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Clinical and radiologic outcomes after stereotactic radiosurgery for meningiomas in direct contact with the optic apparatus: an international multicenter study

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OBJECTIVE Resection of meningiomas in direct contact with the anterior optic apparatus carries risk of injury to the visual pathway. Stereotactic radiosurgery (SRS) offers a minimally invasive alternative. However, its use is limited owing to the risk of radiation-induced optic neuropathy. Few SRS studies have specifically assessed the risks and benefits of treating meningiomas in direct contact with the optic nerve, chiasm, or optic tract. The authors hypothesized that SRS is safe for select patients with meningiomas in direct contact with the anterior optic apparatus.

METHODS The authors performed an international multicenter retrospective analysis of 328 patients across 11 institutions. All patients had meningiomas in direct contract with the optic apparatus. Patients were followed for a median duration of 56 months after SRS. Neurological examinations, including visual function evaluations, were performed at follow-up visits. Clinical and treatment variables were collected at each site according to protocol. Tumor volumes were assessed with serial MR imaging. Variables predictive of visual deficit were identified using univariable and multivariable logistic regression.

RESULTS SRS was the initial treatment modality for 64.6% of patients, and 93% of patients received SRS as a single

ABBREVIATIONS KPS = Karnofsky Performance Status; SRS = stereotactic radiosurgery.

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fraction. Visual information was available for 302 patients. Of these patients, visual decline occurred in 29 patients (9.6%), of whom 12 (41.4%) had evidence of tumor progression. Visual decline in the remaining 17 patients (5.6%) was not associated with tumor progression. Pre-SRS Karnofsky Performance Status predicted visual decline in adjusted analysis (adjusted OR 0.9, 95% CI 0.9–1.0, p < 0.01). Follow-up imaging data were available for 322 patients. Of these patients, 294 patients (91.3%) had radiographic evidence of stability or tumor regression at last follow up. Symptom duration was associated with tumor progression in adjusted analysis (adjusted OR 1.01, adjusted 95% CI 1.0–1.02, adjusted p = 0.02).

CONCLUSIONS In this international multicenter study, the vast majority of patients exhibited tumor control and preservation of visual function when SRS was used to treat meningioma in direct contact with the anterior optic pathways. SRS is a relatively safe treatment modality for select patients with perioptic meningiomas in direct contact with the optic apparatus.

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KEYWORDS stereotactic radiosurgery; radiation necrosis; visual decline; perioptic meningiomas; Gamma Knife; meningiomas

Meningioma is the most frequently diagnosed primary brain tumor, constituting a third of all primary brain and central nervous system tumors in the United States.[1] Perioptic meningioma in close proximity to the anterior optic apparatus is often treated surgically using microsurgical or endoscopic techniques.[2,3] However, resection carries a risk of injury and postoperative visual deficit in 2.6%–13.7% of patients.[4,5] Stereotactic radiosurgery (SRS) is an alternative treatment modality for meningioma in various locations.[6,7] Whereas SRS is widely used for residual or recurrent tumors, it is gaining ground as the initial therapeutic option for patients with meningioma that is difficult to surgically access or adjacent to critical structures, as well as for patients whose surgical options are limited by age or existing comorbidities.[8] It is also often chosen by patients because of its low risk profile. SRS results in sustained local tumor control rates exceeding 90% in patients with skull base meningioma.[7]

To date, SRS use has been restricted for meningioma close to the optic apparatus owing to the risks of optic neuropathy and visual deficit.[9,10] Radiation-induced optic neuropathy may occur due to vascular occlusion, damage to the blood-brain barrier, free radical injury, DNA damage, or demyelination.[11] Painless visual loss, visual field defects, changes in color vision, and pupillary abnormalities may occur months to years after exposure.[10,12] Due to these risks, a cumulative radiation dose limit of 8–12 Gy administered in a single fraction to the optic nerves has been recommended.[13–15] Hypofractionated treatment may increase the safety margin of SRS and decrease the risk of optic neuropathy.[2,16] We recently evaluated the outcomes of patients with perioptic meningioma.[17] However, to date, studies are limited that specifically address outcomes after SRS for patients with meningioma in direct contact with the optic apparatus. The aim of this international multicenter study was to evaluate the safety and efficacy of SRS for meningioma in direct contact with the anterior optic apparatus.

