Stereotactic radiosurgery for vestibular schwannomas: average 10-year follow-up results focusing on long-term hearing preservation

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OBJECTIVE The aim of this study was to reappraise long-term treatment outcomes of stereotactic radiosurgery (SRS) for vestibular schwannomas (VSs). The authors used a database that included patients who underwent SRS with a unique dose-planning technique, i.e., partial tumor coverage designed to avoid excess irradiation of the facial and cochlear nerves, focusing on tumor control and hearing preservation. Clinical factors associated with post-SRS tumor control and long-term hearing preservation were also analyzed.

METHODS This institutional review board–approved, retrospective cohort study used the authors' prospectively accumulated database. Among 207 patients who underwent Gamma Knife SRS for VSs between 1990 and 2005, 183 (who were followed up for at least 36 post-SRS months) were studied. The median tumor volume was 2.0 cm³ (range 0.05–26.2 cm³). The median prescribed dose at the tumor periphery was 12.0 Gy (range 8.8–15.0 Gy; 12.0 Gy was used in 171 patients [93%]), whereas tumor portions facing the facial and cochlear nerves were irradiated with 10.0 Gy. As a result, 72%–99% of each tumor was irradiated with the prescribed dose. The mean cochlear doses ranged from 2.3 to 5.7 Gy (median 4.1 Gy).

RESULTS The median durations of imaging and audiometric follow-up were 114 months (interquartile range 73–144 months) and 59 months (interquartile range 33–109 months), respectively. Tumor shrinkage was documented in 110 (61%), no change in 48 (27%), and enlargement in the other 22 (12%) patients. A further procedure (FP) was required in 15 (8%) patients. Thus, the tumor growth control rate was 88% and the clinical control rate (i.e., no need for an FP) was 92%. The cumulative FP-free rates were 96%, 93%, and 87% at the 60th, 120th, and 180th post-SRS month, respectively. Six (3%) patients experienced facial pain, and 2 developed transient facial palsy. Serviceable hearing was defined as a pure tone audiogram result better than 50 dB. Among the 66 patients with serviceable hearing before SRS who were followed up, hearing acuity was preserved in 23 (35%). Actuarial serviceable hearing preservation rates were 49%, 24%, and 12% at the 60th, 120th, and 180th post-SRS month, respectively. On univariable analysis, only cystic-type tumor (HR 3.36, 95% CI 1.18–9.36; $p = 0.02$) was shown to have a significantly unfavorable association with FP. Multivariable analysis followed by univariable analysis revealed that higher age (≥ 65 years: HR 2.66, 95% CI 1.16–5.92; $p = 0.02$), larger tumor volume (≥ 8 cm³: HR 5.36, 95% CI 1.20–17.4; $p = 0.03$), and higher cochlear dose (mean cochlear dose > 4.2 Gy: HR 2.22, 95% CI 1.07–4.77; $p = 0.03$) were unfavorable factors for hearing preservation.

CONCLUSIONS Stereotactic radiosurgery achieved good long-term results in this series. Tumor control was acceptable, and there were few serious complications in patients with small- to medium-sized VSs. Unfortunately, hearing preservation was not satisfactory. However, the longer the observation period, the more important it becomes to compare post-SRS hearing decreases with the natural decline in untreated cases.

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KEY WORDS stereotactic radiosurgery; vestibular schwannoma; Gamma Knife; long-term; cochlea; hearing preservation

ABBREVIATIONS FP = further procedure; IQR = interquartile range; PTA = pure tone audiography; SDS = speech discrimination scores; SRS = stereotactic radiosurgery; VS = vestibular schwannoma.

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MANAGEMENT options for patients with vestibular schwannoma (VS) include observation, microsurgical resection, stereotactic radiosurgery (SRS) alone, and palliative surgery followed by SRS. Although debate continues as to which therapeutic option is optimal for small- to medium-sized VSs,³⁰ SRS is generally regarded as either a primary or a postoperative procedure for VSs with a diameter smaller than 3.0 cm.¹⁴ According to a database of the International Leksell Gamma Knife Society, as of the end of 2014, the number of patients with VS who have been treated with Gamma Knife SRS worldwide since 1991 exceeded 85,000. Although considerable numbers of retrospective studies have been published, accumulated knowledge as to post-SRS long-term results is not yet considered sufficient. In particular, post-SRS long-term hearing preservation is a problem that still requires discussion, as emphasized by Carlson et al.⁴

Our aim was to reappraise long-term treatment outcomes of SRS for VSs using our database, which includes patients who underwent SRS with our unique dose-planning technique, i.e., partial tumor coverage designed to avoid excess irradiation of the facial and cochlear nerves, focusing on tumor control and hearing preservation. We also analyzed clinical factors associated with post-SRS tumor control and long-term hearing preservation.

