Hearing Preservation in Stereotactic Radiosurgery for Vestibular Schwannoma

Anthony M. Tolisano¹ Jacob B. Hunter¹

¹Department of Otolaryngology, University of Texas Southwestern Medical Center, Dallas, Texas, United States

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Address for correspondence Jacob B. Hunter, MD, Department of Otolaryngology, University of Texas Southwestern Medical Center, G7-218, 2001 Inwood Road, Dallas, TX 75235, United States (e-mail: jacob.b.hunter@gmail.com).

Abstract

Keywords

- ▶ vestibular schwannoma
- ▶ acoustic nerve
- ▶ hearing
- ▶ radiosurgery

Despite no universally accepted definition of hearing preservation following vestibular schwannoma (VS) treatment, numerous variables have been identified as possible factors that may affect hearing outcomes following radiotherapy. Age, pretreatment hearing, radiation dose, tumor location and size, length of follow-up, fractionation, and timing of radiation have all been explored, among other variables, as factors related to hearing outcomes following radiation. These variables and associated hearing outcomes will be explored in detail, summarizing the literature to date to improve patient counseling for those patients who present with serviceable hearing and are considering their VS management options.

Introduction

Vestibular schwannomas (VSs) represent 90% of retrocochlear tumors, and hearing loss is the most common presenting symptom in the majority of patients.^{1,2} With the establishment of radiotherapy as a safe and effective treatment for VS, long-term hearing outcomes are now being reported. Over the years, the percentage of VS patients presenting with serviceable hearing has steadily increased as a result of earlier tumor detection secondary to widespread availability of magnetic resonance imaging (MRI). For instance, while only 21% of patients presented with a speech discrimination score of at least 70% in the 1970s, this increased to 57% in 2008.³

The American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) and the Gardner-Robertson (GR) hearing classification scales are the two most commonly applied measures used to quantify hearing outcomes in VS patients.^{4,5} Both define serviceable hearing as having at least a 50% speech discrimination score and at most a 50-dB pure-tone average (PTA). Nevertheless, there is no universally accepted definition for serviceable hearing. A strict definition for hearing preservation could include maintenance of pretreatment pure-tone thresholds or speech discrimination score, while a more functional definition could include maintaining serviceable hearing (▶ Fig. 1).

There are numerous factors to consider when determining an appropriate management plan for VS patients, of which pretreatment hearing status is one key variable. In general, patients have the option of pursuing observation, microsurgery, or radiation. Stereotactic radiosurgery (SRS), delivered as a single fraction, and fractionated stereotactic radiotherapy (SRT), delivered as multiple fractions over several sessions, are two modalities widely used for radiotherapy in VS patients. Although radiation is a nonsurgical management plan (▶ Fig. 2), it is not without risk, including continued VS growth, dizziness, hearing loss, and trigeminal neuropathy. Despite no universally accepted definition of hearing preservation following VS treatment, numerous variables have been identified as possible factors that may affect hearing outcomes following radiotherapy (▶ Fig. 3). Broadly, these include patient-specific variables, tumor characteristics, radiation dose, timing, and delivery method. Herein, we summarize the hearing outcomes and related variables following radiation therapy for VS.

Etiology of Hearing Loss after Radiotherapy

Accelerated hearing loss following radiation to the head and neck is a well-known phenomenon that predates the development of current stereotactic methods for treating tumors

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Fig. 1 Seventy-one-year-old man presented with excellent word recognition scores bilaterally (A) and a right-sided vestibular schwannoma (B) who underwent Gamma Knife radiosurgery with 13 Gy to the tumor margin, maintaining serviceable hearing (C) with noted tumor shrinkage (D) at the last follow-up 26.8 months following treatment.

of the internal auditory canal (IAC). In fact, up to one-third of patients treated with radiation to the head and neck have been shown to develop late sensorineural hearing loss.⁶ Animal models and temporal bone specimens obtained from postirradiated patients suggest that the stria vascularis, outer hair cells, and spiral ganglion cells are most likely affected by radiation.⁷ Mechanistically, (1) direct damage to cochlear primary sensory neurons and (2) injury of the cochlear and auditory nerve fibers have been suggested as causes for hearing loss after radiotherapy.^{8,9} Radiation may obliterate microvessels leading to intimal thickening, vessel narrowing, or axonal damage, although the exact mechanism is still unknown.¹⁰ Some have also argued that radiogenic tumor swelling may result in nerve conduction block as a result of compression forces,¹¹ whereas others have failed to demonstrate this relationship.¹²

