Multisession Stereotactic Radiosurgery for Vestibular Schwannomas: Single-Institution Experience With 383 Cases

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BACKGROUND: Single-session stereotactic radiosurgery (SRS) treatment of vestibular schwannomas results in excellent tumor control. It is not known whether functional outcomes can be improved by fractionating the treatment over multiple sessions.

OBJECTIVE: To examine tumor control and complication rates after multisession SRS.

METHODS: Three hundred eighty-three patients treated with SRS from 1999 to 2007 at Stanford University Medical Center were retrospectively reviewed. Ninety percent were treated with 18 Gy in 3 sessions, targeting a median tumor volume of 1.1 cm^3 (range, 0.02-19.8 cm^3).

RESULTS: During a median follow-up duration of 3.6 years (range, 1-10 years), 10 tumors required additional treatment, resulting in 3- and 5-year Kaplan-Meier tumor control rates of 99% and 96%, respectively. Five-year tumor control rate was 98% for tumors $<$ 3.4 cm^3. Neurofibromatosis type 2–associated tumors were associated with worse tumor control (P = .02). Of the 200 evaluable patients with pre-SRS serviceable hearing (Gardner-Robertson grade 1 and 2), the crude rate of serviceable hearing preservation was 76%. Smaller tumor volume was associated with hearing preservation (P = .001). There was no case of post-SRS facial weakness. Eight patients (2%) developed trigeminal dysfunction, half of which was transient.

CONCLUSION: Multisession SRS treatment of vestibular schwannomas results in an excellent rate of tumor control. The hearing, trigeminal nerve, and facial nerve function preservation rates reported here are promising.

KEY WORDS: Acoustic neuroma, CyberKnife, Fractionated radiotherapy, Hearing preservation, Radiosurgery, Toxicity, Vestibular schwannoma

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Vestibular schwannoma (VS; also known as acoustic neuroma) is a benign Schwann cell–derived tumor arising from the vestibular portion of the eighth cranial nerve. The overall incidence is 1 per 100 000, with approximately 3000 cases diagnosed per year in the United States. Likely because of the wide use of imaging, there is a rise in both the incidence and earlier detection of VS.[1] Common presenting symptoms include hearing loss, tinnitus, vertigo, and balance and gait disturbance. Tumor progression can lead to brainstem compression, cranial neuropathies, and hydrocephalus. Treatment options are observation, microsurgical resection, conventionally fractionated radiotherapy, and stereotactic radiosurgery (SRS).

ABBREVIATIONS: NF2, neurofibromatosis type 2; **SRS,** stereotactic radiosurgery; **VS,** vestibular schwannoma

Reports of excellent tumor control rates after single-session SRS[2-15] have established SRS as a good treatment option. Treatment-related cranial nerve complications after single-session SRS can include hearing loss, facial nerve palsy, and trigeminal dysfunction. In an effort to improve functional outcomes, the dose for single-fraction SRS has been reduced from previous doses of 16 to 20 Gy to the currently accepted dose of 12 to 13 Gy.[3,16-18] According to radiobiological principles, administration of radiation over multiple fractions may decrease the

risk of normal tissue toxicity compared with single-session treatments.[19] Our practice has been to reduce the dose radiobiologically through the use of multiple treatment sessions to lessen the risk of cranial nerve complications. Our preliminary experience showed comparable rates of tumor control with a suggestion of improved toxicity profile compared with single-session SRS.[20] Here, we present our tumor control and complication results of multisession SRS treatment of VS. To the best of our knowledge, this is the largest published series investigating this technique.

METHODS

Patient Characteristics

Patient data were obtained from Stanford University institutional review board–approved review of a prospectively maintained database of patients treated with SRS at Stanford University Medical Center. From 1999 to 2007, 474 patients with VSs were treated with SRS. Ninety-one patients had either no (n = 62) or < 1 year of imaging (n = 29) follow-up information. Three hundred eighty-three patients with > 1 year of follow-up data were analyzed. Facial nerve function, hearing, and tumor volume/mass effect were classified with the House-Brackman,[21] Gardner-Robertson,[22] and Koos scales,[23] respectively.