Methods

Study Design and Patient Selection

This institutional review board–approved, retrospective cohort study used our prospectively accumulated database, including 207 patients who underwent Gamma Knife SRS for VSs between 1990 and 2005. Among the 207 patients, 14 were treated at Tokyo Women's Medical University before June 1998; thereafter, 193 were treated at the Katsuta Hospital Mito GammaHouse. One coauthor (M.Y.) performed every SRS procedure in all 207 patients.

Among the 207 patients, we studied 183 (88%) in whom long-term outcomes (at least 36 post-SRS months) were available. Twenty-four patients were excluded; 20 of them were lost to follow-up before 36 months and 4 died due to unrelated diseases before the 36th post-SRS month. Characteristics of the 183 patients are summarized in Table 1. The median age was 56 years (range 11–80 years). The median tumor volume was 2.0 cm³ (range 0.05–26.2 cm³). Cystic-type tumor, defined as the cyst accounting for more than 60% of the total tumor volume, was observed in 39 (21%) patients. The Koos classification was used to evaluate tumor extension. Facial and cochlear nerve functions were graded using House-Brackmann grading¹¹ and pure tone audiography (PTA), respectively. Among the 183 patients, 47 (26%) already had facial nerve disturbances prior to SRS. Of these 47 patients, 29 were classified as having House-Brackmann Grade II function and 17 of the other 18 as having Grades III–V function. The latter 17 patients had previously undergone surgery. Before SRS, 74 patients (41%) patients had serviceable hearing on the tumor side.

Radiosurgical Technique

Before SRS, the treatment strategy was explained in detail to each patient, and at least 1 adult relative (by M.Y.).

TABLE 1. Baseline characteristics of 183 patients

Characteristic	Value*
Sex	
M	83 (45)
F	100 (55)
Age in yrs, median (range)	56 (11–80)
Neurofibromatosis Type II	10 (5)
Hx of sudden deafness	14 (8)
Side	
Rt	98 (54)
Lt	85 (46)
Prior surgical intervention	
Tumor removal	56 (31)
VP shunt	6 (3)
Pre-SRS growth	57 (31)
Tumor characteristic	
Cystic†	39 (21)
Solid	144 (79)
Tumor vol in cm ³ , median (range)	2.00 (0.05–26.2)
Koos classification, stage	
I	20 (11)
II	73 (40)
III	56 (31)
IV	34 (19)
Trigeminal neuropathy	6 (5)
House-Brackmann grade	
I	136 (74)
II	29 (16)
III	10 (5)
IV	4 (2)
V	4 (2)
Gardner-Robertson scale, dB‡	
≤30	40 (22)
>30 & ≤50	34 (19)
>50	109 (59)

Hx = history; VP = ventriculoperitoneal.

* All values are expressed as no. of patients (%) unless otherwise specified.

† Volume of cyst(s) exceeded 60% of the entire tumor volume.

‡ Scale described in Gardner and Robertson.⁶

Written informed consent was obtained from all patients. Radiosurgery was performed using a Gamma Unit model B (Elekta Instrument AB). Between 1988 and June 2003, SRS was performed using a Leksell GK model B unit (Elekta); thereafter, a Leksell GK model C unit (Elekta) was used. A Leksell model G stereotactic coordinate frame (Elekta Instrument AB) was applied while patients were under local anesthesia. For target coordinate determination and dose planning, stereotactic gadolinium-enhanced T1-weighted axial MR images with a slice thickness of 1 or 2 mm, depending on tumor size, were obtained. Also, 3D constructive interference in steady state axial MR images and CT axial images without contrast enhancement were routinely used to identify cranial nerves and bone structures.

