0.25-26.90)	5.90 (0.96-16.04)	5.35 (0.25-26.90)	.384
No. of SRS fractions	1	1	1	—

SRS, stereotactic radiosurgery.

Data reported as median (range).

additional surgical resection. Patients who underwent primary SRS showed significantly better LTC rates than those who underwent salvage SRS (HR [hazard ratio] 3.79, 95% CI 1.09-13.15, $P = .024$, Figure 1). Patients from both groups were prescribed with a 13 Gy margin dose, and there were no significant difference in OGM tumor volumes between primary SRS and salvage SRS group (4.39 cc vs 3.40 cc, $P = .331$, Table 2). The representative images of OGM managed with primary and salvage SRS are shown in Figures 2 and 3.

Overall Survival

The 5, 10, 15, and 20-year OS rates were 90.2%, 82.3%, 64.6%, and 43.1%, respectively. In total, 15 patients died during the follow-up interval. None of the patients succumbed to OGM progression. The OS for all OGM patients was 17 years (range, 0.8-24.3 years). None of the patients were deceased due to intracranial disease progression. For patients who underwent primary SRS, the median OS was 17 years. At the last follow-up, 8 patients of the primary SRS cohort were deceased. The median follow-up for patients who underwent salvage SRS was 13.7 years. Seven patients who underwent salvage SRS were deceased at last follow-up. No statistically significant OS differences were observed between patients receiving primary SRS and patients receiving salvage SRS (HR 1.75, 95% CI 0.63-4.88, $P = .28$, Figure 4).

On univariate analysis, age at SRS ≥ 62 years ($P = .03$), tumor volume ≥ 3.9 cc ($P = .01$), and the presence of pre-SRS anosmia (total or partial) ($P = .04$) were associated with poorer OS. On multivariate analysis, only tumor volume ≥ 3.9 cc ($P = .01$) was associated with inferior OS.

Neurological Outcomes

Detailed neurological outcomes are presented in Table 3. Thirty-nine patients who underwent primary SRS were

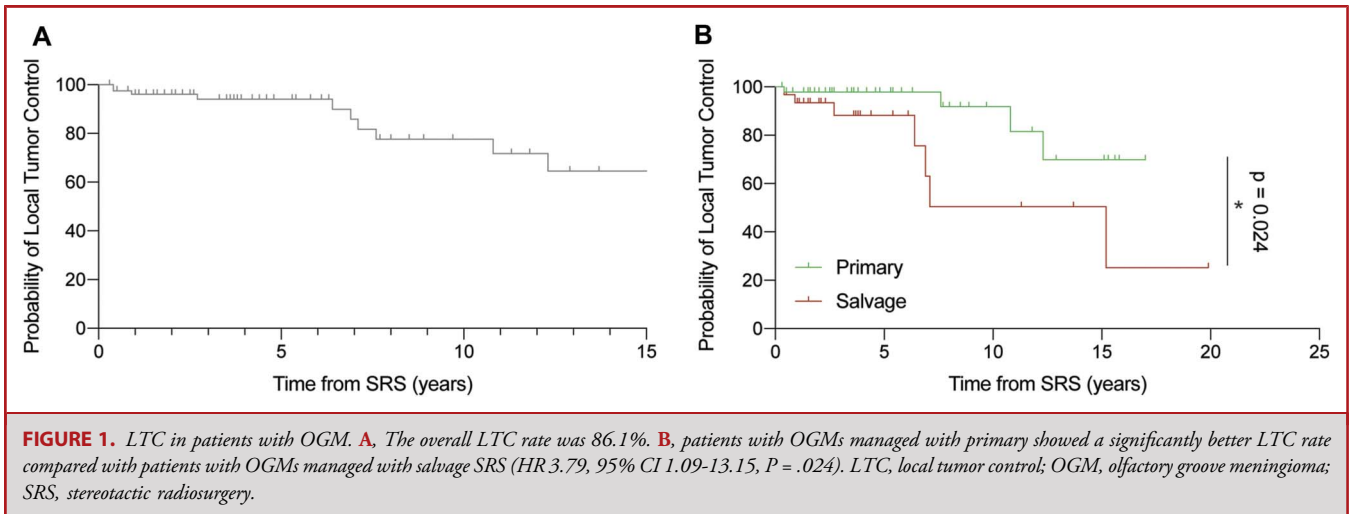
symptomatic at the time of SRS. After SRS, 37 patients (94.87%) patients enjoyed improved symptomology or had stable symptoms (27 patients reported clinical improvement; 10 patients had stable symptoms). Six patients reported new symptoms including changes in behavior ($n = 2$), visual dysfunction ($n = 2$) total anosmia ($n = 1$), headache ($n = 1$), and seizures ($n = 1$). One patient with delayed tumor progression developed total anosmia 12.25 years and underwent repeat SRS. One patient reported a new seizure of unknown etiology with no radiographic change and was controlled with anti-epileptic medications. Twenty-six patients receiving salvage SRS were symptomatic at SRS. After SRS, 23 patients (88.46%) reported symptom reduction or had stable symptoms. Six patients reported reduced symptoms. Three patients reported worsened symptoms.