Methods

Patients and Clinical Data

A total of 328 patients were included from 11 institutions. Study inclusion criteria were 1) diagnosis of meningioma based on MRI or histological examination, 2) meningioma in direct contact with the anterior optic pathways, defined as the optic nerves, chiasm, or immediate portion of the optic tracts, and 3) treatment with single-session or hypofractionated SRS. Patients with a history of fractionated radiation therapy for an index lesion were included in the study.

Data collection was approved by the institutional review board at each participating center. Written patient consent was not required for this retrospective analysis of de-identified data. Baseline clinical parameters were assessed, including age at diagnosis, sex, presenting symptoms, pre-SRS functional status, ophthalmological function, therapies that preceded SRS, World Health Organization tumor grade, and imaging characteristics of the lesion. Patients without a prior histological diagnosis of brain tumor were included if neuroimaging was consistent with meningioma, including contrast enhancement of the tumor, extra-axial location, signs of calcification, and/or dural tail and no history of active cancer. Data were collected by the individual sites and sent to the International Radiosurgery Research Foundation study coordinator who checked for adherence to study requirements. Data were then sent to the study coordinating team at the University of Virginia.

SRS Approach

SRS was performed according to standard protocols and a conformal dose plan with isocentric targeting was achieved.[18] Gamma Knife units (Elekta AB) were utilized with a frame-based or frameless approach. The decision to use single-session or hypofractionated SRS was made at the discretion of the local treating team. Maximal doses to critical structures were kept to within tolerance using a conformal and multi-isocentric dose-planning technique. Biologically effective dose for fractionated therapy was calculated using an α/β ratio of 3 Gy.[19,20]

Follow-Up

Imaging and clinical follow-up was performed at 3- to 6-month intervals for the first 2 years after SRS, with annual follow-up thereafter. Tumor volume was measured on postcontrast T1-weighted MR images using the ABC/2 method.[21] Volume of perioptic meningioma at the latest imaging follow-up was compared with pre-SRS imaging data and was categorized as stable (change within

TABLE 1. Baseline patient demographic characteristics

Characteristic	Value
Age, yrs	50.4 ± 12.2
Female	78.7
Pretreatment KPS	85.7 ± 14.4
Symptom duration, mos	20.1 ± 30.8
Prior surgery	35.4
Previous radiation therapy	2.8
Hypothyroidism	2.1
Diabetes insipidus	0.6
Tuberculum tumor	32.6
Clinoid tumor	38.4
Cavernous sinus invasion	32.0
Tumor vol, mm^3	174.7 ± 1482.5

Values are shown as mean ± SD or percentage.

20%), regressed (> 20% decrease), or progressed (≥ 20% increase).[22,23] Time to tumor volume change and/or death was recorded.

Visual follow-up was obtained with ophthalmic visual field examinations at outpatient clinic visits. Formal visual field testing was performed as indicated and per protocol at the individual sites. Visual status change at the last follow-up was categorized by the treating team as not changed, improved, or declined. SRS-related adverse events were categorized according to the Radiation Therapy Oncology Group central nervous system toxicity criteria.[24]

Statistical Analysis

Baseline characteristics were presented as mean ± SD or as proportions. Agreement between clinical outcomes was assessed using kappa statistics. Association between treatment parameters and clinical outcomes was assessed using univariable or multivariable logistic regression adjusted for age and sex. In this study, $p < 0.05$ on 2-tailed tests was considered statistically significant. Figures were prepared using GraphPad Prism 6.0 software. Statistical analysis was conducted using Stata 14/IC software (StataCorp LP).

