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REVIEW

A review of treatment modalities for vestibular schwannoma

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Abstract Vestibular schwannomas are benign intracranial tumors arising from the vestibular nerve. Treatment options include observation, stereotactic radiosurgery, fractionated radiotherapy, and microsurgery. We review the evidence describing efficacy and side-effect profiles of each of these modalities. This was accomplished by outlining the results of published meta-analyses and performing a systematic search of the literature for individual studies published between 2004 and June 2009. Without intervention, 29–54% of tumors will grow and 16–26% of patients require additional treatment, with 54–63% preserving functional hearing. With radiosurgery, only 2–4% require additional treatment and hearing preservation is accomplished in 44–66% of cases. Reviewing contemporary studies, it appears that reduced marginal doses may have decreased morbidity risks associated with radiosurgery without sacrificing efficacy. With fractionated radiotherapy, 3–7% will require additional treatment and hearing preservation is reported at 59–94% of patients, although long-term outcomes are not known. Microsurgery is an alternative for eligible patients, with fewer than 2% requiring additional treatment; however, the risk of hearing loss, facial neuropathy, and other morbidities is relatively high. There are significant limitations with comparing the efficacy and morbidity rates across interventions because of selection bias and confounding factors. Additional prospective comparative trials and randomized studies are needed to improve our understanding of the relative benefits of each modality.

Keywords Vestibular schwannoma · Acoustic neuroma · Radiosurgery · Microsurgery · Radiotherapy · Observation

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Introduction

Vestibular schwannomas (VSs), also called acoustic neuromas, are benign intracranial neoplasms arising from Schwann cells, which myelinate the vestibular portion of the eighth cranial nerve. Incidence of these tumors is approximately one per 100,000 person-years, a rate that has increased over time [1]. While advances in diagnostic capabilities offer a logical explanation for this trend, incidence of similar tumors remains static suggesting an undetermined etiology may be at play.

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Patients with VS experience dysfunction of structures sharing anatomical proximity with their tumor. Typically, a VS originates within the internal acoustic meatus. Tumors confined within this structure are dubbed *intracanalicular*, while those extending beyond the petrous portion of the temporal bone are designated *extracanalicular*. Mass effect of extracanalicular VSs, which project into the cerebellopontine angle, may compromise function of additional cranial nerves, brainstem nuclei, or the cerebellum. Therefore, unilateral VS can present with a spectrum of ipsilateral symptoms and signs.

Matthies and Samii provide a summary of typical clinical presentations associated with VS based on the experiences of 1,000 patients [2]. Hearing loss was the most common problem, affecting 95% of patients based on subjective assessment. The next most common was tinnitus, affecting over 60% of patients. Notably, nearly half of deaf patients experienced tinnitus. Symptoms associated with vestibular function also caused problems for a significant number of patients. Vertigo reportedly occurred in 28%, dizziness in 22%, and disequilibrium in 40%. The unsteadiness experienced may also be attributable, in part, to compression of the cerebellum, especially in those with very large extracanalicular tumors. Finally, some patients experienced dysfunction of additional cranial nerves. Signs of trigeminal neuropathy occurred in 12–19%, although only 7–9% complained of symptoms of reduced facial sensation. Facial neuropathy was exhibited by 17% of patients, with 5% noting symptoms of paresis. Caudal cranial nerves (IX–XII) were rarely involved, identified in 3% of patients with VS.

The presence of symptoms and signs caused by VSs is indicative of an intracranial lesion, which should provoke physicians to perform a more thorough evaluation. Patients with hearing loss often undergo audiometric evaluation, and those with vestibular disturbances may undergo vestibular testing. Confirmation of asymmetric sensorineural hearing loss, or defects in other cranial nerves, indicates the need for imaging workup. Gadolinium enhanced magnetic resonance imaging (MRI) of the internal acoustic meatus remains the standard method for diagnosing VS. Diagnosis typically occurs in the fifth or sixth decade of life, with a median age at diagnosis of 50 years in a large epidemiological study [1].

Following diagnosis with VS, patients have several options for managing their tumor. These include observation by MRI, stereotactic radiosurgery (SRS), fractionated radiotherapy (FRT), and microsurgery (MS). Selection of a treatment modality depends on tumor size, associated symptoms and signs, patient age, patient health, and patient preference. Unfortunately, some evidence suggests that a predictor of treatment choice is the discipline of the attending physician [3]. This may be attributed partly to the limited evidence-based guidelines for treating VS. There remains no level 1 evidence comparing the modalities, and the majority of data is level 3 or worse, coming from retrospective studies [4, 5]. Until additional prospective comparisons or randomized trials can be accomplished, systematic meta-analysis of the available literature offers the most powerful guidance for clinical decisions. However, such data must be interpreted with caution when comparing modalities, as there is a strong potential for selection bias in the different treatment categories.

We present a summary of the available evidence describing the efficacy and side-effect profiles of the major treatment modalities for VS. Specifically, we tabulated the outcomes from existing meta-analysis published in the literature. Additionally, we performed a systematic search to identify individual studies published in the past 5 years, some of which may not have been included in published meta-analyses. These represent the most current data on VS treatment, reflecting the impact of evolving treatment techniques over the past decade. Our goal is to provide a comprehensive and contemporary review of observation, radiosurgery, radiotherapy, and MS as options for managing patients with VS. This review also offers a concise presentation of the available evidence for guiding patients and practitioners in clinical decision making.

Methods

Literature search for systematic meta-analyses

Seeking existing meta-analyses examining the treatment modalities used in VS management, we searched *PubMed* using the *Clinical Queries* service (http://www.ncbi.nlm.nih.gov/corehtml/query/static/clinical.shtml). We used the query "acoustic neuroma OR vestibular schwannoma" in the *Find Systematic Reviews* field. This search yielded 84 articles. Papers were selected which included systematic reviews of observation, SRS, FRT, or MS. Only those that described treatment outcomes were included in this review.

Literature search for studies published in the past 5 years

In order to identify contemporary studies describing VS treatment modalities, we performed a systematic PubMed search. The following query was used, incorporating appropriate headings from the *MeSH database*; '"Neuroma, Acoustic/prevention and control"[Majr] OR "Neuroma, Acoustic/radiotherapy"[Majr] OR "Neuroma, Acoustic/surgery"[Majr] OR "Neuroma, Acoustic/therapy"[Majr]'. Limits on the article type, used to pair down the results, were "Clinical Trial, Randomized Controlled Trial, Comparative Study, Evaluation Studies, Validation Studies." This yielded 91 studies for further analysis.

