Published in final edited form as:

Otol Neurotol. 2018 March ; 39(3): 273–283. doi:10.1097/MAO.0000000000001672.

Systematic Review of Hearing Preservation after Radiotherapy for Vestibular Schwannoma

Adam R Coughlin, MD¹, Tyler J Willman, MD¹, and Samuel P Gubbels, MD²

¹University of Wisconsin School of Medicine and Public Health; K4/7 Clinical Science Center; 600 Highland Avenue; Madison, WI; 53792. 608-262-6376

²University of Colorado School of Medicine, Department of Otolaryngology, Anschutz Medical Campus; 12631 E. 17th Ave., B-205; Aurora, CO 80045. 303-724-7500

Abstract

Objective—To determine the long-term hearing preservation rate for spontaneous vestibular schwannoma treated by primary radiotherapy.

Data sources—The MEDLINE/PubMed, Web of Science, Cochrane Reviews, and EMBASE databases were searched using a comprehensive Boolean keyword search developed in conjunction with a scientific librarian. English language papers published from 2000 to 2016 were evaluated.

Study selection—Inclusion criteria: full articles, pre-treatment and post-treatment audiograms or audiogram based scoring system, vestibular schwannoma only tumor type, reported time to follow-up, published after 1999, use of either Gamma Knife[®] or linear accelerator radiotherapy. Exclusion criteria: case report or series with fewer than five cases, inadequate audiometric data, inadequate time to follow-up, neurofibromatosis type 2 exceeding 10% of study population, prior treatment exceeding 10% of study population, repeat datasets, use of proton beam therapy, and non-English language.

Data extraction—Two reviewers independently analyzed papers for inclusion. Class A/B, 1/2 hearing was defined as either PTA ≤ 50db with SDS ≤ 50%, AAO-HNS Hearing Class A or B, or Gardner-Robertson Grade I or II. Aggregate data was used when individual data was not specified.

Data synthesis—Means were compared with student t-test.

Conclusions—47 articles containing a total of 2195 patients with preserved Class A/B, 1/2 hearing were identified for analysis. The aggregate crude hearing preservation rate was 58% at an average reporting time of 46.6 months after radiotherapy treatment. Analysis of time-based reporting shows a clear trend of decreased hearing preservation extending to ten-year follow-up. This data encourages a future long-term controlled trial.

Correspondence to: Samuel P Gubbels.

Disclosures: SG serves on the advisory boards for Applied Genetic Technologies Corporation and Roche Pharmaceutical Research both of which are not relevant to the topic of this manuscript.

Conflict of interest: none

Keywords

vestibular schwannoma; acoustic neuroma; hearing preservation; radiotherapy; radiosurgery; GammaKnife; CyberKnife

Introduction

Vestibular schwannoma (VS), also known as acoustic neuroma, is a benign tumor arising from the nerve sheath of the eighth cranial nerve. The incidence as determined by modern population-based studies is between 1.1–1.9 per 100,000 (1–4). The majority of tumors are unilateral and sporadic. Neurofibromatosis type 2 is associated with bilateral tumors which have a worse prognosis for hearing preservation (5,6). Currently, management of VS includes three broad options: conservative management, microsurgery, and radiotherapy. There is a paucity of prospective, randomized comparison data for the three options. Therefore, the patient and physician must rely largely on cohort data to inform the initial individualized management strategy. Control of the tumor is the primary outcome, but cranial neuropathies including audiovestibular function and facial nerve function, as well as quality of life, are also of utmost importance. Therefore, in order to counsel the patient, an accurate estimation of hearing preservation rates of each therapy option should be presented.

The otolaryngologist is usually well-versed in the neurotologic manifestations of VS presentation and treatment sequelae, as well as the various microsurgical approaches to the cerebellopontine angle. However, when a radiotherapy based approach is used, this is often undertaken by a neurosurgeon or a radiation oncologist. A brief history of localized radiation therapy treatment is informative in this context. Lars Leksell, a pioneering neurosurgeon at the Karolinska Institute in Stockholm, Sweden, introduced the term ‘radiosurgery’ in 1951 when he described in principle narrow beams of high dose radiation targeted to intracranial structures using a semicircular frame (7). Twenty years later, he described treatment of VS with the cobalt radiation-based stereotactic device that later became the Gamma Knife[®] (8). Over the subsequent years, frame-based stereotactic radiosurgery (SRS) has become widely used to treat intracranial and skull base tumors (9,10). The actual techniques and dose regimens vary based on device and institution. There are three common sources of radiation. Gamma radiation is emitted from a cobalt-60 source; the Gamma Knife[®] is a common application for SRS manufactured by Elekta AB (Stockholm, Sweden). Linear accelerator (LINAC) devices produce high energy X-ray radiation which can be adapted to SRS techniques; CyberKnife[®] is a robotically adapted and image-guided LINAC radiosurgery application produced by Accuray (Sunnyvale, CA). Proton beam therapy is available but less commonly used in treatment of VS. With regards to the patient setup during delivery of the radiation, the Gamma Knife[®] system traditionally used a fixed stereotactic frame, although Elekta AB now produces a model capable of frameless and fractionated treatments. The linear accelerator based systems are more variable but most often use either a moldable face mask or relocatable head frame for fixation; the tumor is localized most often with MRI and CT fusion imaging. Most often, radiosurgery refers to a single dose of therapy. Fractionated stereotactic radiotherapy is traditionally thought of as conventional doses of 2 Gy or less delivered multiple times over the course of several weeks. In between there is a point of

contention in the nomenclature, with the current consensus of the definition of radiosurgery being five or fewer sessions (often times called multi-session radiosurgery) (11). As with the technology, the terminology is evolving and inconsistently used by even the authors in the field (12,13).

Current literature reporting on the outcomes of VS do not universally report hearing outcomes; furthermore, when the hearing results are reported, audiometric-based methods are not always used. Two scales based on audiometric data have been widely adopted. The Gardner-Robertson scale was designed in 1988 to characterize hearing outcomes after acoustic neuroma surgery (14). In 1995, the American Academy of Otolaryngology-Head & Neck Surgery (AAO-HNS) released a similar grading scale (see Supplemental Digital Content for comparison) as well as guidelines on uniform reporting mechanisms (15). The '50/50 rule', that is, PTA of 50dB or less and SDS 50% or greater, has been promoted by some authors as one definition of adequately preserved hearing (16,17). More recently, the AAO-HNS has advocated a newer scattergram reporting scheme to improve the resolution of hearing outcomes (18).

Much of the literature published on the outcomes of radiation therapy for VS is not published in otolaryngology journals, and the data is heterogeneous in both radiation technique and reporting outcomes (19). Not surprisingly, the reported rates of hearing preservation vary widely with reported rates between 10–90%. (20–23). The aim of this paper is to review the literature to more accurately characterize the objective, audiogram-based long-term hearing preservation rate after treatment of sporadic VS with primary radiotherapy so as to inform clinical decision making in the management of vestibular schwannomas.

Methods

Literature search and selection

A systematic search of the literature was completed using the PubMed/MEDLINE, EMBASE, and Cochrane Library databases for articles on radiation treatment for vestibular schwannoma published between January 2000 and December 2016. We chose a cutoff of January 2000 as the treatment regimens prior to this are quite different than the modern dosages. A comprehensive search term was developed with the aid of a scientific librarian using Boolean keywords: hearing, gamma knife, radiosurgery, radiotherapy, stereotactic, stereotaxic, acoustic neuroma(s), vestibular schwannoma(s) (exact search terms available upon request). Duplicates were removed. Two reviewers (AC, TW) independently screened abstracts for relevance. The same reviewers then evaluated full text articles based on predetermined inclusion criteria and exclusion criteria. Studies from the same institution were evaluated to determine the likelihood of overlapping datasets based on authorship and dates of treatment and eliminated. The reference list of included articles were then examined to identify any articles not identified in the database search. An overview of the methodology schema is outlined in Figure 1.

