Vestibular schwannomas (VSs), also known as acoustic neuromas, are benign primary intracranial tumors that arise from the Schwann cells of the vestibulocochlear nerve. The incidence of VS is estimated to be 1 per 100,000 individuals per year, and it accounts for approximately 8% of all intracranial tumors in adults. These tumors are typically slow growing (0–3.9 mm per year), but without management, most VS tumors will grow within 3 years.

For many years, microsurgical resection remained the most commonly recommended treatment for patients with newly diagnosed unilateral VS. Although surgical outcomes have improved over the last 30 years, resection of VS was frequently associated with impaired facial nerve function and loss of hearing. The recurrence rate of VS has been shown to be 2.6%–11.0% after gross-total resection, and 20%–50% of VS tumors progress after sub-total resection. Since the development of the Gamma Knife (GK) technology, stereotactic radiosurgery (SRS) has become an increasingly used alternative or adjuvant VS management tool that eliminates many risks associated with resection.

Stereotactic radiosurgery offered a safe and effective long-term management strategy for VS patients whose tumors remained or recurred after initial microsurgery.
thy rates in 1%–5% of patients. Stereotactic radiosurgery has also become an important approach for treating patients with recurrent or residual tumors after initial resection. The present study extends our patient series and the length of follow-up from our previous report. We analyzed the outcomes of GK SRS for VS patients who had recurrent or residual tumors after 1 or more previous resections.

Methods

Patients

Between February 1988 and February 2011, 190 patients (of a cohort of 1770 patients with VS) underwent GK SRS at the University of Pittsburgh Medical Center for a recurrent VS after undergoing at least 1 resection to control the growth of the tumor. Two patients were excluded because of associated neurofibromatosis Type II, 1 patient was excluded because of a previous fractionated radiosurgery, and 19 patients were lost to follow-up. Of the 19 patients lost to follow-up, 2 were deceased and 5 were from other countries. The remaining 168 patients included in the present study underwent a total of 173 GK SRS procedures.

Overall, 231 resections of 173 tumors were performed in these patients. The extent of tumor resection was determined from operative notes and postoperative MRI scans or CT images. Forty tumors (23%) were totally resected before SRS, and 96 (55%) were subtotally resected and displayed regrowth before SRS. The remaining 37 tumors were subtotally resected and were managed with early SRS to prevent regrowth. The overall median length of the interval between the last tumor resection and SRS was 42 months (range 2–329 months). For patients who underwent SRS because of confirmed tumor progression after resection, the median interval length was 59 months (range 5–329 months). Patients who underwent early SRS to prevent tumor regrowth had SRS at a median interval of 4 months (range 2–7 months) after resection. None of the patients in this series was prospectively staged, that is, no VS management strategy involved planned initial microsurgical debulking followed by SRS. Table 1 summarizes the characteristics of the patients whose outcomes could be evaluated.

Radiosurgical Technique

Gamma Knife SRS was performed with models U, B, C, 4C, or the Perfexion Leksell GK system (Elekta AB). Our radiosurgical technique has been previously described in detail. The procedure begins with the fitting of a model G Leksell stereotactic frame under intravenous conscious sedation and local scalp anesthetic. Contrast-enhanced CT was used as the neuroimaging modality for dose planning and local scalp anesthetic. Contrast-enhanced CT was used as the neuroimaging modality for dose planning in 27 procedures (15.6%) that were performed before mid-1991. Magnetic resonance imaging was used for dose planning in 146 procedures (84.4%) after mid-1991. Images were exported to a computer workstation for dose planning with software available in the year of treatment (KULA dose planning software in early years and thereafter GammaPlan software). We used an approach that consisted of creation of a highly conformal and selective dose plan that encompassed the 3D geometry of the tumor.