For inclusion, studies must have been published in English after 2003, have a study size ≥25 patients, have a mean follow-up ≥24 months, and have reported a measurement of treatment success. When multiple articles meeting our criteria were published from the same center, we included data from the most recent study. If appropriate, we included multiple studies from the same center because they described different outcomes. Finally, for SRS, we only included studies that used Gamma Knife; and for FRT, we omitted studies on hypofractionation.

We also sought to identify articles not found in our initial PubMed query. First, references cited in papers already selected for inclusion were evaluated. Second, we searched for additional articles from identified study centers, using the city name paired with "AND acoustic neuroma" in a PubMed query. Those additional manuscripts identified in this fashion were evaluated using our inclusion criteria.

Data analysis

Appropriate data was captured from studies, which were identified using the search criteria above. Extracted data points included measurements of treatment success and permanent morbidities, such as hearing preservation rates and facial neuropathy rates. Treatment success was identified as the fraction of patients requiring additional treatment during the follow-up period in the form of radiation or surgery. Outcomes specific to observation included the number of tumors growing and the mean growth rate. In the radiosurgery and radiotherapy categories, tumor arrest was defined as no growth or regression at last follow-up, based on post-treatment MRI measurements. Growth was not uniformly defined across studies, but typically represented a net increase in tumor dimension >2 mm at last follow-up. Serviceable hearing was based on audiometric data and the Gardner–Robertson scale, defined as a pure tone average or speech reception threshold ≤50 dB and speech discrimination score ≥50% [6]. Hearing preservation refers to the retention of serviceable hearing at last follow-up in those patients with serviceable hearing prior to treatment. Facial neuropathy rate was defined as the permanent loss of good facial nerve function following treatment. Good facial nerve function corresponds to House–Brackmann grade of I or II [7]. In some cases, data extracted from the literature had to be recalculated to obtain the outcomes described above, because of differences in reporting summary statistics across studies. For meta-analyses, this included calculating weighted means, weighted by study size (*N*), for those papers that presented overall outcomes as a simple mean. Data from individual studies was summarized in a similar fashion, using weighted means.

Discussion of treatment modalities

Observation

Slow growth rates of some VSs suggest that some patients may be managed conservatively, without active intervention aimed at controlling the size of their tumor. Patients undergoing this approach are monitored using MRI until progression of symptoms or tumor growth warrants more invasive treatment. This allows patients freedom from the potential adverse effects of radiation treatments or surgery.

Observation is not without risks, however, because growth rates vary with time and some VSs have been observed to increase in size at rates tenfold faster than the average tumor [8]. Few variables are predictive of the magnitude of future growth [9]. Previous growth, large size, and young age are the only indicators identified [10]. Furthermore, even small, static, or slowly growing tumors may eventually cause symptom progression and require additional treatment [10]. Regular follow-up is a key component to this strategy, but evidence suggests patient compliance may not be ideal [9].

The efficacy of observation is measured by tumor growth rate, freedom from additional intervention, and preservation of normal cranial nerve function. We present evidence on these subjects from currently available meta-analyses in Table 1 [9, 11–15]. No individual studies were identified in our search that both met our inclusion criteria and were not already included within those meta-analyses. Therefore, we did not tabulate individual studies describing observation. The mean follow-up times reflected in the observation literature were typically just over 3 years. Patients included in this cohort had a mean tumor size hovering around 10 mm in diameter. During observation, tumor growth was identified in 29–54% of patients, with a mean growth rate between 1 and 3 mm per year. Of patients who underwent observation, 16–26% eventually required treatment in the form of radiation or MS. The two systematic reviews that objectively measured hearing preservation report rates of 54% and 63% [13, 14].

Observation offers a low-risk option for some patients with VS. Patients considering this management strategy should be informed that many tumors continue to grow, and approximately one in five people ultimately require intervention. Furthermore, progression of symptoms remains a possibility regardless of tumor size or growth. For those presenting with serviceable hearing, preservation rates are over 50%. Notably, these outcomes are witnessed over a mean follow-up of 3 years and, in the long term, additional patients may experience worsening symptoms and require intervention. This option may be indicated for older patients; those with small, intracanalicular tumors, and those committed to undergoing regular following up

Table 1 Observation, meta-analyses

First author (year)	Studies (patients)	Follow-up (months)	Tumor size (mm)	Tumors growing (%)	Growth rate (mm/year)	Additional treatment rate (%)	Hearing preservation rate (%)
Sughrue (2009) [13][a]	34 (982)	[26–52]	11.3		2.9	16	54
Battaglia (2006) [11]	6 (427)	42 [29–80]	9.5 [8–11]	29 [18–39]	1.2 [0.7–2.9]	18 [8–59]	
			n = 383		*n = 336*	*n = 383*	
Yoshimoto (2005) [15]	26 (1,340)	38 [6–64]	11.1 [5–21]	46 [15–85]	1.2 [0.4–2.9]	18 [16–21]	
			n = 1,163		*n = 964*	*n = 930*	
Smouha (2005) [9]	21 (1,345)	38	11.8	43	1.9	20	49[b]
			n = 900	*n = 1,244*	*n = 793*	*n = 1,001*	*n = 347*
Yamakami (2003) [14]	13 (903)	37 [24–53]	10 [5–16]	51 [29–82]	1.9 [0.3–3.2]	20 [8–33]	63
				n = 879	*n = 879*	*n = 804*	*n = 60*
Selesnick (1998) [12][a]	13 (571)	36 [18–60]	11.8	54 [14–74]	1.8 [0.5–3.2]	26 [0–50]	
		n = 524	*n = 442*	*n = 558*	*n = 508*		

Data points include weighted mean, the range (square brackets), and the sample size (italics). For hearing preservation, the sample size represents the number of patients with functional hearing prior to observation

[a] Data not available to calculate weighted means

[b] Unspecified criteria for hearing preservation

with serial MRI. Progression of symptoms or signs of tumor growth should prompt evaluation for additional treatment.

Stereotactic radiosurgery

SRS is an alternative intervention to surgical resection for VSs. It involves the precise administration of a single dose of radiation to the tumor volume, with the goal of arresting tumor growth. This is accomplished by immobilizing the patient's head, defining a coordinate system to the cranium, and mapping the tumor volume within this frame of reference. Multiple beams of ionizing radiation are oriented such that they sum to a highly conformal dose at the tumor margin. Gamma Knife radiosurgery accomplishes this feat using 201 fixed Cobalt-60 sources, while the linear accelerator uses a single source rotated about the target in radiation arcs. In this review, we focus on the efficacy of Gamma Knife radiosurgery. Since no intracranial manipulation is required, radiosurgery offers minimal invasiveness compared to MS.