Inclusion and exclusion criteria

Inclusion criteria: 1) complete journal articles, 2) hearing outcomes recorded pre-treatment and post-treatment with audiograms or audiogram-based scoring system, 3) vestibular schwannoma (acoustic neuroma) only tumor type, 4) documented time to follow-up, 5) published after 1999, 6) use of either Gamma Knife[®] or linear accelerator radiotherapy.

Exclusion criteria: 1) opinion, editorial, or review articles; 2) case report or series with fewer than five cases, 3) inadequate audiometric data, 4) lack of documented time to follow-up, 5) neurofibromatosis type 2 exceeding 10% of study population, 6) prior treatment exceeding 10% of study population, 7) repeat datasets, 8) use of proton beam therapy, 9) non-English language.

Data extraction and synthesis

Two reviewers (AC, TW) independently analyzed papers for inclusion; discrepancies were settled by consensus. “Preserved Class A/B, 1/2 hearing” was defined as either PTA ≤ 50db and SDS ≤ 50%, AAO-HNS Hearing Class A or B, or Gardner-Robertson Grade I or II. Aggregate data was used when individual data was not specified. When applicable and not otherwise specified, actuarial hearing loss data were extracted from Kaplan-Meier curves. Mean time to follow-up was preferentially recorded when available, when not, median was used for average time to follow-up. Crude hearing preservation rate was defined as the ratio of patients with preserved Class A/B, 1/2 hearing at last follow-up to the number with Class A/B, 1/2 hearing prior to treatment; these were recorded at the average follow-up period. Some authors also reported hearing preservation rates either at specific follow-up intervals (e.g. all patients had an audiogram at exactly two and five years after treatment) or calculated actuarial hearing preservation rates based off survival curves; these specific time-based hearing preservation rates (in comparison to the non-specific ‘at last follow-up’ crude rate) were also noted. Also recorded: journal, year of publication, institution, study type, number of subjects in the study, radiotherapy technique and dose, tumor size, patient age, patient gender, number of patients with NF-2, number of patients with prior surgery. Fractionated radiation therapy was operationally defined as any technique using more than one fraction or treatment session. Data for the complete case series was used when desired subgroup data was not reported. These data were documented in a predesigned Microsoft Excel (Redmond, WA) spreadsheet. Means were compared with the with student t-test and one-way ANOVA.

Results

State of the literature

Forty-seven papers met the inclusion and exclusion criteria (Table 1) (20–67). Of the 151 full-text articles reviewed, 43 were excluded for exceeding either the 10% limit of included study population with NF-2 or prior treatment without breaking out these populations for separate analysis; these two variables have known impact on hearing outcomes. Of the included articles, the minority were in otolaryngology journals (21%, Figure 2A). The articles represented diverse contributions from around the world (Figure 2B). The vast majority (90%) were either single institution retrospective case series or retrospective

reviews of a prospectively maintained institutional database. There were four single-institution single arm non-randomized prospective studies and one two-institution study. There were no controlled trials.

Systematic review analysis

These 47 included papers represent a total 4689 of patients, of which 2195 (47%) were analyzed with pre-treatment Class A/B, 1/2 hearing and adequate post-treatment audiometric evaluation.

The unweighted average crude hearing preservation rate was 58% (SD=19%) at 46.6 months (SD=34.9 months) after treatment; this is irrespective of tumor size, treatment technique, or age at treatment. Weighting for sample size of the Class A/B, 1/2 hearing portion of the study, the average crude hearing preservation rate remained 58% at 48.2 months. Crude hearing preservation rates varied from 14% to 92% with a range of average time to follow-up of 6 to 118 months.

There is a statistically significant difference in hearing preservation rates with time to follow-up after radiotherapy (Figure 3). Using available crude, actual, and actuarial hearing preservation rates, the rate of hearing preservation is 73% at less than two years of follow-up, 60% from 2 to less than 5 years, 48% from 5 to less than 10 years, and is 23% at greater than 10 years of follow-up; these are significantly different on ANOVA comparison of means ($p = .00001$). This relationship of time-dependent hearing preservation is seen with both crude and time-based (actuarial and actual) hearing preservation rates (Figure 4 A & B).

The unweighted average of the mean age at treatment was 56 years old (SD=4.6, range 45–69). The average mean tumor diameter was 15.0 mm (SD=4.12, range 7.1–21) and tumor volume 1.48 cm³ (SD=0.92, range 0.098–3.8). For single dose radiosurgery, the average mean marginal dose was 12.5 Gy (SD=0.7, range 11–18). Twenty-eight studies used GKS (60%) representing 1488 patients (67.5%) with Class A/B, 1/2 hearing, 18 used linear accelerator technologies (38%) representing 675 patients (31.1%), and one study with 32 patients (1.4%) used both (2%). Thirty-two studies used SRS (68%) representing 1622 patients (73.9%) with Class A/B, 1/2 hearing, 12 used fractionated dosing (26%) representing 476 patients (21.7%), and three studies with 97 patients (4.4%) used both (6%). The hearing preservation rate was not dependent on tumor size, patient age, radiotherapy technique, fractionation or SRS dose on univariate analysis (Table 2).

Discussion

Hearing preservation is an important factor when considering treatment options for patients initially presenting with vestibular schwannoma. There are many single institution case series in the literature for radiotherapy treatment of vestibular schwannoma but a paucity of controlled trials. The aim of this study was to aggregate these case series data with a focus on the preservation of hearing at audiometric levels of better than 50 dB pure tone average and better than 50% word recognition. We found the long-term rate of preserved Class A/B, 1/2 hearing after treatment of VS with primary radiotherapy on average was 58% at 47

months of follow-up. There is strong evidence for progressive hearing loss as the time to follow-up extended; there is a sequential and statistically significant difference between hearing preservation from 73% at less than two years of follow-up, 59% at two to five years of follow-up, 48% at five to ten years follow-up, and 23% at ten years or greater. Importantly, hearing preservation rates continue to decline out to the longest-term follow-up of about ten years. This is evident in the strong trends seen in Figure 4.

We did not find any significant differences in hearing preservation outcomes with respect to tumor size, patient age, radiotherapy technique, fractionation or SRS dose on univariate analyses. The power of these subgroup analyses is somewhat diluted secondary to the fact that the analysis was completed using the averages of each study as the individual patient datapoints were not available. This also limits multivariate analysis. Furthermore, our exclusion criteria intentionally limit some of the variation in the data in order to focus only on the current best practices with a focus on hearing outcomes. For example, limiting the publication date to no earlier than the year 2000 intentionally decreased the range of marginal doses; of the 32 SRS studies, only two had an upper range of mean marginal dose higher than 14 Gy.

The strength of this paper is its broad inclusion of radiotherapy techniques and dose regimens while at the same time focusing on high quality audiometric reporting with long-term follow-up. Previous reviews of radiosurgical outcomes for treatment of VS lacked one or both of these features (19, 68–71), although the average crude hearing preservation rate of 58% at 47 months is in agreement with Yang (68) whose GKS review reported a 51% AAO-HNS Class A/B or Gardner-Robertson Class 1/2 hearing preservation rate at 44 months.