Results

Patient and Treatment Attributes

In total, 328 patients from 11 centers underwent SRS during this study. Patient demographic data are summarized in Table 1. The mean age was 50.4 years, and 78.7% of patients were female. At SRS, the average Karnofsky Performance Status (KPS) was 85.7. All patients underwent SRS for meningioma in immediate contact with the anterior optic apparatus. In total, 107 patients (32.6%) had tuberculum meningioma, 126 (38.4%) had clinoid meningioma, and 105 (32%) had tumor involving the cavernous sinus. Average maximum tumor diameter was 3.5 cm. In total, 116 patients (35.3%) underwent SRS after partial resection; in the remaining 64.6% of patients, SRS was the initial treatment modality. SRS was delivered as a single fraction to 93% of patients. The mean maximal radiation doses to the optic nerve, optic chiasm, and optic tract were 8.7 Gy, 7.7 Gy, and 6.2 Gy, respectively. Treatment parameters are summarized in Supplemental Table S1. The median follow-up after SRS was 56 months. Posttreatment outcomes are summarized in Supplemental Table S2.

Visual Function

Follow-up visual data were available in 302 patients. Of these patients, visual function was stable or improved in 273 patients (90.4%), of which 89 patients (29.5%) had improvement in vision. Visual decline occurred in 29 patients (9.6%), mostly in a delayed fashion after SRS (median [IQR] [range] follow-up 55 [64.2] [0.2–193] months) (Fig. 1A). Four patients (1.3%) became blind. Of patients with visual decline, 12 (41.4%) had radiographic evidence of tumor progression (89.9% agreement, kappa 0.39, $p < 0.01$), and this association was significant after adjustment for age and sex (adjusted OR 14.6, 95% CI 5.6–37.8, $p < 0.01$).

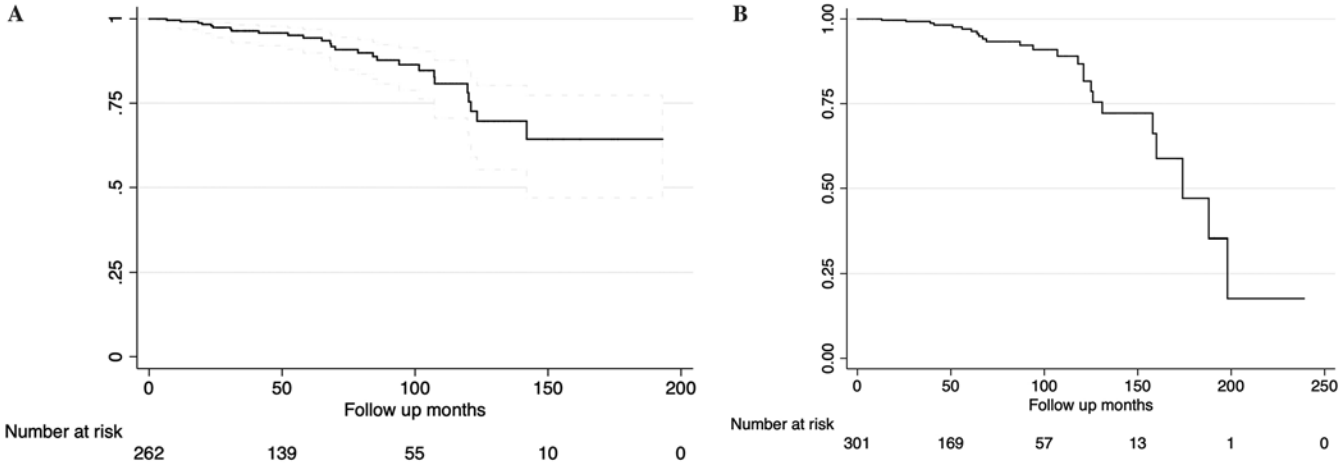

FIG. 1. Kaplan-Meier curves of worsening vision (**A**) and treatment failure (**B**) after SRS.