While radiosurgery is less invasive than surgery by nature, radiation exposure comes with related risks. With the treatment of VSs, dose profiles may overlap structures adjacent to the tumor, potentially resulting in dysfunction of cranial nerve or brainstem structures. For instance, post-operative hearing loss has been associated with increased dose to the cochlea or associated brainstem nuclei [16–18]. Post-treatment hydrocephalus is another adverse outcome experienced by some patients. Radiation exposure also poses a small risk of secondary malignancy; however, follow-up times reported in the literature are likely too short to deduce the true risk to patients treated for VS.

Over the past two decades, side-effect profiles associated with radiosurgery have improved along with treatment techniques. Advances in radiosurgical treatment come in the form of high-resolution MRI and treatment planning software [16, 19]. These allow physicians the ability to achieve more precise dose conformality about the tumor volume. Additionally, the dose prescribed to the tumor margin has been gradually reduced, with similar efficacy being reported with doses below 13 Gy [20]. Evidence suggests that minimizing the radiation exposure to extraneous cranial structures, achieved by modern treatment techniques and reduced doses, minimizes morbidity rates associated with SRS without sacrificing efficacy [19–21]. In recent meta-analyses, statistically significant improvements in hearing preservation and facial neuropathy rates were identified, with doses ≤12.5 and ≤13 Gy, respectively [22, 23].

The efficacy of Gamma Knife radiosurgery has been the subject of several meta-analysis identified by our search [11, 14, 22–26]. Table 2 reports key measures of treatment outcome captured from those reviews, measured at a mean follow-up of 25–60 months. The radiosurgical literature typically reports tumors by volume rather than diameter, and those treated in this cohort had mean sizes between 2.7 and 4.0 cm^3. As mentioned previously, doses have

Table 2 Stereotactic radiosurgery, meta-analyses

First author (year)	Studies (patients)	Tumor volume (cm^3)	Dose (Gy)	Follow-up (months)	Tumor control rate (%)	Additional treatment rate (%)	Hearing preservation rate (%)	Facial neuropathy rate (%)
Yang (2009) [23]	23 (2,204)	3.0 [0.2–15] *n=1,782*	13.7 [12–19.6] *n=2,107*	60 [12–119] *n=2,161*	94.7 [0–100]			4.0 [0–100] *n=1,908*
Yang (2009) [22]	74 (5,825)	4.0	16	41	94		57 *n=2,083*	
Weil (2006) [26]	35 (3,307)	3.0 [0.6–7.6] *n=1,908*	14.1 [12–18]	43 [16–135] *n=3,230*	94.6 [86–100] *n=3,074*			
Battaglia (2006) [11]	3 (397)		[12–13]	30 [24–60]	92.7 [86–100]	1.6 [1–4]		
Yamakami (2003) [14]	9 (1,475)	2.7 *n=390*	13.8 [12–17] *n=663*	46 [22–62] *n=1,148*	92.6 [88–97] *n=841*	4.2 [2–7]	66 [47–81] *n=271*	9 [1–17] *n=967*
Shin (2003) [25]	7(731)			[12–120]	94.1 [93–96] *n=262*		53 [40–69] *n=142*	7.4[a] [0–20]
Kaylie (2000) [24][b]	8 (875)	16.1 mm[d]	17.3	25	91 *n=805*		44 *n=219*	19 *n=717*

Data points include weighted mean, the range (square brackets), and the sample size (italics). For hearing preservation, the sample size represents the number of patients with functional hearing prior to observation

[a] Unspecified criteria for facial neuropathy

[b] Data not available to calculate weighted means

[c] Includes transient hypesthesia

[d] Linear measurement of tumor size

gradually decreased since the first use of radiosurgery for treating acoustic neuromas, so the mean doses reported in the meta-analyses range from 12 to 17 Gy. Arrest of tumor growth was achieved in 91–95% of cases. The fraction of patients needing additional treatment after SRS was 1.6% and 4.2% from the data in two meta-analyses [11, 14]. Hearing preservation rates with radiosurgery range from 44% to 63%. Permanent facial neuropathy was experienced by 4–19% of patients; however, in all meta-analyses published after 2000, the rate was below 10%. In reviews that evaluated permanent trigeminal neuropathy following radiosurgery rates ranged from 11% to 16%, and hydrocephalus occurs in only 2–3% of patients treated (not shown in Table 2).

Evaluating contemporary studies on Gamma Knife radiosurgery for VS may reflect the advantages offered by lower marginal doses and improved radiosurgical techniques. We present the data identified in our literature search in Table 3, including mean statistics weighted by study size (*N*) [27–34]. A total population of 1,850 patients was included in the analysis, with a mean tumor volume of 2.3 cm^3. They were treated with a mean dose of 12.6 Gy and half of the patients underwent a mean follow-up of just under 6 years. Tumor arrest was observed at rates comparable to, but not within, the range of those reported in existing meta-analyses (mean 89%). Two studies determined 10-year actuarial rates of tumor arrest slightly over 90% [27, 28]. The mean number of patients requiring additional treatment was 3.9 %, based on data from six of the seven studies. Hearing preservation was achieved in 60% of 411 patients who presented with serviceable hearing. The rates of facial and trigeminal neuropathy were lower than those reported in other systematic reviews, 1.5% and 1.2%, respectively (data for trigeminal neuropathy is not shown in Table 3). This may reflect a reduction in cranial nerve toxicity as a result of lower doses and more precise treatment planning. However, determining a quantitative association will require more robust examination. Finally, hydrocephalus was observed in 2.7% of patients following treatment (not reported in Table 3), which does not deviate from the range of values reported in Table 2.