Dose planning was performed using a Kula system (Elekta Instrument AB) before 1995 and, thereafter, using a Leksell GammaPlan system (Elekta Instrument AB). In 93% of all cases, the target volume was covered with a 60% isodose gradient to obtain 12.0 Gy at the tumor periphery. Figure 1 shows our actual treatment plan, describing our SRS policy. To avoid excess irradiation to the facial and cochlear nerves, the anterior part of the tumor was covered with a 10.0-Gy isodose gradient in patients whose pre-SRS facial and/or cochlear functions were maintained. Therefore, 72%–99% of the entire tumor volume was irradiated with 12.0 Gy. Table 2 summarizes radiosurgical parameters, i.e., radiosurgical doses, coverage, Paddick conformity²⁸ and gradient²⁹ indices, and cochlear doses. Cochlear doses were determined based on CT scan results, with the bone window level set according to previously reported methods,^{2,3,9,19,25,35} i.e., mean and maximum doses. Cochlear doses were available in 67 of 74 patients with serviceable hearing but were not available in the other 7 due to the outdated computer system used in our earliest cases.

Recommended follow-up includes these measures: 1) neurological examinations, particularly of fifth, seventh, eighth, and lower cranial nerve functions; 2) MR images, tumor size, enhancement changes, and ventricular size; and 3) PTA at 3-month intervals through the 18th post-SRS month, followed by 6-month intervals through the 36th post-SRS month and, thereafter, at 12-month intervals. MRI follow-up was performed at our facility in 100 (55%) of the 183 patients. In these 100 patients, tumor volume was estimated at every examination using the Leksell GammaPlan system. All PTA was performed in the referring hospitals.

In patients who underwent follow-up MRI at our facility, volume was measured using the GammaPlan system. However, in patients who underwent follow-up MRI at other facilities, the same volume measurement technique

In considerable numbers of patients, sequential MR images showed transient tumor expansion, which was regarded as tumor growth followed by shrinkage to the pre-SRS size or smaller within the 36th post-SRS month.²⁷ Clinical tumor control was defined as there being no need for further procedures (FPs), i.e., salvage surgical removal or re-SRS. The FP-free survival time was defined as the interval between SRS and the day of salvage surgery or re-SRS. An FP was judged to be necessary based not only on

Parameter	Value, Median (range)
Radiosurgical doses, Gy	
Min	12.0 (8.8–15.0)*
Mean†	14.8 (13.0–18.0)
Max	20.2 (15.1–30.0)
Coverage, %	92.0 (72.0–99.0)
Paddick conformity index	0.72 (0.14–0.88)
Paddick gradient index	3.30 (2.61–5.09)
Cochlear doses, Gy‡	
Mean	4.1 (2.3–5.7)
Max	5.6 (2.8–11.4)

‡ Cochlear doses were calculated in patients with pre-SRS useful hearing. Doses could not be determined due to an outdated dose-planning system used for the earliest 7 patients.

a tumor volume increase but also symptom progression. As to the end point, failures were regarded as events and any others as censored.

The PTA results were calculated using the following formula: $PTA = (a + 2b + c)/4$, where a, b, and c are threshold levels of 500 Hz, 1000 Hz, and 2000 Hz, respectively. According to the PTA classification of the Gardner-Robertson grading system,⁶ all patients were categorized into 3 groups: 1) ≤ 30 dB, 2) > 30 dB and ≤ 50 dB, and 3) > 50 dB. Serviceable hearing was defined as $PTA \leq 50$ dB. Hearing deterioration-free survival time was defined as the interval between SRS and the day on which a PTA decrease to ≤ 50 dB was documented. Regarding the end point, failures were regarded as events and any others as censored.

Statistical Analysis

All data were analyzed according to the intention-to-treat principle. For baseline variables, summary statistics were constructed using frequencies and proportions for categorical data; and medians, means, and standard deviations for continuous variables.

For time-to-event outcomes, the cumulative incidences of FPs and hearing deterioration were estimated using the Kaplan-Meier method.¹⁷ Also, to identify baseline and clinical variables associated with FPs and hearing deterioration, univariable and multivariable analyses were performed with Cox proportional hazards regression models. For continuous variables, cutoff values were determined using receiver operating characteristic curves. Statistical analyses were performed using JMP 10.0 (SAS Institute). All comparisons were planned, and the tests were 2-sided. A p value < 0.05 was considered a statistically significant difference.