TABLE 2. Univariable and multivariable logistic regression of predictors of visual decline

Variable	Univariable		Multivariable*	
	OR (95 % CI)	p Value	OR (95% CI)	p Value
Female sex	0.7 (0.3–1.7)	0.434	0.7 (0.3–1.8)	0.498
Age	1.0 (1.0–1.0)	0.374	1.0 (1.0–1.0)	0.415
KPS	0.9 (0.9–1.0)	0.001†	0.9 (0.8–1.0)	0.004†
Symptom duration	1.0 (1.0–1.0)	0.144	1.0 (1.0–1.0)	0.188
Tumor vol	1.0 (1.0–1.0)	0.691	1.0 (1.0–1.0)	0.695
Max dose	1.0 (0.9–1.1)	0.722	1.0 (0.9–1.1)	0.739
Margin dose	1.0 (0.9–1.2)	0.752	1.0 (0.9–1.2)	0.775
Max optic nerve dose	1.0 (0.9–1.2)	0.73	1.0 (0.9–1.2)	0.712
Max optic tract dose	1.0 (0.8–1.2)	0.981	1.0 (0.8–1.2)	0.83
Max chiasm dose	1.0 (0.9–1.2)	0.83	1.0 (0.9–1.1)	0.873
No. of isocenters	1.0 (1.0–1.1)	0.596	1.0 (1.0–1.1)	0.648
Prior surgery	1.4 (0.6–3.0)	0.433	1.5 (0.7–3.3)	0.348

* Adjusted for age and sex.
† Significant ($p < 0.05$) according to the 2-tailed test.

We assessed for other clinical parameters associated with visual decline. We found that lower pre-SRS KPS predicted visual decline (OR 0.9, 95% CI 0.9–1.0, $p < 0.01$). This finding remained significant after adjustment for age and sex (adjusted OR 0.9, adjusted 95% CI 0.8–1.0, adjusted $p < 0.01$). Nine patients (3%) had undergone prior radiotherapy. Of these patients, treatment doses were available for 7 patients, as follows: 12.5 Gy in a single fraction; 15 Gy with an unrecorded number of fractions; 54 Gy in 1.8 Gy fractions; 60 Gy in 30 fractions; 40 Gy in 10 fractions; 26 Gy in 4 fractions; and 50 Gy in 25 fractions. There was no association between previous radiotherapy and worsened vision in multivariable logistic regression (adjusted $p = 0.78$). Other clinical parameters, including tumor volume, maximum SRS dose, margin dose, maximum dose to the optic nerve, maximum dose to the optic chiasm, and maximum dose to the optic tract, did not significantly predict visual decline (Table 2). None of the tested clinical variables predicted blindness (Supplemental Table S3).

Radiographic Tumor Response

Complete follow-up imaging data were available for 322 patients. Of these patients, 294 patients (91.3%) had radiographic evidence of stability or tumor regression at last follow-up (Fig. 2). Tumor growth was seen in 28 patients (8.7%) after SRS. Tumor growth typically appeared to show steady progression, suggesting failure to respond to SRS (Fig. 1B). Thirteen patients (46%) with initial tumor progression underwent repeat SRS during the duration of the study. We tested for clinical parameters predictive of radiographic tumor progression after SRS. Symptom duration was marginally associated with tumor progression (OR 1.01, 95% CI 1.0–1.02, $p = 0.05$), and this association became significant after adjustment for age and sex (adjusted OR 1.01, adjusted 95% CI 1.0–1.02, adjusted $p = 0.02$). There was no association between tumor growth and principal tumor location, radiation dose, or number of isocenters (Table 3).