Table 3 Stereotactic radiosurgery, contemporary studies

First author (year)	*N*	Tumor volume (cm^3)	Dose (Gy)	Follow-up (months)	Tumor control rate (%)	Additional treatment rate (%)	Hearing preservation rate (%)	Facial neuropathy rate (%)
Lasak (2008) [29]	33	1.5	12.9 [12–13]	25 [6–51]	93.9		90 *n=10*	0
Regis (2004) [33] (2007) [34]	927	1.3 [0.02–14]	12	[>36]	85	3	60 *n=175*	[<1%][a]
Chopra (2007) [27]	216	1.3[a]	12.9	68	96.8	1.4	56.6 44.5[b]	0
		[0.08–38]	[12–13]		90.8[b]	1.7[b]	*n=163*	
Pollock (2006) [31]	208	3.2	14.4	56 [24–132]	93.3	1.9		
Pollock (2006) [32]	46	12.3 mm[e]	12.2	42 [12–62]	96	4.3	63 *n=30*	0
Hasegawa (2005) [28]	317	5.6 [0.2–37]	13.2 [10–18]	93	93 92[b]	9	58 *n=90*	1.6[c]
Myrseth (2005) [30]	103	[<30 mm][e]	12.2 [10–20]	71 [12–170]	89.2	4.9		5.2
Weighted mean	264	2.3	12.6	71	89	3.9	60	1.5
Patients (n)	*1,850*	*1,701*	*1,850*	*923*	*1,850*	*1,817*	*411*	715

Data points include weighted mean, the range (square brackets). For hearing preservation, the sample size (italics) represents the number of patients with functional hearing prior to observation

[a] Median

[b] 10-year actuarial rate

[c] Unspecified criteria for facial neuropathy

[d] Facial neuropathy defined as House–Brackmann grade>1

[e] Linear measurement of tumor size

Given the available evidence, SRS is an effective alternative to surgery for the treatment of VS. Physicians can confidently advise patients that radiosurgery will arrest tumor progression in approximately 90% or more cases and only about 4% will require additional treatment. While it remains possible that with longer follow-up this may prove an overestimation, 10-year actuarial rates of arrested growth are reported at greater than 90%. For patients with serviceable hearing prior to treatment, preservation of function is reported at between 44% and 63%. Patients should be informed that major adverse outcomes associated with radiosurgical intervention include trigeminal neuropathy (1–17%), facial neuropathy (2–19%), and hydrocephalus (2–3%). It appears that current treatment protocols, which typically prescribe below 13 Gy, these side effects will be limited to fewer than one in ten patients, and likely closer to one in 50. The risk of radiation-induced neoplasm has not been determined in patients treated for VS; however, patients should be informed that it is a possibility. This modality may be well suited for patients exempt from surgical intervention, those with small tumors (<30 mm diameter), those with serviceable hearing, and those who prefer not to undergo surgical resection because of preference or anxiety.

Fractionated radiotherapy

FRT is akin to SRS in that it uses ionizing radiation to treat intracranial tumors in a minimally invasive fashion. Similar to radiosurgery, the patient's head is immobilized and assigned a coordinate system, allowing for the orientation of external radiation beams to achieve a conformal dose encompassing the tumor volume. The primary difference is that radiotherapy involves the sequential administration of numerous dose fractions over a series of weeks, which ultimately sum to one large dose. The goal is to administer significant dose to the tumor, while the surrounding tissue, which receives minimal dose with each fraction, will be capable of healing between treatments. However, questions exist as to whether FRT will offer long-term efficacy comparable to radiosurgery [16].

We identified no systematic reviews evaluating the efficacy of FRT, although a number of individual studies published in the last 5 years were available. The data captured is outlined in Table 4, and includes six studies and 404 patients [35–40]. As summary statistics we calculated weighted means, weighted by study size (*N*).

Patients treated in this cohort had a mean tumor volume of 4.1 cm^3 and received a mean total dose of 52 Gy, administered in fractions of 1.8 or 2.0 Gy. Overall, a mean follow-up of 53 months was reported. The mean rate of tumor arrest was 96%. Based on four studies, the 5-year actuarial rate was 94% [36–39]. From three reporting studies, the rate of additional treatment was 5.4% [36, 39, 40]. Hearing preservation was achieved in 79% of 261 patients with serviceable hearing prior to intervention and facial neuropathy was experienced by 1.0%. Adverse events also included trigeminal neuropathy (1.8%) and hydrocephalus (3.8%; not shown in Table 4). It should be noted that two centers preferentially guided patients with serviceable hearing to receive FRT, potentially confounding the results and limiting comparison of radiotherapy to other modalities [35, 40].

While long-term outcomes are yet to be evaluated, available results indicate FRT is an efficacious option for treatment of VS. The major downside is that FRT requires the administration of more than 25 treatments over a period of weeks. Patients should be made aware of this treatment modality as an alternative to radiosurgery. While it may offer a similar success rate and improved hearing preservation relative to SRS, the results in this review are not sufficient to prove or disprove a significant difference in relative outcomes. Such conclusions can only come from prospective comparative studies or randomized trials, which limit confounding and provide adequate power to elucidate differences between SRS and FRT. Results in the FRT literature should also be evaluated with the awareness that they represent a mean follow-up period of just over 4 years and the long-term outcomes are yet to be determined. FRT may appeal to patients with small tumors, similar to those well suited for radiosurgery, who desire to maximize the possibility of preserving of cranial nerve function. However, at this point, there is inadequate evidence to recommend it over SRS in the treatment of vestibular schwannomas.

Microsurgery

Surgical intervention for VSs was first performed over a century ago. Unfortunately, early efforts involved significant mortality rates, as reviewed in [4]. The advent of the surgical microscope and improvement in surgical practices has eliminated much of that risk. Today, surgery offers the possibility of excellent tumor control. Also, since this intervention seeks to remove all or part of the tumor, while SRS or FRT only seek to prevent additional growth, surgery is appropriate for use in treating larger tumors. Furthermore, despite its invasiveness, microsurgical approaches

Table 4 Fractionated radiotherapy, contemporary studies

First author (year)	*N*	Tumor volume (cm^3)	Dose (Gy)	Fractions (Gy)	Follow-up (months)	Tumor control rate (%)	Additional treatment rate (%)	Hearing preservation rate (%)	Facial neuropathy rate (%)
Andrews (2009) [35][c]	89	1.6	48.5	1.8	68	97.8		73.3 *n = 89*	0.0
Koh (2007) [38]	60	4.9 [0.3–49]	50.0	2.0	32 [6–107]	96.7 96.2[b]		77.3 *n = 22*	0.0
Thomas (2007) [40][c]	34	1.1 [0.3–9.6]	50.0	2.0	48	94.1	2.9	59 56[b] *n = 34*	0.0
Maire (2006) [39]	45		50.4	1.8	80 [4–227]	88.9 86[b]	6.7		
Combs (2005) [37]	106	6.6 [2.7–31]	57.6[a]	1.8	48.5 [3–172]	95.3 93[b]		94.0 *n = 65*	2.3[d]
Chan (2005) [36]	70	4.5 [0.05–21]	54[a]	1.8	45	98.6 98[b]	5.7	84[e] *n = 51*	1.4
Weighted mean	67	4.1	52.4	1.8	53	95.8	5.4	79	1.0
Patients (n)	*404*	*359*	*404*	*404*	*404*	*404*	*149*	*261*	*359*

