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Controversy and Consensus in the Management of Small Vestibular Schwannomas in Patients with Intact Hearing

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Vestibular Schwannoma (VS) is a benign lesion from the Schwann cells around the vestibular nerve. It is more often a slow-growing tumor that initially causes symptoms related to dysfunction of the vestibular and cochlear nerves. The management of intracanalicular small VS has witnessed a sea change in the last half a century. Though the natural history of the disease remained unreliable, early discovery of small VS has significantly increased because of better radiology techniques, especially magnetic resonance imaging (MRI). The early identification of VS poses two crucial questions; a, if the treatment is required or not; and b, what is the most appropriate treatment option, determining these patients' functional quality of life (QOL).(1)

The microsurgical era has transformed the management of VS from a daunting task to respectful outcomes(2). Frustrated with the persistently poor functional outcomes, Lars Leksell pioneered the treatment of VS with Gamma knife radiosurgery (GKRS). In 1971, Lars Leksell published the inaugural account of the VS treatment with GKRS(3). The evolutionary changes in microsurgery and radiosurgery have shifted the pendulum towards functional outcomes rather than disease eradication(4). Currently, the treatment options are compared to primary benchmarks of hearing preservation, facial preservation, and long-term tumor control(5). Unfortunately, there is no conclusive evidence of consistent data in the literature on VS. The criteria of hearing preservation, tumor growth control, useful hearing, and serviceable hearing are not uniformly followed and published. It resulted in an extensive data set of random variables with no statistical significance. The published literature has great variability in the natural history and management options, and a definite consensus is still awaited(6, 7).

Incidence of Small VS

VS are relatively uncommon intracranial tumors with an annual incidence of <1.0 per 100,000 person-years, but they comprise 6-8% of all brain tumors. In different series, Koos grade I VS comprise 8-33% of all VS(8, 9) (Figure 1). The focus of management of small VS has shifted from mere tumor control to maintenance of oncofunctional fleece. Among all VS, small intracanalicular VS (Koos grade 1) and with some protrusion inside the cerebellopontine angle (CPA) cistern (Koos grade 2) are mostly asymptomatic or paucisymptomatic. The management options are observation, proactive stereotactic radiosurgery (SRS), fractionated radiation therapy, and microsurgical resection(10, 11).

Natural History of Vestibular Schwannoma

Since the 1917 milestone monograph on acoustic tumors by Harvey Cushing, many studies have commented on the natural history of VS. Yet, the literature suffers from a great discrepancy in the tumor behavior and growth patterns, further confusing the management options. Various studies have reported growth frequency ranging from 12% to 85%. Further adding to the confusion, most studies suffer from inaccuracies in tumor growth measurement as only a linear increase in the size has been quoted. Being a three-dimensional structure, the comparative volumetric assessment provides the best chance of tumor growth assessment(6).

Literature search and reporting patterns highlight a higher incidence of small VS diagnosed in the early course of the natural history. Detection at an early stage has started a trend of a policy of observation in some instances with serial imaging and regular clinical examination(12). Early detection allows for better counseling of the patient, options of available treatment modalities, and a chance to study the natural history of the disease(13). There has been a disturbing trend in the incidence of VS cases based on the registry in Denmark, from 7.8 to 12.4 cases per million from 1976 to 1995(14). Cellular phones play a role in the early detection of hearing loss, which has increased the detection of small vestibular schwannoma! European and North American studies report the usual size of 10-12 mm at the time of diagnosis. At the same time, large and giant tumors represent only 6% of all tumors(15). The average growth rate of untreated VS is 2.9 mm per year(16).

Stangerup *et al*. analyzed a database of more than 2500 VS patients over 35 years and observed the natural history of these tumors. They suggested a strategy to decide on VS management based on these lesions' growth patterns(17). Contrary to the meager rates of tumor growth reported in the Stangerup study, other studies on the natural history