Clinical Outcomes

Assessment prior to SRS revealed hypothyroidism in 7 patients (2.1%), estrogen or testosterone deficiency in 2 patients (0.6%), and diabetes insipidus in 2 patients (0.6%). After SRS, only 1 patient had residual hypothyroidism that was present prior to SRS. All other patients had normal estrogen, testosterone, and growth hormone levels. No patients had diabetes insipidus after SRS, indicating overall improvement in endocrine function.

Eleven patients (3.4%) died over the duration of the study. Cause of death was available for 6 patients. Of these, 1 patient died of an unrelated lung cancer complication, 1 died of hepatorenal syndrome, and the other patients died of causes unrelated to the SRS procedure. Post-SRS mortality was higher in older patients (OR 1.1, 95% CI 1.0–1.2, $p < 0.01$) and lower in females (OR 0.1, 95% CI 0.0–0.5, $p = 0.02$). No other variables predicted mortality after SRS.

Discussion

SRS is a minimally invasive alternative to resection of skull base meningiomas, particularly for lesions that are difficult to access, tumors adjacent to critical structures, and patients with significant contraindications to surgery.[7] SRS is commonly used for residual tumor control but has gained more prominence as the first line of treatment for many meningiomas. In our study, 64.6% of patients underwent SRS as the initial treatment. To date, adoption of SRS to treat patients with meningiomas in direct contact with the optic apparatus has been tempered with caution owing to concerns for radiation-induced optic neuropathy, but only a few studies have specifically addressed this limitation. Herein, we performed a multicenter international study to evaluate outcomes after SRS for meningiomas in immediate contact with the optic nerves, chiasm, or proximal portion of the optic tracts.

