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ORIGINAL ARTICLE - TUMOR - SCHWANNOMA

Long-term follow-up results of stereotactic radiosurgery for vestibular schwannomas larger than 8 cc

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Abstract

Background Accumulated stereotactic radiosurgery (SRS) experience for large vestibular schwannomas (VSs) based on over 5 years of follow-up are as yet insufficient, and chronological volume changes have not been documented.

Method Among 402 patients treated between 1990 and 2015, tumor volumes exceeded 8 cc in 30 patients. We studied 19 patients with follow-up for more than 36 post-SRS months or until an event. Median tumor volume was 11.5 cc (range; 8.0 to 30.6). The target volume was basically covered with 12.0 Gy.

Results The median magnetic resonance imaging and clinical follow-up periods were both 98 months (range 49 to 204). Tumor shrinkage was documented in 13 patients (72%), no change in 2 (11%), and growth in the other 3 (17%). Therefore, the crude growth control rate was 83%. All three patients with tumor enlargement needed salvage treatment. Thus, the crude clinical control rate was 84%. Actuarial further procedure-free rates were 91%, 83% and 76%, at the 60th, 120th, and 180th post-SRS month. Among six patients followed chronologically, transient tumor expansion was observed in three (43%) and two cystic VSs showed rapid tumor growth. Transient trigeminal neuropathy occurred in two patients (11%). No patients experienced facial nerve palsy. None of the six patients with useful hearing pre-SRS maintained serviceable hearing. Ventricular-peritoneal shunt placement was required in three patients.

Conclusions Long-term tumor control with SRS was moderately acceptable in large VSs. In terms of functional outcome, trigeminal neuropathies and facial palsies were rare. However, hearing preservation remains a challenge. In the long term, chronological tumor volumes were generally decreased after SRS. However, caution is required regarding rapid increases in tumor size, especially for cystic type VSs. Further studies are needed to optimize clinical positioning of SRS for large VSs.

Keywords Stereotactic radiosurgery · Large vestibular schwannoma · Long term · Volume change · Rapid cystic enlargement

This article is part of the Topical Collection on Tumor - Schwannoma

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Introduction

In modern management of patients with relatively small vestibular schwannomas (VSs), stereotactic radiosurgery (SRS) is widely applied as either the primary or a post-operative procedure [6, 11]. According to the International Leksell Gamma Knife Society database, covering the 1991–2016 period, the number of VS patients who underwent gamma knife (GK) SRS worldwide reached 100,610. It is widely believed that patients with relatively large VSs are unfavorable candidates for SRS as the initial treatment due to the potential risk of further brain stem compression arising from transient swelling [4]. There is no question that surgical removal is the gold standard for relatively large VSs, i.e., those with a maximum diameter > 3 cm. However, some patients have contraindications for general anesthesia due to advanced age or systemic disorders or refuse to undergo surgery due to anxieties about

craniotomy. Although several reports on SRS for relatively large VSs have described long-term tumor control rates of 84–94% and reasonable neurological function [4, 15, 19, 26, 28], accumulated SRS experiences with large VSs based on longer follow-up periods are as yet insufficient. In particular, most previous studies were based on relatively short observation periods, i.e., the average was 5 years of post-SRS follow-up. Furthermore, although these previous studies showed crude incidences of tumor control, chronological long-term post-SRS changes in VS volumes were not examined.

We have already reported our post-SRS results, in detail, based on our cohort of patients undergoing SRS for VS [25]. Herein, we performed a subset study to reappraise long-term treatment outcomes after GK SRS for patients with VSs > 8.0 cc, i.e., tumor growth control based on chronological tumor volume changes, clinical control, and functional outcomes.

Methods

Study design and patient selection

This institutional review board (IRB)-approved, retrospective cohort study used our prospectively accumulated database including 402 patients who underwent gamma knife SRS for VSs between 1990 and 2015 (Tokyo Women's Medical University IRB No. 2071). Among these 402 patients, 14 were treated at Tokyo Women's Medical University before June, 1998, and, thereafter, the other 388 were treated at the Katsuta Hospital Mito GammaHouse. One (M.Y.) of the co-authors performed every SRS procedure in all 402 patients.

