Stereotactic Radiosurgery of Central Skull Base Meningiomas—Volumetric Evaluation and Long-Term Outcomes

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■ BACKGROUND AND OBJECTIVE: **Complete resection of a central skull base meningioma (CSM) is possible, but it is often associated with high morbidity. Stereotactic radiosurgery (SRS) plays an appreciable role in the management of skull base meningiomas. This study aims to apply volumetric methods to assess the CSM response after SRS and correlate it with clinical outcomes.**

■ MATERIALS AND METHODS: **The cohort consisted of 219 patients, of whom 73.9% were female ($n = 162$), with a median age of 55 years (19–88). SRS was the primary treatment for 45.7% ($n = 100$), while 37.9% ($n = 83$) underwent treatment for residual tumors, 14.2% ($n = 31$) for recurrence, and in 5 with others reasons. The median tumor volume was 4.9 cm^3 (0.3–105 cm^3) to a median margin dose of 14 Gy (5–35 Gy). Volumetric analysis of CSM was performed on the SRS scan and each available magnetic resonance image thereafter.**

■ RESULTS: **The median clinical and imaging follow-ups of the cohort were 72 (24–298) and 66 (18–298) months, respectively. The overall tumor control rate was 83.4% ($n = 183$) at last follow-up with tumor regression 72.1% ($n = 158$). Neurologic symptoms were improved after SRS in 6.8% ($n = 15$), stable in 72.6% ($n = 159$), and worsened in 20.5% ($n = 45$). The clinical deterioration usually occurred in the patients with tumor progression ($P < 0.001$). Following SRS, the volumetric analysis confirmed that tumor response at 3 years reliably projected volumetric change and tumor control at 5 years ($R^2 = 0.694$) with $P < 0.001$ and 10 years ($R^2 = 0.571$) with $P = 0.001$.**

■ CONCLUSION: **SRS affords effective tumor volumetric control and neurologic stability or improvement in the majority of patients with CSMs. The radiologic response of CSM as determined by volumetry at 3 years post-SRS is predictive of long-term tumor response at 5 and 10 years following SRS.**

INTRODUCTION

Meningiomas are the most common intracranial primary extra-axial brain tumors, comprising around one third of all intracranial primary tumors.[1,2] Central skull base meningiomas (CSMs) are defined as meningiomas that arise from locations involving the tuberculum sellae, anterior clinoid, dorsum sellae, cavernous sinus, posterior clinoid, and upper part of the petroclival region. These lesions are closely associated with critical neurovascular structures, which make complete resection difficult.[3] The incidence of mortality rates was up to 9% with a median of 3.6% and transient or permanent resection-related cranial nerve deficits as high as 44% and 56%, respectively.[4,5] In a study from 2016, the mean recurrence rate in the upfront SRS group was 7.5% as opposed to 15.6% in the surgery with or without radiation, and ranges varied widely.[6] The mortality rates were up to 9% with a median of 3.6% and transient or permanent initial resection-related cranial nerve deficits as high as 44% and 56%,

Key words
- Central skull base
- Gamma Knife
- Meningioma
- Middle fossa
- Parasellar
- Petroclival
- Stereotactic radiosurgery
- Volumetry

Abbreviations and Acronyms
CN: Cranial nerve
CSM: Central skull base meningioma
GKRS: Gamma Knife radiosurgery
Gy: Gray
MRI: Magnetic resonance imaging
SRS: Stereotactic radiosurgery
WHO: World Health Organization

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respectively.[4,5] The high rate of recurrence of up to 24.5% for these meningiomas has been described even in recently published series using contemporary microsurgical approaches.[7]

Stereotactic radiosurgery (SRS) has been an important part of the treatment of patients with skull base meningiomas. However, there have been few large studies defining its use with CSMs and even fewer with long-term follow-up.[8-26] Moreover, while many recommend volumetric measurements for tumor follow-up, the technical and logistical constraints have yet precluded its widespread use in prior published series by our group or others.[27-30] In the current study, we evaluated the quantitative volumetric changes observed in the short to intermediate term to see if they were predictive of long-term response to SRS. We also evaluated the relationship between tumor volumetry and clinical outcomes in patients with benign central skull base meningiomas including cavernous sinus, middle cranial fossa, petroclival, and petrous apex lesions treated with single-session SRS.