Adverse Radiation Effects

Four primary SRS patients developed symptomatic ARE. Imaging revealed increased peritumoral edema at a median time of 5 months (range, 4-12 months). All 4 patients responded to a short course of oral corticosteroids. The median percentage edema volume reduction was 82% (range, 2%-100%). No symptomatic AREs were identified in the salvage SRS group, although temporary asymptomatic radiographic changes were not included.

DISCUSSION

Although the literature on SRS for skull base meningiomas is extensive, no previous studies have evaluated the difference in LTC and neurological outcomes between patients who underwent primary SRS vs salvage SRS performed after resection. The present study evaluated tumor control and neurological outcomes comparing primary and salvage SRS for OGMs and provides additional evidence that primary SRS is an important option for



patients with newly diagnosed or enlarging tumors not associated with acute neurological symptoms.

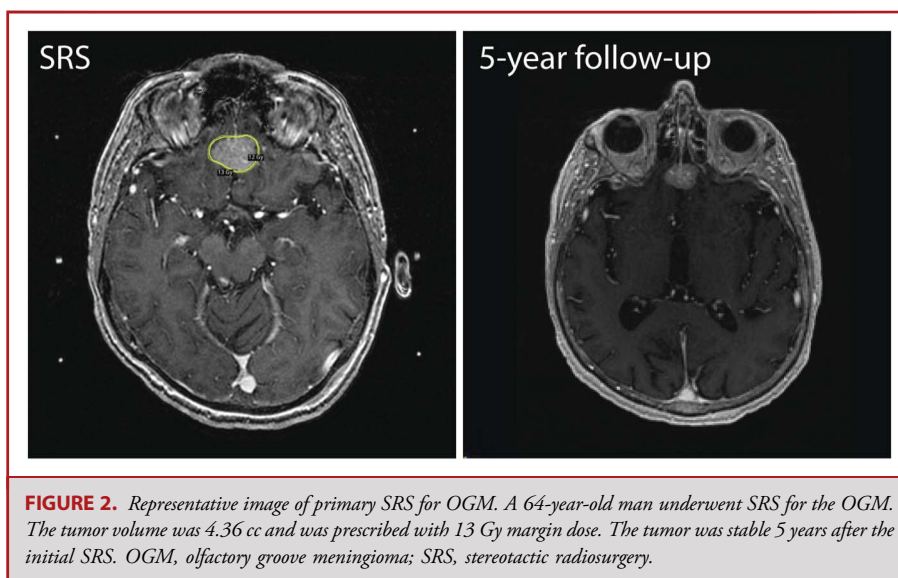
The Role of Surgical Resection

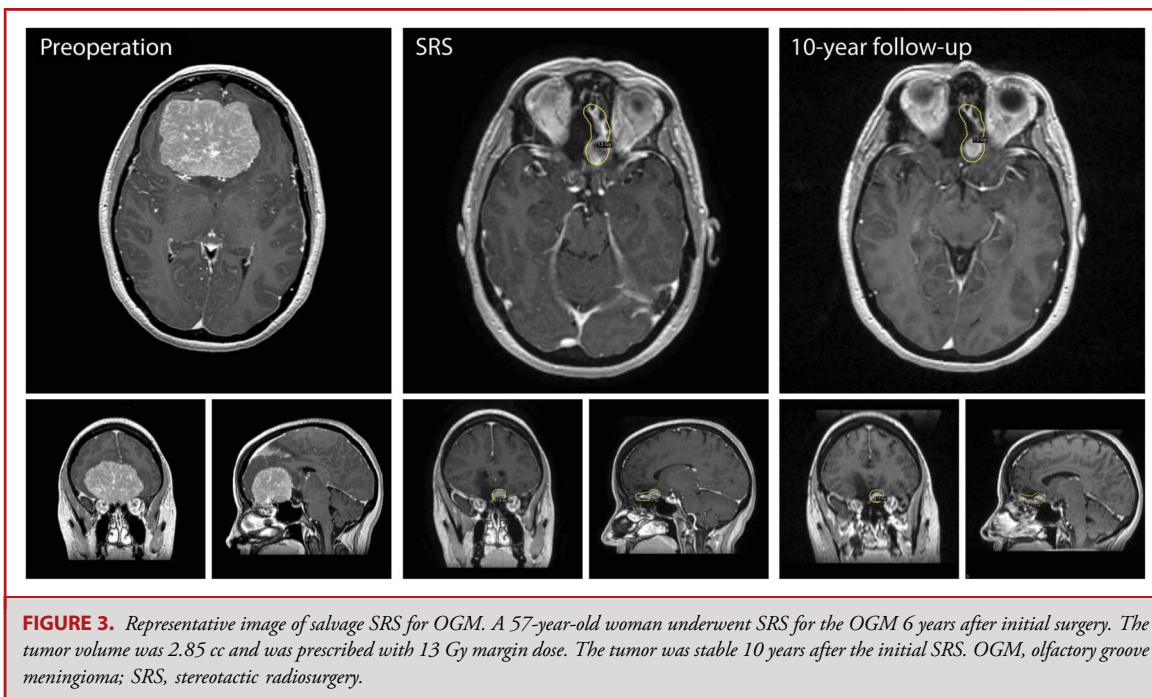
Surgical resection remains the initial strategy for large symptomatic OGMs. Although surgical morbidity and mortality associated with OGM resection has lessened considerably, Simpson Grade I resection for OGMs still prove to be challenging.¹ Initial resection has been associated with risks of neurological injury, brain edema, and seizures. The prevalence of postoperative anosmia varies from 9%-38% regardless of the surgical method used.^{9,10} In the present study, we found that frequent symptoms after initial surgical resection in 26 out of

31 patients including anosmia, visual dysfunction, seizures, and oculomotor weakness. Preservation of anatomic integrity of olfactory nerves during open transcranial or endoscopic surgical resection of OGMs can be limited by the intimate contact of OGMs with neural structures, limited visualization of olfactory bulbs, olfactory nerve avulsion or ischemic injury during microsurgical resection, or intentional sacrifice of the nerve to maximize surgical resection.^{11,12}