In 30 of the 402 patients, tumor volume exceeded 8 cc, which is nearly equivalent to a tumor diameter of 2.5 cm. Among these 30 patients, we studied 19 in whom long-term imaging follow-up (more than 36 post-SRS months or an event) results were available; 11 were excluded, i.e., 9 lost to follow-up before 36 months and 2 who died due to unrelated diseases before the 36th post-SRS month (described in Fig. 1).

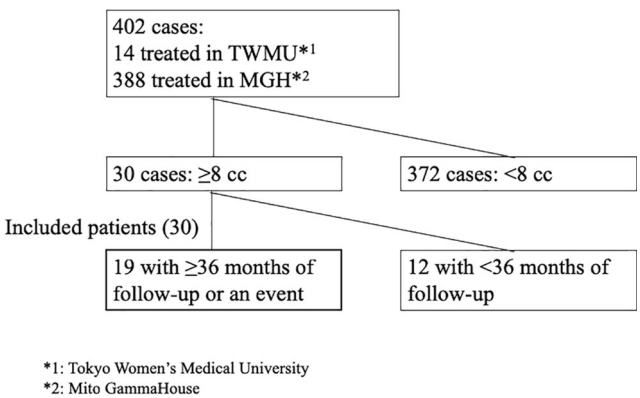

Fig. 1 Patients included: 18 cases were followed up for ≥ 36 months or until an event

In these 9 patents, the reason for exclusion was lack of data since the time of SRS in 4, while the latest follow-up ranged from 6.7 to 20.8 months in the remaining 5 patients.

Characteristics of the 19 patients are summarized in Table 1. Median age was 71 years with a range of 29 to 91 years. The median tumor volume was 11.5 cc, ranging from 8.0 to 30.6 cc. Cystic-type tumor, defined as the cyst accounting for more than 60% of the entire tumor volume, was observed in 11 patients (58%). The Koos classification was used to evaluate tumor extension [14]. Functions of the facial and cochlear nerves were graded using the House-Brackmann system [9] or pure tone audiography (PTA), respectively. Among the 19 patients, 4 (21%) already had facial nerve disturbances prior to SRS. Of these four patients, the House-Brackmann grade was II and III in two each. The latter two patients had previously undergone surgery. Seven patients (37%) had serviceable hearing on the tumor side before SRS.

Table 1 Baseline characteristics

Characteristic	Value
Sex	
Female, *n* (%)	11 (58)
Age median [range], years	71 [29–91]
Side	
Right, (%)	7 (37)
Left, (%)	12 (63)
Prior surgical intervention	
Tumor removal, *n* (%)	9 (47)
VP shunt, *n* (%)	3 (16)
Tumor volume median [range], cc	11.5 [8.0–30.6]
Pre-SRS growth	8 (42)
Tumor characteristic	
Cystic,[a] *n* (%)	11 (58)
Solid, *n* (%)	8 (42)
Koos classification	
Stage I, (%)	0
Stage II, (%)	0
Stage III, (%)	2 (11)
Stage IV, (%)	17 (89)
Trigeminal neuropathy, *n* (%)	3 (16)
House-Brackmann grade[9]	
Grade I, *n* (%)	15 (79)
Grade II, *n* (%)	2 (11)
Grade III–V, *n* (%)	2 (11)
Pure tone audiogram	
≤ 30 dB, *n* (%)	4 (21)
> 30 dB and ≤ 50 dB, *n* (%)	3 (16)
> 50 dB, *n* (%)	12 (63)

V-P ventricular-peritoneal, *SRS* stereotactic radiosurgery

[a] Volume of cyst(s) exceeded 60% of the entire tumor volume

Two patients underwent ventriculo-peritoneal shunt placement before SRS. Pre-SRS, surgical removal had been performed in nine patients.