Data points include weighted mean, the range (square brackets). For hearing preservation, the sample size (italics) represents the number of patients with functional hearing prior to observation

[a] Median

[b] 5-year actuarial rate

[c] Patients with serviceable hearing selectively assigned to FRT treatment

[d] Unspecified criteria for facial neuropathy

[e] Hearing preservation based on subjective assessment

can offer some patients the chance to preserving serviceable hearing. Unfortunately, even technological and procedural advances have not eliminated the risk of adverse events associated with surgical resection. Damage to cranial nerves, cerebrospinal fluid (CSF) leak, and infection occur in a significant fraction of patients. There is also a significant learning curve associated with VS resection, and small tumor size and the surgeon's experience have been associated with facial nerve preservation [10]. Whether this site-specific variability is specific to surgical approaches, as opposed to SRS or FRT is not clear. Despite its invasiveness, surgery remains a mainstay in VS treatment.

Two meta-analyses were identified evaluating the use of surgery in over 7,500 patients with VS [14, 24]. Data collected from the studies is compiled in Table 5. These reviews represent a population with a range of tumor sizes who were treated with a variety of surgical approaches. Surgery offers excellent efficacy, with additional treatments utilized in 1.4% and 1.8% of the cohort. The preservation of serviceable hearing is accomplished in 36–44% of cases. Notably, hearing preservation was 49% in a cohort of 926 patients with tumors smaller than 30 mm in diameter, which more closely aligns with the population typically treated with radiation. The most prevalent side effect is facial nerve injury or transection, with permanent facial neuropathy occurring in 13–19% of patients treated, and 10% of those with tumors smaller than 30 mm. CSF leak is the most common complication of surgery, affecting 6–11% of patients (not shown in Table 5). Mortality associated with VS resection occurs 0.3–0.6% of cases.

Our search for individual studies published after 2003 yielded five papers consisting of 813 patients total treated with a variety of surgical approaches [30, 32, 41–43]. Results, including means weighted by study size (*N*), are presented in Table 6. Tumor size was not consistently reported, but it should be noted that a significant portion of patients had large tumors compressing the cerebellum or brainstem, which would not typically be treated with radiation. With a mean follow-up of just over 5 years, the mean fraction of patients requiring additional treatment was 1.1% with MS. Hearing preservation was only reported in two studies, one of which involved a more lenient criteria for serviceable hearing (see Table 6 footnotes), and the mean rate was 44% out of 148 patients eligible for preservation. Permanent facial neuropathy was experienced by 29% of patients. The most common acute morbidity was CSF leak in 7% of cases on average (not shown in Table 6). Similar to the data presented in existing meta-analyses, mortality was rare, occurring in 0.4% of surgeries.

MS remains an efficacious treatment for acoustic neuromas. It offers patients excellent efficacy, with approximately 1% requiring additional treatment. Patients and physicians must weight this against the risks associated with surgical intervention. For patients with serviceable hearing, preservation is achieved in 32–44% of cases, although the rate may approach 50% for those with smaller tumors. While advances in surgical technique have reduced the risk of death to 0.3–0.6%, morbidity rates remain significant. Between 14% and 29% of patients experience permanent facial neuropathy and 6–11% will have post-operative CSF leak. For patients with VS who are candidates for surgery, microsurgical resection is indicated for those whose tumors progress after previous intervention, those with large tumors (>30 mm diameter).

Table 5 Microsurgery, meta-analyses

First author (year)	Studies (patients)	Tumor size (mm)	Surgical approach	Follow-up (months)	Additional treatment rate (%)	Hearing preservation rate (%)	Facial neuropathy rate (%)	Mortality rate (%)
Yamakami (2003) [14]	16 (5,155)	All sizes		66	1.8	36	13	0.6
				[61–70]	[0–20]	[15–59]	[3–34]	[0–2]
				n = 295	*n* = 2,997	*n* = 1,448	*n* = 4,241	*n* = 3,969
	(1,869)	[<30]				49	10	
						[26–78]	[1–41]	
						n = 926	*n* = 1,645	
Kaylie (2000) [24][a]	11 (2,579)	All sizes	SO/RS (58%) TL (34%) MF (7%)	24	1.4	43	19	0.3
					n = 776	*n* = 599	*n* = 1,192	*n* = 2,320

Data points include weighted mean, the range (square brackets), and the sample size (italics). For hearing preservation, the sample size represents the number of patients with functional hearing prior to observation

SO Suboccipital, *RS* retrosigmoidal, *TL* translabyrinthine, *MF* middle fossa

[a] Data not available to calculate weighted means

Table 6 Microsurgery, contemporary studies

First author (year)	*N*	Tumor size (mm)	Surgical approach	Follow-up (months)	Additional treatment rate (%)	Hearing preservation rate (%)	Facial neuropathy rate (%)	Mortality rate (%)
Samii (2006) [42]	200	NC (54%) C (46%)	RS	24 [9–45]	0.5	51[a] *n= 126*	19[b]	0
Pollock (2006) [32]	36	14.1	RS (69%) MF (6%) T (25%)	42	0	5 *n= 22*	17	0
Schmerber (2005) [43]	91	NC (85%) C (15%)	TL	132 [60–252]	0		25	
Myrseth (2005) [30]	86	[<30 mm]	TL (62%) SO (38%)	71 [12–170]	5.8		20	1.2
Darrouzet (2004) [41]	400	NC (62%) C (38%)	TL (57%) RL (32%) RS (11%)	70 [12–212]	0.7		29	0.5
Weighted mean	163			64	1.1	44	29	0.4
Patients (n)	*813*			*813*	*813*	*148*	*813*	*722*

Data points include weighted mean, the range (square brackets). For hearing preservation, the sample size (italics) represents the number of patients with functional hearing prior to observation

NC non-compressing with respect to cerebellum, *C* Compressing with respect to cerebellum, *RS* retrosigmoidal, *MF* middle fossa, *TL* translabyrinthine, *SO* suboccipital, *RL* retrolabyrinthine

[a] Functional hearing defined as SRT <60 dB & SDS >40%

[b] House–Brackmann grade IV or V (excludes III)

Comparative studies

Of the studies included in this review, five involved direct comparison of VS treatment modalities. Three meta-analyses evaluated historical outcomes (see Table 7) [11, 14, 24]. Kaylie et al. [24] represented early outcomes in the field of radiosurgery, the reason that the mean marginal dose was 17 Gy, which was likely the reason the authors favored microsurgical resection until results of low-dose treatment strategies were available. Battaglia et al. [11] reviewed more recent data and drew no clear conclusion regarding the efficacy of radiosurgery relative to conservative management with observation. Yamakami et al. [14] also failed to identify any clear guidelines for implementing observation, radiosurgery, or microsurgery in vestibular schwannoma treatment. Similar to results of this review, existing meta-analyses clearly organize the outcomes of many individual studies but suffer from the inability to draw comparative conclusions from such results (see "Limitations of this review" section below).