Results

Tumor Control and FP-Free Interval

The median MRI follow-up period was 114 months (interquartile range [IQR] 73–144 months). During this period, tumor shrinkage was documented in 110 (61%) patients, no change in 48 (27%), and growth in the other 22 (12%). Therefore, the crude growth control rate was 88% in the present study. Actuarial tumor control rates were 93%, 87%, and 82% at the 60th, 120th, and 180th post-SRS month, respectively. Among the 22 patients with tumor enlargement, 9 were carefully observed and have received no treatment thus far because no neurological deterioration has occurred. Salvage treatment was needed in the remaining 13. In addition to these 13 patients, 2 underwent salvage treatment due to rapid growth followed by shrinkage or facial palsy. As a result, an FP was required in 15 (8%) patients, i.e., surgery in 9 (5%), surgery followed by repeat SRS in 1 (0.5%), and repeat SRS alone in 5 (3%). Thus, the crude clinical tumor control rate was 92%. Figure 2 shows the FP-free survival interval. Actuarial FP-free rates were 96%, 93%, and 87% at the 60th, 120th, and 180th post-SRS month, respectively. Among the 100 patients who were followed in our facility (in whom tumor volume size was calculated at every follow-up visit), transient tumor expansion was observed in 50 (50%).

FIG. 2. Actuarial clinical control rates after SRS. GKRS = Gamma Knife radiosurgery.

Table 3 demonstrates pre-SRS factors possibly related to the necessity of an FP. Among various clinical factors, only cystic-type tumor (HR 3.36, 95% CI 1.18–9.36; $p = 0.02$) was shown to be significantly unfavorable. Also, univariable analysis failed to show any correlation between the minimum dose and tumor control (≥ 14 Gy vs < 14 Gy: HR 5.93, 95% CI 0.93–21.5; $p = 0.06$).

Post-SRS Functional Outcomes

During the median clinical follow-up period of 114 months (IQR 73–144 months), trigeminal neuropathy occurred in 6 (3%) patients: at the 6th post-SRS month in 2 and at the 9th, 16th, 36th, and 96th post-SRS month in 1 each. Trigeminal neuropathy occurrence was associated with a tumor volume increase in 2 patients. Two of the 6 patients have received meticulous follow-up observation because of mild symptoms, and the other 4 were administered carbamazepine. However, the trigeminal neuropathy was transient in 5 patients. Only 1 patient experienced prolonged trigeminal neuropathy.

Two patients experienced transient facial nerve palsy at 18 and 91 months after SRS. In the patient with earlier fa-

TABLE 3. Pretreatment clinical factors and radiosurgical parameters possibly related to clinical tumor control

Variable	HR	95% CI	p Value
Age, ≥ 65 vs < 65 yrs	0.78	0.22–2.29	0.67
Pre-SRS growth, yes vs no	1.07	0.33–2.02	0.90
Prior removal, yes vs no	2.06	0.72–5.74	0.17
Tumor characteristic, cystic vs solid	3.36	1.18–9.36	0.02
Koos classification, Stage IV vs I–III	2.51	0.78–7.07	0.12
Tumor vol category, ≥ 8.0 vs < 8.0 cm ³	2.65	0.60–8.33	0.17
Mean tumor dose, ≥ 14.3 vs < 14.3 Gy	1.09	0.30–7.02	0.91
Paddick conformity index, ≥ 0.75 vs < 0.75 Gy	1.85	0.63–5.40	0.25
Coverage, < 0.79 vs ≥ 0.79	2.70	0.15–13.46	0.40

FIG. 3. Actuarial useful hearing preservation rates after SRS.

cial nerve palsy, the tumor volume increased from 0.9 cm³ at the time of SRS to 1.6 ml at the 18th post-SRS month. Steroid treatment was continued for 90 days; thereafter, facial nerve functions normalized and have not deteriorated to date. The tumor gradually shrank to 0.27 cm³ at the 158th post-SRS month. In the patient with facial palsy at the 91st post-SRS month, the tumor volume had decreased from 0.68 cm³ at the time of SRS to 0.29 cm³ at the 84th post-SRS month. At the 91st post-SRS month, the tumor volume was 0.61 cm³. This patient underwent a second SRS and received steroid therapy for 30 days. Thereafter, facial nerve functions normalized and have not deteriorated to date. The tumor gradually shrank to 0.23 cm³ at the 132nd post-SRS month. We retrospectively reviewed the dose planning for both of these patients. It was, however, impossible to determine whether the tumors had recurred from the portion irradiated with a lower dose. None of our patients experienced irradiation-related facial nerve disturbances.