In neurofibromatosis type-2 patients, metabolic neurotoxins have been found in higher concentrations and are associated with more rapid hearing decline, suggesting that hearing loss

may result from accumulation of noxious intralabyrinthine toxins secondary to cochlear aperture obstruction.¹³ Other groups have found significantly better pretreatment PTAs in patients with limited cochlear hyperintensities on MRI as compared with those patients with extensive hyperintensities.^{14,15} While it is unclear which mechanism is most important, it is likely that radiotherapy-induced hearing loss is a combination of the aforementioned etiologies.

Patient Demographics and Pretreatment Hearing Levels

Certain patient-specific factors may portend a worse hearing outcome following treatment of VS with radiotherapy. Multiple studies have suggested that advanced age results in poorer hearing outcomes,^{16–20} while others have found no such relationship.²¹ Tamura and colleagues assessed age as a continuous variable and found no significant association between maintaining the same GR class on univariate and

Fig. 2 Gamma Knife radiosurgery plan for a left-sided vestibular schwannoma. The 50% isodose line is outlined in yellow and the cochlea is outlined in orange.

multivariate analyses.¹⁰ However, Yang and colleagues performed a literature review and found a trend toward improved hearing preservation rates in those patients older than 65 years of age, albeit not significantly different.²²

In patients treated with radiation for head and neck tumors other than VS, two studies have reported higher hearing loss rates in males as compared with females.^{18,19} Otitis media and the presence of a cerebrospinal fluid shunt in children have been associated with increased risk of hearing loss, as well.^{16,18,19}

By and large, patients with better pretreatment hearing tend to have a higher probability for retaining serviceable hearing postirradiation. Jacob and colleagues, in a review of 59 VS patients treated with SRS, reported 1-, 2-, and 3-year estimated serviceable hearing rates of 96, 83, and 57%, respectively.⁷ On multivariate analysis, they found that there was a 2.4-fold increased risk in developing nonserviceable hearing for every 10 dB increase in pretreatment PTA.⁷ Mousavi and colleagues subclassified 166 VS patients with GR Class 1 hearing into those with no subjective hearing loss (Class 1-A) and those with subjective hearing loss (Class 1-B). The latter group was further separated into whether the PTA in the affected ear was within 10 dB as compared with the contralateral ear (Class 1-B1 and Class 1-B2, respectively).²³ Following SRS, with a median follow-up of 65 months,

serviceable hearing was preserved in Class 1-A, Class 1-B1, and Class 1-B2 patients in 98, 73, and 33%, respectively, and was significantly associated with the pretreatment GR class on multivariate analysis after controlling for age and gender.²³

Similarly, in a cohort of 77 VS patients, Kano and colleagues found that 71.4% of patients retained serviceable hearing with a median follow-up of 20 months after SRS and that GR Class 1 hearing before treatment was the only predictor for maintaining serviceable hearing.⁸ In a separate analysis, Hasegawa and colleagues reported on the outcomes of 117 VS patients with serviceable hearing treated with SRS utilizing a tumor margin dose of 12 Gy. Kaplan-Meier analysis calculated 3-, 5-, and 8-year serviceable hearing preservation rates of 55, 43, and 34%, respectively.²⁴ They found that those patients with pretreatment GR Class 1 hearing had significantly better hearing preservation rates as compared with those patients with GR Class 2 hearing.²⁴ While Kano et al and Hasegawa et al do not comment directly on why pretreatment hearing leads to better hearing preservation rates, Jacob and colleagues, noting that hearing loss following radiation of other cerebellopontine angle tumors, such as petroclival meningiomas, is a rare event, believe that there are “more significant tumor-related factors beyond cochlear dose that ultimately dictate hearing outcomes.”⁷

Fig. 3 Seventy-two-year-old woman presented with excellent word recognition scores bilaterally (A) and a right-sided vestibular schwannoma (B) who underwent Gamma Knife radiosurgery with 13 Gy to the tumor margin, losing serviceable hearing in the right ear (C) with slight tumor enlargement (D) at the last follow-up 59.1 months following treatment.