Radiosurgical technique

Our radiosurgical technique was detailed in a prior report and, therefore, is not described herein [25]. The treatment strategy was fully explained to each patient, and at least one adult relative, by one of the co-authors (M.Y.) before SRS. Because all patients were referred to our institution by their primary neurosurgeons, the decision to undergo SRS had already been made when they first came to our institute. However, the first author (M.Y.) still explained the obvious advantages of surgical removal as compared with SRS to each patient. Nevertheless, the 19 patients refused surgery. Written informed consent was obtained from all patients. Radiosurgery was performed using a Gamma Unit Model B (Elekta Instrument AB, Stockholm, Sweden). Before June of 2003, SRS was performed using a Leksell GK Model B unit (1988–2003, Elekta); a Leksell GK Model C unit (2003–2014, Elekta); and, thereafter, a Lesell GK Model Perfection unit (Elekta). A Leksell Model G stereotactic coordinate frame (Elekta Instrument AB) was applied under local anesthesia. For target coordinate determination and dose-planning, stereotactic gadolinium-enhanced T1-weighted axial magnetic resonance (MR) images with a slice thickness of 1 or 2 mm, depending on tumor size, were obtained. Also, three-dimensional constructive interference in steady-state axial MR images and computed tomographic (CT) axial images without contrast enhancement were routinely used for identifying cranial nerves and bone structures.

Dose planning was performed using a Leksell GammaPlan system (Elekta Instrument AB). Table 2 summarizes radiosurgical parameters, i.e., radiosurgical doses, coverage, and Paddick's conformity index [21], as well as the gradient [22] indices. In 18 (95%) of the 19 procedures, the target volume was basically covered with a 60% isodose gradient to obtain 12.0 Gy at the tumor periphery. 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, 88–98% of the entire tumor volume was irradiated with 12.0 Gy. A 10 Gy dose was selected for the one other procedure.

Table 2 Radiosurgical parameters

Parameter	Value median (range)
Radiosurgical doses, Gy	
Minimum[a]	12.0 (10.0–12.0)
Mean	14.7 (13.0–17.0)
Maximum	20.3 (20.0–24.8)
Coverage, %	93.0 (88.0–99.0)
Paddick's conformity index	0.81 (0.72–0.85)
Paddick's Gradient index	2.98 (2.80–3.25)

[a] A minimum (marginal) dose of 12.0 Gy was selected for 17 patients (94%)

Post-SRS follow-up

Recommended follow-up includes (1) neurological findings, particularly, Vth, VIIth, VIIIth 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. MR imaging follow-up was performed at our facility in 8 (42%) of the 19 patients. In these 8 patients, tumor volume was determined at every examination using the Leksell GammaPlan system. Therefore, the event of transient tumor expansion was applied to numerically estimate tumor volume changes, allowing accurate evaluation in these seven patients. PTA was performed by the referring otolaryngologist.

Clinical outcomes

Regarding tumor growth control, because the slice level and angle were not consistent among all MR imaging examinations and, whether using a computer system or not, 25%/10% measurement errors were anticipated for an estimated volume/diameter, volume ≥ 125% or diameter ≥ 110% relative to the pre-treatment baseline was regarded as "growth," volume ≤ 75% and/or diameter ≤ 90% as "shrinkage," and all other observations as "no change." As for transient tumor expansion, this event was defined as tumor growth followed by shrinkage to the pre-SRS size or smaller within 36 post-SRS months [20]. In addition to the crude outcome, tumor change trends were estimated employing a line graph. Clinical tumor control was defined as there being no necessity for further procedures (FP), 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/re-SRS or the day of the latest follow-up. FP was judged to be necessary based not only on a tumor volume increase but also symptom progression. As to the endpoint, failures were regarded as events, any others as censored.

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. Hearing levels were graded into three groups: (1) ≤ 30 dB, (2) > 30 dB and ≤ 50 dB, and (3) > 50 dB. Serviceable hearing was defined as PTA ≤ 50 dB. Hearing deterioration-free survival time was defined as the interval between SRS and the day that a PTA decrease to ≤ 50 dB was documented or the

day of the latest follow-up. As to the endpoint, failures were regarded as events, any others as censored.

Statistical analysis

For baseline variables, summary statistics were constructed employing frequencies and proportions for categorical data, medians, means, and standard deviations for continuous variables. For time-to-event outcomes, the cumulative incidences of FP were estimated using the Kaplan-Meier method [12]. Statistical analyses were performed using JMP 10.0 (SAS Institute, Cary, NC).