An inherent challenge when studying long-term hearing loss in an adult population is that there is expected hearing loss with aging, and furthermore, an apparent progressive hearing loss attributable to the pathology of VS with respect to the eighth cranial nerve. It is therefore difficult to attribute a certain portion to natural hearing loss and another portion to post-treatment neuropathy. An ideal study of long-term hearing outcomes after VS treatment would account for the effect of the natural, age-related decline in hearing and also to make comparisons to patients with untreated, observed tumors. A few studies have looked at using the contralateral ear as a control. Carlson et al (49) examined 44 patients undergoing GKS with a median audiometric follow-up time of 9.3 years. Their study included an interaural correction and showed, in the contralateral ear, a 8.5 dB increase in PTA and a 1.8% drop in SDS over the long follow-up course. Even accounting for this adjustment, the treated ear demonstrated continued hearing loss throughout the course of long-term follow-up. Roos et al (42) reviewed their experience with single dose LINAC SRS. While they lacked speech discrimination scoring, they reported hearing preservation relative to interaural PTA differences and similarly showed a relative decline in the ipsilateral useful hearing preservation rate (defined in their paper as interaural PTA $\leq$ 50 dB) with a crude rate of 38% at 65 months median follow-up. Rather than comparing to the contralateral ear for control, Rasmussen et al (44) retrospectively compared 21 patients with pretreatment GR Class 1 hearing treated with fractionated stereotactic radiotherapy to an untreated control group matched for pre-treatment speech discrimination scores. The control group had an approximately 30% better hearing preservation rate out to ten years of follow-up.

Audiometric testing reporting is also widely variable in the current literature. This review eliminated papers with subjective hearing scores or otherwise poor audiometric reporting. Twenty-six of the 962 articles were eliminated on abstract screening, and another 38 of the 148 full text screening articles failed to pass the audiometric exclusion criteria. However, even for papers with good audiometric hearing outcomes, there is a not insignificant difference between the widely reported grading systems. The Gardner-Robertson (GR) scale was designed by the otolaryngologist Gale Gardner and neurosurgeon Jon Robertson of Memphis, Tennessee in their 1988 microsurgical case series with review of the literature as a modification of the Silverstein (72) classification which calculates pure tone average at 0.5, 1.0, and 2.0 kHz. The need for more standardized reporting has long been recognized; it was even discussed by Drs. Gardner and Robertson in their paper, and has been addressed twice by the AAO-HNS. The 1995 position paper (15) used a similar scale and nomogram calculated with the addition of a fourth frequency at 3kHz (see Supplemental Digital Content for comparison). The addition of a higher frequency is an important difference as high frequencies are important in speech quality, localization, and intelligibility (73). The addition of another high frequency in the calculation of PTA using the AAO-HNS system may receive a less favorable overall grade compared to the same patient under the GR score. Some authors even favor using speech discrimination alone without pure tone average with the argument that, in part, amplification is more successful with retained speech discrimination than retained pure tone average or speech reception thresholds; the Word Recognition Score (WRS) (74) is one such classification. None of the included papers used the current recommended AAO-HNS reporting standard of a scattergram (18). Furthermore, optimally going forward, future studies would include not only audiometric data, but also patient reported outcomes such as the Hearing Handicap Inventory for Adults (75) to better assess overall hearing ability. The combination of audiometric data and patient reported outcomes would come closer to the ideal of assessing overall hearing function. In addition to these technical differences in scoring system calculations, there is the further problem of grouping scores together and assigning descriptive terms to these groups. The terms 'serviceable' and 'useful' abound in the literature; however, there is no consensus definition of these terms nor guidelines in how to use such descriptions. Furthermore, the connotation that a patient with Class 2 hearing has 'serviceable hearing' implies that they should be able to adequately function, but this may not be the case. It is for this reason that the authors decided to use the term 'preserved Class A/B, 1/2 hearing' as a composite of the AAO-HNS and Gardner-Robertson scales rather than any descriptive terms, even when the original paper reported the results with such terminology.

A systematic review is, by definition, dependent upon the quality of the data in the included articles. There are some limitations to this. Oftentimes, there were not discrete datapoints for individuals or groups of individuals. Therefore, averages for the entire case series were assumed to be the same for the group analyzed. For example, while the subset of the case series with pre-treatment Class A/B, 1/2 hearing may have only been 25% of the given study population, the tumor size was reported for the entire group and may not be representative of the subset used in this paper's analysis. Another common datapoint which required grouping is the time to follow-up. This may have been either clinical, radiographic, or audiometric follow-up but was not often specified or broken down for audiometric only; when not

otherwise specified, audiometric follow-up was assumed to be the same as overall follow-up. Furthermore, the lack of homogeneity in the individual case series inclusion criteria, patient demographics, and treatment techniques, combined with the need to group patients as a whole rather than individuals limited the statistical analysis and precluded true metaanalysis. This also limits a risk of bias analysis, as recommended by the PRISMA statement (76), as treatment choices are not attempted to be completed in a randomized fashion.

There are additional limitations which must be acknowledged. Stereotactic radiosurgery is an evolving technology. The outcomes of radiation therapy are, of course, dependent on the technique of radiation delivery, among many other factors. The exact treatment planning details which optimize patient hearing outcome while maximizing tumor control remains an active ongoing area of research. There is evolving evidence that cochlear dose (43, 44, 56, 77), pretreatment hearing class (42, 43, 45, 49), and tumor size (49, 77) are important factors affecting hearing preservation. As an attempt to include high quality modern studies, the inclusion criteria limited to publications from 2000 and later; thus eliminating higher dose earlier reports. Still, case series reporting specific technical metrics such as cochlear dose or conformity index are not the norm; the dosimetry and complete treatment planning details are often absent from these case series, and the degree of conformality and other quality metrics cannot be fully assessed. These important factors remain an uncontrolled variable for this study and other such reviews of the literature.

Another aspect of the evolving technologies of radiosurgery lies in the controversy between frame-based and frameless devices. Stereotactic radiosurgery was initially designed with a frame mechanically connecting the patient to radiation source to maximize target localization. As the technology has evolved, relocatable frames (for example, the Gill-Thomas-Cosman frame (78)) and image-guided frameless technologies (for example, an optical bite-plate fiducial array (79)) have evolved with the purported benefits of decreased invasiveness for the patient and increased ease of fractionated regimens. Like other areas of controversy in this field, there is at this time a lack of comparative or long-term trials to answer the question of whether precision is as good with these newer techniques as compared to the fixed frame techniques. Regardless of the specific techniques used, there must be a strong emphasis by the treating physicians to design a treatment field with accuracy and precision, and in the case of fractionated treatment repeatability, to irradiate the tumor while sparing the important nearby cochlear and nerve structures. Overall, to the best of our ability, the studies included in this analysis represent case series in which the authors used modern conformal techniques with intent on hearing preservation therapy. While the techniques are variable, the goal was uniform, and therefore the results should be broadly applicable.

Due to the strict inclusion criteria, several studies with relatively large numbers of patients with long-term data were not included. This includes several of the more well-known articles in this field. Most commonly, these were excluded as they represented overlapping institutional datasets or exceeded the allowed number of patients with prior treatment or NF-2. For example, the non-overlapping case series from Chopra (32) and Kano (22) were chosen to represent the University of Pittsburgh GKS experience rather than perhaps the better-known larger Lunsford article from 2005 (80). A sampling of long-term case series

not included in this analysis report hearing preservation rates of 37–74% (77, 80–84) - all with at least five years average follow-up. Of particular interest is an excellent recent paper from Watanabe (77) which retrospectively reviewed 183 patients who underwent GKS and included a calculated 15-year actuarial hearing preservation rate of 12%; they also identified age 65, tumor volume 8cm³ and mean cochlear dose > 4.2 Gy as predictive for poor hearing preservation.