Follow-Up Review

The patients’ clinical characteristics and the radiosurgical parameters were prospectively entered into a computer database at the time of SRS. At present, cochlear nerve function was assessed with an audiogram and graded with the Gardner-Robertson (G-R) scale. Facial nerve function was graded by clinical examination using the House-Brackmann (HB) scale. Clinical examinations and CT or MRI studies were requested at 6, 12, 24, and 48 months after SRS. Patients with no evidence of VS tumor growth 4 years after SRS were scheduled to undergo repeat imaging examinations every 2 years thereafter. Follow-up data were obtained as previously described. The tumor was measured 3 times (1 time in each axis) on follow-up MRI scans, and the measured dimensions were compared with those of the measurements on images acquired at the time of SRS. An increase or decrease of 2 mm in 1 or more plane was recorded as a change in tumor size. We used Kaplan-Meier survival analysis to create a progression-free survival curve.

Assessments of improved, worsened, or new neurological deficits were based either on the results of physical examinations or on subjective reports from the patient. We used the chi-square test to determine whether any patient characteristics resulted in significant differences in outcomes. Clinical and radiographic follow-up results were entered into the database as they became available. Patients for whom follow-up data were not available within 1 year were contacted by telephone to update the database.

### Table 1. Patient and tumor characteristics and SRS parameters

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Resections</th>
<th>Entire Series</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of tumors managed w/SRS (%)</td>
<td>128 (74)</td>
<td>173 (100)</td>
</tr>
<tr>
<td>Median age in yrs</td>
<td>57</td>
<td>57</td>
</tr>
<tr>
<td>M/F ratio</td>
<td>54.74</td>
<td>72.101</td>
</tr>
<tr>
<td>Median interval b/twn last resection &amp; SRS in mos</td>
<td>42</td>
<td>42</td>
</tr>
<tr>
<td>Median tumor vol in cm³ (range)</td>
<td>2.5 (0.2–18)</td>
<td>2.7 (0.2–22)</td>
</tr>
<tr>
<td>Median dose at tumor margin in Gy (range)</td>
<td>13 (11–20)</td>
<td>13 (11–20)</td>
</tr>
<tr>
<td>Median follow-up post-SRS in mos (range)</td>
<td>70 (6–285)</td>
<td>74 (6–285)</td>
</tr>
</tbody>
</table>

* Overall, 168 patients underwent a total of 173 GK procedures.
and to maximize the follow-up data for this study. The median length of the clinical review follow-up period was 74 months (range 6–285 months), and the median length of the neuroimaging review follow-up period was 67 months (range 6–275 months).

Results

Tumor Control

Overall, SRS successfully controlled VS growth in 163 (94%) of the 173 tumors. The actuarial tumor progression-free survival rate determined with Kaplan-Meier analysis was 97% at 3 years, 95% at 5 years, and 90% at 10 years after SRS.

Hearing Function

After the initial microsurgical resection, 161 patients (93%) were completely deaf (i.e., had G-R Class V hearing), 6 patients (3.5%) had G-R Class III hearing, and 5 patients (2.9%) had G-R Class I hearing. Only 1 (2.2%) of the 45 patients who underwent more than 1 resection retained any measurable hearing after the final resection; that patient’s hearing was G-R Class III. The patient characteristics at the time of SRS are summarized in Table 2.

Facial Function

Table 3 summarizes the changes in cranial nerve function after SRS, and Table 4 subdivides the lesions into 3 groups: those in patients who underwent initial subtotal resection followed by tumor regrowth, those in patients who underwent initial subtotal resection followed by regrowth, and those in patients who underwent a subtotal resection and early SRS to preempt regrowth. After the microsurgical resection, 81 patients (47%) overall had facial neuropathy (i.e., facial function with an HB grade of ≥ III). Fifty-one (40%) of 128 patients who underwent only 1 surgery had facial function with an HB Grade of III or greater. However, 30 (67%) of 45 patients who underwent more than 1 surgery had facial neuropathy. Patients who had undergone only 1 resection had significantly better facial nerve function than those who had undergone more than 1 resection (p < 0.01, chi-square test). Twenty patients (12%) had significantly greater incidence of complications (p < 0.05).