Results

Tumor control and FP-free interval

We recently experienced a patient of advanced age a 30.55 cc VS, successfully treated with SRS, as illustrated in Fig. 2.

The median MR imaging follow-up period was 98 months (range; 49–204, IQR; 60–145). Table 3 shows post-SRS clinical and neuroimaging results. Table 4 lists all 19 patients. During this observational period, tumor shrinkage was documented in 13 patients (72%), no change in 2 (11%) and growth in the other 3 (17%) but imaging data were unavailable for one. Therefore, the crude growth control rate was 83% in the

Table 3 Post-radiosurgical clinical and neuro-imaging results

Outcome	Value
Follow-up period, median (range)	
Clinical follow-up[a], months	97.7 (49.2–204.4)
Imaging follow-up[a], months	97.7 (49.2–204.4)
Tumor volume, value (%)	
Shrinkage	13 (72)
No change	2 (11)
Growth	3 (17)
Further procedure	3 (16)
Surgery	2 (11)
Surgery followed by SRS	1 (5)
Transient tumor expansion[b]	3 (43)
Trigeminal neuropathy[c]	2(11)
Facial palsy	0
Loss of useful hearing[d]	7 (100)
Hydrocephalus[e]	3 (19)

[a] One patient experienced the last MRI at 9 post-SRS months and FP at 11.2 post-SRS months and was thus censored before 36 post-SRS months

[b] Transient tumor expansion was estimated in 7 patients followed-up for more than 36 post-SRS months without FP

[c] Trigeminal neuropathies, experienced by 2 patients, were both transient

[d] Loss of useful hearing occurred in 7 patients with useful pre-SRS hearing

[e] Post-SRS hydrocephalus was diagnosed in 16 patients without V-P shunting before SRS