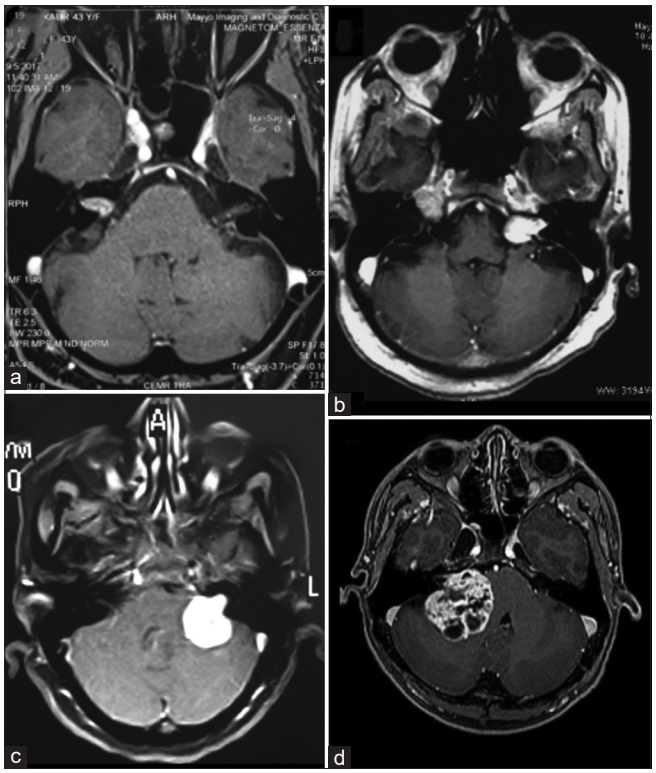

Figure 1: Neurotopographic classification of the vestibular schwannoma according to the Koos grade ((a) Koos grade 1, intracanalicular VS; (b) Koos grade 2, extracanalicular tumor extending into cerebellopontine angle but not touching brain stem; (c) Koos grade 3, cerebellopontine angle cistern tumor touching brainstem but not distorting it; (d) Koos grade 4, large VS distorting brain stem) (VS, vestibular schwannoma)

of VS have shown significantly higher growth rates(15, 18, 19). Of 325 patients observed during three years, Bakkouri *et al*. found that 42% of tumors showed growth while 61% of intracanalicular tumors became extracanalicular(20). Breivik *et al*. followed 124 patients with an average tumor volume of 1.2 cm^3 who underwent observation of their tumors and reported that tumor volumes doubled over 3.3 years, and 50% of patients underwent intervention at five years because of an increase in size(21). Sughrue *et al*. (16) performed a meta-analysis of 34 observational studies with a total of 982 patients and found a mean growth rate of 2.9±1.2 mm/year within a follow-up period of 2 to 4 years. This knowledge that most small tumors kept on observation will grow and eventually require intervention has to be understood by the treating doctor and the patient when a decision to adopt a wait-and-watch policy is taken(22).

What is more interesting is that even though the tumor incidence appears to increase, the size at the time of diagnosis is falling, and the median age remains the same. The "large & giant" variants are also decreasing in numbers, probably due to early detection. The number of patients requiring treatment is not as high as the incidence suggests, hinting at a probability that many do not end up needing treatment (slow growth)(23).

The management options for VS include surgery that achieves complete excision, except that it carries the risk of morbidity. Radiosurgery, although well tolerated, has long-term tumor control issues and the risk of radiation-induced malignant transformations. There is an ongoing debate about making subsequent surgery difficult if needed. Patients with small lesions, advanced age, and significant medical conditions are candidates for a conservative approach. Another patient population that falls in the observation category is the residual lesion after planned partial resection (residual left to preserve function)(24).

What is a serviceable hearing?

A serviceable hearing is defined by a pure tone average (PTA) of 50 decibels or less and a speech discrimination score (SDS) of 50% of more (Also known as the 50/50 rule). A simple method

for clinical assessment of serviceable hearing in an outpatient clinic is to inquire if the patient can talk on the phone with the receiver on the ear. It must be stressed if the patient understands what is being spoken to him and does not just perceive some sound (SDS). This simple question crudely differentiates serviceable hearing from non-serviceable hearing(25) (Table 1).

Hearing preservation is an important but difficult-to-achieve goal of VS treatment. Hearing deterioration occurs as a progression of the natural history of the disease, as reported by Pennings *et al*.(26). Sughrue's analysis showed that even though the hearing was preserved in up to 54% of patients who were conservatively managed, this dropped to 32% when tumors grew more than 2.5mm per year(16).

Is there any tinnitus?

Tinnitus is a bothersome symptom that significantly affects the quality of life. Tinnitus at presentation indicates an aggressive growth pattern (nearly three times higher). Marseille group treated 175 patients with a VS and functional preserved hearing with GKRS with a follow-up longer than three years. The rate of functional hearing preservation at three years was 77.8% in patients with grade I hearing, 80% in patients with tinnitus as a first symptom, and 95% when the patient had both grade I hearing and tinnitus(27). Though SRS does not provide any definite relief from tinnitus, it is an indirect indicator of a non-innocuous growth rate. CNS guidelines support SRS for asymptomatic VS patients with tinnitus (Level III evidence)(10).

Management of an asymptomatic vestibular schwannoma patient

Management of an asymptomatic VS is perhaps the most complex and challenging aspect for the clinician and the patient. An asymptomatic patient may have completely preserved hearing or suffer from partial but serviceable hearing loss. It is vital to document baseline hearing at the time of primary presentation. Any extent of hearing loss needs to be carefully evaluated as subclassification of hearing loss is an essential guiding parameter for patient selection to either observation or radiosurgery(28). Different neurosurgical societies have carefully reviewed the published literature and generated evidence-based guidelines for managing patients with VS(12, 29, 30).