After SRS, hearing deteriorated in 3 (50%) of the patients who had G-R Class III hearing and in 2 (40%) of the patients who had G-R Class I hearing before SRS (Table 3).
had complete facial palsy (i.e., HB Grade VI facial function) at the time of SRS. Twelve of these patients (60%) had more than 1 resection (p < 0.001, chi-square test).

At the time of SRS, 95 (70%) of 136 patients whose tumors had confirmed regrowth following resection had facial dysfunction (i.e., facial function of HB Grade ≥ II), while only 20 (54%) of 37 patients who underwent subtotal resection without regrowth had facial nerve dysfunction.

Eight (5.5%) of 145 patients with some facial function had deterioration in this function after SRS, indicated by an HB grade change of at least one at the last follow-up. Twenty-two (19%) of 116 patients with some facial dysfunction had an improvement in facial function. Among 78 patients with at least a 24-month interval between microsurgery and SRS, 10 (13%) had facial function improvement. Table 5 shows the effect of tumor margin dose on facial nerve function in 123 patients with preoperative HB grades of I–III. After SRS, the facial function in 5 (4.1%) of these patients deteriorated. Of 130 patients who received a margin dose of 11–14 Gy, only 3 (2.3%) had worsening facial function after SRS. Patients who were treated with higher margin doses had significantly higher rates of worsening of facial nerve function than those treated with lower doses (p < 0.01).

Other Cranial Neuropathies

Overall, 87 patients (50%) had varying degrees of trigeminal neuropathy at the time of SRS. Patients who underwent more than 1 resection had significantly more trigeminal neuropathy than those who underwent a single microsurgical procedure (p < 0.05, chi-square test). At the time of the last follow-up, 17 patients (20%) with some trigeminal dysfunction had improved trigeminal function, but 10 (5.8%) developed new or had worsened trigeminal neuropathy. Among 55 patients with at least a 24-month interval between microsurgery and SRS, 10 (18%) had an improvement in trigeminal nerve function.

At the time of SRS, 71 patients (41%) reported imbalance or disequilibrium difficulties, with a disproportionately higher number among those who had multiple resections (p = 0.051, chi-square test). After SRS, disequilibrium improved in 4 of these patients (5.6%), but 20 patients (12%) reported new or worsened balance disorders. Thirteen patients (7.5%), all of whom reported significant balance difficulties at the time of SRS, underwent shunt placement. Of 47 patients with at least a 24-month interval between microsurgery and SRS, 3 (6.4%) had balance improvement. Other commonly reported symptoms and signs were residual tinnitus or vertigo. Preoperatively, 49 patients (28%) reported having tinnitus, and 13 (7.5%) had vertigo. After SRS, tinnitus resolved in 17 patients (35%), and 6 (4.8%) of 124 patients previously without tinnitus reported new onset of tinnitus. Four (24%) of 17 patients with tinnitus who underwent SRS less than 24 months after resection reported that their tinnitus had resolved. Eight (62%) of the 13 patients who reported vertigo had undergone more than 1 resection. After SRS, intermittent vertigo in 5 (38%) of these patients resolved, and 6 (3.8%) of 160 patients without vertigo before SRS developed ver-
Two (40%) of 5 patients with vertigo who underwent SRS less than 24 months after the resection reported that their vertigo had resolved. Four (80%) of the 5 patients in whom vertigo resolved had undergone only 1 resection. Of 8 patients with multiple resections and vertigo, 1 (13%) had vertigo resolution. Patients who had more than 1 microsurgery were significantly (p < 0.01) more likely to have vertigo and significantly (p < 0.05) less likely to have vertigo resolution.