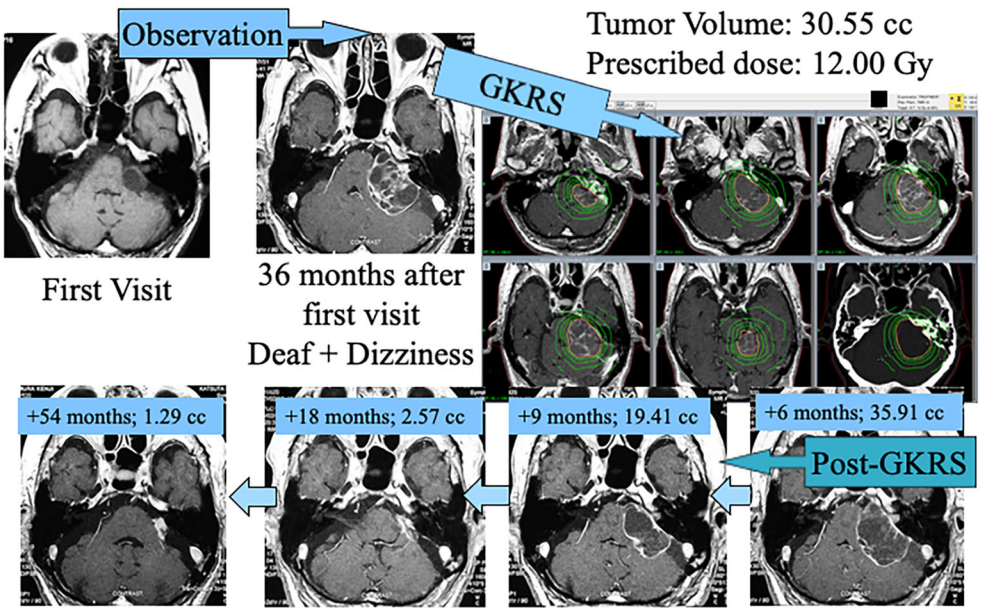

Fig. 2 Clinical course of an illustrative case. A 91-year-old male patient with a large VS. MR imaging showed a small VS in the left cerebropontine angle cistern. The referring neurosurgeon selected observation because of the patient's advanced age. He had no neurological symptoms other than left-sided deafness. Three years later, he experienced dizziness caused by extreme enlargement of the tumor with multi-lobulated cysts. He underwent GK SRS. The tumor (volume; 30.55 cc) was irradiated with a marginal dose of 12 Gy (maximum dose; 20 Gy). The brainstem received a mean of 6.7 ± 2.8 Gy (range 2.1 to15.0). Brainstem volumes receiving > 5/10 Gy were 13.79 cc/3.16 cc. The cystic tumor transiently expanded to 35.91 cc at the 6th post-GKS month, followed by remarkable shrinkage to 19.41 cc, 7.09 cc, 3.57 cc, 1.78 cc, 1.76 cc, and 1.49, at the 9th, 12th, 24th (the last examination at data cut-off), 36th, and 54th (the most recent examination) post-SRS months, respectively. He remains healthy, to date. GKRS; gamma knife radiosurgery

Table 4 List of 19 patients with large VSs studied

Age	Sex	Tumor volume	Tumor nature	Koos classification	Trigeminal neuropathy	H-B grade	PTA	Marginal Dose	Imaging F/U	Clinical F/U	Tumor control	Further procedure(s)
45	F	15.5	Solid	IV	(−)	III	Deaf	10	98.3	61.3	Increase	(+)
74	F	9.4	Cystic	IV	(+)	I	Deaf	12	98.0	98.0	Shrinkage	(−)
76	F	8.0	Cystic	III	(−)	I	15.0	12	84.0	101.7	Shrinkage	(−)
71	F	11.2	Cystic	IV	(−)	I	Deaf	12	122.8	122.8	Shrinkage	(−)
75	F	13.4	Cystic	IV	(−)	I	Deaf	12	145.0	166.6	Shrinkage	(−)
77	M	12.6	Cystic	IV	(−)	I	81.3	12	66.7	66.7	Shrinkage	(−)
53	F	11.5	Solid	IV	(−)	I	50.0	12	203.8	203.8	Shrinkage	(−)
50	F	8.9	Solid	III	(−)	1	22.0	12	204.4	204.4	Shrinkage	(−)
59	M	12.8	Cystic	IV	(−)	I	Deaf	12	9.0	11.2	Increase	(+)
76	F	12.0	Cystic	IV	(+)	I	Deaf	12	84.2	85.1	Increase	(+)
72	M	12.0	Cystic	IV	(−)	I	Deaf	12	156.2	156.2	Shrinkage	(−)
42	M	8.1	Cystic	IV	(−)	I	Useful	12	191.9	191.9	Shrinkage	(−)
37	F	9.7	Solid	IV	(−)	I	38.8	12	97.7	97.7	Shrinkage	(−)
52	M	26.2	Solid	IV	(−)	III	Deaf	12	51.0	51.0	No change	(−)
79	M	9.1	Cystic	IV	(−)	I	Deaf	12	49.2	49.2	NE	(−)
73	F	8.1	Solid	IV	(−)	II	30.0	12	107.7	107.7	Shrinkage	(−)
62	F	10.3	Solid	IV	(−)	II	Deaf	12	59.9	62.7	Shrinkage	(−)
29	M	11.6	Solid	IV	(+)	I	8.8	12	60.4	60.4	No change	(−)
91	M	30.6	Cystic	IV	(−)	I	Deaf	12	56.0	56.0	Shrinkage	(−)

VSs vestibular schwannomas, *H-B grade* House-Brackmann grade, *PTA* pure tone audiogram, *F/U* follow-up period, *F* female, *M* male, *NE* not examined

present study. Salvage surgery was needed in all three patients with tumor enlargement, one of whom underwent re-SRS (5%). Thus, the crude clinical control rate was 84%. Figure 3 shows the FP-free survival interval. Actuarial FP-free rates were 91%, 83%, and 76%, respectively, at the 60th, 120th, and 180th post-SRS month. In the eight patients who were followed in our faculty, tumor volume was determined at every follow-up MR examination. One patient was judged as showing treatment failure before the 36th post-SRS month. Among the remaining seven patients, transient tumor expansion was observed in three. Tumor volume changes are illustrated in Fig. 4. Tumor volumes decreased chronologically until the last follow-up in five patients. However, two cystic VSs showed rapid tumor growth.

