Gamma Knife surgery for trigeminal schwannoma

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Object. Trigeminal schwannomas are rare intracranial tumors. In the past, resection and radiation therapy were the mainstays of their treatment. More recently, neurosurgeons have begun to use radiosurgery in the treatment of trigeminal schwannomas because of its successful use in the treatment of vestibular schwannomas. In this article the authors evaluate the radiological and clinical outcomes in a series of patients in whom Gamma Knife surgery (GKS) was used to treat trigeminal schwannomas.

Methods. Twenty-six patients with trigeminal schwannomas underwent GKS at the University of Virginia Lars Leksell Gamma Knife Center between 1989 and 2005. Five of these patients had neurofibromatosis and one patient was lost to follow up. The median tumor volume was 3.96 cm³, and the mean follow-up period was 48.5 months. The median prescription radiation dose was 15 Gy, and the median prescription isodose configuration was 50%. There was clinical improvement in 18 patients (72%), a stable lesion in four patients (16%), and worsening of the disease in three patients (12%). On imaging, the schwannomas shrank in 12 patients (48%), remained stable in 10 patients (40%), and increased in size in three patients (12%). These results were comparable for primary and adjuvant GKSs. No tumor growth following GKS was observed in the patients with neurofibromatosis.

Conclusions. Gamma Knife surgery affords a favorable risk-to-benefit profile for patients harboring trigeminal schwannomas. Larger studies with open-ended follow-up review will be necessary to determine the long-term results and complications of GKS in the treatment of trigeminal schwannomas.

KEY WORDS • trigeminal schwannoma • neurofibromatosis • Gamma Knife surgery • radiosurgery

TRIGEMINAL schwannomas are the second most common type of intracranial schwannoma; the vestibular variety is the most common. Despite this distinction, trigeminal schwannomas remain relatively rare and constitute between 0.8 and 8% of all intracranial schwannomas and less than 0.5% of all intracranial tumors. Complete resection can be curative; however, even in the best of hands it is associated with a risk of significant neurological complications and death. Even more disheartening is the fact that gross-total resection is not always feasible, and lesion recurrence afterwards is not uncommon.

With the success of GKS in the treatment of VSs, it seems a natural extension to use radiosurgery in the treatment of trigeminal schwannomas. The relative rarity of this tumor type has resulted in a paucity of significant series of patients treated radiosurgically for this disease. The present study details our experience with GKS for both the primary and secondary treatment of trigeminal schwannomas.

Clinical Material and Methods

Patient Population

During a 16-year period at the University of Virginia Lars Leksell Gamma Knife Center, 26 patients with trigeminal schwannomas underwent 27 GKS procedures. The patient who underwent two GKSs was initially treated for a lesion in the Meckel cave and had a favorable response in tumor reduction. A prepontine cistern portion of the tumor was discovered later and treated in a second procedure.

The mean age of patients at the time of GKS was 50 years (range 19–76 years). There were nine men and 17 women. Eight patients had undergone at least one prior tumor resection and three had undergone two previous resections. Those who had undergone prior resections presented for GKS at a mean interval of 23.3 months after the first procedure (range 6–66 months). In this group the histological characteristics of the tumors analyzed at resection were consistent with trigeminal schwanna. Eighteen patients underwent GKS as the primary treatment for trigeminal schwannomas. The lesions in these patients were diagnosed on the basis of neuroimaging findings and the presence of typical clinical features of trigeminal nerve dysfunction (such as facial pain and numbness). Neuroimaging findings in this group included evidence of an extraaxial, uniformly enhancing tumor involving the middle and/or posterior cranial fossae without evidence of a dural tail and with predominant clinical signs of trigeminal nerve dysfunction. Prior to GKS, preoperative neuroimaging studies were reviewed both by the treating neurosurgeon (either L.S. or J.S.) and by a neuroradiologist at the University of Virginia.
Virginia Health System; both the neuroradiologist and neurosurgeon agreed that the lesion in each case was most consistent with trigeminal schwannoma. The characteristics of the five patients with neurofibromatosis are summarized in Table 1. The clinical signs and symptoms in all patients are summarized in Table 2. The mean interval between the onset of primary symptoms and GKS was 31.4 months (range 3 weeks–12 years). The most common initial symptom was facial numbness, reported by 62% of patients.