Impact on Daily Life

Most patients were able to return to normal activities within 2 days after SRS with no long-term impact on daily life. Eight patients (4.6%), all of whom reported a new permanent neuropathy after SRS) reported a negative impact on their daily life after SRS. Six of these patients (75%) considered balance difficulties as the major impairment after SRS. One patient reported severe headaches and swallowing difficulties. Another patient underwent repeat microsurgery because of sustained tumor growth, but had further deterioration in cranial nerve function after the repeat surgery.

Additional Symptoms or Signs After SRS

All of the aforementioned changes in symptoms and signs were observed during long-term follow-up. Fifteen patients (8.7%) reported transient additional symptoms in the first few weeks after SRS. Four patients (2.3%) developed peritumoral reactive edema verified by MRI findings during this period. Two of these patients noted fatigue, headaches, dizziness, and facial numbness that began 2–5
months after SRS. Moreover, 2 patients (1.2%) reported diplopia and balance difficulties. In 1 of these patients, reactive peritumoral edema was noted 1 year after the patient’s third SRS for a refractory recurrent VS. Whereas this patient had received radiation doses of 15 Gy and 16 Gy in his second and third treatments, respectively, the other 3 patients had received doses of only 12–13 Gy. Tumor control was achieved in all of these patients, and transient treatment with corticosteroids resolved all symptoms.

Two patients (1.2%) developed a peritumoral cyst and underwent microsurgical cyst fenestration. Three patients (1.7%) exhibited temporary trigeminal symptoms, 1 of whom also developed facial weakness. One patient reported taste dysfunction for 2 years. One patient (0.6%) reported temporary onset of ipsilateral facial spasms 1 year after SRS, and 2 patients (1.2%) reported development of transient headaches.

Two patients (1.2%) underwent additional surgery during the follow-up period. A new CSF leak via a skull-base defect was repaired 11 years after microsurgery and 1 year after SRS. One patient (0.6%) developed progressive hydrocephalus, which was managed with shunt placement. Transient symptoms were more likely to be detected in patients treated early when tumor margin doses exceeded 14 Gy.

### Tumor Progression and Additional Treatments

Follow-up MRI or CT results were available for all patients. Ten VS tumors (5.8%) showed radiological evidence of growth at a median interval of 34 months (range 18–108 months) after SRS. Two of these tumors were recurrences managed with SRS after a total resection. Three were tumors that had been subtotally resected and had regrown before SRS. The remaining 5 tumors had been subtotally resected and were managed with SRS to reduce the risk for regrowth. One patient’s tumor increased by 2 mm over the 30 months after SRS. None of the patients had malignant tumor transformation or development of radiation-related neoplasms.

Because of confirmed tumor progression, 4 patients (2.3%) underwent repeat resection at a median interval of 25 months (range 19–33 months) after SRS. After the repeat resection, additional neurological decline was noted in all but 1 of these patients.

At a median of 35 months (range 23–64 months) after the first SRS, 4 patients (2.3%) underwent a repeat SRS, which successfully controlled tumor growth in 3 (75%) of these patients. The facial function of 1 of these patients improved from HB Grade VI to Grade III. Only 1 patient had tumor progression after a second SRS; 25 months after the repeat SRS, follow-up imaging showed new VS growth in this patient in a previously untreated area. A third SRS procedure targeting only the new nodule was successful in curtailing tumor progression in this patient. After recovering from postoperative complications following the initial resection, this patient’s clinical condition remained stable with HB Grade IV facial function and some trigeminal neuropathy.

### Discussion

Only a few studies have reported the outcomes of SRS for VS that recurred or remained after a microsurgical resection.20,21,27 Table 6 summarizes the findings of these previous reports and of our study. The present study represents the largest series to date and provides an update to our 1998 report.2 Overall, the observed outcomes among patients in the current series are consistent with those previously reported for patients treated with radiosurgery for VS. In each series, a high rate of tumor control and relatively low rate of complications was observed after SRS. The patients in the present series had significantly fewer new or worsened neurological deficits after GK SRS than those in our previous report. This reduction may have been the result of a combination of lower treatment dosages and improved planning software. In both studies, a median dose of 13 Gy resulted in fewer permanent dysfunctions than higher median doses.