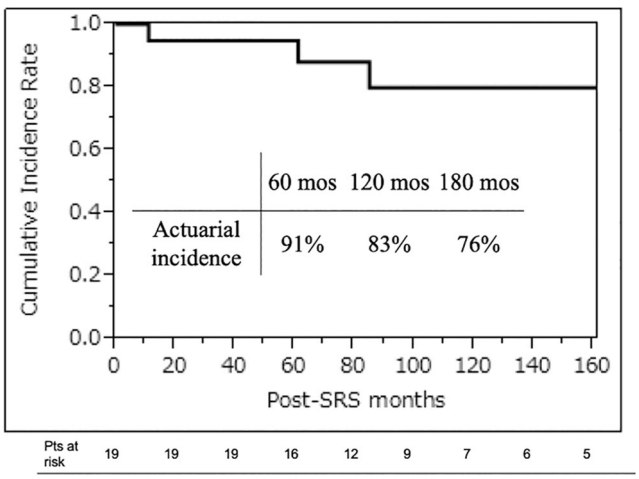

Fig. 3 Actuarial clinical control rates after stereotactic radiosurgery (SRS). Pts; patients

Post-SRS functional outcomes

During the median clinical follow-up period of 98 months (range; 49–204, IQR; 60–145), trigeminal neuropathy occurred in 2 patients (11%), at the 6th and 95th post-SRS month. Trigeminal neuropathy was associated with tumor volume increase in one patient, while in the other, the treated tumor showed remarkable shrinkage. The former patient was meticulously followed with no medication, symptoms were mild, and the other was administered carbamazepine. In both patients, the trigeminal neuropathy was transient. No patients experienced facial nerve palsy. Follow-up PTA was performed at a median post-SRS interval of 24 months (range; 6 to 199). None of six patients with useful hearing pre-SRS maintained serviceable hearing, though in one patient with pre-SRS useful hearing, no post-SRS PTA results were available. Ventricular-peritoneal shunt placement for symptomatic hydrocephalus

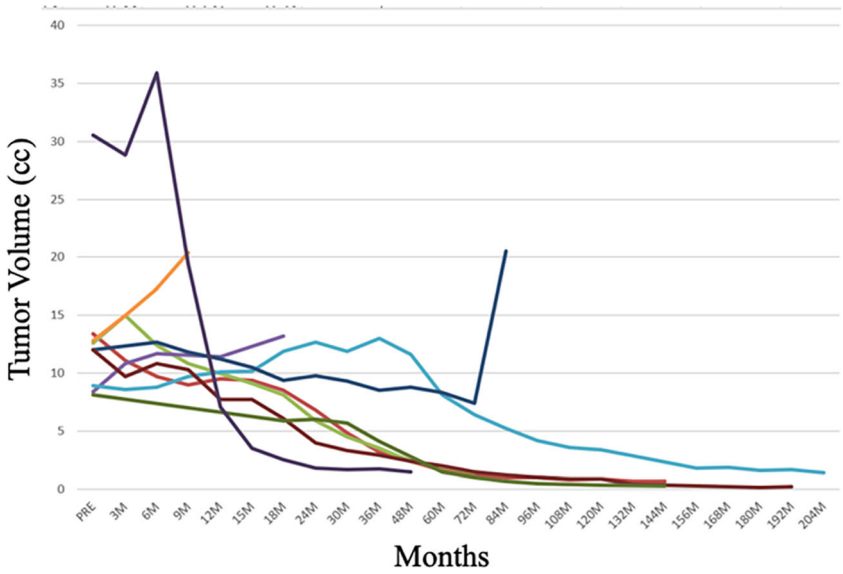

Fig. 4 Chronological tumor volume changes determined using Leksell GammaPlan system (Elekta, AB, Stockholm)

was required in three patients at respective median post-SRS intervals of 33, 36, and 85 months.