Follow-up PTA was performed at a median post-SRS interval of 59 months (IQR 33–109 months). Among the 66 patients, serviceable hearing was maintained in 23 (35%). Figure 3 shows hearing deterioration–free survival. Actuarial rates of hearing preservation were 49%, 24%,

and 12% at the 60th, 120th, and 180th post-SRS month, respectively. Table 4 demonstrates pre-SRS clinical factors possibly related to hearing worsening. With multivariable analysis followed by univariable analysis, we found that more advanced age (≥ 65 years: HR 2.66, 95% CI 1.16–5.92; $p = 0.02$), larger tumor volume (≥ 8 cm³: HR 5.36, 95% CI 1.20–17.4; $p = 0.03$), and higher cochlear dose (mean cochlear dose > 4.2 Gy; this cutoff value was calculated using the receiver operating characteristic curve based on our own data set: HR 2.22, 95% CI 1.07–4.77; $p = 0.03$) were unfavorable factors for hearing preservation. The actuarial survival curves for hearing preservation, divided according to these 3 significant factors, are shown in Fig. 4.

Post-SRS Hydrocephalus

Six patients had undergone ventriculoperitoneal shunt placement before SRS. After SRS, ventriculoperitoneal shunt placement for symptomatic hydrocephalus was required in 11 patients at a median post-SRS interval of 33 months (range 5 to 85 months).

Discussion

As detailed in the description of our dose-planning technique above, the tumor was not totally covered with a prescribed peripheral dose in most of our cases. The crude tumor growth and clinical control rates (88% and 92%, respectively) and actuarial FP-free fractions of 96%, 93%, and 87% at the 60th, 120th, and 180th post-SRS month, respectively, were nonetheless considered to be favorable compared with previously reported results, ranging from 82% to 98%, as listed in Table 5.^{4,7,8,19,23,24,26} Although various definitions of tumor growth were applied in prior studies, favorable tumor control rates did not differ widely among the previously reported results. Therefore, Gamma Knife SRS with the recently applied low-dose protocol, approximately 12 Gy at the tumor margin for small- to medium-sized VSs, is expected to achieve good long-term tumor control, similar to that reported with shorter-term follow-up results.

Our dose-planning technique, which avoids excess ir-

TABLE 4. Pretreatment clinical factors and radiosurgical parameters possibly related to hearing deterioration

Variable	Univariable Analysis			Multivariable Analysis		
	HR	95% CI	p Value	HR	95% CI	p Value
Age, ≥ 65 vs < 65 yrs	3.42	1.61–6.99	0.002	2.66	1.16–5.92	0.02
Neurofibromatosis Type II	1.45	0.23–4.92	0.63			
Pre-SRS growth, yes vs no	1.14	0.48–2.41	0.75			
Hx of sudden deafness	0.69	0.21–1.76	0.47			
PTA level > 30 vs ≤ 30 dB	1.69	0.87–3.33	0.11			
Prior removal, yes vs no	1.36	0.32–3.82	0.63			
Tumor characteristic, cystic vs solid	1.18	0.56–2.32	0.65			
Koos class, Stage IV vs I–III	1.84	0.74–4.03	0.18			
Tumor vol, ≥ 8.0 vs < 8.0 cm ³	4.75	1.10–14.45	0.04	5.36	1.20–17.4	0.03
Paddick gradient index, ≥ 3.21 vs < 3.21	0.56	0.29–1.11	0.10			
Mean cochlear dose, > 4.2 vs ≤ 4.2 Gy	2.54	1.28–5.23	0.01	2.22	1.07–4.77	0.03

Age: ≥ 65 years vs < 65 years **Tumor Volume: $\geq 8 \text{ cm}^3$ vs $< 8 \text{ cm}^3$** **Cochlear dose: $> 4.2 \text{ Gy}$ vs $\leq 4.2 \text{ Gy}$**

FIG. 4. Actuarial hearing preservation rates after SRS according to 3 significant clinical factors. There were significant differences between 2-sided data in age ($p = 0.0004$), tumor volume ($p = 0.01$), and cochlear dose ($p = 0.01$).