TABLE 1. Patient Characteristics

Parameter	
Age, median (range), y	54 (11-91)
Sex, n (%)	
Male	202 (53)
Female	181 (47)
Location, n (%)	
Right	195 (51)
Left	188 (49)
Prior surgery, n (%)	
Yes	41 (11)
No	342 (89)
Neurofibromatosis type II, n (%)	
Yes	15 (4)
No	368 (96)
Symptoms at presentation, n (%)	
Trigeminal paresthesia	28 (7)
Trigeminal neuralgia	9 (2)
House-Brackman facial nerve function grade	
I	350 (91)
II	7 (2)
III	9 (2)
IV	4 (1)
V	7 (2)
VI	6 (2)
Hemifacial spasm	8 (2)
Hearing loss	353 (92)
Tinnitus	188 (49)
Ataxia/disequilibrium	176 (46)

Patient demographic information is summarized in Table 1. One hundred eighty-one female patients (47%) and 202 male patients (53%) were treated at a median age of 54 years (range, 11-91 years). The tumor was located on the left in 188 patients (49%) and right in 195 patients (51%). Forty-one patients (11%) had received prior microsurgical resection. Fifteen patients (4%) had a diagnosis of neurofibromatosis type 2 (NF2). Before SRS, 324 patients (85%) presented with symptoms related to VS, most commonly hearing loss of some degree (92%). Additional symptoms at presentation included tinnitus (49%), ataxia/disequilibrium (46%), diminished sensation of the ipsilateral trigeminal nerve dermatome(s) (7%), trigeminal neuralgia (2%), facial weakness (9%),[21] and hemifacial spasm (2%).

Treatment Characteristics

Table 2 summarizes treatment characteristics. The tumor volume ranged from 0.02 to 19.8 cm^3 (median, 1.1 cm^3). Ninety percent of the patients (n = 368) were treated with 18 Gy in 3 sessions. Twenty-two patients (9.6%) were NF2 patients (n = 15) or were treated before 2000 (n = 7) when the treatment dose was decreased. In an attempt to decrease complication risks from SRS further, our total dose was decreased from 21 to 18 Gy in 3 sessions in early 2000. This was analogous to the dose de-escalation trend observed with single-session SRS, demonstrating decreased cranial nerve injury without compromising tumor control.[18,24] Those who had no useful hearing before SRS were treated with a single dose of 12 to 15 Gy (n = 13). The prescription isodose line ranged from 65% to 95% (median, 80%). Conformity index ranged from 1.03 to 3.39 (median, 1.41).

Radiosurgical Technique

The CyberKnife Robotic Radiosurgical System (Accuray, Sunnyvale, California) was used to deliver the radiosurgical treatments. A high-resolution thin-slice (1.25 mm) computed tomogram (CT) was obtained with a GE Light Speed 8i or 16i Scanner (Milwaukee, Wisconsin) after administration of 125 mL Omnipaque intravenous contrast (Iohexol, 350 mg I/mL; GE Health Care, Princeton, New Jersey). The stereotactic magnetic resonance imaging (MRI) scan was fused to the CT scan in all patients except those patients with contraindication for MRI scan or those few patients who refused MRI because of claustrophobia. Figure 1 shows a sample CT fusion with MRI SRS plan of a patient with a VS.

TABLE 2. Treatment Characteristics

Characteristics	
Tumor volume, median (range), cm^3	1.1 (0.02-19.8)
Koos classification, n (%)	
I	84 (22)
II	123 (32)
III	96 (25)
IV	80 (21)
Sessions, n/total dose, Gy, n (%)	
1/12-15	13 (0.3)
2/16	1 (0.03)
3/18	346 (90)
3/21	22 (9.64)
5/24	1 (0.03)