Discussion

Tumor control and chronological volume change after SRS for large VSs

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 demonstrated by previous studies [3, 7, 8, 13, 16, 17, 19, 23, 25]. Huang et al. reported that tumor volume ≥ 15 cc is a significant factor predicting poor tumor control following GK radiosurgery [10]. Table 5 shows previous studies on SRS for large VSs, yielded by a PubMed search. Median or mean follow-up periods in these reports ranged from 30 to 97 months. In general, longer follow-up was meaningful for analyzing SRS results. During our median follow-up period of 98 months (range 49–204), which is the longest period among reported series, our crude tumor growth and clinical control rates were 83% and 84%, and the actuarial FP-free fractions were 91%, 83%, and 76% at the 60th, 120th, and 180th post-SRS month. Also, prior studies showed relatively favorable post-SRS results, i.e., rates of tumor control and clinical control ranged from 82% to 98% and 80% to 96%, respectively. Even when our unique dosing technique, intentional partial coverage, was applied, post-SRS results were essentially the same as those of other reported studies. Nevertheless, as we foresaw, these control rates were slightly lower than the post-SRS results obtained for small-to-medium sized VSs [3, 7, 8, 13, 16, 17, 19, 23, 25]. Mandl et al. stated that morbidity rates were increased in patients with large VSs treated with stereotactic radiotherapy or SRS, as compared to the results of published series on smaller-sized VSs [18]. Chung et al. concluded that radiosurgery plays an important role, i.e., satisfactory results can be expected, in managing relatively large VSs for carefully selected patients [4]. Also, Williams et al. concluded that GK SRS has efficacy for some large VSs and represents a reasonable treatment option for carefully selected patients [26]. Bailo et al. concluded that GK SRS can be considered a safe and effective option in certain patients who are not good candidates for surgery [2]. Nowadays, SRS for large VSs should not be the first treatment choice, though some VS patients may benefit from SRS, as illustrated by the case described above.

Information on post-SRS chronological volume changes has been limited, especially transient tumor expansion and subsequent shrinkage. Furthermore, no study has shown long-term chronological volume changes in large VSs after SRS. Our study demonstrated that, in relatively large VSs, gradual tumor shrinkage was generally observable through the 10th post-SRS year and, thereafter, no size changes were detected. However, continuous volume reduction was observed even after the 10th post-SRS year in one case (Fig. 4). In contrast, two tumors showed rapid growth and salvage surgery was required. Both tumors were of the cystic type. Teo et al. stated that cystic tumors tended to require cerebrospinal fluid diversion after interventions [24]. Clinicians should be aware of the possibility of rapid tumor growth of large cystic VSs and follow such patients closely. In clinical situations, rapid growth may also be temporary, such that surgical intervention timing is a very important issue. Further studies are needed to clarify the mechanism underlying this phenomenon.

Table 5 Summary of published reports of post-radiosurgical follow-up for large vestibular schwannomas

Author and year	Number	Tumor volume (cc)	Dose (Gy)	F/U periods [a](months)	Tumor control (%)	Freedom of FP (%)	Hydrocephalus (%)	Hearing preservation (%)	Facial palsy (%)	Trigeminal neuropathy (%)
Inoue 2005	18	Mean 15.2	Median 12	≥72	93	94	–	80	0	–
Mandl et al. 2010	29	Mean 15.3	13 or 5 × 5 Fr	Median 36	84	96	17	38	44	36
Chung et al. 2010	21	Mean 17.3	Mean 12	Mean 66	91	90	10	–	0	0
Langenberg et al. 2011	33	Mean 8.8	Mean 13	Median 30	88	88	6	58	6	9
Milligan et al.2012	22	Median 9.4	Median 12	Median 66	82 (5 years)	89	14	30	14	14
Williams et al. 2013	24	Median 9.5	Median 11–12	Median 83	89	89	9	25	33	13
Casentini et al. 2015	33	Median 9.4	Median 18*[3]	Median 48	94	94	6	88	0	3
Teo et al. 2016	30	Median S 9.2/C 8.9	18 × 3 Fr	Median 97	S77 C88	83	3	38	12	–
Bailo et al.2016	59	Mean 6.0	Median 13	Mean 79	98	92	19	31	5	7
Huang et al. 2017	35	Median 14.8	Median 11	Median 48	86	80	6*[2]	33	0	0
Our study 2019	19	Median 11.5	Median 12	Median 98	83	84	19	0	0	11