radiation to the facial and cochlear nerves, was shown to preserve facial nerve function; no patients experienced additional permanent deterioration of facial nerve function after SRS. However, regarding hearing preservation, our results—a crude preservation rate of 35% and cumulative

rates of 49%, 24%, and 12% at the 60th, 120th, and 180th post-SRS month, respectively—were not as favorable as we had hoped. As for hearing preservation, previous reports showed that the longer the follow-up period was, the lower the preservation rate tended to be. The longer follow-up periods might have resulted in lower hearing preservation rates in the time ranges examined; reported hearing preservation rates were 34% at the 8th post-SRS year and 23% at the 10th post-SRS year.^{4,8}

As for clinical factors contributing to loss of serviceable hearing, there were statistically significant correlations between hearing deterioration and more advanced age, larger tumor volume, and higher cochlear dose. Although there are a few reports on fractionated stereotactic radiation therapy of VSs,^{1,20} these studies did not have sufficiently long posttreatment observation periods. We must carefully monitor further long-term treatment results to determine whether our protocol achieves better outcomes than those of single-session SRS.

Notably, we obtained no evidence that tumor progression occurred at the anterior part of an intracranial tumor, i.e., the lower coverage area. Rather, in all cases with tumor progression, the cisternal portion enlarged in all directions, i.e., medial, posterior, anterior, upward, and/or downward. Thus, it was difficult to determine the part(s) that had actually enlarged.

Tumor Control and Larger Tumor Volume

Among various pre-SRS clinical factors and radiosurgical parameters, a larger tumor volume is generally recognized as being significantly unfavorable for tumor growth control, as shown by both our present results and previous reports.^{4,5,8,10,19,23,24,26,32} However, 2 groups, Liu et al.²³ and Milligan et al.,²⁶ reported good long-term tumor control rates (82%–97%) after SRS for relatively large VSs, i.e., mean tumor volumes were 10.8 cm^3 in the former and 9.4 cm^3 in the latter study.

Hearing Outcomes and Cochlear Dose

Reported hearing preservation rates after SRS varied markedly (from 28% to 79%) in long-term follow-up studies.^{4,8,23,24,27,34} According to most previous reports, a larger tumor volume including Koos stage and an older patient age were shown to be unfavorable predictive factors for hearing preservation.^{5,9,33,36} However, Yang et al.³⁶ performed a systematic review of SRS for VS and concluded that large tumors and older patient ages do not appear to be associated with any increased risk for hearing loss after SRS compared with younger patients and/or those with smaller tumors. Although Franzin et al.⁵ and Hasegawa et al.⁹ reported that the only positive predictive factor for hearing preservation was having Gardner-Robertson Class I hearing prior to treatment, hearing preservation rates in our study did not differ significantly between patients in Gardner-Robertson Classes I and II. Franzin et al.⁵ reported that patients with presenting symptoms other than hearing loss have better hearing outcomes. Further studies are needed to clarify the impacts of these factors.

In addition to the aforementioned factors, cochlear dose was recently recognized as likely to be related to a de-

TABLE 5. Summary of published reports of postradiosurgical long-term follow-up for VSs

Authors & Year	No. of Pts	Tumor Vol, cm ³	FU, Mos	Tumor Control, %	Freedom of FP, %	Rate of Hearing Preservation, %
Kondziolka et al., 2004	157	—	Median 109.2	98	98	47
Lunsford et al., 2005	252	Mean 2.5	≥10 yrs in 252 pts	—	97 (10 yrs)	79 (6 yrs)
Liu et al., 2006	74	Mean 10.8	Median 68	96	97	79
Carlson et al., 2013	44	Mean 1.7	Median 112	97	97	23 (10 yrs)
Milligan et al., 2012	22	Median 9.4	Median 66	82 (5 yrs)	82	28 (5 yrs)
Hasegawa et al., 2013	440	Median 2.8	Median 150	92	92	34 (8 yrs)
Present study, 2016	183	Median 2.0	Median 114	88	92	35

FU = follow-up; pts = patients; — = no data.

crease in hearing acuity after SRS.^{2,3,9,16,21,22,25,33–35} Several in vivo studies have examined radiation effects on the cochlea, as previously reported. Hulcrantz et al. stated that in a pregnant mouse model, scanning electron microscopy revealed that both inner and outer hair cells were missing in large numbers of exposed animals, irrespective of the irradiation dose, and that remaining hair cells, as well as pillar cells, showed signs of degeneration.¹³ Furthermore, a dose-dependent, time-related damage pattern was demonstrated in the cochlea, with pathological changes affecting both outer and inner hair cells.¹² These studies support the idea that hair cells are the most vulnerable structures in the cochlea. Thus, radiation-induced damage to the cochlea might account for the difference in hearing decrease between the 2 sides. Therefore, lowering of cochlear doses has been discussed in relation to better hearing preservation rates after SRS. The cutoff points applied in our study, which were mainly between 3 Gy and 4 Gy, are presented in Table 6.