Radiosurgical Technique

The GKS procedure has been detailed elsewhere. Briefly, a stereotactic frame was attached to the patient’s head and anesthesia was induced. Magnetic resonance imaging was used for treatment planning. The Leksell Gamma Unit Model U was used until July 2001, when it was replaced with the Model C (Elekta Instruments, Inc.). The dose delivered per minute by the Model U varied from 3.66 Gy in March 1989 to 1.59 Gy in October 1995. The radiation source was reloaded at that time and the dose delivered per minute was 3.56 Gy from November 1995 to 2.31 Gy in July 2001 when the Model C was installed. The dose dispensed from the Model C unit was 3.67 Gy/minute in July 2001 and 2.30 Gy/minute in December 2004. Kula software was used for dose planning before June 1994 and was replaced with Gamma Plan software thereafter (both obtained from Elekta Instruments, Inc.).

The median tumor volume at the time of GKS was 3.96 cm³ (range 0.63–8.5 cm³). The median prescription isodose was 50% (range 30–50%) and the median prescription dose was 15 Gy (range 10.2–17 Gy). The mean maximum dose was 35 Gy (range 26–50 Gy). The mean number of isocenters used per patient was six (range two–16).

Follow-up Review

Clinical follow-up data were obtained by physical examination or through written and verbal communication with the patients and referring physicians. Follow-up MR imaging was performed at 6-month intervals. Additional imaging studies were acquired in the interim if new or worsening clinical symptoms developed. All films were reviewed by neurosurgeons and neuroradiologists and subjected to computer-calculated tumor volumetry. The tumors were classified as having an increased, stable, or decreased volume. The films were also assessed for radiation-induced changes in the brain.

### TABLE 1

**Patients with neurofibromatosis and trigeminal schwannomas who underwent GKS**

<table>
<thead>
<tr>
<th>Age (yrs), Sex</th>
<th>Associated Lessons</th>
<th>Prior Treatment</th>
<th>Delay Between Last Treatment &amp; GKS</th>
</tr>
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<tbody>
<tr>
<td>52, F</td>
<td>VS</td>
<td>microsurgery</td>
<td>12 yrs</td>
</tr>
<tr>
<td>63, M</td>
<td>lower cranial nerve schwannoma</td>
<td>GKS</td>
<td>concomitant GKSs</td>
</tr>
<tr>
<td>76, F</td>
<td>VS</td>
<td>none</td>
<td>NA</td>
</tr>
<tr>
<td>58, F</td>
<td>bilat VS</td>
<td>microsurgery</td>
<td>23 &amp; 13 yrs</td>
</tr>
<tr>
<td>28, F</td>
<td>rt TS &amp; L4–5</td>
<td>surgery</td>
<td>5 yrs</td>
</tr>
</tbody>
</table>

* NA= not applicable; TS = trigeminal schwannoma.

### Results

Clinical and neuroimaging follow-up data were obtained in 25 of 26 patients. One patient was lost to follow up. Two patients underwent resection of their tumors after GKS, and their cases were censured at the time of their microsurgeries. One patient died of unrelated causes 95 months after GKS. The mean follow-up period was 48.5 months (range 12–104 months). Thirteen patients (52%) were followed up for longer than 4 years.

**Clinical Outcomes**

Improvement in preexisting neurological deficits was observed in 18 (72%) of 25 patients. Twelve (75%) of 16 patients with facial numbness, seven (64%) of 11 patients with facial pain, six (75%) of eight patients with facial paresthesias, nine (82%) of 11 patients with diplopia, seven (88%) of eight patients with headaches, and one (50%) of two patients with dizziness reported improvement in symptoms after GKS. Four patients (16%) reported no change in their initial symptoms. Three of these four were on a regimen of Tegretol at the time of their last follow-up examination.

Three patients (12%) experienced worsening facial pain after GKS. Two of these three underwent resection of the lesion; one was found to have a new prepontine portion of tumor and underwent GKS a second time. This patient remains clinically stable since her second GKS. No patient experienced clinical deterioration related to adverse radiation effects.

**Imaging Outcomes**

Of the 25 patients followed up with imaging, in 12 patients (48%) tumor regression was demonstrated, in 10 (40%) there was no change, and in three (12%) the tumor enlarged (Figs. 1–4). One of the patients whose tumor enlarged underwent resection because of continuing trigeminal neuropathy. In two others there was only mild tumor enlargement, and serial follow-up neuroimaging studies were performed in these patients. In the patient in whom a second GKS procedure was required to treat a prepontine cistern portion of the tumor, both the originally and subsequently treated portions of the tumor showed no growth on
the last follow-up images. In the one patient who died of an unrelated cause in this series, the trigeminal schwannoma remained stable without evidence of growth on the last follow-up MR image, which was obtained 86 months after GKS.