In 2019, the Congress of Neurological Surgeons (CNS) published a consensus guideline for predetermined clinical scenarios. They tried to identify the overall probability of maintaining serviceable hearing following single fraction radiosurgery using ≤13 Gy, utilizing modern dose planning to the tumor margin in patients with serviceable hearing or documented AAO-HNS class A or GR grade 1 hearing in the ipsilateral ear before treatment at two, five-, and ten-years following treatment. They provided a level 3 recommendation that individuals who meet these criteria should be counseled that there is a moderately high probability (>50-75%) of hearing preservation at two and five years. There was a moderately low probability (>25-50%) of hearing preservation at ten years. The most consistent predictive features associated with maintenance of serviceable hearing were good preoperative word recognition and PTA thresholds with variable cut-points reported, smaller tumor volume, marginal tumor dose ≤12 Gy, and cochlear dose ≤4 Gy. Age and sex were not strong predictors of hearing preservation outcome(10).

Wait and Watch Strategy

Wait and watch strategy may be followed for many patients if they prefer to be observed rather than receive any interventional treatment. In 1985, Wazen *et al*. published an article stating that observation might be less risky in the elderly age group than microsurgery(31). Many other articles resonated with this opinion solidifying the concept that observation could be a valid management option(32-35). This option is justified if there is evidence

Table 1: Gardner Robertson Hearing Grading

Grade	Description	Pure Tone Average (PTA, dB)	Speech Discrimination Score (SDS,%)
1	Good, excellent	0-30	70-100
2	Serviceable	31-50	50-69
3	Non-serviceable	51-90	5-49
4	Poor	91-100	1.4
5	None-Could not test	0	

of either no growth or negligible growth, posing no immediate or long-term danger to the patient. It is practically impossible to identify that subgroup of the patient who remains at risk of an unexpectedly higher growth rate. This remains a debatable issue, and even literature is not supported due to the lack of uniformity of methodology and data collection in this disease. It is easier to observe linear increase or volumetric change in a large volume VS, but in a small volume VS, it is difficult to register any change. Though the size is a valuable parameter, it has little correlation with hearing preservation, and it remains exciting and confusing if any size change translates into poor auditory outcomes(36, 37).

The meta-analyses and systematic reviews suggest a growth rate of 1.5 mm/year, and the failure rate of conservative management is around 19%. The failure of conservative management is termed when some intervention is done. The reasons for failure are significant growth of the tumor, symptoms/signs progressing, and patient decision. Overall tumor size increased by more than 5 mm/year, and/or the extracanalicular part exceeding 20mm are criteria for discontinuing conservative treatment(38, 39) (Table 2) (17, 18, 21, 40-46).

Predicting the time frame in which the tumor growth occurs is very difficult, leading to failure detection late. This merits a close clinical follow and frequent MRI imaging at appropriate intervals. Patient compliance for follow-up is paramount to a successful observation policy. This is more so because, in a vestibular schwannoma, hardly any clinical sign will help detect early growth. Some evidence is available but inconclusive that tumor growth during one year is a predictor of growth rate and pattern. There have been cases of tumor growth happening late in the follow-up after initial no growth and vice versa. On average, 50% of the tumors may be expected to grow over a five-year follow-up period. Another unresolved issue is the imaging to be done on follow-up. The initial imaging to diagnose the tumor might be a screening MRI, so comparing on follow-up might not be an issue. Follow-up for at least five years is the consensus for now. The imaging frequency is based on resources available, tumor characteristics, tumor behavior, clinical findings, and, lastly, equally important resource limitations(12).

The chances of hearing preservation were the same with observation in a nongrowing VS with serviceable hearing loss with no significant difference from GKRS. On the other hand, any documented growth in the tumor volume was associated with a substantial reduction in long-term hearing preservation. In patients with confirmed hearing loss of AAO-HNS class A or GR grade 1 and nongrowing tumor, there is a moderately high probability (>50-75%) of hearing preservation at two years and five years. However, there is insufficient data to determine hearing preservation in this population subset at ten years(10).

VS often surprises us with worsening symptomatology without any radiographic growth. The actual reason for audiological symptoms is still not entirely known. Many patients suffer progressive or sudden hearing loss without radiographic tumor growth. There might be no new histopathological changes, such as interactive mural microhemorrhages in fibrosis or immunological reactions. It might be secondary to vascular phenomena such as labyrinthine artery infarct(47).