Previous studies have not analyzed the effect of multiple resections before SRS on outcomes. On the basis of our results, we conclude that patients who had more than 1 surgical procedure before SRS may have had more aggressive tumors that were unexpectedly difficult to manage with resection. Such patients tended to have worse outcomes, both before and after SRS. Freeman et al. found that 8 (30%) of 27 patients who underwent 1 repeat resection underwent additional treatment for tumor progression,29 indicating a tumor control rate after repeat resection of 70%.

### Tumor Control After SRS

In the current series, SRS controlled tumor progression in 94% of the patients. To achieve tumor control after a single SRS treatment failed to control VS, 4 patients underwent a second SRS treatment, and 1 patient had a third treatment. Five of these 10 tumors had been preemptively managed with SRS to reduce the likelihood of tumor progression after the initial resection.

### Neurological Outcomes

In this series, 93% of patients were deaf (i.e., had G-R Class V hearing) after the initial microsurgical resection. Among the patients who had more than 1 resection, 98% were deaf after the final resection. In none of these patients did hearing improve after SRS, an observation consistent with outcomes after repeat microsurgery.23 At the time of undergoing SRS, 28% of the patients had tinnitus, and 35% of these patients reported that the tinnitus had resolved after SRS, whereas 4.8% developed new tinnitus.

Almost half of the patients in the current series had facial neuropathy (i.e., facial function with an HB grade ≥ III) at the time of SRS. A disproportionate number of these patients had undergone more than 1 resection. This disproportional representation of patients with more than
1 resection was even more significant among patients with complete facial palsy (i.e., HB Grade VI facial function). Only 4.6% of patients developed new or had worsened facial nerve function after SRS. The risk for worsened facial neuropathy was significantly greater in patients treated with a higher tumor margin prescription dose. Only 2.3% of the patients who received a margin dose of 11–14 Gy had new or worsened facial function. Of the patients with some facial dysfunction before SRS, 19% had improvement of facial function by at least 1 HB grade at the time of the last examination.

Facial function improved in 6 (30%) of 20 patients with facial nerve dysfunction after microsurgery who were treated early with SRS. This higher rate of symptom improvement may be related to a surgical decision to perform subtotal resection to anatomically preserve the facial nerve.

Compared with observations reported in previous studies of repeat resection of VS tumors,16,17 the findings in the present study suggest that our patients may have had an enhanced rate of preservation of facial nerve function. The authors of 1 study noted that facial nerve function deteriorated in 5 (42%) of 12 patients who underwent a repeat resection; 3 (30%) of 10 patients with preoperatively good facial function (i.e., of an HB grade of I–II) developed reduced or absent facial nerve function (of HB Grade ≥ III).12 Another study reported that facial function in 3 (50%) of 6 patients with an HB grade of I–II worsened to HB grades of III–VI after repeat surgery.23 The largest study to date reported that 16 (46%) of 35 patients had worsening facial function 1 year after repeat surgery (1 patient’s facial function was already HB Grade VI). Twelve (57%) of 21 patients with HB Grade I–II facial function at the time of revision surgery had deterioration of facial function.

Consistent with observations in previous studies,16,17 disequilibrium and vertigo symptoms were the most significant factors that negatively affected daily life of the patients in the present series. Overall, 7.5% of patients had vertigo before SRS. Of interest, 18% of those who underwent multiple resections had vertigo, compared with only 3.9% of those who underwent a single resection. After SRS, vertigo resolved in 80% of patients who underwent only 1 resection, but in only 13% of patients with multiple resections.