Two studies included in this review represent comparative studies of radiosurgery versus microsurgery in patients treated at a single institution (see Table 8) [30, 32]. Pollock et al. [32] represents the only prospective cohort study, and the highest quality evidence encountered using our inclusion criteria. The studies favored SRS because similar efficacy and greater freedom from treatment associated morbidity. Both studies include a relatively small cohort of patients and involve statistically significant confounders such as patient age and pre-treatment hearing status, the latter present only in the Myrseth et al. [30] study. Therefore, the strength of their conclusions remains limited. However, the reader should be aware that the only comparative studies identified in our review of the literature suggest that SRS offers greater functional outcomes compared to surgical resection of vestibular schwannomas.

Limitations of this review

This review seeks to present a summary of the recent literature describing VS management. It is necessary to acknowledge inherent biases in our methods and the limitations of our review. For example, our search for publications on this topic was relatively narrow and convergent. We utilized a number of restrictions in our search criteria, including omitting primary studies published prior to 2003 and restricting our search to PubMed's MeSH headings or the *Clinical Queries* database. Our goal was to provide a comprehensive yet concise review of the current literature, yet there are certainly selection biases present by neglecting additional resources.

There are also significant problems with comparing the evidence associated with individual modalities. The patient population undergoing each treatment modality suffers from selection biases, making it impossible to compare the outcomes associated with each one. For instance, patients undergoing observation had mean tumor sizes around 10 mm. Although a poor estimation, if we assume a

Table 7 Results from within comparative meta-analyses

First author (year)	Treatment modality	Patients (*n*)	Follow-up (months)	Additional treatment rate (%)	Hearing preservation rate (%)	Facial neuropathy rate (%)
Battaglia (2006) [11]	Observation	427	42	18		
	Stereotactic radiosurgery	397	30	2		
Yamakami (2003) [14]	Observation	903	37	20	63 *n= 60*	
	Stereotactic radiosurgery	1,475	46	4	66 *n= 271*	9 *n= 967*
	Microsurgery	5,155	66	2	49[a] *n= 926*	10[a] *n= 1,645*
Kaylie (2000) [24]	Stereotactic radiosurgery	875	25	9[b]	44 *n= 219*	19 *n= 717*
	Microsurgery	2,579	24	1	43 *n= 599*	19 *n= 1,192*

Data points represent weighted means. For hearing preservation, the sample size (italics) represents the number of patients with functional hearing prior to observation

[a] Results for tumors smaller than 30 mm maximum diameter

[b] Rate of tumor progression (fraction growing post-treatment)

spherical volume then the mean diameter of tumors treated with SRS or FRT were 16 and 20 mm, respectively. MS, on the other hand, includes many large tumors greater than 30 mm, which are rarely considered for management with another option. Therefore, comparing modality-specific rates of treatment success reported in this review is challenging and should be performed with significant skepticism.

Evaluating the relative probability of hearing preservation for each modality is equally troublesome. While it may be postulated that those with serviceable hearing prior to treatment may be relatively homogenous across cohorts, this is not always the case. For instance, surgical series typically involve larger tumors than radiosurgical data, and meta-analysis by Yamakami et al. [14] identified a large difference in hearing preservation even among those treated with MS when the entire patient population was compared with a subset of those with tumors smaller than 30 mm (see Table 5). Additionally, hearing preservation rates in the surgical and FRT literature often reflect a population of patients selected with the specific goal of hearing preservation, based on age, symptom profile, or tumor characteristics such as size. In this review, it was not always possible to clearly differentiate which results may have been subject to this confounder, although it was clearly present in two studies [35, 40]. Such results would be more appropriately compared with others reflecting a matched cohort of patients treated with alternative modalities. For instance, several recently published studies of SRS have evaluated hearing preservation in select patients; however, these were not identified using our search criteria and therefore have not been included in our data [44, 45]. Since hearing preservation statistics do not necessarily measure the same outcome across studies or represent similar cohorts of

Table 8 Results from within comparative prospective trials

First author (year)	Treatment modality	Patients (*n*)	Follow-up (months)	Additional treatment rate (%)	Hearing preservation rate (%)	Facial neuropathy rate (%)
Pollock (2006) [32]	Stereotactic radiosurgery	46	42	4	63 *n= 30*	0
	Microsurgery	36	42	0	5 *n= 22*	17
Myrseth (2005) [30]	Stereotactic radiosurgery	103	71	5		5
	Microsurgery	86	71	6		20

Data points represent weighted means. For hearing preservation, the sample size (italics) represents the number of patients with functional hearing prior to observation

patients, it remains difficult to draw sound conclusions by cross-examining the results tabulated in this review. It would be most appropriate to compare hearing preservation rates across matched populations, with respect to age, tumor size, and pre-treatment hearing status, a feat that may be accomplished in a future review or comparative studies.

We hope the reader will recognize that this review seeks to present the evidence in a concise fashion for use in clinical decision making, but that it does not have sufficient capacity to facilitate comparative conclusions or treatment guidelines with regard to VS management. Problems exist with selection bias and different ways of reporting outcomes in the observation, microsurgery, and radiosurgical literature. Surgeon experience has been identified to impact microsurgical outcomes, so that even comparisons between different study centers reporting on the same treatment modality must be evaluated carefully [10]. Experience likely also plays a role in radiosurgical outcomes between different treatment centers. For these reasons, the information provided throughout this paper and within the tables should be utilized judiciously, for confounders are undoubtedly present that weaken conclusions that might be formed regarding the relative efficacy and safety of each treatment modality.

Higher quality evidence is the only means to develop more robust set of treatment guidelines for VS. This comes in the form of prospective studies, prospective comparisons, and ultimately randomized controlled trials with regards to the treatment modalities. Better guidelines will also be facilitated by uniformly reporting precise measures of tumor volume, treatment success, and morbidity rates. Furthermore, outcomes must be measured at greater follow-up intervals, such as a minimum of 5-year post-treatment, as conclusions are limited when they represent the experience after an average follow-up of similar duration. We hope that this compilation of currently available evidence will encourage VS treatment centers to engage in more powerful, well-designed studies.