Table 2: Literature review of Wait and Watch Policy of Vestibular Schwannoma (excluding Neurofibromatosis-2)

Start Year	Observation Period	Cases	Author
1974	17.2 years (maximum observation period)	70	Rosenberg
1976	16(median)	2500	Stangerup & Caye-Thomasen
1976	9.5(median), 27 (maximum observation period)	1261	Huang *et al*
1986	3(median), 13 (maximum observation period)	576	Patnaik *et al*
1988	4.8(median), 15.6 (maximum observation period)	114	Fayad *et al*
1994	7.9(median), 17.8(maximum observation period)	145	Jufas *et al*
2000	3.6(median), 9.6(maximum observation period)	193	Breivik *et al*
2000	5(maximum observation period)	355	Varughese *et al*
2000	6.2(median), 14(maximum observation period)	155	Wolbers *et al*
2002	5.6(median)	94	Jethanamest *et al*

Table 3: Literature review on the radio surgical management of small vestibular schwannoma (*FU*, Median follow-up in months; *GKS*, Gamma Knife surgery; *MS*, percentage of patients who had already undergone operation on the same lesion by microsurgical approach)

Author and Year	No. of Patients	Radiosurgical Technique	Dose (Gy)	FU (mo)	MS (%)	Failure (%)	Volume (cm^3)	Control Rate (%)	VIII (%)	VII (%)	V (%)
Prasad *et al.*, 2000	153	GKS	13	51.2	37	7.2	2.8	92.8	60	1.3	3.2
Lunsford *et al.*, 2005	829	GKS	13	72	19.9	3	2.5	97	70.3	1	3
Pollock *et al.*, 2006	46	GKS	12.2	42	0	4.3	1.5	95.7	63	0	2.
Chopra *et al.*, 2007	216	GKS	12-13	68	0	1.7	1.3	98.3	74	0	6.8
Régis *et al.*, 2007	927	GKS	12.57	52	9	2.3	1.2	97.7	60	0.7	0.6
Hasegawa *et al.* 2013	440	GKS	12.8	149	21	1	2.8	92	55% @ 3 Y	0.3	1
Johnson *et al.* 2019	871	GKS	13	62		6	0.9	94	51.4% @ 10 Y	1.6	5.8
Tukcer *et al.* 2019	117	GKS	12.5	68			1.8	94		0	
Kawashima *et al.* 2020	214	GKS	14	133			1.3	93.9		2	

Role of Radiosurgery

Unlike microsurgical approaches, SRS offers a minimally invasive day care treatment. There is no doubt in the long-term tumor control with no facial paresis with GKRS. The only challenge is the maintenance of functional hearing. To justify the role of proactive SRS, hearing preservation must be better than observation alone or microsurgery. Many studies have carefully evaluated functional hearing preservation (Grade 1 and 2) after GKRS for VS. The rate of functional hearing preservation after GKRS in different series has ranged from 33-74% at different follow-up periods(48, 49). There is a high probability of functional hearing preservation after GKRS (Table 3)(50-57).

Maniakas and Saliba published the review after comparing the outcomes of conservative management and SRS in studies with a minimum of five years of follow-up. 58.5% of patients preserved functional hearing at an average of 7.75 years with conservative management. 73.3% maintained functional hearing after a mean follow-up of 6.4 years following SRS. The same authors published the second literature review comparing long-term hearing and tumor control outcomes between microsurgery and SRS for a small VS (<2 cm) with a minimum of five years of follow-up (Figure 2). SRS offered a greater probability of durable hearing preservation compared to microsurgery ($p<0.001$). With tumor control defined as radiographic growth arrest or no requirement for further intervention, literature on the efficacy of RS has reported high tumor control rates of 92 to 98% in medium-term follow-up(58, 59). Chopra *et al*. described their series of 216 patients who underwent RS for primarily small tumors; they had 98% ten-year actuarial control rates; 3 patients had to undergo surgery for expanding tumors(53). In a Japanese series of 80 patients with mean tumor volumes of 6.3 cm^3, the actuarial ten year progression free survival was 83% with 9 patients requiring resection(54).

Before the introduction of GKRS, microsurgical approaches intended to preserve hearing in small VS were proposed (retro sigmoid or middle cranial fossa approach). However, the literature is greatly skewed in favor of GKRS compared to microsurgical approaches regarding hearing preservation. Two studies have class II evidence in comparison of microsurgery with SRS. In 2006, Pollock *et al*. reported a comparative prospective nonrandomized study of 82 patients (36 in the surgical and 46 in the SRS arm). Preservation of serviceable hearing was greater for the SRS arm than microsurgical arm at three months (77% vs. 5%, $p<0.001$), one year (63% vs. 5%, $p<0.001$), and last follow-up (63% vs. 5%, $p<0.001$)(50). Similarly,

Table 4: House-Brackmann facial paralysis scale

Grade	Impairment
I	Normal
II	Mild dysfunction (slight weakness, normal symmetry at rest)
III	Moderate dysfunction (obvious but not disfiguring weakness with synkinesis, normal symmetry at rest) Complete eye closure w/maximal effort, good forehead movement
IV	Moderately severe dysfunction (obvious and disfiguring asymmetry, significant synkinesis) Incomplete eye closure, moderate forehead movement
V	Severe dysfunction (barely perceptible motion)
VI	Total paralysis (no movement)