VS vestibular schwannoma, *F/U* follow-up, *Growth* growth control rate, *FP* further procedure, *Fr* fractions *S* solid, *C* cystic, *pts* patients

[a] F/U periods are the clinical follow-up periods

[b] Two patients (5.7%) who developed a symptomatic cyst underwent placement of a cystoperitoneal shunt rather than a V-P shunt

[c] In this study, SRS was performed in multiple sessions and delivered at 15 Gy in 3 fractions, 16 Gy in 4 fractions, or 17.5 Gy in 5 fractions

Functional outcomes of SRS for large VSs

Post-SRS facial and trigeminal neuropathy reportedly occurred in 0 to 44% and 0 to 36% of patients, respectively, as shown in Table 5. None of our patients experienced facial nerve palsy. Trigeminal neuropathy occurred in two patients (11%) but was transient. As noted in our previous report, our dose-planning technique, avoiding excess irradiation to the facial and cochlear nerves, showed preservation of facial nerve function. However, regarding long-term preservation of cochlear function, our results were not as favorable as we had hoped.

According to previous reports, hearing preservation rates ranged from 25 to 88%. The longer the follow-up period was, the lower the preservation rate tended to be [3]. This might be an unavoidable irradiation effect exerted on normal neural tissues. There are a few reports on fractionated SRT for VSs [18, 24]. However, in these studies, post-treatment observation periods were not long enough to draw final conclusions. We must carefully monitor further long-term treatment results to determine whether our protocol achieves better outcomes than those of single-session SRS. Hearing preservation remains an important clinical challenge. Clinical positioning of SRS for VS between surgical interventions is based mainly on small-to-medium-sized VS [27]. The discussion of SRS, especially for large VSs, should focus on choosing between SRS and microsurgery. Hearing is an important aspect of this discussion.

Weaknesses of our study

The major weakness of this study might be that it was retrospective with the clinical factors being unavoidably heterogeneous. However, we feel that the heterogeneity of our patient group well reflects actual clinical practice situations. In fact, clinicians often encounter inhomogeneous patient factors. The more homogeneous a patient group, the more scientific the study results are. However, those results pertain only to a highly select patient group, making them ever less applicable to actual practice. The next weakness of this study might be its small sample size. Only patients with a large VS, an uncommon diagnosis, are referred to us for SRS. In addition, although regular neuroimaging follow-up is crucial, not all follow-up procedures were performed in our facility. Another weakness of this study might be lack of vertigo or dizziness data. Vertigo and a "sense of imbalance" affecting patients treated with SRS for vestibular schwannoma are symptoms inconsistently impacted by either RS or surgery. These relatively uncommon complaints, along with tinnitus, have not been adequately studied in this patient population, despite their significant impact on quality of life [5].

Long-term follow up itself is another potential study weakness. It is true that the longer the follow-up, the less uniformity a study shows as technologies advance. In general, technological advancements improve treatment conformity. The

conformity index is a tool used for estimating treatment conformity. In brain metastasis, the lower the conformity index, the lower the reported local progression rates were [1], contrary to the majority opinion that dose planning with a higher conformity index results in good post-SRS results. However, for VSs, further studies are needed to clarify the relationship between conformity and outcome. Another possible weakness of this study is the lack of meticulous neuro-otologic examinations before and after SRS. Only PTA was available in all cases. Ideally, hearing functions should be evaluated using both PTA and the Speech Discrimination Score.

In conclusion, the tumor control rate obtained with SRS was acceptable in patients with VSs > 8 cc, though post-SRS results were slightly inferior to those of small-to-medium-sized VSs. Functional outcomes, i.e., incidences of facial and trigeminal neuropathies, were acceptably low. However, long-term, useful hearing preservation remains a clinical challenge. Further studies are needed to optimize clinical positioning of SRS for large VSs.

Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (name of institute/committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

For this type of study, formal consent is not required.

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