The Role of SRS in OGMs Tumor Control

The 5-year tumor control rates of SRS for meningiomas varies between 87% and 98.5%.¹³⁻¹⁵ In a large multicenter study reviewing the outcomes of SRS for OGMs of 278 patients,





Bunevicius et al¹¹ reported that local control was achieved in 97% of the patients at a median follow up of 39 months. In a previous single-institution study of OGM patients, Gande et al¹ reported that tumor control was achieved in 95% of patients at a median follow-up of 65 months. Excellent LTC of OGMs treated with the SRS is consistent with previously documented LTC of benign intracranial meningiomas of other locations. A 2012 multi-institution analysis of 4565 patients (5300 meningiomas) reported 92.5% of patients had a stable or reduced lesion volume.¹⁶ Similarly, a 2012 study of 255 patients with skull base meningiomas reported 86% of patients had no change or decrease in tumor volume at last follow-up.⁶

In the present study, 48 patients underwent primary SRS and 31 patients underwent salvage SRS had stable tumor volume or tumor regression (Table 3). In this long-term follow-up span over 35 years, 86.1% patients had documented tumor controlled at the last clinical follow-up. Our result showed that patients who underwent primary SRS showed significantly better LTC rates than those who underwent salvage SRS ($P = .024$). We hypothesize that the improved outcomes after primary SRS in part may be attributed to more distinct imaging defined tumor margins in unoperated patients. This facilitates more precise dose planning. The finding that primary SRS provided superior LTC rates compared with salvage SRS becomes relevant in the initial