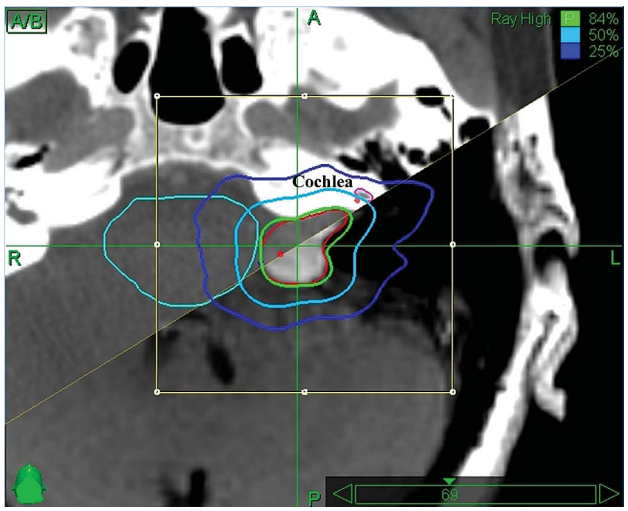

FIGURE 1. *Radiosurgery treatment plan of a left-sided vestibular schwannoma. The left cochlea is outlined as critical structure.*

The neurosurgeon, radiation oncologist, and radiation physicist performed tumor delineation, dose selection, and planning. Treatment plans were generated with the CyberKnife nonisocentric iterative inverse treatment planning software. Quality of treatment plans was assessed by evaluating target coverage, dose heterogeneity, and conformality. The conformity index (prescribed isodose volume/tumor volume encompassed by the prescription isodose line) and the modified conformity index ([prescribed isodose volume × tumor volume encompassed by the prescription isodose line]/tumor volume^2) were calculated.[25-28] Digitally reconstructed radiographs were synthesized computationally to allow real-time patient tracking throughout radiosurgery. Informed consent for treatment was obtained from all patients. Patients received 4 mg dexamethasone immediately after each treatment. For multisession treatments, the typical interfraction time interval was 24 hours.

Follow-up

Patients were followed up with MRI scan, audiogram, and clinic visits (including detailed neurological examination) every 6 months for the first 2 years. After the fourth post-SRS year, follow-up visits were conducted every 2 years.

Statistics

All statistical analyses were performed with Stat View, version 5.0.1 (SAS Institute Inc, Cary, North Carolina). The tumor control rate, defined as the absence of the need for additional surgical or radiosurgical intervention, was calculated with the Kaplan-Meier product-limit method.[29] Tumor/local control rate is defined as needing no additional treatment (ie, microsurgical resection, repeat SRS). Time to local failure was calculated from the date of SRS to the date of intervention; otherwise, patients were censored at the time of their last follow-up MRI scan. Preservation of serviceable hearing is defined as maintenance of Gardner-Robertson grade 1 to 2 hearing after SRS.

Log-rank test and univariate Cox proportional hazard regression were used to assess categorical and continuous variables, respectively. Univariate tests were not adjusted for multiple comparisons. Differences between the groups were assessed with the Fisher exact test and a 2-tailed *t* test for categorical and continuous data sets, respectively.

RESULTS

Tumor Control

Of the 383 patients, 10 tumors exhibited progressive growth requiring additional treatment (microsurgical resection [n = 9] and repeat SRS [n = 1]; Table 3). With a median follow-up duration of 3.6 years (range, 1-10 years), the 3- and 5-year Kaplan-Meier resection/repeat SRS-free tumor control rates were 99% and 96%, respectively (Figure 2). The median time from SRS to date of additional treatment was 3.4 years (range, 1.8-5.7 years). Complications from post-SRS microsurgical resection included new or worsening facial weakness (n = 3) and worsening trigeminal neuropathy (n = 2). All of these patients had no useful hearing before post-SRS microsurgical resection.

Multisession SRS was used in 370 patients; the 3- and 5-year Kaplan-Meier tumor control rates for patients treated with multisession SRS were 99% and 96%, respectively. On univariate analysis, tumor volume, as a continuous variable, was associated with a trend toward treatment failure ($P = .12$); the 3- and 5-year Kaplan-Meier tumor control rates for the largest quartile tumors (> 3.4 cm^3) were 99% and 89%, respectively, compared with 99% and 98% for the rest ($P = .07$). The NF2-associated tumors had worse tumor control compared with sporadic tumors. The 3- and 5-year Kaplan-Meier tumor control rates for sporadic vs NF-2–associated tumors were 99% and 96% compared with 93% and 84%, respectively ($P = .03$). Factors not associated with tumor control included location (right vs left; $P = .9$), prior surgery ($P = .34$), and conformity index ($P = .8$).