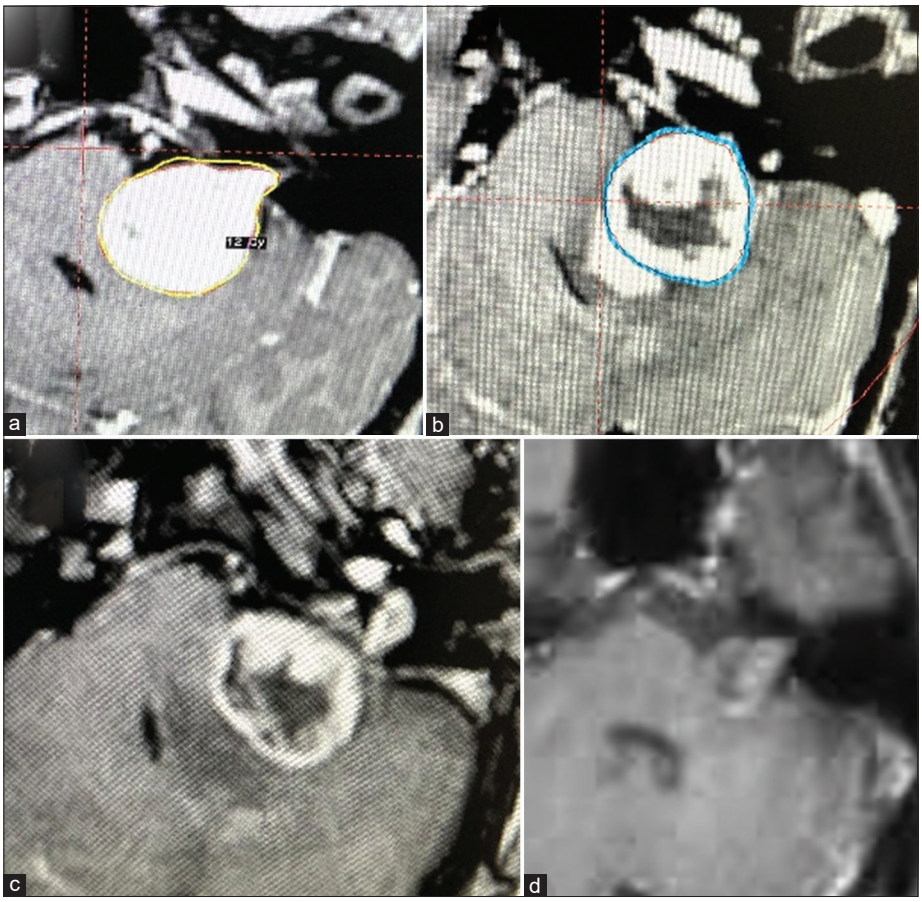

Figure 2: (a) At time of GKRS (volume 3.2 cc); (b) MRI at 8 months showing central necrosis with pseudoprogression of the tumor (volume 4.1 cc) with no clinical deterioration; (c) spontaneous regression of pseudoprogression with reduction in the size of the tumor at 12 months MRI (volume 2.9 cc); (d) significant volumetric reduction of the tumor at 32 months MRI (volume 1.9 cc)

Myrseth *et al*., in 2009, reported comparative outcomes of 63 patients receiving GKRS and 28 patients receiving microsurgery. At two years interval time, the GKRS cohort had a statistically significant better hearing outcome(60, 61).

In 2003, Yamakami *et al*. published an extensive review comparing outcomes following all three significant radiation cohorts therapy, microsurgery, and observations. Overall, chances of retaining functional hearing following observation, radiation therapy, and surgery were respectively 63%, 57%, and 36%. However, this study was criticized because many patients were treated with higher dose radiosurgery (average marginal dose of 14.5 Gy) than commonly used. Similarly, the proportion of patients undergoing hearing preservation microsurgery had larger tumor volumes(62).

There is sufficient evidence that untreated small VS eventually grows and damages hearing. In the first published article on this topic, Regis *et al*. evaluated small

intracanalicular VS. 47 patients in the study were observed until the tumor grew or hearing deteriorated. The tumor showed growth in 74% of patients observed compared to only 3% of the GKRS cohort. The functional hearing was preserved at five years in 60% of the GKRS group and 14% of the observed group. The tumor volume was relatively less in the observed group still hearing preservation was better in the GKRS group(52).

Similarly, the Pittsburgh group showed that observed patients were most likely to experience tumor growth after ten years. Moreover, observation was associated with a greater frequency of hearing loss over five years than with radiosurgery. Further supporting this data Pittsburgh group found that patients treated within two years of the diagnosis were in an advantageous position of retaining 88% serviceable hearing compared to 55% among patients treated beyond two years of diagnosis(50).