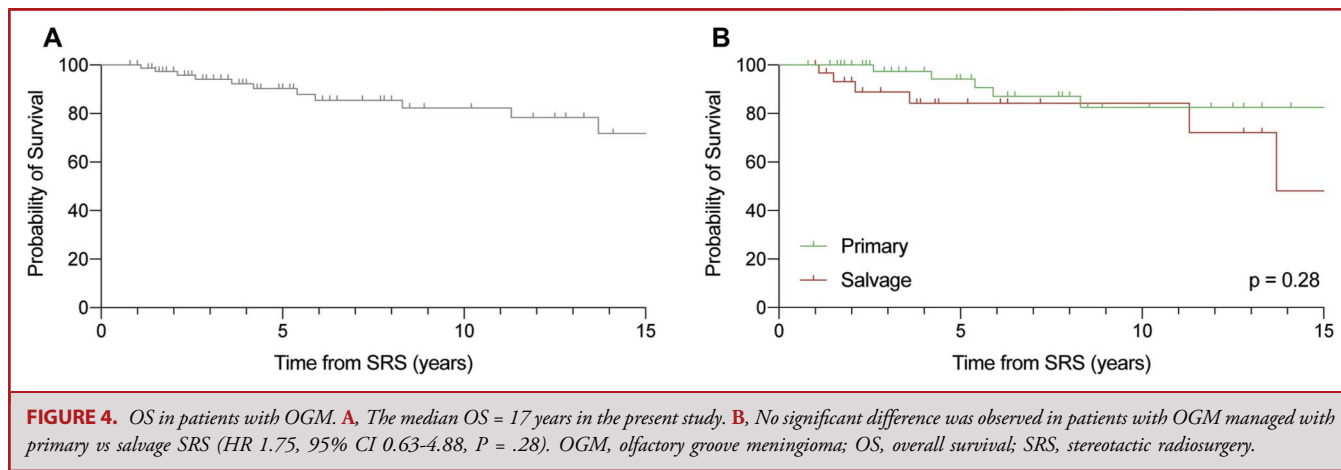


TABLE 3. Clinical Outcomes for 79 Patients Treated for Olfactory Groove Meningioma

Outcome	Value			P-value
	Overall cohort	Primary SRS	Salvage SRS	
Death, n. of patients (%)	15 (18.99%)	8 (16.67%)	7 (22.58%)	—
Neurological symptom (improved/stable/worsened/new)				
Total anosmia	2/14/0/1	2/1/0/1	0/13/0/0	
Partial anosmia	3/7/0/0	3/4/0/0	0/3/0/0	
Headache	23/8/4/2	19/5/2/1	4/3/2/1	
Changes in behavior	3/0/0/2	3/0/0/2	0/0/0/0	
Visual dysfunction	4/10/1/3	3/3/0/2	1/7/1/1	
Seizures	6/4/2/0	4/2/0/1	2/2/2/0	—

SRS, stereotactic radiosurgery.

Data reported as number of patients (%) or median (range).

Clinical outcomes reported as number of patients *Improved/Stable/Worsened/New*.

clinical management. In view of the morbidity of both endoscopic and craniotomy approaches for OGMs, the need for initial cytoreductive strategy may need reconsidered. For patients with residual or recurrent tumor progression, SRS achieved tumor control in 24 patients. Nonetheless, additional tumor management including repeat SRS and additional surgery was required in 7 patients in the salvage SRS cohort. With recent advances in the molecular biology of meningiomas, biological differences, such as proliferative indices or radiosensitivity-related mutations (eg, SMO, AKT), were not uniformly assessed in our cohort and may have contributed to differences in treatment response. These factors underscore the complexity of interpreting outcomes in retrospective studies and may offer important insights for future approaches to meningioma management.