Our analysis was not primarily designed to identify treatment or demographic factors influencing hearing preservation rates. On univariate analysis of tumor size, patient age, radiation source, dose fractionation, or marginal dose, none were found to be significant predictors of hearing preservation. As mentioned above, other papers investigating factors influencing hearing preservation rates have identified initial speech discrimination scores (43,85,86), marginal dose (68), and cochlear dose (56, 64, 84, 87) to be important factors. The effect of fractionation on hearing preservation is still not settled. While some earlier reports described very favorable hearing preservation rates (88–90), more recent comparative studies with low-dose treatments show similar hearing preservation outcomes between radiosurgery and fractionated radiotherapy (91–93).

Hearing preservation in the treatment of vestibular schwannoma remains a challenge regardless of treatment modality. In the long-term analysis from the large Danish cohort of observed patients (86), of the 178 patients with AAO-HNS Class A hearing at the start of observation, Class A hearing was preserved in 46% at 10 years. Quist et al (94) reported five-year follow-up results of patients treated by middle cranial fossa surgical approach. Of the 49 patients with AAO-HNS Class A or B hearing preoperatively, 55% maintained Class A/B hearing immediately post-operative. Of these patients followed for five years, 75% maintained Class A/B hearing. Similarly, Meyer (74) and Woodson (95) reviewed the University of Iowa experience with small tumors resected via middle cranial fossa surgery. Meyer showed a 57% AAO-HNS Class A/B hearing preservation rate immediately post-operative; Woodson showed that of these patients with initial preserved post-operative AAO-HNS Class A/B hearing, the long-term crude hearing preservation rate at minimum two years of follow-up was 65%, and when corrected for contralateral hearing loss it was 93%. Mazzoni (96) reviewed 200 cases of retrosigmoid approach to VS: 47% had immediate post-operative AAO-HNS Class A/B hearing, and of these 87% maintained Class A/B hearing at a minimum of six years and median nine year follow-up. Chee et al (97) also reviewed outcomes after the retrosigmoid approach. Thirty-four percent of 126 cases had initial hearing preservation, and of the cases with initial preservation, at last follow-up, 65% of patients with AAO-HNS Class A/B hearing maintained hearing at these levels; the minimum follow-up was 36 months and the mean was 113.6 months. Selection bias greatly limits direct comparison of these results. Regardless of selection criteria however, long-term hearing preservation rates remain lower than desired for all current treatment strategies, especially for larger tumors or patients with less than excellent initial hearing.

For future directions, ideally one would design a multi-institutional long-term prospective, randomized control trial of primary radiosurgery versus primary hearing-preservation approach microsurgery (i.e. via middle fossa or retrosigmoid craniotomy approaches) versus conservative wait-and-scan management in patients with Class A/B, 1/2 hearing without

tumor compressive symptoms. Treatment techniques would be homogeneous and hearing would be measured at set intervals with audiograms and patient-reported functional analysis. In the likely absence of this, standardized high quality reporting criteria should continue to be encouraged across disciplines. Fundamental to this is the current American Academy of Otolaryngology-Head & Neck Surgery standardized format of scattergram hearing outcomes using PTA calculated at 0.5-, 1-, 2-, and 3-kHz and a minimum 50-word list word recognition score. An effort should be made to encourage our colleagues treating vestibular schwannoma of all disciplines to continue to strive to report high quality, standardized hearing outcome measures in both the short and long terms.

Conclusions

The crude rate of preserved hearing at audiometric levels of better than 50 dB pure tone average and better than 50% word recognition after treatment of vestibular schwannoma with primary radiotherapy on average was 58% at 47 months of follow-up. There is strong evidence for progressive hearing loss as the time to follow-up extended; there is a sequential and statistically significant difference between hearing preservation from 73% at less than two years of follow-up, 59% at two to five years of follow-up, 48% at five to ten year follow-up, and 23% at ten years or greater. Importantly, the hearing preservation rate continues to decline with long-term follow-up - with the current longest term follow-up averaging about ten years after treatment. This highlights the need to state the time to follow-up when reporting hearing outcomes in future studies, as well as the need to explain to patients the progressive nature of possible hearing loss that can occur following treatment of vestibular schwannoma rather than quoting a hearing preservation rate in isolation. Hearing preservation rate after primary radiotherapy was not dependent on tumor size, patient age, radiation source, dose fractionation or marginal dose in this study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Grant support: SG receives research funding support from the NIH/NIDCD (R01 DC013912-01) for studies unrelated to the topic of this manuscript.

Stephen Johnson, MLS, senior academic librarian for aiding in constructing the database search terms and managing the search results. Glen E Levenson, PhD for guidance on statistical methodologies.

References

1. Stangerup SE, Caye-Thomasen P. Epidemiology and natural history of vestibular schwannomas. *Otolaryngol Clin North Am.* 2012; 45:257–68. [PubMed: 22483814]
2. Babu R, Sharma R, Bagley JH, Hatef J, Friedman AH, Adamson C. Vestibular schwannomas in the modern era: epidemiology, treatment trends, and disparities in management. *J Neurosurg.* 2013; 119:121–30. [PubMed: 23432451]
3. Carlson ML, Habermann EB, Wagie AE, et al. The Changing Landscape of Vestibular Schwannoma Management in the United States--A Shift Toward Conservatism. *Otolaryngol Head Neck Surg.* 2015; 153:440–6. [PubMed: 26129740]