Although our follow-up patient examinations did not use validated quality of life (QOL) scoring methods, our results generally parallel those of Carlson et al. who reported that microsurgery results in worse QOL scores than SRS does.5 In that report, patients who underwent microsurgery had worse Penn Acoustic Neuroma QOL Scale scores in facial function, balance, and pain. Microsurgery patients also scored worse on the Glasgow Benefit Inventory in general and physical health.

Weaknesses of the Present Study

This report represents a longitudinal but retrospective review of a large series of patients with unilateral VS who underwent SRS because of tumor regrowth or because of concern that a residual tumor would regrow after an incomplete initial resection. The outcomes were determined through serial observations, supplemented by additional discussion with the patients by authors who were not part of the initial treatment team. We did not have the exact dates of symptom changes for many patients, a limitation that made it difficult to determine whether any clinical improvements resulted from SRS or reflected the expected natural history of VS after resection. To obtain conservative estimates of clinical improvements attributable to SRS alone, we used an interval of at least 24 months between resection and SRS. Although the median length of clinical follow-up was 74 months (range 6–285 months), 11 patients were followed up for less than 1 year, a length of follow-up that may not be sufficient to fully assess the response of VS tumors to SRS. Because of the 28-year length of this study, outcomes analysis began before the use of validated QOL-scoring methods that might have enhanced the analysis of the outcomes among the patients in the current study.

Conclusions

It is estimated that most patients with VS in the United States are counseled to undergo initial microsurgical tumor removal if an intervention is eventually recommended.3,5,28 Because 8.8%–44% of patients with VS will have incomplete resection or tumor recurrence, such patients may undergo additional treatment to control tumor growth.2,3,12,24,25 We note that during our 28-year experience of managing VSs with SRS, 18% of our patients previously underwent 1 or more microsurgical resections. Gamma Knife SRS for recurrent VS was associated with a high rate of tumor control and a relatively low risk for additional complications. Radiosurgery can be successfully used to treat patients with recurrent VS tumors after complete resection and also patients whose tumors were incompletely removed.

References


### Table 6. Summary of studies on the outcomes of radiosurgery for recurrent VS after previous resection

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Patients</th>
<th>Median Tumor Vol in cm³ (range)</th>
<th>Median Dose (Gy)</th>
<th>Tumor Control Rate (%)</th>
<th>Deterioration in Trigeminal Nerve Function (%)</th>
<th>Deterioration in Facial Function (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pollock et al., 1998</td>
<td>78</td>
<td>2.8 (0.2–15.7)</td>
<td>15</td>
<td>94</td>
<td>12</td>
<td>21</td>
</tr>
<tr>
<td>Unger et al., 2002</td>
<td>50</td>
<td>3.4 (0.2–23.1)</td>
<td>13</td>
<td>96</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pollock &amp; Link, 2008</td>
<td>55</td>
<td>3.0 (0.1–18.1)</td>
<td>14</td>
<td>94</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Present study</td>
<td>173</td>
<td>2.7 (0.2–21.6)</td>
<td>13</td>
<td>94</td>
<td>5.8</td>
<td>4.1</td>
</tr>
</tbody>
</table>

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Outcomes of SRS for recurrent vestibular schwannoma


Disclosures

Dr. Lunsford is a consultant for AB Elekta and is on the Data Safety Monitoring Board and is a stockholder of AB Elekta.

Author Contributions

Conception and design: Kano, Huang. Acquisition of data: all authors. Analysis and interpretation of data: Kano, Huang. Drafting the article: Huang. Critically revising the article: Huang, Lunsford. Approved the final version of the manuscript on behalf of all authors: Kano. Statistical analysis: Kano, Huang. Administrative/technical/material support: Kano, Huang, Niranjian, Arai, Flickinger. Study supervision: Kano, Niranjian, Lunsford.

Supplemental Information

Previous Presentations

Portions of this work were presented as a talk at the 83rd Annual Meeting of the American Association of Neurological Surgeons, Washington, DC, May 2–6, 2015.

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