The factors determining hearing preservation

Multiple parameters determine the hearing outcome. Prabhu *et al*. differentiated a healthy cochlea from a sick cochlea based on signal intensity in the cochlea on the T2 weighted images. A decreased signal intensity is associated with poor hearing outcomes, suggesting that the tumor may alter endolymph protein concentration, affecting the protein cochlea health(63). Mousavi *et al*. reported that chances of long-term hearing preservation are significantly high if the SRS is performed before the subjective hearing loss. In patients with subjective hearing loss, the difference in the PTA between the affected and normal ear was an essential factor in long-term hearing preservation(64). The role of concomitant medical therapy, such as steroids, bevacizumab, etc., is still disputed(65).

In a review of 45 series on hearing preservation after SRS, Yang *et al*. estimated that 50% of patients will have preserved hearing 3-4 years after the procedure(66). Akpinar *et al*. compared hearing preservation after early (within two years of diagnosis) and delayed (after two years of diagnosis) SRS. He described that after five years, an estimated 88% of the early treatment group retained serviceable hearing, and 77% retained normal hearing, compared with 55% with serviceable hearing and 33% with normal hearing in the late treatment group(38). In a recent survey of neurosurgeons and otolaryngologists, both sets of practitioners alike reported that SRS should not be considered a long-term hearing preservation strategy(67). A recent CNS review also shared that the long-term rate of hearing preservation after RS is similar to patients having MS(10). In an update on VS, hearing preservation rates after SRS were reported to vary from 63-93%(68).

Another anatomical parameter is the lateral extent of the tumor in the IAC. The chances of hearing preservation are much higher if there is a CSF-free space between the tumor's tip and the tumor's lateral wall. Contrary to this, tumors extending into the fundus have poor auditory outcomes(69). At present, there is no definite account of the effect of age on maintaining hearing after radiosurgery.

Dose of GKRS

In GKRS for VS, the prescribed dose is 11-13 Gy at 50% isodose. Any dose exceeding 13 Gy is associated with a higher risk of neuropathy, especially with the loss of functional hearing(70, 71). In their short-term follow-up analysis, Massager *et al*. identified that patients with lower intracanalicular tumor volume (<100 mm^3) and lower integrated dose delivered to the intracanalicular part of the tumor (<1.5mJ) had a higher chance of maintaining their hearing at pretreatment levels(72). In their recent experience, Lunsford *et al*. could keep functional hearing in >90% of their Koos grade I VS with a prescription dose of 13 Gy (median)(28, 55). In an interesting take on dose planning, Teyateeti *et al*. reported higher hearing preservation with prescription at 40% isodose rather than at 50%. Theoretically, it provides a steeper dose falloff while maintaining a higher dose deposition inside the tumor. This needs further validation as this approach also risks marginal tumor failure(73).

The vestibular nerve is sensory and is a radiosensitive structure. Contrary to the facial nerve (motor in nature), the vestibular nerve has a high chance of injury after radiation therapy(71). While treating VS, a radio surgeon must spare the surrounding organs at risk, such as the basal turn of the cochlea and brain stem(74). Contrary to microsurgery, hearing loss after radiosurgery is a delayed onset phenomenon (if any)(75). A sudden hearing loss

post radiosurgery has been rarely reported in cases of intratumoral hemorrhage(76). There is only a limited case reported for this rare phenomenon. There is no evidence of loss of hearing related to the pseudoprogression of the VS(77). Pseudoprogression is transient edema in the tumor following SRS, supposedly associated with central tumor necrosis, and has been implicated as a cause of deterioration of hearing. A remote possibility is radiation-induced obliteration of certain micro-vessels or axonal damage. In GKRS, the typical dose prescription is 11-13 Gy; any dose less than 14 Gy does not appear to cause any such possibility(69).

Biologically effective dose (BED) and dose rate are under evaluation criteria. It has been observed that dose rates had practically no effect on tumor control. However, slower dose rates (<2.675 Gy/min) appeared to correlate with reduced cranial nerve toxicity and better hearing outcomes(78).

Dose to cochlea

The tolerance of OARs is differential, with cochlea being the most radiosensitive structure. The basal turn of the cochlea houses the outer and inner hair cells, which are highly radiosensitive (Figure 3). Regis *et al*. advocated sparing cochlea from 4 Gy radiation exposure in a single session SRS in their landmark article. Patients receiving <4 Gy exposure to cochlea have a significant advantage over patients receiving >4 Gy radiation (p=0.014). Regis *et al*. reported preserved functional hearing (GR 1 or 2) in 78.4% of patients, while 100% maintained hearing in the Koos grade I subgroup at the latest follow-up evaluation(27). Paek *et al*. have reported that a lower maximum dose delivered to the cochlear nucleus in pons is associated with better hearing preservation. But, this could not be replicated in other studies(79). Such studies have kindled interest in identifying a holy grail; however, there is significant interstudy diversity for cochlear dose. The cochlear dose is one of the variables dictating the hearing outcome, but there is no definite guideline if the point dose vs. mean dose. Vs. the maximum dose to the cochlea is relevant. Literature has no consensus on the true mean or maximum dose permissible to the cochlear nerve or dose to the cochlear nuclei.