4. Kleijwegt M, Ho V, Visser O, Godefroy W, van der Mey A. Real Incidence of Vestibular Schwannoma? Estimations From a National Registry. *Otol Neurotol*. 2016; 37:1411–7. [PubMed: 27525713]
5. Mathieu D, Kondziolka D, Flickinger JC, et al. Stereotactic radiosurgery for vestibular schwannomas in patients with neurofibromatosis type 2: an analysis of tumor control, complications, and hearing preservation rates. *Neurosurgery*. 2007; 60:460–8. [PubMed: 17327790]
6. Samii M, Matthies C, Tatagiba M. Management of vestibular schwannomas (acoustic neuromas): auditory and facial nerve function after resection of 120 vestibular schwannomas in patients with neurofibromatosis 2. *Neurosurgery*. 1997; 40:696–705. [PubMed: 9092842]
7. Leksell L. The stereotactic method and radiosurgery of the brain. *Acta chirurgica*. 1951; 104:316–19.
8. Leksell L. A note on the treatment of acoustic tumors. *Acta Chir Scand*. 1971; 137:763–65. [PubMed: 4948233]
9. Flickinger JC, Lunsford LD, Linskey ME, Duma CM, Kondziolka D. Gamma knife radiosurgery for acoustic tumors: multivariate analysis of four year results. *Radiother Oncol*. 1993; 27:91–8. [PubMed: 8356233]
10. Foote RL, Coffey RJ, Swanson JW, et al. Stereotactic radiosurgery using the gamma knife for acoustic neuromas. *Int J Radiat Oncol Biol Phys*. 1995; 32:1153–60. [PubMed: 7607937]
11. Barnett GH, Linskey ME, Adler JR, et al. American Association of Neurological Surgeons; Congress of Neurological Surgeons Washington Committee Stereotactic Radiosurgery Task Force. Stereotactic radiosurgery--an organized neurosurgery-sanctioned definition. *J Neurosurg*. 2007; 106(1):1–5.
12. Chang SD, Gibbs IC, Sakamoto GT, Lee E, Oyelese A, Adler JR Jr. Staged stereotactic irradiation for acoustic neuroma. *Neurosurgery*. 2005; 56(6):1254–61. [PubMed: 15918941]
13. Torrens M, Chung C, Chung HT, et al. Standardization of terminology in stereotactic radiosurgery: Report from the Standardization Committee of the International Leksell Gamma Knife Society: special topic. *J Neurosurg*. 2014; 121(Suppl):2–15.
14. Gardner G, Robertson JH. Hearing preservation in unilateral acoustic neuroma surgery. *Ann Otol Rhinol Laryngol*. 1988; 97:55–66. [PubMed: 3277525]
15. Monsell EM, Balkany TA, Gates GA, et al. Committee on Hearing and Equilibrium guidelines for the evaluation of hearing preservation in acoustic neuroma (vestibular schwannoma). American Academy of Otolaryngology-Head and Neck Surgery Foundation, INC. *Otolaryngol Head Neck Surg*. 1995; 113:179–80. [PubMed: 7675475]
16. Sanna M, Zini C, Mazzoni A, et al. Hearing preservation in acoustic neuroma surgery: middle fossa versus suboccipital approach. *Am J Otol*. 1987; 8:500–6. [PubMed: 3501673]
17. Walsh RM, Bath AP, Bance ML, Keller A, Rutka JA. Consequences to hearing during the conservative management of vestibular schwannomas. *Laryngoscope*. 2000; 110:250–5. [PubMed: 10680925]
18. Gurgel RK, Jackler RK, Dobie RA, Popelka GR. A new standardized format for reporting hearing outcome in clinical trials. *Otolaryngol Head Neck Surg*. 2012; 147:803–7. [PubMed: 22931898]
19. Bassim MK, Berliner KI, Fisher LM, Brackmann DE, Friedman RA. Radiation therapy for the treatment of vestibular schwannoma: a critical evaluation of the state of the literature. *Otol Neurotol*. 2010; 31:567–73. [PubMed: 20300044]
20. Lin VY, Stewart C, Grebenyuk J, et al. Unilateral acoustic neuromas: long-term hearing results in patients managed with fractionated stereotactic radiotherapy, hearing preservation surgery, and expectantly. *Laryngoscope*. 2005; 115:292–6. [PubMed: 15689753]
21. Rutten I, Baumert BG, Seidel L, et al. Long-term follow-up reveals low toxicity of radiosurgery for vestibular schwannoma. *Radiother Oncol*. 2007; 82:83–9. [PubMed: 17182142]
22. Kano H, Kondziolka D, Khan A, Flickinger JC, Lunsford LD. Predictors of hearing preservation after stereotactic radiosurgery for acoustic neuroma. *J Neurosurg*. 2009; 111:863–73. [PubMed: 19284227]
23. Horiba A, Hayashi M, Chernov M, Kawamata T, Okada Y. Hearing Preservation after Low-dose Gamma Knife Radiosurgery of Vestibular Schwannomas. *Neurol Med Chir*. 2016; 56:186–92.

24. Unger F, Walch C, Schröttner O, Eustacchio S, Sutter B, Pendl G. Cranial nerve preservation after radiosurgery of vestibular schwannomas. *Acta Neurochir Suppl.* 2002; 84:77–83. [PubMed: 12379008]
25. Ottaviani F, Neglia CB, Ventrella L, Giugni E, Motti E. Hearing loss and changes in transient evoked otoacoustic emissions after gamma knife radiosurgery for acoustic neurinomas. *Arch Otolaryngol Head Neck Surg.* 2002; 128:1308–12. [PubMed: 12431177]
26. Régis J, Pellet W, Delsanti C, et al. Functional outcome after gamma knife surgery or microsurgery for vestibular schwannomas. *J Neurosurg.* 2002; 97:1091–1100. [PubMed: 12450031]
27. Williams JA. Fractionated stereotactic radiotherapy for acoustic neuromas. *Acta Neurochir.* 2002; 144:1249–54. [PubMed: 12478335]
28. Rowe JG, Radatz MW, Walton L, Hampshire A, Seaman S, Kemeny AA. Gamma knife stereotactic radiosurgery for unilateral acoustic neuromas. *J Neurol Neurosurg Psychiatry.* 2003; 74:1536–42. [PubMed: 14617712]
29. Muacevic A, Jess-Hempfen A, Tonn JC, Wowra B. Results of outpatient gamma knife radiosurgery for primary therapy of acoustic neuromas. *Acta Neurochir Suppl.* 2004; 91:75–8. [PubMed: 15707028]
30. Myrseth E, Møller P, Pedersen PH, Vassbotn FS, Wentzel-Larsen T, Lund-Johansen M. Vestibular schwannomas: clinical results and quality of life after microsurgery or gamma knife radiosurgery. *Neurosurgery.* 2005; 56:927–35. [PubMed: 15854240]
31. van Eck AT, Horstmann GA. Increased preservation of functional hearing after gamma knife surgery for vestibular schwannoma. *J Neurosurg.* 2005; 102(Suppl):204–6.
32. Chopra R, Kondziolka D, Niranjan A, Lunsford LD, Flickinger JC. Long-term follow-up of acoustic schwannoma radiosurgery with marginal tumor doses of 12 to 13 Gy. *Int J Radiat Oncol Biol Phys.* 2007; 68:845–51. [PubMed: 17379451]
33. Thomas C, Di Maio S, Ma R, Vollans E, et al. Hearing preservation following fractionated stereotactic radiotherapy for vestibular schwannomas: prognostic implications of cochlear dose. *J Neurosurg.* 2007; 107:917–26. [PubMed: 17977261]
34. Massager N, Nissim O, Delbrouck C, et al. Irradiation of cochlear structures during vestibular schwannoma radiosurgery and associated hearing outcome. *J Neurosurg.* 2007; 107:733–39. [PubMed: 17937216]
35. Bush ML, Shinn JB, Young AB, Jones RO. Long-term hearing results in gamma knife radiosurgery for acoustic neuromas. *Laryngoscope.* 2008; 118:1019–22. [PubMed: 18364592]
36. Iwai Y, Yamanaka K, Kubo T, Aiba T. Gamma knife radiosurgery for intracanalicular acoustic neuromas. *J Clin Neurosci.* 2008; 15:993–7. [PubMed: 18617402]
37. Lasak JM, Klish D, Kryzer TC, Hearn C, Gorecki JP, Rine GP. Gamma knife radiosurgery for vestibular schwannoma: early hearing outcomes and evaluation of the cochlear dose. *Otol Neurotol.* 2008; 29:1179–86. [PubMed: 18931646]
38. Kim CH, Chung KW, Kong DS, et al. Prognostic factors of hearing preservation after gamma knife radiosurgery for vestibular schwannoma. *J Clin Neurosci.* 2010; 17:214–8. [PubMed: 20056421]
39. McWilliams W, Trombetta M, Werts ED, Fuhrer R, Hillman T. Audiometric outcomes for acoustic neuroma patients after single versus multiple fraction stereotactic irradiation. *Otol Neurotol.* 2011; 32:297–300. [PubMed: 21192276]
40. Brown M, Ruckenstein M, Bigelow D, Judy K, Wilson V, Alonso-Basanta M, Lee JY. Predictors of hearing loss after gamma knife radiosurgery for vestibular schwannomas: age, cochlear dose, and tumor coverage. *Neurosurgery.* 2011; 69:605–13. [PubMed: 21471832]
41. Park CE, Park BJ, Lim YJ, Yeo SG. Functional outcomes in retrosigmoid approach microsurgery and gamma knife stereotactic radiosurgery in vestibular schwannoma. *Eur Arch Otorhinolaryngol.* 2011; 268:955–9. [PubMed: 21479879]
42. Roos DE, Potter AE, Zacest AC. Hearing preservation after low dose linac radiosurgery for acoustic neuroma depends on initial hearing and time. *Radiother Oncol.* 2011; 101:420–4. [PubMed: 21741718]
43. Hasegawa T, Kida Y, Kato T, Iizuka H, Yamamoto T. Factors associated with hearing preservation after Gamma Knife surgery for vestibular schwannomas in patients who retain serviceable hearing. *J Neurosurg.* 2011; 115:1078–86. [PubMed: 21961962]