Hearing Preservation

Of the 383 patients, 96 (25%) had nonserviceable hearing (ie, Gardner-Robertson grade 3, 4, or 5) before SRS. Pretreatment

TABLE 3. Treatment Outcomes

Treatment Outcomes	
Tumor control rate, %	
3 year Kaplan-Meier tumor control rate	99
5 year Kaplan-Meier tumor control rate	96
Hearing preservation, %	
Crude rate	76
Koos I	83
Koos II, III, and IV	73
Other complications, n (%)	
Overall	19 (5)
Increased trigeminal paresthesia	6 (1.6)
Trigeminal neuralgia	2 (0.5)
New facial nerve paresis	0 (0)
Hemifacial spasm	8 (2)[a]
Hydrocephalus	4 (1)[a]

[a]One patient with both hemifacial spasm and hydrocephalus.

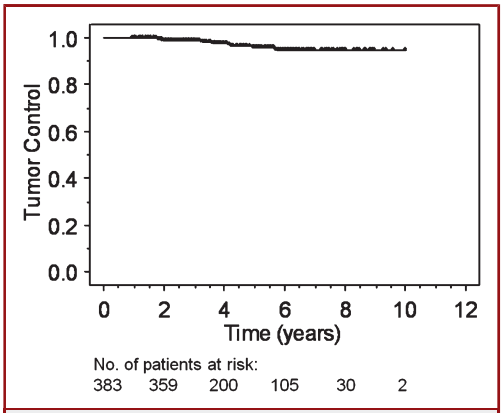

FIGURE 2. *Kaplan-Meier curve showing tumor control in 383 patients treated with radiosurgery for vestibular schwannoma.*

audiogram information was not available for 47 patients; 40 patients were missing posttreatment audiograms. Thus, 200 patients were evaluable for hearing outcome (198 patients treated with multisession SRS). During a median follow-up period of 3.0 years (range, 1.0-8.9 years), 151 patients maintained serviceable hearing, yielding a crude serviceable hearing preservation rate of 76%.

Smaller tumor volume was associated with a higher hearing preservation rate after SRS (P = .001, with tumor volume as a continuous variable). Tumors < 3 cm^3 had a serviceable hearing preservation rate of 80% compared with 59% for tumors ≥ 3 cm^3 (P = .009). There was a trend toward hearing preservation for younger age (P = .06) and intracanalicular tumors (P = .19); crude hearing preservation rates for Koos stage I compared with Koos stage II, III, and IV tumors were 83% vs 73%, respectively (P = .19).

Nonauditory Complications

There were 19 total cases of nonauditory complications. There were 8 trigeminal nerve complications (2%): 6 patients developed facial paresthesias, 2 of whose symptoms resolved completely. Two patients reported transient trigeminal neuralgia–like pain; both remain symptom free. Additionally, the degree of facial numbness in each of these patients was mild and not bothersome. There was no case (0%) of post-SRS facial weakness. Hemifacial spasm occurred in 8 patients (2%). The symptoms of 7 of 8 patients were self-limited and disappeared over time. Four patients (1%) required ventriculoperitoneal shunt placement; however, none had fourth ventricular obstruction as the cause of hydrocephalus. Larger tumor volume was associated with risk of nonauditory complications (P = .009, with tumor volume as a continuous variable), with largest quartile tumors (3.4 cm^3) having a complication rate of 9.6% compared with 3.5% for the rest (P = .03). Similarly, the rate of nonauditory complications for Koos stage IV tumors was 9.3% compared with 3.8% for Koos stage I, II, and III tumors (P = .05).

DISCUSSION

Since Dr Lars Leksell first reported the use of Gamma Knife for VS,[30] SRS has evolved considerably. High rates of tumor control have been reported with the Gamma Knife–based[2-4,7-11,13,15,31,32] and linear accelerator–based SRS,[6,33,34] conventionally fractionated stereotactic radiotherapy,[35-44] and proton beam irradiation.[45-47] Given the excellent rates of tumor control, more attention is being paid to functional outcomes such as hearing, trigeminal nerve, and facial nerve preservation. The radiobiological rationale behind fractionation is to minimize radiation-induced normal tissue complications. However, conventionally fractionated radiotherapy schedules, requiring 5 to 6 weeks of daily treatments, are inconvenient for some and impossible for those living distant from a radiation facility. What is not known is whether fractionating over 3 sessions would confer benefit over single-session treatments. Based on the radiobiological principals of fractionation and encouraged by our previously published experience of treating VSs using 21 Gy in 3 sessions resulting in a 77% hearing preservation rate,[48] our practice has been to treat VSs with multisession SRS.[20] We retrospectively reviewed the outcomes of these patients to determine the rates of tumor control, hearing preservation, and nonauditory complications.