However, despite sharp dose fall out, inverse planning, and beam blocking, it is not always feasible to spare the cochlea. Lesions extending deep inside the canal remain at higher risk for the same reason. Despite the reported variation, the controversy is still persistent, and the author (MT) does not advocate sparing the cochlea at the expense of tumor coverage or control(72, 74).

Complications with radio surgical management of VS

"A fool with a tool is still a fool." Radiosurgery, similar to any other interventional tool, may result in complications if the neurosurgeon does not comply with the standard safety

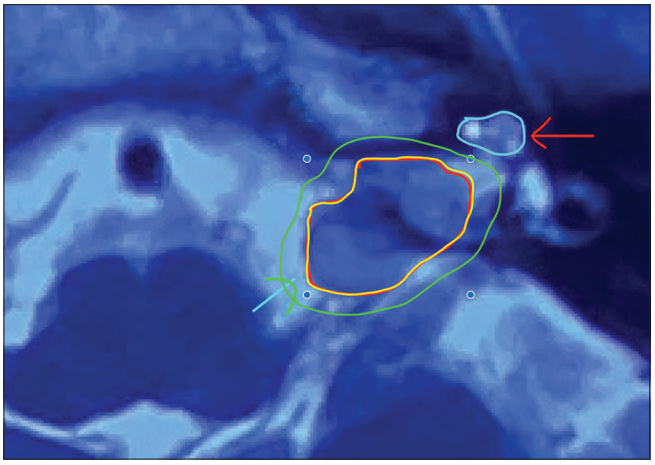

Figure 3: Relationship between Koos grade II vestibular schwannoma (green arrow) and basal turn of cochlea (red arrow; organ at risk). Note the cerebrospinal fluid between the tip of tumor and the distal end of the canal. Tumor margin marked in red, radiosurgery plan delivering 12 Gy at the periphery of the tumor (yellow periphery). Basal turn of cochlea is spared from 4 Gy radiation exposure (Green periphery). (Figure for radio surgical planning representation)

parameters. The primary requirement is the exact target definition and surrounding organs at risk. The usual imaging sequence required is pre- and post-contrast volumetric T1 and T2 sequences. Additionally, the CISS/FIESTA sequences may be obtained to better visualize the cranial nerves in the basal cisterns(69).

A transient reversible swelling in the vestibule Schwannoma post radiosurgery is a well-known phenomenon also known as "pseudoprogression" (Figure 2B). VS quite often swells up after radiosurgery without any clinical deterioration hence with no requirement of any further intervention. The swelling is radiation-induced edema that subsides on its own with mere observation. It has been observed that a volumetric increase of 30% or more was significantly more likely to produce dysfunctions. An increase to such an extent may cause transient facial and trigeminal neuropathy, which subsides on its own when the temporary swelling resolves(80). There is no definite correlation between pseudo-progression and hearing loss. It has been observed that patients suffering from hearing loss secondary to pseudoprogression have a poor recovery prognosis. A plausible explanation is a vascular compression within the rigid confines of the IAC(81).

Radiosurgery-induced facial neuropathy is a rare phenomenon Table 4. The prescription dose must not cross the drawing of the target margin, especially in the upper part of the internal auditory meatus anterior to the intracanalicular portion of the tumor. With modern planning software, the incidence of facial nerve dysfunction is less than 1%(71). One of the most controversial topics against radiosurgery are chances of radiosurgery induced malignant transformation of VS. Radiation treatments do increase the risk of malignant change to a rate over 20 years estimated at 15.6 per 100,000 in sporadic tumors. This risk is equivalent to a risk of spontaneous malignant transformation in a tumor even in the absence of any radiation therapy. The risk of malignant transformation are slightly higher in syndromic patients such as NF 2 compared to sporadic VS. This is a very small risk set against the risk of not treating growing VS. However patients must be made aware of this remote and unlikely complication while discussing various management options(69).