44. Rasmussen R, Claesson M, Stangerup SE, et al. Fractionated stereotactic radiotherapy of vestibular schwannomas accelerates hearing loss. *Int J Radiat Oncol Biol Phys.* 2012; 83:e607–11. [PubMed: 22560549]
45. Han JH, Kim DG, Chung HT, et al. Hearing preservation in patients with unilateral vestibular schwannoma who undergo stereotactic radiosurgery: Reinterpretation of the auditory brainstem response. *Cancer.* 2012; 118:5441–7. [PubMed: 22570121]
46. Yomo S, Carron R, Thomassin JM, Roche PH, Régis J. Longitudinal analysis of hearing before and after radiosurgery for vestibular schwannoma. *J Neurosurg.* 2012; 117:877–85. [PubMed: 22937934]
47. Hayden Gephart MG, Hansasuta A, Balise RR, et al. Cochlea radiation dose correlates with hearing loss after stereotactic radiosurgery of vestibular schwannoma. *World Neurosurg.* 2013; 80:359–63. [PubMed: 22484770]
48. Lin MC, Chen CM, Tseng HM, Xiao F, Young YH. A proposed method to comprehensively define outcomes in acoustic tumor patients undergoing CyberKnife management. *Stereotact Funct Neurosurg.* 2013; 91:177–85. [PubMed: 23446119]
49. Carlson ML, Jacob JT, Pollock BE, et al. Long-term hearing outcomes following stereotactic radiosurgery for vestibular schwannoma: patterns of hearing loss and variables influencing audiometric decline. *J Neurosurg.* 2013; 118:579–87. [PubMed: 23101446]
50. Baschnagel AM, Chen PY, Bojrab D, et al. Hearing preservation in patients with vestibular schwannoma treated with Gamma Knife surgery. *J Neurosurg.* 2013; 118:571–8. [PubMed: 23216466]
51. Litre F, Rousseaux P, Jovenin N, et al. Fractionated stereotactic radiotherapy for acoustic neuromas: a prospective monocenter study of about 158 cases. *Radiother Oncol.* 2013; 106:169–74. [PubMed: 23219253]
52. Karam SD, Tai A, Strohl A, et al. Frameless fractionated stereotactic radiosurgery for vestibular schwannomas: a single-institution experience. *Front Oncol.* 2013; 17(3):121.
53. Champ CE, Shen X, Shi W, Mayekar SU, et al. Reduced-dose fractionated stereotactic radiotherapy for acoustic neuromas: maintenance of tumor control with improved hearing preservation. *Neurosurgery.* 2013; 73:489–96. [PubMed: 23756743]
54. Su CF, Lee CC, Yang J, Loh TW, Tzou JH, Liu DW. Long-term outcome of gamma knife radiosurgery treatment in patients with tiny intracanalicular vestibular schwannomas detected by three-dimensional fast imaging employing steady-state acquisition magnetic resonance. *Tzu Chi Medical Journal.* 2014; 26:132–7.
55. Vivas EX, Wegner R, Conley G, et al. Treatment outcomes in patients treated with CyberKnife radiosurgery for vestibular schwannoma. *Otol Neurotol.* 2014; 35:162–70. [PubMed: 24335934]
56. Jacob JT, Carlson ML, Schiefer TK, Pollock BE, Driscoll CL, Link MJ. Significance of cochlear dose in the radiosurgical treatment of vestibular schwannoma: controversies and unanswered questions. *Neurosurgery.* 2014; 74:466–74. [PubMed: 24476904]
57. Kranzinger M, Zehentmayr F, Fastner G, et al. Hypofractionated stereotactic radiotherapy of acoustic neuroma: volume changes and hearing results after 89-month median follow-up. *Strahlenther Onkol.* 2014; 190:798–805. [PubMed: 24638268]
58. López Carratalá I, Escorihuela García V, Orts Alborch M, de Paula Vernetta C, Marco Algarra J. Radiosurgery as treatment for acoustic neuroma. Ten years' experience. *Acta Otorrinolaringol Esp.* 2014; 65:327–31. [PubMed: 24846561]
59. Boari N, Bailo M, Gagliardi F, et al. Gamma Knife radiosurgery for vestibular schwannoma: clinical results at long-term follow-up in a series of 379 patients. *J Neurosurg.* 2014; 121(Suppl): 123–42.
60. Elliott A, Hebb AL, Walling S, Morris DP, Bance M. Hearing preservation in vestibular schwannoma management. *Am J Otolaryngol.* 2015; 36:526–34. [PubMed: 25771841]
61. Tveiten OV, Carlson ML, Goplen F, Vassbotn F, Link MJ, Lund-Johansen M. Long-term Auditory Symptoms in Patients With Sporadic Vestibular Schwannoma: An International Cross-Sectional Study. *Neurosurgery.* 2015; 77:218–27. [PubMed: 25850598]