Of the 18 patients who underwent GKS as the initial treatment, follow-up imaging was available in 17 patients; in nine (53%) of these patients there was tumor shrinkage, in six (35%) there was no sign of tumor enlargement, and in two (12%) there was tumor growth. Eight patients underwent GKS as a secondary treatment following microsurgery; in three (37.5%) of these patients the tumor decreased in size, in four (50%) it remained stable, and in one patient (12.5%) the lesion enlarged. In the five patients with neurofibromatosis, there was a reduction in the size of the tumor in three patients (60%) and no tumor enlargement in two patients (40%) following GKS.

Discussion

Trigeminal schwannomas are benign and relatively rare tumors. Historically the standard treatment for trigeminal schwannomas has been resection. More recently, radiosurgery has been used as either a primary or secondary treatment for such tumors. For benign intracranial tumors, radiosurgery offers the advantages of a low rate of morbidity, good spatial precision, and the radiobiological efficacy of a single dose for late-responding tissues. In our 25 patients there was a favorable clinical outcome in 88%. Either tumor shrinkage or no growth was noted in 80% of patients at a mean of 48.5 months after GKS.

Microsurgery for Trigeminal Schwannomas

Exirpation has been the mainstay of treatment for trigeminal schwannomas. A number of groups have reported their results after resection of trigeminal schwannomas. Al-Mefty et al. detailed results in 25 patients and found a 12% rate of new cranial nerve palsy development. These authors also observed tumor recurrence in three patients at an average of 22.3 months postoperatively. In a series of 12 patients with trigeminal schwannomas who participated in follow-up review for 12 to 60 months, Samit et al. reported new cranial nerve palsies in 33% of patients and tumor recurrence in 17%. In a series of 14 patients, McCormick and colleagues reported new cranial nerve palsies in 86% and tumor recurrence in 36% of patients. Other reported complications after resection of trigeminal schwannomas include death, infection, cerebrospinal fluid leak, and postoperative hematomas. Despite the use of different skull-base surgical approaches performed by specialized neurosurgical teams, the rate of new cranial nerve palsies, other complications, and tumor recurrence speaks to the

![Fig. 1. Coronal (A and B) and axial (C) contrast-enhanced MR images obtained at the time of GKS in a 50-year-old woman who presented with left trigeminal neuralgia and facial numbness.](image1)

![Fig. 2. Coronal (left panels) and axial (right panels) MR images obtained in the same patient as in Fig. 1 demonstrating tumor regression at 9 (A and B), 27 (C and D), and 58 (E and F) months post-GKS.](image2)
need for improvement in the outcome after treatment of trigeminal nerve schwannomas.

**Fractionated Radiation Therapy for Trigeminal Schwannomas**

There are relatively little data in the literature to support the use of conventional fractionated radiation therapy to treat trigeminal schwannomas. In a small series from the University of California at San Francisco, 45 patients received adjuvant radiation therapy after undergoing incomplete resection. Unfortunately, this approach failed to prevent local recurrence in nearly 50% of patients. Zabel et al. 49 used fractionated radiation therapy in a series of 13 patients with nonvestibular schwannomas. Using a median dose of 57.6 Gy with a 1.8-Gy fraction dose, tumor shrinkage or no new growth was seen in all 13 patients at a median follow up of 33 months. Such a series, albeit small and with short follow-up periods, demonstrates that radiation therapy may be effective for halting the growth of trigeminal schwannomas.

**Previous Radiosurgical Studies**

With the successful treatment of VSs using radiosurgery, its use on trigeminal schwannomas would appear to represent a natural extension. However, given the relative rarity of this tumor type, few cases are reported in the literature. Most radiosurgical series are small and have relatively short follow-up periods (Table 3). In some of these studies, investigators use the Kaplan–Meier method to illustrate “tumor control” and rely on the plateau at the right end of the curve. However, as Peto and colleagues 31 noted, the plateau to the right of the Kaplan–Meier plot must be interpreted cautiously, particularly if it is based on a statistically small number of observations. In these published series, linear accelerator radiosurgery was used to treat 14 patients and GKS was used in 149 patients. Many previous reports in the literature focus on other, nonvestibular schwannomas rather than just on trigeminal schwannomas.