We observed visual decline in 9.6% of patients with tu-

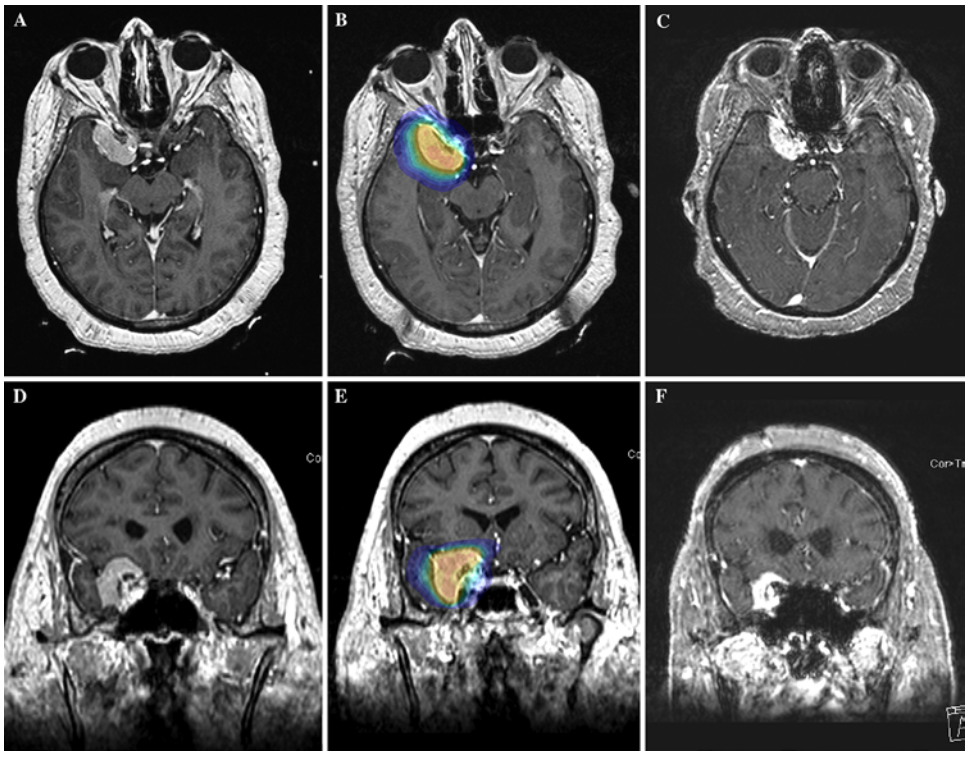

FIG. 2. Contrast-enhanced T1-weighted MR images. An illustrative case is presented of a 74-year-old female who received frame-based SRS for a right-sided sphenoid wing meningioma in direct contact with the right optic nerve. At 10-year follow-up, she had radiographic tumor regression and both visual acuity and visual fields were normal. **A and D:** Axial and coronal images obtained at the time of presentation showing a meningioma measuring 31.9 × 17.5 × 22.8 mm. **B and E:** The patient received 15 Gy to the 50% isodose line (*orange*) in a single fraction, and 9.1, 7.9, and 9.1 Gy were administered to the optic nerve, tract, and chiasm, respectively. **C and F:** Ten-year follow-up scans showing tumor regression. Figure is available in color online only.

TABLE 3. Univariable and multivariable logistic regression of predictors of treatment failure, defined as tumor growth after SRS

Variable	Univariable		Multivariable*	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Female	0.6 (0.3–1.5)	0.293	0.6 (0.2–1.4)	0.239
Age	1.0 (0.9–1.0)	0.139	1.0 (0.9–1.0)	0.116
KPS	1.0 (0.9–1.1)	0.929	1.0 (0.9–1.1)	0.89
Symptom duration	1.01 (1.00–1.02)	0.046†	1.01 (1.00–1.02)	0.02†
Tumor vol	1.0 (1.0–1.2)	0.7	1.0 (1.0–1.0)	0.847
Tuberculum tumor	1.0 (0.4–2.3)	0.985	1.0 (0.4–2.2)	0.926
Clinoid tumor	0.6 (0.3–1.5)	0.276	0.7 (0.3–1.6)	0.353
Cavernous tumor	1.4 (0.6–3.2)	0.388	1.4 (0.6–3.2)	0.384
Tumor vol	1.0 (1.0–1.0)	0.915	1.0 (1.0–1.0)	0.921
Max dose	1.0 (1.0–1.1)	0.398	1.0 (1.0–1.1)	0.39
Margin dose	0.9 (0.8–1.1)	0.452	0.9 (0.8–1.1)	0.455
Max optic nerve dose	1.0 (0.8–1.1)	0.618	1.0 (0.8–1.1)	0.553
Max optic tract dose	0.9 (0.8–1.1)	0.468	0.9 (0.8–1.1)	0.341
Max chiasm dose	0.9 (0.8–1.1)	0.326	0.9 (0.8–1.1)	0.295
No. of isocenters	1.0 (0.9–1.0)	0.532	1.0 (0.9–1.0)	0.627
Prior surgery	1.7 (0.8–3.7)	0.192	1.5 (0.7–3.4)	0.29
No. of fractions	0.8 (0.4–1.5)	0.496	0.8 (0.4–1.5)	0.509

* Adjusted for age and sex.
† Significant ($p < 0.05$) according to the 2-tailed test.

mors in direct contact with the optic apparatus, of which 4% were associated with treatment failure and continued tumor growth. Therefore, only 5.6% of patients whose tumors responded to SRS developed post-SRS visual decline. We did not note any differences in visual function between patients with tumors in direct contact with the optic nerves versus those with tumors in contact with the chiasm or anterior optic tracts. Likewise, within the range of doses used in the current study, we noted no correlations with maximum SRS dose. Of the variables tested, only low pretreatment KPS predicted visual decline after SRS. Low preoperative KPS predicts poor outcomes after meningioma resection,[25] and it also predicts shorter progression-free survival after SRS in patients with meningiomas.[26] Our data corroborate these findings and indicate that patients do better if they have increased pretreatment functional reserve.[27] Thus, it may be advantageous to treat patients with meningiomas in direct contact with the anterior optic pathways earlier with SRS rather than waiting until overall performance status declines. In our study, 93% of patients received SRS in a single fraction. The impact of fractionated SRS on the safety profile of SRS, particularly as it relates to optic neuropathy, remains to be defined;[2] however, we found no association between fractionated therapy and visual decline or tumor response in our study. Further studies are needed to assess delayed visual decline years after SRS.