62. Ikonomidis C, Pica A, Bloch J, Maire R. Vestibular Schwannoma: The Evolution of Hearing and Tumor Size in Natural Course and after Treatment by LINAC Stereotactic Radiosurgery. *Audiol Neurotol*. 2015; 20:406–15. [PubMed: 26571111]
63. Klijn S, Verheul JB, Beute GN, Leenstra S, Mulder JJ, Kunst HP, Hanssens PE. Gamma Knife radiosurgery for vestibular schwannomas: evaluation of tumor control and its predictors in a large patient cohort in The Netherlands. *J Neurosurg*. 2016; 124:1619–26. [PubMed: 26430848]
64. Bennion NR, Nowak RK, Lyden ER, Thompson RB, Li S, Lin C. Fractionated stereotactic radiation therapy for vestibular schwannomas: Dosimetric factors predictive of hearing outcomes. *Pract Radiat Oncol*. 2016; 6:e155–62. [PubMed: 26961715]
65. Schumacher AJ, Lall RR, Lall RR, et al. Low-Dose Gamma Knife Radiosurgery for Vestibular Schwannomas: Tumor Control and Cranial Nerve Function Preservation After 11 Gy. *J Neurol Surg B Skull Base*. 2017; 78:2–10. [PubMed: 28180036]
66. Kessel KA, Fischer H, Vogel MM, et al. Fractionated vs. single-fraction stereotactic radiotherapy in patients with vestibular schwannoma: Hearing preservation and patients' self-reported outcome based on an established questionnaire. *Strahlenther Onkol*. 2017; 193:192–199. [PubMed: 27803960]
67. Putz F, Müller J, Wimmer C, et al. Stereotactic radiotherapy of vestibular schwannoma: Hearing preservation, vestibular function, and local control following primary and salvage radiotherapy. *Strahlenther Onkol*. 2017; 193:200–212. [PubMed: 27928625]
68. Yang I, Sughrue ME, Han SJ, Aranda D, Pitts LH, Cheung SW, Parsa AT. A comprehensive analysis of hearing preservation after radiosurgery for vestibular schwannoma. *J Neurosurg*. 2010; 112:851–9. [PubMed: 19747043]
69. Murphy ES, Suh JH. Radiotherapy for vestibular schwannomas: a critical review. *Int J Radiat Oncol Biol Phys*. 2011; 79:985–97. [PubMed: 21353158]
70. Maniakas A, Saliba I. Conservative management versus stereotactic radiation for vestibular schwannomas: a meta-analysis of patients with more than 5 years' follow-up. *Otol Neurotol*. 2012; 33:230–8. [PubMed: 22222572]
71. Maniakas A, Saliba I. Microsurgery versus stereotactic radiation for small vestibular schwannomas: a meta-analysis of patients with more than 5 years' follow-up. *Otol Neurotol*. 2012; 33:1611–20. [PubMed: 22996165]
72. Silverstein H, McDaniel A, Norrell H, Haberkamp T. Hearing preservation after acoustic neuroma surgery with intraoperative direct eighth cranial nerve monitoring: Part II. A classification of results. *Otolaryngol Head Neck Surg*. 1986; 95:285–91. [PubMed: 3108775]
73. Monson BB, Hunter EJ, Lotto AJ, Story BH. The perceptual significance of high-frequency energy in the human voice. *Front Psychol*. 2014; 5(587):1–11. [PubMed: 24474945]
74. Meyer TA, Canty PA, Wilkinson EP, Hansen MR, Rubinstein JT, Gantz BJ. Small acoustic neuromas: surgical outcomes versus observation or radiation. *Otol Neurotol*. 2006; 27:380–92. [PubMed: 16639278]
75. Newman CW, Weinstein BE, Jacobson GP, Hug GA. The Hearing Handicap Inventory for Adults: psychometric adequacy and audiometric correlates. *Ear Hear*. 1990; 11(6):430–3. [PubMed: 2073976]
76. Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009; 339:b2535. [PubMed: 19622551]
77. Watanabe S, Yamamoto M, Kawabe T, et al. Stereotactic radiosurgery for vestibular schwannomas: average 10-year follow-up results focusing on long-term hearing preservation. *J Neurosurg*. 2016; 125:64–72. [PubMed: 27903183]
78. Kooy HM, Dunbar SF, Tarbell NJ, et al. Adaptation and verification of the relocatable Gill-Thomas-Cosman frame in stereotactic radiotherapy. *Int J Radiat Oncol Biol Phys*. 1994; 30:685–91. [PubMed: 7928501]
79. Bova FJ, Buatti JM, Friedman WA, Mendenhall WM, Yang CC, Liu C. The University of Florida frameless high-precision stereotactic radiotherapy system. *Int J Radiat Oncol Biol Phys*. 1997; 38:875–82. [PubMed: 9240657]

80. Lunsford LD, Niranjan A, Flickinger JC, Maitz A, Kondziolka D. Radiosurgery of vestibular schwannomas: summary of experience in 829 cases. *J Neurosurg.* 2005; 102:195–199.
81. Hasegawa T, Kida Y, Kobayashi T, Yoshimoto M, Mori Y, Yoshida J. Long-term outcomes in patients with vestibular schwannomas treated using gamma knife surgery: 10-year follow up. *J Neurosurg.* 2005; 102:10–6. [PubMed: 15658090]
82. Liu D, Xu D, Zhang Z, Zhang Y, Zheng L. Long-term outcomes after Gamma Knife surgery for vestibular schwannomas: a 10-year experience. *J Neurosurg.* 2006; 105(Suppl):149–53. [PubMed: 18503349]
83. Nagano O, Higuchi Y, Serizawa T, et al. Transient expansion of vestibular schwannoma following stereotactic radiosurgery. *J Neurosurg.* 2008; 109:811–6. [PubMed: 18976069]
84. Combs SE, Welzel T, Kessel K, et al. Hearing preservation after radiotherapy for vestibular schwannomas is comparable to hearing deterioration in healthy adults and is accompanied by local tumor control and a highly preserved quality of life (QOL) as patients' self-reported outcome. *Radiother Oncol.* 2013; 106:175–80. [PubMed: 23333012]
85. Stangerup SE, Caye-Thomasen P, Tos M, Thomsen J. Change in hearing during 'wait and scan' management of patients with vestibular schwannoma. *J Laryngol Otol.* 2008; 122:673–81. [PubMed: 18088451]
86. Stangerup SE, Thomsen J, Tos M, Cayé-Thomasen P. Long-term hearing preservation in vestibular schwannoma. *Otol Neurotol.* 2010; 31:271–5. [PubMed: 19887973]
87. Massager N, Lonnenville S, Delbrouck C, Benmebarek N, Desmedt F, Devriendt D. Dosimetric and clinical analysis of spatial distribution of the radiation dose in gamma knife radiosurgery for vestibular schwannoma. *Int J Radiat Oncol Biol Phys.* 2011; 81:e511–8. [PubMed: 21621339]
88. Poen JC, Golby AJ, Forster KM, et al. Fractionated stereotactic radiosurgery and preservation of hearing in patients with vestibular schwannoma: a preliminary report. *Neurosurgery.* 1999; 45:1299–305. [PubMed: 10598696]
89. Sawamura Y, Shirato H, Sakamoto T, et al. Management of vestibular schwannoma by fractionated stereotactic radiotherapy and associated cerebrospinal fluid malabsorption. *J Neurosurg.* 2003; 99:685–92. [PubMed: 14567604]
90. Combs SE, Volk S, Schulz-Ertner D, Huber PE, Thilmann C, Debus J. Management of acoustic neuromas with fractionated stereotactic radiotherapy (FSRT): long-term results in 106 patients treated in a single institution. *Int J Radiat Oncol Biol Phys.* 2005; 63:75–81. [PubMed: 16111574]
91. Collen C, Ampe B, Gevaert T, et al. Single fraction versus fractionated linac-based stereotactic radiotherapy for vestibular schwannoma: a single-institution experience. *Int J Radiat Oncol Biol Phys.* 2011; 81:503–9.
92. Anderson BM, Khuntia D, Bentzen SM, et al. Single institution experience treating 104 vestibular schwannomas with fractionated stereotactic radiation therapy or stereotactic radiosurgery. *J Neurooncol.* 2014; 116:187–93. [PubMed: 24142200]
93. Combs SE, Engelhard C, Kopp C, et al. Long-term outcome after highly advanced single-dose or fractionated radiotherapy in patients with vestibular schwannomas – pooled results from 3 large German centers. *Radiother Oncol.* 2015; 114:378–83. [PubMed: 25702864]
94. Quist TS, Givens DJ, Gurgel RK, Chamoun R, Shelton C. Hearing preservation after middle fossa vestibular schwannoma removal: are the results durable? *Otolaryngol Head Neck Surg.* 2015; 152:706–11. [PubMed: 25628370]
95. Woodson EA, Dempewolf RD, Gubbels SP, et al. Long-term hearing preservation after microsurgical excision of vestibular schwannoma. *Otol Neurotol.* 2010; 31:1144–52. [PubMed: 20679955]
96. Mazzoni A, Zanoletti E, Calabrese V. Hearing preservation surgery in acoustic neuroma: long-term results. *Acta Otorhinolaryngol Ital.* 2012; 32:98–102. [PubMed: 22767970]
97. Chee GH, Nedzelski JM, Rowed D. Acoustic neuroma surgery: the results of long-term hearing preservation. *Otol Neurotol.* 2003; 24:672–6. [PubMed: 12851563]

Figure 1.
Literature database search and data synthesis methodology.