Pollock and colleagues 33 reported tumor shrinkage or growth cessation in nine of 10 patients with trigeminal schwannomas; in three of these patients new or worsened trigeminal nerve dysfunction developed. Nettel et al. 26 reported on 23 patients, 12 of whom had undergone one or more resections for a trigeminal schwannoma. Tumor shrinkage or no new growth was observed in 91% of patients (20 of 22 patients who could be examined). Wowra and coworkers 46 treated 15 trigeminal schwannomas at a mean follow up duration of 68.4 months; all tumors were well controlled after GKS. To date, Pan and coworkers 30 have reported the largest series of 56 patients, 14 of whom had undergone resection previously. Tumor shrinkage or growth cessation was observed in 52 (93%) of these patients after a mean follow-up period of 68 months.

We observed tumor shrinkage or growth cessation in 88% of our patients. With longer follow-up periods, it has been our experience that benign tumors tend to fall into one of two categories following GKS: those that display shrinkage and those that exhibit enlargement. 24 As such, we pre-

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Fig. 3. Axial (A and B) and coronal (C) MR images obtained at the time of treatment in a 68-year-old man who underwent GKS for a right trigeminal schwanna (tumor volume 3.2 cm³).

Fig. 4. Axial (left panels) and coronal (right panels) and axial postoperative MR images obtained in the same man as in Fig. 3, at 14 (A and B) and 25 (C and D) months post-GKS demonstrating significant tumor shrinkage.
fer not to use the term “tumor control” for benign tumors after radiosurgery. In 10 patients we saw no tumor growth after GKS. Longer follow-up periods for patients with trigeminal schwannomas who have undergone GKS and linear accelerator radiosurgery are needed to determine the true incidence of tumor shrinkage or growth cessation after radiosurgery compared with the natural history of slow-growing benign tumors such as schwannomas.

With regard to clinical outcome after GKS, the incidence of neurological deterioration reported in the literature ranges from 0 to 33% (Table 3).15,26,33,46 The highest rate of neurological deterioration was noted by Wowra et al.,42 who reported a 33% increase in cranial neuropathy after 9 to 15 Gy of radiation was administered to the tumor margin. We observed no new cranial nerve deficits in any of our patients after GKS. Moreover neuropathy after GKS for a trigeminal schwannoma is usually limited to the trigeminal nerve, which is not the case in patients who have undergone resection. Most of our patients had substantial trigeminal nerve dysfunction prior to GKS and few were at risk for a significant new decline in their neurological conditions. In addition, it is well known from the radiosurgical literature on trigeminal neuralgia that the trigeminal nerve is fairly radioresistant.32 Our results and those reported by others (see Table 3) suggest that the current prescription doses of 12 to 15 Gy, although effective for suppressing tumor growth, rarely cause a decline in trigeminal nerve function, even in a nerve that appeared dysfunctional at baseline.14,26,30,33,46 Moreover, as with VSs, such prescription doses delivered to small and moderately sized trigeminal schwannomas are well below the doses that typically result in radiation-induced changes or necrosis.42 However, the long-term clinical benefits and risks of GKS for trigeminal schwannomas can only be ascertained after studies with larger patient cohorts and longer follow-up periods have been conducted.

Although GKS avoids certain types of complications associated with open surgery, radiosurgery does have the potential for at least one complication not seen after extirpation. Akiyama et al.1 reported on a case of pseudocapsule formation after GKS was performed for trigeminal schwannoma. The fibrotic capsule and cyst formation occurred at the target site approximately 15 months after GKS, necessitating surgery to decompress the brainstem and alleviate worsening facial pain and diplopia. Close neuroimaging and clinical follow up is necessary for all patients who undergo GKS for trigeminal schwannomas.

### Optimal Treatment Dose and the Role of GKS

At the time of diagnosis not all patients with trigeminal schwannomas are good candidates for GKS. If the tumor volume is large, the patient may benefit from lesion extirpation. In the present study, we were successful in treating lesions as large as 8.5 cm³ that were causing brainstem compression.

The small number of patients in our cohort and in the literature prevents us from making a firm recommendation about the radiation dose required to treat trigeminal schwannomas. Extrapolating from the literature on VSs, however, it would seem that higher radiation doses provide better control but also risk a higher rate of complications.7,10 For trigeminal schwannomas, one must select a dose based on tumor volume, the patient’s radiation treatment history, and the lesion’s proximity to critical structures such as other cranial nerves, major vessels, and the brainstem. At present we believe the optimal dose is 12 to 14 Gy. Open-ended follow up is needed to determine if low-dose radiosurgery (such as a 12-Gy margin dose) effectively prevents tumor growth.