Nevertheless, other groups have found that pretreatment hearing has no association with hearing preservation. Horiba and colleagues reviewed 49 VS patients with serviceable hearing prior to treatment and found that GR class was not significantly associated with hearing preservation.²⁵ Despite this study, the body of evidence suggests that the better the patients' hearing is at diagnosis, the more likely they will preserve serviceable hearing following treatment.

Effect of Radiation Dose

Logically, higher doses of radiation would be expected to result in poorer hearing outcomes. This has been substantiated in numerous studies by evaluating tumor margin dose and the dose delivered to the cochlea. Unfortunately, there is a high degree of variability when experts are asked to determine tumor margins. In one study, a 231% variance in the degree of three-dimensional conformity for tumors

was found among 16 different radiosurgery teams.²⁶ Moreover, inconsistency of reporting cochlear dosing in the literature often precludes comparisons across studies. Reporting only the mean cochlear dose as an average over the entire cochlear volume fails to account for higher doses delivered to more susceptible portions of the cochlea.^{27,28} For this reason, reporting both mean and maximum doses to the cochlea is advisable. Jacob and colleagues noted that many studies utilize the modiolar point dose as the reference cochlear dose.⁷ However, recognizing that MRI-based modalities are more common, the authors found that there is significantly greater agreement between observers when using computed tomography (CT) to determine the modiolar point dose as compared with MRI, and "therefore assigning a cochlear dose value based on a single pixel is problematic."⁷

A recent systematic review of the literature regarding hearing preservation following SRS for VS found an overall serviceable hearing preservation rate of 51% in patients

treated with a mean radiation dose of 14.2 ± 2.4 Gy (median follow-up: 35 months).²² It was found that patients who received ≤ 13 Gy to the tumor margin had significantly greater hearing preservation rates when compared with patients who received >13 Gy.²² In a separate analysis, Foote and colleagues noted that a tumor margin dose <12 Gy was hearing protective.²⁹

With respect to cochlear dosing, Paek and colleagues showed that there was a significantly larger maximum cochlear nucleus dose in patients who lost useful hearing as compared with those patients whose hearing was preserved (11.1 ± 3.9 vs. 6.9 ± 4.5 Gy).³⁰ Hasegawa and colleagues found a significant difference in hearing preservation rates when 6 Gy was used as a cutoff for the dose delivered to the cochlea. In their retrospective analysis, 3-year hearing preservation rates for those patients with a cochlear dose <6 and ≥ 6 Gy were 63 and 31%, respectively, while 5-year hearing preservation rates were 50 and 15%, respectively.²⁴ Other groups have found that a mean cochlear dose exceeding 4 Gy has been associated with failure to preserve hearing.^{21,31} Massager and colleagues found that patients with preserved hearing received an average cochlear dose of 3.7 Gy (range, 1.3–7.1 Gy), compared with 5.33 Gy (range, 1.9–10.0 Gy) in patients with worsened hearing.²⁸

However, it is important to note that not all studies have concluded that cochlear dose predicts hearing outcomes. Gabert and colleagues found no significant relationship between hearing outcomes and cochlear radiation exposure in 175 VS patients treated with a mean tumor margin dose of 12.74 Gy and a mean cochlear dose of 4.66 Gy.³² Similarly, Kano and colleagues with 77 VS patients and Horiba and colleagues with 49 VS patients failed to find a relationship between cochlear radiation dose and hearing preservation rates.^{8,25} That said, Kano and colleagues highlighted that all 12 patients with pretreatment serviceable hearing under 60 years of age who received less than 4.2 Gy to the cochlea maintained serviceable hearing at the last follow-up.⁸ While Pan and colleagues reported that 81.2% of patients maintained serviceable hearing with a dose of 12 Gy prescribed to the 50% isodose line, they found that cochlear and brainstem doses did not predict hearing outcomes.³³

Tumor Characteristics and Location

Tumor location can dictate the degree to which the cochlea is affected by radiation. In an effort to improve hearing outcomes in patients with substantial lateral tumor extension into the IAC, some authors have suggested use of beam channel blocking and modification of dosimetry to protect the cochlea.²⁸ Nevertheless, the radiation dose delivered to the cochlea may still exceed acceptable limits. Linskey and colleagues measured radiation doses delivered to the modiolus near the basal turn after SRS for VS. They found that radiation doses exceeding 12 Gy or the tumor margin dose were delivered in 10.8 and 9.3% of cases, respectively.²⁶ When they assessed those radiation dose parameters at the inferiormost extension of the cochlea, these doses were exceeded in 14.8 and 2.8% of cases, respectively.²⁶