MATERIALS AND METHODS

Patient Population

This study consists of a retrospective study of a prospectively maintained and Institutional Review Board—approved database at the University of Virginia. The database was searched for patients with a benign meningioma involving the central skull base region who were treated with single-session SRS between 1986 and 2014. Inclusion criteria were clinical and radiologic features consistent with a benign World Health Organization (WHO) grade I meningioma involving the planum sphenoidale, sella, parasellar, cavernous, tuberculum sellae, dorsum sellae, petrous apex, and upper one third petroclival region areas of the skull base, as well as a minimum of 3 available follow-up magnetic resonance imaging (MRI) scans in the follow-up after SRS. Patients who exhibited typical imaging and clinical features consistent with a benign CSM and underwent primary SRS were included, too. Typical imaging features of WHO grade 1 meningioma included an extra-axial location, the presence of a dural tail, uniform enhancement after administration of IV gadolinium, and/or calcifications. Patients were excluded if they had a WHO grade II or grade III meningioma, prior history of cancer, CT imaging alone, or multiple meningiomas indicative of neurofibromatosis type II or other tumor-related genetic predispositions. The final study cohort included 219 patients. All complications that occurred prior in the study population were included in the study results.

SRS Technique

Details of the SRS technique used at the University of Virginia have been illustrated in a prior publication.[25] In summary, the Leksell Gamma Knife Unit Model U was used until July 2001, Model C until September 2007, and the Gamma Knife Perfexion after that. For dose planning, 2 types of software were used during the study period. Kula (Elekta Instruments, AB) was used until June 1994, from which point onwards Gamma Plan (Elekta Instruments, AB) was employed. The dosimetry and other radiosurgical factors were developed under the direction of the treating neurosurgeon in collaboration with a medical physicist and radiation oncologist.[27] High-resolution stereotactic MRI was performed after Leksell stereotactic frame fixation. Thin-slice axial and/or coronal plane squared images were acquired after intravenous contrast administration. The particulars of stereotactic imaging for SRS planning changed over time, but the planning generally comprised precontrast and postcontrast volumetrically obtained gradient echo pulse sequences reconstructed into axial and coronal image stacks. The voxel sizes varied over the period including from 1 mm $\times$ 1 mm $\times$ 3 mm to 1 mm $\times$ 1 mm $\times$ 1.3 mm.

PATIENT AND TUMOR CHARACTERISTICS

Patient and tumor features were outlined in Tables 1 and 2. The final cohort consisted of 219 patients, of whom 73.9% were female ($n = 162$), with a median age of 55 years (19—88). SRS was the primary treatment for 45.7% ($n = 100$), while 37.9% ($n = 83$) underwent treatment for residual tumors, 14.2% ($n = 31$) for recurrence, and in 5 others the nature of the tumor was difficult to verify as residual or recurrence of tumor. The most common neurologic symptom was diplopia (33.9%, $n = 74$), followed by visual changes (32.9%, $n = 72$), headache (30.5%, $n = 67$), facial numbness or paresthesias (22.3%, $n = 49$), facial pain (7.3%, $n = 16$), facial paresthesia (3.6%, $n = 7$), and hormonal dysfunction (3.7%), which occurred in combination or alone. The most common cranial nerve deficit was trigeminal (37.4%, $n = 82$) followed by the optic (32.8%, $n = 72$), oculomotor (32%, $n = 70$), abducens (22.4%, $n = 49$), and trochlear (4.6%, $n = 20$). Tumor locations of the CSMs were mentioned as in Table 1. The mean volume of the central skull base meningiomas was 5.3 cc (range 0.2—54.8 cc). The median time interval from the development of associated neurologic symptoms to treatment with SRS was 12 months (range 0—361 months).

CLINICAL AND RADIOLOGIC FOLLOW-UP

After treatment with SRS, clinical and radiologic follow-up were performed approximately every 6 months for the first 2 years and yearly thereafter. An attending neurosurgeon and neuroradiologist at the University of Virginia reviewed each neuroimaging study. The response of the tumors was determined to be unchanging on the basis of volumetric analysis if it was within $\pm$10% of the targeted tumor volume at the time of treatment (original volume), was considered increased if it was >10% of the original volume, or decreased if it was at least 10% smaller than its original volume.[16] Tumor control was defined as either tumor regression or stability on volumetric assessment. Adverse radiation effects were defined as new or worsening perilesional hyperintensity noted in T2-weighted imaging or fluid-attenuated inversion recovery MRI sequences in the post-SRS follow-up.

TUMOR VOLUMETRIC ASSESSMENT

The Gamma Knife planning software (Gamma Plan, Elekta, AB, Stockhold, Sweden) for the initial volumetric assessment on the planning stereotactic MRI or *Image-J* software (National Institutes of Health, Bethesda, MD) for all follow-up MRIs was used for volume calculations, as previously described based on the