The rates of tumor shrinkage and growth cessation in our patients who underwent GKS as the primary or secondary treatment for trigeminal schwannomas were 88 and 87.5%, respectively. Thus, radiosurgery appears to be comparably effective for treating both initially diagnosed and recurrent trigeminal schwannomas.

Tumor shrinkage or no growth was observed in all five patients with neurofibromatosis who were treated with GKS in this series. The authors of other publications have also reported on the efficacy of GKS for treating VSs associated with neurofibromatosis.14,36,37 However, VSs in patients with neurofibromatosis may not respond as well to radiosurgery as those that arise spontaneously.1,27 The rarity of trigeminal schwannomas, the small subgroup size presented here, and the difference in underlying pathophysiological characteristics between neurofibromatosis-associated schwannomas and spontaneous schwannomas demand cautious interpretation of this finding.25,28

In the present study, only eight patients (31%) received histological confirmation of a trigeminal schwannoma. The other patients received a diagnosis based on radiological findings, past medical history, and clinical signs and symptoms. The differential diagnosis for such lesions includes meningiomas and metastatic tumors.10,18,19,23,24 Given the high operative risks, we believe that these tumors do not

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**TABLE 3**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Treatment Method</th>
<th>No. of Patients</th>
<th>Tumor Margin Dose (Gy)</th>
<th>Tumor Shrinkage or No Regrowth (%)</th>
<th>Presence of CN Deficit (%)</th>
<th>Mean FU (mos)</th>
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</thead>
<tbody>
<tr>
<td>Kida et al., 1997</td>
<td>GKS</td>
<td>19</td>
<td>13, mean</td>
<td>100</td>
<td>19.8</td>
<td>14.3</td>
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<tr>
<td>Mahanta et al., 1999</td>
<td>LINAC</td>
<td>7</td>
<td>13.1, mean</td>
<td>100</td>
<td>17</td>
<td>32</td>
</tr>
<tr>
<td>Zabel et al., 2001</td>
<td>FR</td>
<td>7</td>
<td>57.6, median†</td>
<td>100</td>
<td>0</td>
<td>33.6</td>
</tr>
<tr>
<td>Pollock et al., 2002</td>
<td>GKS</td>
<td>10</td>
<td>18, median</td>
<td>96</td>
<td>30</td>
<td>43</td>
</tr>
<tr>
<td>Nett et al., 2004</td>
<td>GKS</td>
<td>23</td>
<td>15, median</td>
<td>91</td>
<td>8.6</td>
<td>40</td>
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<tr>
<td>Wowra et al., 2004</td>
<td>GKS</td>
<td>15</td>
<td>13.5, mean</td>
<td>100</td>
<td>33</td>
<td>68.4</td>
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<tr>
<td>Pan et al., 2005</td>
<td>GKS</td>
<td>56</td>
<td>13.3, mean</td>
<td>93</td>
<td>7.1</td>
<td>68</td>
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<tr>
<td>present study</td>
<td>GKS</td>
<td>26</td>
<td>15, median</td>
<td>88</td>
<td>0</td>
<td>48.5</td>
</tr>
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</table>

* CN = cranial nerve; FR = fractionated radiosurgery; FU = follow up; LINAC = linear accelerator.
† In 1.8-Gy fraction dose.
categorically require verification via an open resection or biopsy sampling because these tumor types also lend themselves well to GKS.

Even with the addition of the present study to the literature, little is known about the long-term clinical and radiological outcomes of GKS for trigeminal schwannomas. The radiosurgical literature does, however, provide some long-term outcomes following GKS for VSs. If one can extrapolate from these studies, one can postulate that GKS may provide beneficial and durable results for patients with trigeminal schwannomas. Larger studies with open-ended follow up will, however, be needed to prove this point.

Conclusions

Trigeminal schwannomas are rare intracranial tumors that are sometimes associated with neurofibromatosis. Ex- tirpation performed even by an experienced neurosurgeon is associated with a high risk of complications and tumor recurrence. Gamma Knife surgery affords a favorable risk- to-benefit profile for the treatment of small to moderately sized trigeminal schwannomas. Larger studies with open- ended follow up are needed to determine the optimal radiation dose as well as the long-term results and complication rates of GKS for trigeminal neuralgia.

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