Massager and colleagues found that the degree of tumor involvement within the IAC, measured as quartiles, approximated hearing preservation rates, such that hearing preservation rates were negatively correlated to IAC tumor involvement. With IAC tumor involvement of 0 to 25, 25 to 50, 50 to 75, and 75 to 100%, they reported hearing preservation rates of 100, 77, 65, and 50%, respectively.²⁸ In an earlier study, the same authors found that intracanalicular tumor volume was significantly larger in those patients who developed worsened hearing following treatment; however, loss of serviceable hearing was not related to the mean dose delivered.³⁴

Ohata and colleagues created a classification scheme to define lateral tumor extension.³⁵ Utilizing this scheme, Tamura and colleagues found that the degree of extension into the IAC was significantly associated with maintenance of pretreatment GR class after radiation.¹⁰ On multivariate analysis, Park and colleagues reported that a distance within 20 mm between the center of the tumor and modiolus was a significant independent predictive factor for hearing deterioration.³⁶ However, they also demonstrated that large extracanalicular tumors can actually receive higher cochlear radiation doses when compared with small intracanalicular tumors.³⁶ By calculating the slope of the tangent at the point of the 50% isodense line, large extracanalicular tumors were found to have lower slopes as compared with smaller intracanalicular tumors. A lower slope suggests poorer discrimination between tumor and organs to be preserved.³⁶ Other groups have found that intrameatal tumor extension,^{21,25} tumor volume,^{8,21} and fundal cap length⁸ have not been shown to affect hearing preservation rates following SRS. In a recent systematic review, the Congress of Neurological Surgeons concluded that cochlear doses ≤ 4 Gy, marginal tumor doses ≤ 12 Gy, smaller tumor size, and “good preoperative word recognition and/or pure tone thresholds” are the “most consistent prognostic features associated with maintenance of serviceable hearing.”³⁷

It is interesting to note that radiation to non-VS cerebellopontine angle tumors has been found to have different hearing preservation rates when compared with VS patients, despite cochlear doses exceeding 7 to 10 Gy.²⁵ For example, Hasegawa and colleagues reported on 42 patients with facial nerve schwannomas treated with SRS, 20 of whom had PTA ≤ 50 dB before treatment. With a median follow-up of 48 months, 90% of patients maintained their hearing level after receiving a median cochlear dose of 7.3 Gy (range, 2.0–17.8 Gy) and a median tumor margin dose of 12 Gy (range, 10–16 Gy).³⁸ Separately, Pollock and colleagues reviewed 16 patients with meningiomas extending into the IAC who were treated with SRS, nine of whom had GR Class 1 or 2 hearing before treatment.³⁹ With a median follow-up of 36 months (range, 12–123 months) and a median tumor margin dose of 15 Gy, six patients maintained serviceable hearing.³⁹ However, like many VS studies, limited follow-up and small sample sizes may account for the differences in audiometric outcomes. In Hasegawa and colleagues’ review of facial nerve schwannomas, Kaplan–Meier analysis provided 1-, 2-, and 5-year hearing preservation rates of 93, 84, and 42%, respectively, comparable to VS outcomes.³⁸