First, multisession SRS results in excellent tumor control. The tumor control rates reported here (3- and 5-year Kaplan-Meier local control rates of 99% and 96%, respectively) are comparable to those of other large ($>$ 100 cases) series of single-session SRS for VS (90%-98%; summarized in Table 4) and series of conventionally fractionated radiotherapy (Table 5). The majority of patients in this series were treated with 18 Gy over 3 days with a frameless system. Analogous to the dose de-escalation trend observed with single-session SRS, our total dose was decreased starting in early 2000 from 21 to 18 Gy in 3 sessions; the rate of tumor control with the lower dose of 18 Gy is equivalent to our earlier experience of using 21 Gy in 3 sessions.[48] In our series, tumor volumes > 3.4 cm^3 and a diagnosis of NF2 were associated with decreased tumor control. These findings are in agreement with prior studies showing worse tumor control with larger tumors[2,4,13,49] or diagnosis of NF2.[50-52] In contrast, Pollock et al[53] and Arthurs et al[54] did not find a significant association between tumor control and diagnosis of NF2 or tumor size, respectively. Nine patients in the present series underwent delayed microsurgical resection after SRS failure. Of these, there were 3 cases of new or worsening facial weakness and 2 cases of worsening trigeminal neuropathy. Similar rates of complications were reported after delayed postmicrosurgical resection by other investigators.[55-59]

Next, we examined hearing preservation, an important functional outcome for patients with VS. The detrimental effect of radiation on auditory organs is well documented,[42,60-71] but the exact mechanism remains not well understood. Although the

TABLE 4. Literature Summary of Vestibular Schwannomas Treated With Single-Session Stereotactic Radiosurgery (n ≥ 100)[a]

Authors	Year	N	Radiosurgery Technique	Median Tumor Volume, cm^3	Median Radiation Dose at IDL, Gy	Local Control, %	Median Follow-up, mo	n	Serviceable Hearing Preservation, %	New Trigeminal Neuropathy, %	New Facial Neuropathy, %
Prasad et al[8]	2000	153	GK	Mean 2.7	13.2	92 crude	38	36	58 crude	4	2.3
Unger et al[14]	2002	100	GK	3.4	13	96 crude	76	29	55 crude	5	6
Rowe et al[9]	2003	212	GK	3.7	15	97 crude	34	49	75 crude	3.5	4.5
Litvack et al[32]	2003	134	GK	NR	12	98 crude	36	47	62 crude	5.8	2.3
Chung et al[7]	2005	187	GK	Mean 4.1	13	96.8 crude	31	26	60 crude	1.1	1.4
Wowra et al[10]	2005	111	GK	1.6	13	95 (6-y actuarial)	84	NR	NR	11.7	3
Hasegawa et al[4]	2005	301	GK	Mean 5.6	13	93 (5-y actuarial)	94	19	37 crude, 68 crude for dose < 13 Gy	2	1
Hempel et al[5]	2006	116	GK	1.6	13	96.7 crude	Mean 98	NR	NR	5.8	0
Friedman et al[6]	2006	295	LINAC	2.2	12.5	90 (5-y actuarial)	34	NR	NR	3.6 overall, 0.7 for dose < 12.5 Gy	4.4 overall, 0.7 for dose < 12.5 Gy
Chopra et al[11]	2007	216	GK	1.3	13	98.3 ± 1 (10-y actuarial)	68	106	57-74 crude	4.2 ± 1.6	0
Fukuoka et al[13]	2009	152	GK	2	12	94 (5-y actuarial)	>60	59	71 crude	2.6	0
Murphy et al[15]	2011	103	GK	Mean 1.95 ± 2.42	13	95.4 (3-y actuarial)	37.5	NR	NR	1	5

[a]GK, Gamma Knife; IDL, isodose line; LINAC, Linear accelerator; n, number of patients evaluated for serviceable hearing preservation; N, number of patients evaluated for local control; NR, not reported. Only the latest published data from each institution are shown.