Summary

In Tables 1, 2, 3, 4, 5, and 6 we outline the existing evidence, from meta-analyses and contemporary studies, describing the modalities used for treating VS. Observation offers the least risk to patients, but 29–54% of tumors will grow and 16–26% of patients require treatment at approximately 3 years. Gamma Knife radiosurgery arrests growth in 89–95% of tumors after an average of 6 years following treatment. Only 2–4% of patients will require additional treatment, hearing preservation is achieved in 44–66% of treatments, and fewer than 2% of patients experienced facial neuropathy or trigeminal neuropathy in recent studies. The adoption of lower doses may yield even better morbidity rates, and our center has adopted a standard marginal dose of 12 Gy to the 50% isodose line. FRT has not been evaluated with follow-up as long as radiosurgery, but the available data suggests that 3–7% will require additional treatment after 4 years follow-up and associated morbidity rates are similar to SRS. MS is an efficacious treatment for VSs, and fewer than 2% of patients are likely to require additional treatment at 5 years average follow-up. It remains a primary option for patients with very large tumors and those who have failed previous intervention. Despite the invasiveness of intracranial surgery, hearing preservation can be achieved in 32–44% of cases, and higher in those with smaller tumors. However, rates of facial neuropathy and other morbidities are significant.

Comparative studies and randomized trials are lacking, and conclusions regarding the relative efficacy and safety of each modality based on data in this review are limited. Our center advocates counseling patients with VS using the best available evidence for all treatment modalities; but at this point, there are no clear treatment guidelines. Choice of intervention is multifactorial, depending on tumor size, tumor growth rate, symptoms, health status, and the personal preference of the patient. Patients and physicians should be aware of the risks and benefits offered by each modality. Furthermore, it is important to be aware of how advancements in treatment protocols are impacting treatment success and side effect profiles, especially in the rapidly evolving fields of radiosurgery and radiotherapy. With the development of more powerful studies, we may identify more conclusive guidelines for the treatment of VS. Until then, we hope that this comprehensive review will provide a convenient means to evaluate currently available data and help to guide decision making for physicians, radiation oncologists, neuro-otologists, and neurosurgeons in the management of their patients with VS.

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Comments

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Is there one approach superior to the others in the neurosurgical management of vestibular schwannomas?

Vestibular schwannomas (VSs), also known as acoustic neurinomas historically, are benign neoplasms of Schwann cell origin, occurring predominantly on the vestibular division of the cranial nerve VIII at the oligodendroglial/Schwann cell interface at or within the internal auditory meatus (10). VSs have always frustrated and challenged neurosurgeons for more than 100 years because of their benign nature and potentially significant surgical morbidity and mortality related to the complex anatomy of the cerebellopontine angle. The surgical management of VSs has evolved from the pioneering era of the life-saving procedure by intracapsular removal (1), to the curative era with complete tumor resection (2), then to the era of facial nerve sparing (17). In the 1960s and 1970s, microsurgical revolution led to the development of modern neurosurgical strategies with the middle fossa approach (7) and the translabyrinthine route (6). Yasargil (27) refined the microsurgical technique, emphasizing the importance of the brainstem arterial supply, specifically anterior inferior cerebellar artery, and the need to optimize the preservation of facial nerve function. These technical advances have resulted in a 50% reduction in mortality, a rate of complete tumor removal reaching 85% and a rate of the successful anatomical preservation of the facial nerve approaching 80%.

In recent years, development of new diagnostic modalities such as computed tomography, magnetic resonance imaging (MRI) and auditory evoke potentials has resulted in the drastic decrease in the average size of VS at diagnosis. In addition, multidisciplinary team approach and intraoperative monitoring of cranial nerves VII and VIII have led to the dramatic improvement in clinical outcome, namely operative mortality of around 1%, total tumor removal rate close to 95%, and preservation of facial motor function (House–Brackman grade I or II) in significant portion of cases involving small tumors (Koos class I and II). In some expert hands, the preservation of useful hearing (Gardner–Robertson class I or II) has been demonstrated to be achievable in selected small lesions with very good preoperative hearing. In 1997, Samii and Matthies (23) published a series of 962 patients with tumor control rate of 98%, an impressive functional hearing preservation rate of 39%, with associated mortality rate of 1.1%, and a reasonable complication rate of CSF leak (9%), meningitis (1.2%), hydrocephalus (2.3%) and miscellaneous events (5%).

The most recent neurosurgical advance has been that of radiosurgery. Conceived during the microsurgical revolution of the 1960s and 1970s (11, 12), the fantastic image-guided neurosurgical instrument, which Leksell called the Gamma Knife, has realize its full potential with the appearance of modern imaging in the late 1980s, specifically MRI. In the 1990s, radiosurgery became the first-line treatment option for small- to middle-sized VSs, especially in young patients with few symptoms (9, 14, 16, 21). However, microsurgery still remains as the first-line treatment for large VSs (Koos class IV), which is still challenging. In the twenty-first century, the demonstration of the high rate of functional preservation has led us to promote the idea of a combined microradiosurgical approach for large VSs, allowing a dramatic reduction in the rate of facial nerve palsy in large VSs from 50% to less than 20% (5, 8).

The strategy of "surgical removal at all cost" has evolved into the strategy of "cranial nerve preservation whenever possible". Currently, the management of this tumor has become less controversial but continues to fascinate generations of neurosurgeons and neuro-otologists. No tumor provides a greater test of a neurosurgeon's or neuro-otologist's skill than the VSs. However, the need for improved outcomes proved the driving force in the introduction and development of stereotactic radiosurgery as a potent management strategy. Over the years, cranial nerve function preservation rates have dramatically improved and now hearing preservation is a reality.

Our oto-neurosurgical experience of more than 4,500 VSs has led us to consider that, in the modern era, treatment of VSs should be tailored individually and be managed by experienced multidisciplinary teams able to integrate all the microsurgical and radiosurgical approaches in order to provide the highest level of care, the highest probability of functional preservation, and good quality of life.