Hearing Loss over Time

Another variable that must be accounted for when discussing hearing preservation rates is the length of patient follow-up. With radiation, most studies demonstrate a decrease in serviceable hearing over time following treatment (► **Table 1**). This can be differentiated into an early phase within 2 years of treatment, which results in rapid hearing decline, and a late phase characterized by a more gradual hearing decline.⁴⁰ Horiba and colleagues, with a mean marginal dose of 11.9 Gy (range, 11–12 Gy), calculated a 71% hearing preservation rate in 49 VS patients at 1 year posttreatment; this decreased to 33% at 2 years and 14% at 3 years.²⁵ In a cohort of 100 patients who received a slightly higher marginal dose, ranging from 12 to 13 Gy, Lin and colleagues reported serviceable hearing preservation rates of 89, 68, and 63% at 1-, 3-, and 5-years posttreatment.²¹ Excluding all patients who had less than 5 years of follow-up, Carlson and colleagues reviewed 44 VS patients with serviceable hearing treated with SRS and 12 to 13 Gy to the tumor margin with a median audiometric follow-up of 9.3 years (range, 5–14 years).⁴⁰ Through Kaplan–Meier analysis, serviceable hearing preservation rates at 1-, 3-, 5-, 7-, and 10-years following radiosurgery were 80, 55, 48, 38, and 23%, respectively.⁴⁰ This is further supported by a systematic review of hearing preservation rates after radiotherapy for VS, accounting for 47 papers with 4,689 patients, 47% of which had pretreatment serviceable hearing, “the rate of hearing preservation is 73% at less than 2 years of follow-up, 60% from 2 to less than 5 years, 48% from 5 to less than 10 years, and 23% at greater than 10 years of follow-up.”⁴¹

The Congress of Neurological Surgeons published a systematic review and evidence-based guideline meant to synthesize the above findings for hearing preservation outcomes in VS patients with pretreatment serviceable hearing. They reported that following single-fraction therapy, there is a “moderately high probability (>50 to 75%) of hearing preservation at 2 years, moderately high probability (>50 to 75%) of hearing preservation at 5 years, and moderately low probability (>25 to 50%) of hearing preservation at 10 years.”³⁷

Fractionation

Several groups have assessed hearing outcomes with respect to fractionated radiation. In a direct comparison of SRS and SRT, Andrews and colleagues compared outcomes in 69 VS patients treated with Gamma Knife radiosurgery (SRS) at 12 Gy to the 50% isodose line and 56 VS patients treated with linear accelerator (LINAC)-based fractionated radiotherapy (SRT) using 2 Gy fractions for a cumulative dose of 50 Gy.⁴² They found that the SRT group maintained serviceable hearing at a significantly higher rate than the SRS group.⁴² However, other groups have found comparable audiometric outcomes with SRS when reviewing SRT outcomes. Bennion and colleagues summarized the hearing outcomes of 45 VS patients who underwent SRT with a median prescribed dose of 54 Gy (range, 46.8–62.4 Gy) using 1.8 Gy per fraction.⁴³ At last follow-up (median, 33.9 months), 58% maintained ser-

viceable hearing, with 1-, 2-, and 3-year serviceable hearing preservation rates of 83, 75, and 51%, respectively.⁴³ On multivariate analysis, cochlear volume <0.15 mL and mean cochlear dose <40 Gy were significantly associated with preserving serviceable hearing.⁴³

Combs and colleagues compared the outcomes between a total of 200 patients treated with SRS or SRT and found that the maintenance of pretreatment hearing levels was significantly better in the SRT group than the SRS group.⁴⁴ However, when excluding those SRS patients who received >13 Gy, there was no significant difference between hearing outcomes.⁴⁴ Interestingly, the study also evaluated tinnitus and noted that 10.2% had a decrease in tinnitus following SRT, while 6.0% developed tinnitus.⁴⁴ When compared with the SRS cohort, 8.3% had resolution of their tinnitus and 5.6% developed it.⁴⁴

Bhandare and colleagues reviewed the literature and found that hearing impairment occurs between 3 and 24 months following SRS, with a median of 4 months, compared with 18 to 24 months following SRT, though it has been identified as early as 3 months posttreatment.¹⁶

In a systematic review, Fong and colleagues compared VS patients who received single (SRS) and multiple dose (SRT) LINAC radiation therapy. With an average follow-up of 45 months in the SRS cohort, and 38.5 months in the SRT group, 66.3 and 75.3% preserved hearing, respectively.⁴⁵ For patients older than 54 years old, SRT offered higher hearing preservation rates (81%) compared with SRS (61.8%). Although tumor size did not affect hearing preservation rates in patients receiving SRS, patients with tumors of at least 3 cm treated with SRT actually had higher hearing preservation (94%) compared with patients with tumors <3 cm (71%).⁴⁵ The authors postulate that the acoustic nerve may be more prone to injury when the tumor is small, but cautioned against firm conclusions since the analysis did not account for tumor control rates, facial nerve outcomes, and other treatment morbidity. Furthermore, one must acknowledge the short-term follow-up.