Olfactory Outcomes After SRS

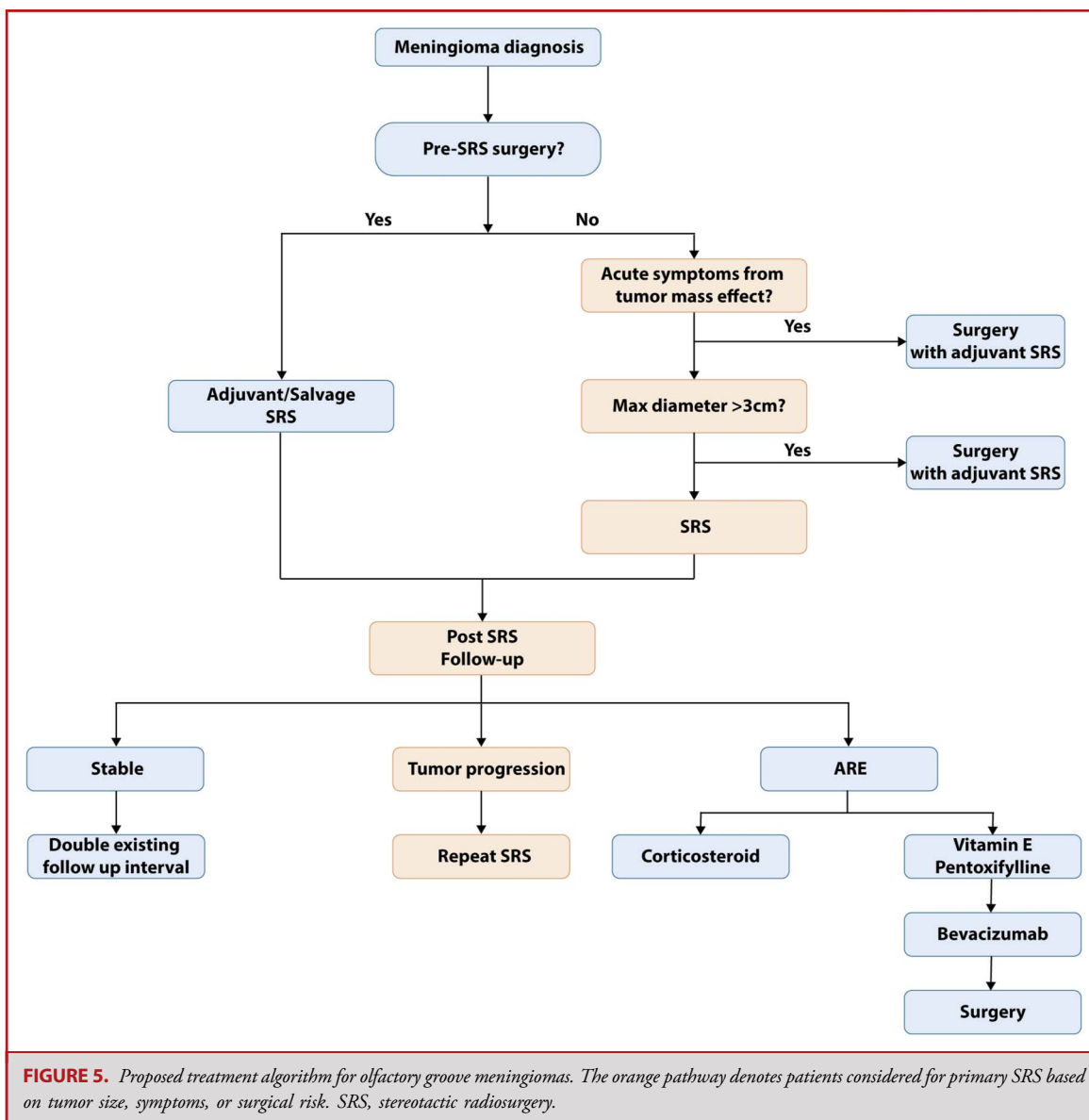
The risk of postoperative anosmia for SRS patients is significantly reduced in patients who had primary SRS. In the salvage SRS group we noted that 7 patients had anosmia after skull base craniotomy, and 9 patients had anosmia after endoscopic transphenoidal approaches.¹⁷⁻¹⁹ Gande et al reported 93% stable and 7% improved olfactory outcomes in their study of 41 OGM patients. Similarly, in an international cohort study of 278 OGM patients, Bunevicius et al reported 90% stable, 8% improved, 2% deteriorated olfaction among patients underwent SRS. Consistent with these studies, there was a low rate of olfactory deterioration after SRS among our patients. Within the primary SRS patient cohort, 2 patients with total anosmia improved after SRS. Three patients with partial anosmia at the time of SRS improved and the remaining 4 partial anosmia patients remained stable after primary SRS. Overall, 10.42% patients improved smell status (n = 5),

87.50% patients (n = 42) had stable smell status, and only 2.08% patients (n = 1) experienced smell deterioration from local tumor progression in the primary SRS patient population.