Arthurs et al. are providing us with a review of the different treatment options in the management of VSs. The authors are comparing Wait & See, microsurgical resection, radiosurgery, and stereotactic radiotherapy in the management of VSs. They are reviewing papers about these several approaches, which correspond to different populations of patients and use different evaluation criterion. This work is a review of the literature, and it does not present any original data, but is attempting to look broadly at the available data from recent years and compile it into a comprehensive review. There are major flaws in their process, which they have attempted to address in the discussion of the paper. For those interested in the modern management of VSs, this work constitutes a useful review under the condition of a clear identification of its flaws and weaknesses.

1. First, the strategy of the authors was to scrutinize published cohort from a specific time period (2004–2009). The authors have decided to investigate *only a sampling of the literature between 2004 and 2009*. To analyze only the modern literature, excluding old papers, which may present a technical gap, is sensible. However, the lower limit of 2004 seems very much restrictive and leads the authors to miss some of the more important papers of the modern literature.

2. The *heterogeneity among the methodology of different papers* reporting their results of the diverse therapeutic strategies is so varied that frequently the authors are performing "forced comparisons", often leading them to somewhat invalid conclusions. In such a comparison, the rules cannot be changed depending on what technique is

evaluated. The efficacy must be defined similarly in Wait & See, Microsurgery, and Radiosurgical populations. For example, Arthur et al. are defining a failure for microsurgery as the requirement for a new surgery (either microsurgery or radiosurgery) and for radiosurgery as a significant tumor growth. Thus, Arthur et al. have decided on different definitions of failure (different rules) for microsurgery and radiosurgery. In radiosurgery, it is a well-known and well-published fact that VSs after radiosurgery frequently increase in size for some time and then stops growing thereafter in long term (in the majority of the patients). Some of the patients with long-term follow-up demonstrating complete arrest of growth for a very long period of time have a tumor that is larger compared to the size before radiosurgery, due to the growth during the first 2 years (3). These patients are clearly considered as "cured" and cannot be considered as failures. Thus, in the abstract, the failure rate of radiosurgery must read 2–4% (success rate 96–98%). Also, the rate of failure after fractionated radiotherapy is 5.4% (2.9–6.7%) and this seems higher.

3. *Selection bias* is the other major weakness of this review. This is especially true for the comparison of hearing preservation rates, which may not be valid because of the selection of the best responders in the radiotherapy and microsurgery groups. Major patient selection bias is obvious in some papers in the literature and makes any attempts of comparison unfair. Even if, in the papers from micro and radiosurgery literature, the useful hearing preservation rate is calculated for those patients with a useful hearing before the operation, there is a major difference related to the selection of "good candidates" for microsurgical attempt for hearing preservation. Frequently in microsurgical series, the rate of hearing preservation is not defined as the number of patients keeping a useful hearing based on the total number of patients with useful hearing before the surgery but based on the smaller group of patients selected, as good candidate, for an attempt to preserve hearing. In several papers, one of the main criteria is a subnormal hearing (Los Angeles A or Garner–Robertson I). Thus, these specific papers from the microsurgical literature must be compared to the results of radiosurgical papers analyzing the results of radiosurgery in this specific group of patient (26). The young age, which is frequently used as a major selection criterion for an attempt to preserve functional hearing in microsurgical series is also demonstrated to influence the chances for hearing preservation (13). Thus, the rate of hearing preservation, already significantly higher with high precision radiosurgery can be even more favorable when considered in this selected group of "good candidate" patients. Series of fractionated radiotherapy also demonstrate this bias when patients retained for fractionation are those who are young with a small lesion and a very good hearing! Any comparison in terms of functional hearing preservation must take into account these strong predictors and must be stratified.

4. *Series with short follow-up* may be especially misleading. In Wait & See strategy, the series are small and follow-up short (compared to the slow-growing natural history of these tumors). The number of patient operated because of growth seems modest at 3 years but with an average growth of 1–2 mm a year, the actuarial rate of patient requiring surgery at 5–10 years is much higher. Thus, the high rates of "success" of the Wait & See strategy claimed by some authors in these small series with short follow-up must be viewed with caution. Thus, the following sentence "Without intervention, 29–54% of tumors will grow; however, observation remains successful in that only 16–26% of patients require additional treatment" is unrealistic at the scale of patient life expectancy. These observations must be replaced in the context of a longer time frame. As a minimum requirement, actuarial rates of failure (growth requiring treatment) at 3, 5, and 10 years must be reported. In fact, the true benefit of these management strategies should be theoretically considered at the scale of patient life expectancy. In a recent prospective study evaluating Wait & See strategy in the management of VSs, the actuarial rate of tumor progression was reported (20). Additionally, in Wait & See series, some authors are using syncretic definition of tumor growth. For example, Stangerup et al. are reporting surprisingly only 17% of tumor increase in a group of 230 Koos I tumors with a mean follow-up of 3.6 years (24). In fact, the authors have decided to define as "growing" only tumors that are becoming extrameatal. Thus, for these authors, a small tumor of 2 mm diameter increasing in size to a 14 mm tumor (from 4 to 420 mm^3) but still in the canal is considered a non-growing tumor! Finally, the quite high rate of hearing loss with this approach must be mentioned (25). Also, vast majority of series of stereotactic radiosurgery also possess this bias (small series and short follow-up) in addition to the selection bias already mentioned. The claim that fractionated stereotactic radiotherapy may be superior to radiosurgery in terms of functional hearing preservation is, until now, not substantiated by the literature (4). In the only two series of radiotherapy reporting significantly better results of hearing preservation than radiosurgical series (Combs et al. 2005 and Chan et al. 2005) the hearing is not systematicaly evaluated by audiometry before and after but based on patient self assessment.

5. *Comparing the results of safety and efficacy of different techniques may be an attempt to answer an inappropriate question since nowadays these approaches are frequently proposed in combination*. Especially in large Koos class IV tumors, centers of excellence, benefiting from many modalities and human skills available to them, are increasingly offering a combination of partial removal under physiological monitoring followed by radiosurgery of the remnant. Consequently, these approaches are not intrinsically antagonistic.

The authors obviously have faced a certain number of methodological difficulties. In order to make relevant and valuable comparisons, we need to be sure to compare the similar type of patients and utilize, as much as possible, the same evaluation criterion for the different techniques.

Surprisingly, while regretting the rarity of the comparative studies, the authors do not pay attention to the existing papers reporting such studies (15, 18, 19, 22). There is a total of five such comparative studies in the literature, very convergent in their conclusion and establishing that the functional outcome after radiosurgery is superior as compared to microsurgery in small to moderate size VSs (even if some of these comparative studies predate 2004). Of course, each of these trials has its methodological limits. However, the level of evidence of these studies is much higher than a forced comparison of retrospective non-comparative cohorts from the literature!

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