TABLE 5. Literature Summary of Vestibular Schwannoma Treated With Conventionally Fractionated Radiotherapy[a]

Author	Year	N	Fractions, n	Median Tumor Volume, cm^3	Median Radiation Dose, Gy	Local Control, %	Median Follow-up, mo	n	Serviceable Hearing Preservation, %	New Trigeminal Neuropathy, %	New Facial Neuropathy, %
Andrews et al[35]	2001	56	25	2.8	50	97 crude	26	27	81 crude	7	2
Sawamura et al[38]	2003	101	23	1.9-cm diameter	48	91 (5-y actuarial)	45	36	71 (5-y actuarial)	4	0
Selch et al[41]	2004	48	30	2.5	54	100 crude	36	42	91 (5-y actuarial)	2.2	2.1
Chan et al[37]	2005	68	30	2.4	54	92 (5-y actuarial)	45	NR	NR	4	1
Maire et al[43]	2006	45	30	3.1-cm diameter	51	86 (15-y actuarial)	80	9	78 crude subjective hearing	0	0
Koh et al[40]	2007	60	25	4.9	50	96 (5-y actuarial)	31.9	22	77 crude	0	0
Horan et al[39]	2007	42	30	2-cm diameter	50	96.9 (2.5-y actuarial)	18.6	20	100 crude subjective hearing	0	3.2
Combs et al[42]	2010	165	30	2.8	57.6	96 (5-y actuarial)	75	94	78 (5-y actuarial)	3	4
Kopp et al[44]	2010	47	30	3.95	54	97.9 crude	32	33	79 crude	8.5	4.3

[a]n, number of patients evaluated for serviceable hearing preservation; N, number of patients evaluated for local control; NR, not reported. Only the latest published data from each institution are shown.

higher rate of hearing preservation reported in the more recent series[3,13,16,24,32,35,37,39-42,44,50,72-77] is encouraging, there is still a great need for improvement.

Two key treatment parameters in SRS are dose and fractionation. First, improved hearing preservation can be achieved with a lower radiation dose. A recent analysis of 45 published articles representing 4234 patients treated with Gamma Knife SRS showed an overall hearing preservation rate of 51%; the authors found dose to be a statistically significant factor associated with hearing preservation (hearing preservation rate of 60.5% at $\leq$ 13 Gy vs 50.4% at $>$ 13 Gy: $P = .001$).[63]

The effect of the second treatment parameter, fractionation, on hearing preservation is less clear. Although the 70% to 100% hearing preservation rate reported with conventionally fractionated radiotherapy (Table 5)[35-44] is promising, no prospective, randomized study has evaluated the effects of fractionation (with either conventional fractionation schedules or 2- to 5-session SRS) on hearing preservation. A retrospective study by Andrews et al[35] reported a 2.5-fold increase in hearing preservation in the conventionally fractionated radiotherapy group compared with SRS; however, studies from 2 other centers failed to confirm this finding.[42,78]

The serviceable hearing preservation rate of 76% in our series is superior to that of the compiled single-session SRS analysis reported by Yang et al[63] (overall hearing preservation rate of 51%; 60.5% hearing preservation with dose $\leq$ 13 Gy) and is in line with some single-institution series results (68%-77%).[4,9,11,13] A shortcoming of the present series is that we have chosen to report hearing outcomes using the Gardner-Robertson scale. This was done to allow comparison of our results with previously published results. However, the Gardner-Robertson scale provides a rather crude estimate of hearing and may overestimate functional hearing outcomes in some cases. Another shortcoming of our series is the number of patients for whom we do not have audiogram results. Thus, on the basis of currently available data, we cannot conclude that there is a hearing preservation outcome difference between single-session and multisession SRS. To this end, to properly examine the effects of fractionation on hearing preservation, a multi-institutionally generated, prospective collection of raw audiometric data is needed to further our understanding of hearing outcomes after SRS.