We determined a tumor control rate of 91% (stability or regression) after SRS. This figure is in line with previous studies.[6,7] In adjusted analysis, only duration of symptoms predicted failure to respond to SRS. The reason for this association is unclear. Long-standing lesions can grow to larger sizes. However, no association was found between lesion size and response to SRS in this study. It is possible that changes in tumor microarchitecture over time may blunt response to SRS. Our data suggest that earlier treatment may be beneficial to improve the odds of tumor response and therefore preservation of visual function. However, in patients with symptomatic compressive optic neuropathy, decompressive surgery before SRS should still be considered.

Study Limitations

The study had the usual limitations inherent to the design of a retrospective study. Treatment approaches and follow-up algorithms varied at the participating sites. We did not review the implications of decompressive surgery followed by radiosurgery that was used to treat some patients. Also, technology varied during the study period owing to improvements in radiosurgical devices, neuroimaging protocols, and radiosurgical dose-planning software systems. We also included patients who underwent prior radiotherapy to avoid selection bias, but this may have affected cumulative doses in patients who underwent repeat treatment. All sites were high-volume SRS centers, typically at tertiary referral institutions. Thus, the results may not be generalizable to lower volume centers. Future studies are needed to address longer term visual findings and their contributions to patient morbidity. Despite these limitations, this remains the largest series to date on this subject.

Conclusions

SRS is a minimally invasive treatment of meningiomas. However, it is used with caution near the radiation-sensitive optic apparatus in order to avoid radiation-induced optic neuropathy. In this international multicenter study of patients with meningiomas in direct contact with the optic apparatus, treatment response after SRS was 91%; among patients with treatment response, worsened vision occurred in 5%. Given its safety margin, SRS is a reasonable option for appropriately selected patients with meningiomas in direct contact with the anterior optic apparatus.

References

1. Wiemels J, Wrensch M, Claus EB. Epidemiology and etiology of meningioma. *J Neurooncol*. 2010;99(3):307–314.
2. Marchetti M, Conti A, Beltramo G, et al. Multisession radiosurgery for perioptic meningiomas: medium-to-long term results from a CyberKnife cooperative study. *J Neurooncol*. 2019;143(3):597–604.
3. Eddleman CS, Liu JK. Optic nerve sheath meningioma: current diagnosis and treatment. *Neurosurg Focus*. 2007;23(5):E4.
4. Taha ANM, Erkmen K, Dunn IF, et al. Meningiomas involving the optic canal: pattern of involvement and implications for surgical technique. *Neurosurg Focus*. 2011;30(5):E12.
5. Schick U, Dott U, Hassler W. Surgical management of meningiomas involving the optic nerve sheath. *J Neurosurg*. 2004; 101(6):951–959.
6. Cohen-Inbar O, Lee CC, Schlesinger D, et al. Long-term results of stereotactic radiosurgery for skull base meningiomas. *Neurosurgery*. 2016;79(1):58–68.
7. Kondziolka D, Mathieu D, Lunsford LD, et al. Radiosurgery as definitive management of intracranial meningiomas. *Neurosurgery*. 2008;62(1):53–60.
8. Dufour H, Muracciole X, Métellus P, et al. Long-term tumor control and functional outcome in patients with cavernous sinus meningiomas treated by radiotherapy with or without previous surgery: is there an alternative to aggressive tumor removal? *Neurosurgery*. 2001;48(2):285–296.
9. Adler JR Jr, Gibbs IC, Puataweepong P, Chang SD. Visual field preservation after multisession CyberKnife radiosurgery for perioptic lesions. *Neurosurgery*. 2006;59(2):244–254.
10. Danesh-Meyer HV. Radiation-induced optic neuropathy. *J Clin Neurosci*. 2008;15(2):95–100.
11. Mihalcea O, Arnold AC. Side effect of head and neck radiotherapy: optic neuropathy. *Oftalmologia*. 2008;52(1):36–40.
12. Whipple KM, Levi L, Lee MS. The delayed cost of treatment. *Surv Ophthalmol*. 2013;58(4):370–376.
13. Milano MT, Grimm J, Soltys SG, et al. Single- and multifraction stereotactic radiosurgery dose tolerances of the optic pathways. *Int J Radiat Oncol*. 2021;110(1):87–99.
14. Minniti G, Amichetti M, Enrici RM. Radiotherapy and radiosurgery for benign skull base meningiomas. *Radiat Oncol*. 2009;4(1):42.
15. Stafford SL, Pollock BE, Leavitt JA, et al. A study on the radiation tolerance of the optic nerves and chiasm after stereotactic radiosurgery. *Int J Radiat Oncol Biol Phys*. 2003; 55(5):1177–1181.
16. Conti A, Pontoriero A, Midili F, et al. CyberKnife multisession stereotactic radiosurgery and hypofractionated stereotactic radiotherapy for perioptic meningiomas: intermediate-term results and radiobiological considerations. *Springerplus*. 2015;4(1):37.
17. Bunevicius A, Anand RK, Suleiman M, et al. Stereotactic radiosurgery for perioptic meningiomas: an international, multicenter study. *Neurosurgery*. 2021;88(4):828–837.
18. Sheehan JP, Starke RM, Kano H, et al. Gamma Knife radio-