Comparison of Hearing Preservation With Natural Hearing Decrease

Our crude hearing preservation rate was 35%, and the actuarial useful hearing preservation rates were 49%, 24%, and 12% at the 5th, 10th, and 15th post-SRS year, respectively. These outcomes are clearly not satisfactory. However, according to previous reports describing long-term outcomes, the longer the follow-up period was, the lower the hearing preservation rate tended to be. When considering the clinical significance of these results, it is important to compare hearing preservation with the course of untreated natural hearing decreases. Previous reports have shown that hearing tends to decrease even in untreated cases. Régis et al. reported that the wait-and-see policy exposes the patient to elevated risks of tumor growth and hearing deterioration, with the probability of long-term functional hearing preservation being very poor (40% at 4 years).³¹ Hajioff et al. stated that hearing deteriorated substantially even in patients whose tumors did not grow, but did so faster when tumors grew significantly.⁷

Weaknesses of the Current Study

The major weakness of this study might be that a retrospective cohort was used and, therefore, the clinical factors are obviously heterogeneous. However, we believe that these heterogeneous patient groups rather closely reflect

actual clinical practice. In fact, as physicians, we often encounter inhomogeneous clinical factors. The more homogeneous a patient group is, the more scientific the study becomes. However, the results obtained are applicable only to a select patient group, making them ever farther from actual clinical practice.

Another possible weakness of this study might be that the only audiometric follow-up method was PTA, i.e., speech discrimination scores (SDS) were not obtained. Thus, our results for hearing preservation may have been overestimated. In fact, patient hearing functions should be estimated using both PTA and SDS. Jacob et al.¹⁵ reported that SDS correlated significantly with time to nonserviceable hearing. We are now collecting SDS after SRS for VS. One Japanese study has already shown a correlation between PTA and SDS in patients with VS. Based on results for 607 ears, Kimitsuki et al.¹⁸ demonstrated that all patients with VS who had PTA ≤ 50 dB maintained ≥ 50% of hearing acuity according to SDS. Thus, PTA ≤ 50 dB in VS cases might be regarded as correlating with ≥ 50% hearing acuity according to SDS.

Conclusions

Stereotactic radiosurgery achieved good long-term results in our series. Tumor control was acceptable, and there were few serious complications in patients with small- to medium-sized VSs. Unfortunately, hearing preservation

TABLE 6. Published reports on cochlear doses

Authors & Year	Cochlear Factors Affecting Hearing Outcomes
Linskey et al., 2003	Intratemporal inner ear
Massager et al., 2007	Mean cochlear dose
Lasak et al., 2008	Mean cochlear dose ≥4.75 Gy
Timmer et al., 2009	Max cochlear dose
Tamura et al., 2009	Modiolus 4.0 Gy
Kano et al., 2009	Mean cochlear dose >4.2 Gy
Wackym et al., 2010	Max cochlear dose
Hasegawa et al., 2011	Mean cochlear dose
Brown et al., 2011	Mean % vol of cochlea >5.3 Gy
Baschnagel et al., 2013	Mean cochlear dose 3.0 Gy, % vol ≥3.0 Gy
Present study, 2016	Mean cochlear dose >4.2 Gy

was not satisfactory. However, the longer the observation period is, the more important it becomes to compare post-SRS hearing decreases with the natural decline in hearing acuity in untreated cases.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Conception and design: M Yamamoto, Watanabe, Kawabe. Acquisition of data: M Yamamoto, Kawabe, Koiso. Analysis and interpretation of data: M Yamamoto, Watanabe. Drafting the article: Watanabe. Critically revising the article: M Yamamoto, Watanabe, T Yamamoto. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: M Yamamoto. Statistical analysis: Watanabe. Administrative/technical/material support: M Yamamoto. Study supervision: M Yamamoto, T Yamamoto, Matsumura, Kasuya.

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