Favorable prognostic factors for hearing preservation in our series include younger age (trend) and smaller tumor volume. Additionally, in agreement with previous reports,[32,75,77,79] Koos stage I tumors (ie, intracanalicular tumors) had a trend toward improved hearing preservation compared with those with higher Koos classification.

Nonauditory complications such as facial nerve palsy and trigeminal dysfunction can be quite disabling. As with hearing preservation, reduction of the prescription dose has resulted in a decreased risk of cranial nerve V and VII injury.[3,80,81] Rates of new-onset permanent and transient facial weakness of 0% to 5% and 1% to 10%, respectively, have been reported after

TABLE 6. Literature Summary of Vestibular Schwannomas Treated With Multisession Stereotactic Radiosurgery[a]

Authors	Year	N	Sessions, n	Median Tumor Volume, cm^3	Median Radiation Dose at IDL, Gy	Local Control, %	Median Follow-up, mo	n	Serviceable Hearing Preservation, %	New Trigeminal Neuropathy, %	New Facial Neuropathy, %
Williams[83]	2003	80	5	1.6-cm mean diameter	25	100 crude	13	19	94 (2-y actuarial)	2.5	0
Meijer et al[78]	2003	80	5	2.5-cm diameter	25	94 (5-y actuarial)	Mean 33	55	61 (5-y actuarial)	2	3
Ishihara et al[84]	2004	38	3	4.7	18	94 crude	27	14	93 crude	0	0
Ju et al[85]	2008	21	3	5.4	18	100 crude	15	NR	76 crude	0	0
Current series	2011	383	3	1.1	18	96 (5-y actuarial)	43	200	76 crude	2	0

[a]IDL, isodose line; n, number of patients evaluated for serviceable hearing preservation; N, number of patients evaluated for local control; NR, not reported.

single-session SRS with 12 to 13 Gy.[2,3,5-7,9-11,13,15,16,31,74,82] Trigeminal dysfunction is another well-recognized complication of SRS, with rates ranging from 0.7 to 5%.[3-5,10,11,13,15,74] Although progress has been made, means to further reduce the risk of nonvestibular nerve complications are desired.

Previously published studies have produced conflicting results regarding the effect of fractionation. In a nonrandomized, retrospective study, 5-fraction SRS resulted in higher trigeminal nerve preservation compared with single-session SRS (98% vs 92%, respectively; $P = .05$).[78] In contrast, nonrandomized, retrospective comparison of SRS and conventionally fractionated RT resulted in no difference in trigeminal nerve outcomes.[35,42]

Tumor control and complication results of published series with single-session SRS, conventionally fractionated radiotherapy, and multisession SRS are summarized in Tables 4, 5, and 6, respectively. Our results of 0% facial nerve weakness and 2% trigeminal dysfunction (half of which was transient) are promising. However, the retrospective nature of our and others' series and the range of complication rates in published reports make direct comparison difficult.

With recent advances in imaging and planning algorithms and lessons learned from previously treated case series, SRS for VS has yielded higher rates of hearing preservation along with less toxicity while maintaining similar tumor control rates[2-4,6,7,10,11,13,15,16,20,32,53,54] compared with the earliest published reports of this technique. However, functional outcomes, particularly preservation of hearing, remain an area where further research may be beneficial. To this end, collaborative efforts to conduct multi-institutional, prospective studies are needed.

CONCLUSION

Multisession SRS with 18 Gy in 3 sessions results in excellent tumor control. The hearing preservation and nonauditory complication rates presented here are promising and comparable to those in other published series. Although hearing preservation rates are improved compared with earlier, higher-dose regimens, research is needed to further optimize the functional outcomes in our patients. Going forward, multi-institutional, prospective studies are desired to better evaluate SRS treatment outcomes.

Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

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COMMENTS

The Stanford group reports their comprehensive experience with CyberKnife multisession radiosurgery in the management of acoustic neuromas. Their data confirm that the evolution of this approach, as practiced by this team, has resulted in a safe and effective option for patients with acoustic neuromas. Stereotactic radiosurgery has increasingly become a preferred treatment for patients, many of whom are now diagnosed earlier in their clinical course. It is important that stereotactic radiosurgery deliver an effective (ie, tumor-controlling) dose to the target (conformality of planning) and high selectivity (dose reduction to adjacent critical structures). Dividing the dose delivery into multiple sessions appears to achieve this balance when CyberKnife technology is used. This report sets the standard for results expectation at centers of excellence using Cyberknife. No doubt such results have been achieved by the multidisciplinary cooperation of thoughtful providers who discuss options with the patients, obtain the necessary high-resolution imaging required, oversee careful planning of the dose, and ensure accurate delivery of the radiation over the course of multiple treatments. Most important, this report serves as an example of what is needed to understand the value of technology introduction that changes the paradigm of how we care for such tumors: a long-term commitment to accurate outcomes analysis.

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The group at Stanford reports a significant update to their series of patients treated with multifraction radiosurgery for vestibular schwannomas. It remains the largest series of its kind, and local control remains outstanding but is not the main focus of the updated experience. It is of substantial interest that, during prolonged follow-up, hearing preservation has remained quite good at 76% and other complications have remained low. Although this is laudable compared with many radiosurgery series, there remains a dearth of reliable, well-controlled comparative literature to enable clinicians and patients to know whether observation, surgery, single-fraction radiosurgery, or multifraction radiosurgery offers the most optimal outcome.

Frequent issues regarding the reporting of hearing preservation remain, including the difficulty of obtaining detailed audiology data. The authors are commended for a relatively complete set of scored audiometric data; however, once these data are obtained, there are a number of scales used in the literature to record hearing data, including the Gardner-Robertson scale in this article and the Word Recognition Score and Speech Discrimination Score. There is also recognition that

hearing preservation after surgery may be scored with less anticipation of progressive deterioration over time compared with the known progressive deficits possible with radiation. There have been reported rates of hearing preservation after surgery for very small tumors as high as 90%, which of course is a select series of intracanalicular tumors. It is well recognized that these series are not directly comparable to the radiosurgery series because the tumor and host features are substantially different. Despite the clear differences and limitations of each, the debate remains.

Unfortunately, despite this report's significant and well-collected additional data, it is unlikely that the substantial controversy concerning the optimal use of surgery, single-fraction stereotactic radiosurgery, and/or multifraction stereotactic radiosurgery will be resolved by even the prolonged follow-up in these ever-more-substantial institutional experiences. It is encouraging that the results and outcomes are excellent, but so are those with single-fraction radiosurgery and surgery. It is unclear whether this type of study will ever address the best that we are capable of or whether 1 method is more advantageous than another. Barring the unlikely advent of a randomized trial that intelligently integrates what is known regarding these benign tumors, the best option for clinicians is to offer alternatives and counsel by an appropriate group of experts who need to recognize both their biases and the facts as they exist. This contribution does add more facts on 1 available option.

When the literature is much cloudier than the biases, the importance of full reporting of such data to patients for consideration of their choice in the selection of therapy is paramount. Understanding the full risks and benefits of surgery, radiosurgery, and multifraction stereotactic radiosurgery is critical.

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The authors report a reasonably large cohort of patients with vestibular schwannomas treated in a uniform manner with a hypofractionated dose scheme of 18 Gy in 3 fractions. Excellent local control and hearing preservation rates at 3 years are reported with this approach, and clearly, this represents another option for patients with vestibular schwannomas in need of treatment. There are 2 cautionary issues to be noted with this series. First, the median tumor volume was relatively small for this cohort of patients (1.1 cm^3; range, 0.02-19.8 cm^3). Second, the median follow-up is 3.6 years. It is well recognized that local control and risks of complications increase with increasing tumor volume, so one is left to wonder whether many of these patients with the smaller tumors in this series would have had similarly excellent results with single-fraction radiosurgery. One aspect of this report that I find very interesting is the low risk of complications also seen with the larger-volume tumors reported with this hypofractionated approach, which leads one to consider approaching this subset of patients with this hypofractionated approach. The other issue relates to a relatively short median follow-up for this population of patients, a problem common to most reports in patients with this diagnosis treated with relatively recently available technologies. As the authors state, only through prospective randomized studies will the relative merits of single-fraction radiosurgery, hypofractionated radiosurgery, or fractionated stereotactic radiotherapy be discerned among different subgroups of patients with vestibular schwannomas, let alone randomized comparisons of some form of radiotherapy and microsurgery.

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