Figure 2. Distribution of publications. The majority of papers were published in the neurosurgery literature (A). There is a wide global distribution of institutions represented (B).

Figure 3. Hearing preservation rate significantly decreases with time from radiotherapy (ANOVA $p < 0.05$).

Figure 4.

Crude hearing preservation rate (A) and time-based hearing preservation rates (B) are dependent on time from radiotherapy. Bubble area is proportional to sample size. Crude hearing preservation rate plotted with minimum time to follow-up of one year and minimum sample size of 13.

Table 1

Summary of reviewed publications and selected data.

Author	Year	Site	Total sample size	Serviceable hearing sample	Hearing preservation rate *	Avg follow-up time (mo.) [†]	Technique	Fractionation	Tumor Size [‡]
Putz	2017	Erlangen, Germany	107	25	72.0%	36.4	Linac	both	13.5 mm
Kessel	2017	Munich, Germany	184	65	63.1%	90	Linac	both	1.96 cm ³
Schumacher	2017	Chicago, IL	30	11	55.0%	42	GKS	single	0.53 cm ³
Horiba	2016	Tokyo Womens Hospital	102	49	57.0%	55	GKS	single	**
Klijn	2016	Tilburg, Netherlands	420	71	60.3%	61	GKS	single	1.4 cm ³
Bennion	2016	Omaha, Nebraska	45	45	58.0%	33.9	Linac	fractionated	0.33 cm ³
Ikonomidis	2015	Lausanne, Switzerland	84	41	36.0%	39	Linac	single	2.1 cm ³
Tveiten	2015	Bergen, Norway & Rochester, MN	240	114	34.2%	87.6	GKS	single	**
Elliot	2015	Halifax, Nova Scotia	123	25	40.0%	43	Linac	fractionated	**
Boari	2014	Milan, Italy	379	96	49.0%	59.9	GKS	single	1.94 cm ³
Llopez	2014	Valencia, Spain	35	32	65.5%	56.4	both	single	15.2 mm
Kranzinger	2014	Salzburg, Austria	21	12	50% (5 yrs)	80.5	Linac	fractionated	0.9 cm ³
Jacob	2014	Rochester, MN	105	59	64.0%	25.2	GKS	single	7.1 mm
Vivas	2014	Pittsburgh, PA	59	28	53.5% (3 yrs)	40	Linac	fractionated	0.81 cm ³
Su	2014	Hualein, Taiwan	13	12	91.7%	118	GKS	single	0.098 cm ³
Champ	2013	Philadelphia, PA	154	87	67.0%	35	Linac	fractionated	2.4 cm ³
Karam	2013	Washington DC	37	14	78.0%	18	Linac	fractionated	1.03 cm ³
Litre	2013	Reims, France	158	61	54.0%	60	Linac	fractionated	2.45 cm ³
Baschnagel	2013	Royal Oak, Michigan	40	40	75.0%	34.5	GKS	single	13 mm
Carlson	2013	Rochester, MN	44	44	18.0%	99.6	GKS	single	1.70 cm ³
Lin	2013	Taipei, Taiwan	20	10	50.0%	24	Linac	fractionated	1.41 mm
Yomo	2012	Marseille, France	154	128	58.1%	52	GKS	single	0.73 cm ³
Han	2012	Seoul, Korea	119	119	57.1%	55.2	GKS	single	1.95 cm ³

Author	Year	Site	Total sample size	Serviceable hearing sample	Hearing preservation rate* (mo.) [†]	Avg follow-up time (mo.) [†]	Technique	Fractionation	Tumor Size [‡]
Rasmussen	2012	Copenhagen, Denmark	42	21	38% (2 yrs)	60	Linac	fractionated	20 mm
Hayden-Gephart	2012	Palo Alto, CA	94	94	74.0%	28.8	Linac	fractionated	**
Hasegawa	2011	Komaki, Japan	117	117	47.9%	38	GKS	single	1.9 cm ³
Roos	2011	Adelaide, Australia	91	50	38.0%	65	Linac	single	21 mm
Park	2011	Seoul, South Korea	31	31	45.0%	43.8	GKS	single	19.3 mm
Brown	2011	Philadelphia, PA	53	31	61.0%	15.5	GKS	single	1.11 cm ³
McWilliams	2011	Pittsburgh, PA	23	7	14.3%	13	linac	both	12 mm
Kim	2010	Seoul	27	27	68.1% (3 yrs)	35.7	GKS	single	17.3 mm
Kano	2009	Pittsburgh, PA	77	77	71.4%	20	GKS	single	0.75 cm ³
Lasak	2008	Wichita, Kansas	33	10	90.0%	24	GKS	single	1.48 cm ³
Iwai	2008	Osaka, Japan	25	16	64.0%	89	GKS	single	8.4 mm
Bush	2008	Lexington, Kentucky	17	12	41.7%	33.6	GKS	single	13.3 mm
Massager	2007	Brussels, Belgium	82	60	65.0%	24	GKS	single	**
Thomas	2007	Vancouver, Canada	34	33	59.0%	36.5	Linac	fractionated	1.06 cm ³
Chopra	2007	Pittsburgh, PA	216	106	56.6%	68	GKS	single	1.3 cm ³
Rutten	2007	Liege, Belgium	26	11	90.1%	45	Linac	single	18 mm
van Eck	2005	Krefeld, Germany	95	30	83.3%	22	GKS	single	2.28 cm ³
Myrseth	2005	Bergen, Norway	103	31	32.2%	70.8	GKS	single	**
Muacevic	2004	Munich, Germany	219	53	49.0%	6	GKS	single	**
Rowe	2003	Sheffield, UK	234	49	76.0%	35	GKS	single	3.71 cm ³
Williams	2002	Baltimore, MD	150	46	80.4%	22.8	Linac	fractionated	1.7 cm ³
Regis	2002	Marseille, France	97	48	50.0%	48	GKS	single	18 mm
Ottaviani	2002	Milan, Italy	30	18	66.7%	24	GKS	single	1.6 cm ³
Unger	2002	Graz, Austria	100	29	55.0%	76	GKS	single	3.8 cm ³

* Hearing preservation rate is crude hearing preservation rate unless otherwise noted.

[†] Average time to follow-up is mean unless only median time to follow-up was available.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Tumor size reported either as diameter or volume as noted;
* indicates non-continuous variable sizes.

Patient, tumor, or treatment effects on serviceable hearing preservation rate. No effect was significant on univariate analysis.

Table 2

Patient or treatment effect	HP rate	number of studies	p-value
Tumor size small *	61%	20	0.50
Tumor size large *	57%	20	
Age < 58 years	56%	27	0.56
Age ≥ 58 years	59%	17	
GKS	59%	28	0.68
Linac	56%	18	
Single dose	58%	32	0.99
Fractionated	58%	12	
Dose <13Gy †	56%	16	0.44
Dose ≥ 13 Gy †	61%	16	

* tumor size small is ≤ 15mm diameter or ≤ 1.5 cm³ volume.

† single dose radiosurgery only