In another comparison study, Kessel and colleagues compared 128 patients treated with SRT (median overall dose 54 Gy with median single dose 1.8 Gy) to 56 patients treated with SRS (median dose 12 Gy). Overall survival and progression free survival were similar between groups, supporting Bhandare and colleagues' data, but patients treated with SRT had median hearing preservation for 48.7 months compared with 36.3 months for SRS, although this did not achieve statistical significance.⁴⁶

In a long-term follow-up study, Lo and colleagues evaluated 49 VS patients with serviceable hearing treated with SRT (50 Gy delivered over 25 fractions) and found hearing preservation rates of 55% at 3 years, 37% at 5 years, and 29% at 7 years.⁴⁷ With a median follow-up of 6 years, ipsilateral PTAs worsened from 27 to 53 dB and word recognition scores decreased from 90 to 68%, posttreatment. Neither pretreatment GR class nor mean dose delivered to the cochlea predicted hearing deterioration on multivariable analysis, although pretreatment PTA did predict hearing preservation on multivariable analysis.⁴⁷ These findings are similar to previously discussed SRS outcomes, with long-term follow-up revealing hearing preservation rates under 30%.

Table 1 Hearing preservation outcomes for single fraction stereotactic radiosurgery, conventional fractionation, and hypofractionation. Medians unless otherwise reported

	Year	Sample size	Age (y)	Dose (Gy)	Other	Volume (cm ³)	Hearing preservation rate							Follow-up (mo)	
							1 year	2 year	3 year	4 year	5 year	7 year	8 year	10 year	
Single fraction SRS															
Andrews et al ⁴² (SRS)	2001	69	61 (mean)	12		2.92	33% maintained serviceable hearing							11.5	
Paek et al ³⁰	2005	25	47	12		3					46%				49
Massager et al ²⁸	2007	82	57	12						56%					24
Tamura et al ¹⁰	2009	74	47.5 (mean)	12.1		1.35 (mean)	78.4% maintained serviceable hearing							48	
Kano et al ⁸	2009	77	52	12.5		0.75	71.4% maintained serviceable hearing							20	
Hasegawa et al ²⁴	2011	117	52	12		1.9			55%		43%		34%		38
Carlson et al ⁴⁰	2013	44	58	12.1 (mean)		1.7	80%		55%		48%	38%		23%	99.6
Jacob et al ⁷	2014	59	58.9 (mean)	12		1.28	96%	83%	57%						25
Akpina et al ⁵⁰ (SRS) early ^a	2016	57	47	12.5		0.74	96%		93%		88%			64%	75
Akpinar et al ⁵⁰ (SRS) late	2016	31	48	12.5		0.67	87%		73%		55%			55%	75
Horiba et al ²⁵	2016	49		11.9 (mean)			71%	33%	14%						56
Kessel et al ⁴⁶ (SRS)	2016	56	63	12	1.8 Gy fractions		Median hearing preservation 36.3 months								
Mousavi et al ²³	2016	166	49	12.5		0.8									65
Class I-A		53	46	12.5		0.74	100%				100%			92%	66
Class I-B1		56	50	12.5		0.69	82%				71%			57%	67
Class I-B2		57	51	12.5		1	65%				35%			26%	65
Lin et al ²¹	2017	100	50.1 (mean)	12.1 (mean)			89%		68%		63%				78
Pan et al ³³	2017	93	58	12		3.14	81.2% maintained serviceable hearing							76.3	
Conventional fractionation															
Andrews et al ⁴² (SRT)	2001	56	56	50 (overall)	25 fractions over 5 wk	2.78	81% maintained serviceable hearing							10.5	
Combs et al ^b	2010	172 (FSRT) 202 (overall)		57.6 (overall), 13 (single dose)			83%		79%		76%			69%	75
Bennion et al ^{43,44}	2016	45	55	54 (overall)	1.8 Gy fractions	0.33	83%	75%	51%						33.9
Kessel et al ⁴⁶ (SRT)	2016	128	59	54 (overall)			Median hearing preservation 48.7 months								
Lo et al ⁴⁷	2017	49	55 (mean)	50	25 fractions over 5 wk	3.6			55%		37%	29%			72
Hypofractionated (Cyberknife)															
Hansasuta et al ⁴⁹	2011	370	54	18	3 fractions at 80% isodose	1.1	76% maintained serviceable hearing at last F/U							36	
Tsai et al ⁵¹	2013	65	57.3 (mean)	18	3 fractions at 80% isodose	4.7	81.5% maintained serviceable hearing at last F/U							64.5 (mean)	
Vivas et al ^c	2013	73	59	18	3 fractions at 80% isodose	0.81	53.5% maintained serviceable hearing at 3 years							40 (mean)	
Teo et al ^d	2016	13	44 (mean)	18	3 fractions at 80% isodose		38.4% maintained serviceable hearing								
Cakir et al ^e	2018	16	50.2 (mean)	17.6			69% maintained serviceable hearing							16.4 (mean)	