surgery for sellar and parasellar meningiomas: a multicenter study. *J Neurosurg*. 2014;120(6):1268–1277.
19. Vernimmen FJAI, Slabbert JP. Assessment of the α/β ratios for arteriovenous malformations, meningiomas, acoustic neuromas, and the optic chiasma. *Int J Radiat Biol*. 2010;86(6):486–498.
20. Shrieve DC, Hazard L, Boucher K, Jensen RL. Dose fractionation in stereotactic radiotherapy for parasellar meningiomas: radiobiological considerations of efficacy and optic nerve tolerance. *J Neurosurg*. 2004;101(suppl 3):390–395.
21. Kothari RU, Brott T, Broderick JP, et al. The ABCs of measuring intracerebral hemorrhage volumes. *Stroke*. 1996;27(8):1304–1305.
22. Yang DY, Sheehan J, Liu YS, et al. Analysis of factors associated with volumetric data errors in gamma knife radiosurgery. *Stereotact Funct Neurosurg*. 2009;87(1):1–7.
23. Chukwueke UN, Wen PY. Use of the Response Assessment in Neuro-Oncology (RANO) criteria in clinical trials and clinical practice. *CNS Oncol*. 2019;8(1):CNS28.
24. Shaw E, Scott C, Souhami L, et al. Single dose radiosurgical treatment of recurrent previously irradiated primary brain tumors and brain metastases: final report of RTOG protocol 90-05. *Int J Radiat Oncol Biol Phys*. 2000;47(2):291–298.
25. Delgado-Fernández J, García-Pallero MA, Gil-Simoes R, et al. Validation of grading scores and outcome prognostic factors in intracranial meningiomas in elderly patients. *World Neurosurg*. 2018;114:e1057–e1065.
26. Ge Y, Liu D, Zhang Z, et al. Gamma Knife radiosurgery for intracranial benign meningiomas: follow-up outcome in 130 patients. *Neurosurg Focus*. 2019;46(6):E7.
27. Theriault BC, Pazniokas J, Adkoli AS, et al. Frailty predicts worse outcomes after intracranial meningioma surgery irrespective of existing prognostic factors. *Neurosurg Focus*. 2020;49(4):E16.

Disclosures

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Supplemental Information

Online-Only Content

Supplemental material is available with the online version of the article.

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