In comparison, surgical modalities have not yielded comparable olfaction preservation. Bassiouni et al¹² evaluated outcomes after 56 OGM surgeries and found that 37% of the patients had worsened sense of smell (partial or complete anosmia) at mean follow-up of 67 months. Romani et al²⁰ reported that 9% patients developed new-onset complete anosmia after a modified pterional (lateral supraorbital) resection of 66 OGMs. Other studies have similarly described increased incidence of postoperative anosmia, with little or no improvement in olfaction status after surgical management of OGMs.^{20,21} Although the primary SRS group showed higher rates of olfactory preservation post-treatment, we acknowledge that this comparison is limited by the absence of standardized preoperative olfactory data.

Response of Preoperative Peritumoral Edema in Primary SRS Patients

Peritumoral edema is a common and clinically significant phenomenon in meningiomas. Although its exact mechanism remains unknown, current hypotheses link it to vasogenic blood flow and cytokine release.¹⁸ Several factors influence edema development, including tumor location, size, and border regularity.²² Convexity and parasagittal meningiomas show higher edema rates compared with skull base tumors,^{13,19} whereas subfrontal meningiomas in the anterior fossa demonstrate higher rates than those in mid- or posterior fossae. Limited data exist on post-SRS edema outcomes, particularly for subfrontal meningiomas. Of the 16 patients with pre-existing peritumoral edema, SRS achieved favorable outcomes with a median edema volume reduction of 82% during follow-up. In a study by



Sheehan et al¹³ examining peritumoral edema after Gamma Knife SRS for parasagittal and parafalcine meningiomas, only a minority of patients experienced worsening edema. The authors found that although transient edema occurred post-SRS, it could be effectively managed to prevent persistent long-term complications. Similarly, in our study, although 4 patients developed symptomatic worsening of peritumoral edema after SRS, the majority demonstrated significant edema reduction, with a median volume decrease of 82%.

Adverse Radiation Effects

Previous studies report ARE development rates between 7% and 20% after SRS for OGMs.^{1,11,23} In the present study, AREs

were reported at a median of 5 months (range, 4-12 months) after SRS. These symptoms improved with a short course of corticosteroids. Our data have shown that SRS can be safely used and the ARE for tumors in this location is exceedingly low. Majority of the patients who presented with peritumoral edema had edema subsided after SRS.

Indication of SRS for OGMs

The proposed management flowchart for OGMs is shown in Figure 5. For patients with small to mid-sized tumors not associated with symptomatic mass effect causing progressive headache or visual loss, we believe that primary SRS offers

effective option that maintains tumor control and preserves the sense of smell. Notably, patients who underwent primary SRS achieved superior tumor control rates and maximal neurological function preservation compared with those treated with salvage SRS. For tumors associated with peritumoral edema, our findings indicate that SRS can be safely used. Surgical resection remains the gold standard for large tumors with symptomatic mass effect or acute neurological compromise. In cases of large OGMs where surgical risks and comorbidities are deemed unacceptable, SRS emerges as a valuable alternative treatment option for select cases without urgent indications for decompression.

Limitations

The current study is limited by its retrospective nature and the small subsets. The objective methods of olfaction testing were unable to be implemented because of the study's restricted design.

Our retrospective Data set lacked consistent documentation of patient comorbidities and quality-of-life metrics, which may influence long-term neurological outcomes. In addition, the absence of molecular data (eg, SMO, and AKT mutations) limits our ability to evaluate biologically driven differences in radiosensitivity between groups.

CONCLUSION

This 35-year single institution study compared primary vs salvage SRS in patients with OGMs. This study showed a high rate of tumor control and neurological function preservation after primary SRS compared with salvage SRS. Patients underwent primary SRS had higher rates of smell preservation, decreased visual deterioration, comparable OS, and improved LTC as compared salvage SRS.

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Disclosures

L. Dade Lunsford is an AB Elekta stockholder and Insightec consultant. Constantinos G. Hadjipanayis is a consultant for Stryker Corp, Hemerion Therapeutics, Integra, Synaptive Medical, and True Digital Surgery. The other authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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