Abbreviations: FSRT, fractionated stereotactic radiotherapy; F/U, follow-up; Gy, gray; mo, months; SRS, stereotactic radiosurgery; SRT, stereotactic radiotherapy.

^aLess than 2 years from diagnosis.^bProbability of preserving the same Gardner–Robinson class.^c73 patients treated, 10 of which were postresection, with 50.5% of patients having serviceable hearing prior to treatment.^dSeparated patients based on solid and cystic tumors.^eOf an original group of 26 patients, three were treated with single fraction therapy.

With respect to hypofractionated protocols consisting of 3 to 5 fractions, there is substantially less data. Teo and colleagues assessed the outcome of hypofractionated SRS for large VS, comparing solid to cystic tumors, but also including 13 patients who had serviceable hearing prior to treatment.⁴⁸ They found that 38.4% of patients maintained serviceable hearing, concluding that their outcome may be indicative of the “high likelihood that patients experience some degree of auditory sequelae after CyberKnife-related VS treatment.”⁴⁸ In the largest series to date, Hansasuta et al reported on 370 VS patients who received multisession SRS with the CyberKnife Robotic Radiosurgical System (Accuray, Sunnyvale, California, United States), with 90% of patients receiving three fractions for a total dose of 18 Gy and a median isodose line of 80%.⁴⁹ With 198 patients with serviceable hearing and a median posttreatment follow-up of 3.0 years, 76% maintained serviceable hearing, with smaller tumor volume associated with higher hearing preservation rates, and a trend toward hearing preservation for younger age and intracanalicular tumors.⁴⁹ While it is reported that the radiobiological rationale for fractionation is to minimize radiation-induced tissue complications, further studies with long-term follow-up are needed to assess the technique of hypofractionated protocols.

Timing of Radiation

One study has found that early radiation may portend better hearing outcomes as compared with delayed radiation. Akpinar and colleagues studied the effect of early treatment (≤ 2 years) versus late treatment (> 2 years) of 88 VS patients with GR Class 1 hearing utilizing SRS.⁵⁰ Both cohorts received an average tumor margin dose of 12.5 Gy (range, 11.5–13 Gy) and had a median follow-up of 75 months (range, 12–169 months). The study found that patients in the early treatment group maintained serviceable hearing significantly longer than those patients in the late treatment group; 1-, 3-, 5-, and 10-year rates of serviceable hearing preservation were 96, 93, 88, and 64% for the early treatment group, compared with 87, 73, 55, and 55% for the late treatment group.⁵⁰ Limitations to this study include its retrospective nature and the fact that the late treatment group had slightly lower speech discrimination scores and significantly higher PTAs as compared with the early treatment group. Nevertheless, future studies exploring the role of radiation timing should be explored to better characterize this interesting finding.

Conclusion

The majority of patients treated with radiotherapy for VS will lose serviceable hearing over time. While the most consistent predictors of hearing preservation include better baseline hearing and younger age at the time of treatment, tumor margin doses < 12 Gy and cochlear doses < 4 Gy have also been demonstrated to maximize hearing preservation rates. With respect to tumor-specific characteristics, lateral tumor extension and tumor volume have variably been associated with hearing preservation. Furthermore, while fractionation

may improve hearing outcomes in the short term, especially in patients with larger tumors exceeding 3 cm, long-term data suggest comparable results to SRS. Although the goal of improving hearing preservation rates is admirable and should be sought aggressively, patients need to be appropriately counseled of the risks of hearing loss following radiation, enabling them to adequately assess their management options when diagnosed with VS.

Conflict of Interest

None.

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