Contemporary Role of Microsurgery in Small Vestibular Schwannomas

MS is the only modality that guarantees a cure and total tumor extirpation. This is especially relevant in younger patients who will witness tumor progression during their life spans. Large surgical series also report excellent tumor control rates (Table 5)(82-86). Arthurs *et al*. in their systematic review of VS treatment, reported that MS is very efficacious across tumor sizes, with only 1% of operated patients requiring further treatment(87). In expert hands and at large volume centers, 98% of complete excision rates are reported(82). The reliable efficacy of MS in achieving tumor control is evident in series reporting smaller numbers. In an 80-patient series of small VSs (Koos grades 1 and 2), Anaizi *et al*. reported 97.5% tumor control, including cure and growth arrest, thus rivaling the results mentioned for RS(88). The described less than 3% recurrence rate for tumors after MS is tempered by the fact that these are applicable only in cases of gross or near

Table 5: Functional preservation after microsurgery for vestibular schwannoma (MCF, middle cranial fossa; RS, radiosurgery; TL, translabyrinthine)

Major series	Hearing Preservation	Facial Preservation	Microsurgical approach used
Samii *et al*. (1997)	51% (37)	94% (37)	
Staecker *et al* (2000)	54% (15)	92% (15)	
Magnan *et al* (2002)	52% (20)	100% (20)	
Mohr *et al* (2005)	50% (8)		
Colletti *et al* (2005)	57% (35)	91 (35)	
Samii *et al* (2006)	57% (22)	90% (22)	
Myrseth E *et al* (2009)	44% (13/28)	100% (28/28)	
Sughrue ME *et al* (2011)		90% (2890)	MCF (85%), TL (81%), RS (78%)
Ansari SF *et al* (2012)	56.4% (96/165)	96/7% (232/240)	MCF
	35.7% (76/213)	92.8% (259/279)	RS
Mastronardi L *et al* (2019)	64.3% (18/28)		RS

total (defined as leaving behind only a microscopic bit of tumor on the facial nerve or the brainstem) excision; after subtotal excision, the recurrence rate is 20-30%(11).

Hearing preservation rate after microsurgery

Mastronardi *et al*. 17 states that small VS in younger patients with preserved hearing should be treated with hearing preservation surgery as the long-term chances of hearing preservation are maximum after MS compared to either observation or RS(89). Anaizi *et al*. 30 claim that MS is suitable for long-term hearing preservation in patients with mild but serviceable hearing loss but should not be resorted to in patients with normal hearing(88). Multiple studies7,38,39,40,41 demonstrate long-term preserved hearing in 60-75% of patients after MS(24, 90-92). In a recent single-surgeon experience comparing MS to RS, the former had a higher hearing preservation rate at five years (71.4 versus 53.3%)(92).

Facial nerve preservation

Conservatively managed patients hardly develop facial paresis from a VS (Table 4). In Sughrue's series it was reported that less than 3% of patients developed facial neuropathy in the long term(16). Myrseth *et al*. in a prospective study of MS vs. RS for tumors less than 25 mm reported 46% rates of poor postoperative facial nerve function (House-Brackmann grade 2 or poorer); in contrast, only one patient out of 60 had it after RS(60). Pollock *et al*. also reported better facial nerve outcomes after RS (98%) compared to MS (83%). With 12-13 Gy dose RS,45 recent series have reported excellent long-term facial nerve outcomes between 94-100%.

MS fares worse when it comes to post-procedure facial nerve dysfunction(50). In a meta-analysis of 79 articles, Sughrue *et al*. found facial nerve preservation rates of 90% for tumors less than 20 mm. The middle fossa approach generally leads to worse facial nerve outcomes than the retrosigmoid approach(93). Even large center data like those reported by Samii *et al*. show facial nerve dysfunction rates as high as 80% after MS; this series includes tumors of all sizes. The aggregate of data suggests that RS may be superior to MS in terms of facial nerve preservation(82, 94).

Salvage microsurgery after radiosurgery for VS

When the management of VS is increasingly shifting to non-surgical methods, a salvage procedure following failed SRS is one of the abiding needs for MS. Husseini *et al*. found that following SRS, surgery for VS is technically tricky with bad planes, worsening of facial nerve function in 73% of patients and almost impossible hearing preservation. They also had one case of malignant transformation(95). Lee *et al* shared similar unfavourable outcomes and opined that those involved in the decision-making process for VS should know about the risks of failure and the potential complications, especially in younger patients(96). Misra *et al* reported that out of 16 patients who required MS after RS, 4 patients had poor facial outcomes(97). Friedman *et al* in a larger series of 73 patients compared outcomes of total and partial removal after surgery for MS and found 21.7% of the total removal group having unsatisfactory facial outcomes (which they described as House-Brackmann grades 5 or 6) compared with 7.1% of patients with partial removal(98). Troude *et al* compared facial nerve outcomes in large VS who underwent primary versus secondary (after failed RS) MS and described good facial nerve outcomes in both sets of patients (84% vs 95%)(99). In all three studies, the authors say that good tumour control rates can be achieved with decent functional outcomes especially if nerve-sparing resections and willingness to leave behind tiny bits of tumour on the facial nerve are adopted(97, 98).

Surgical techniques in the setting of small asymptomatic VS

Hearing preservation approaches in the setting of MS for a small VS include the retrosigmoid and middle fossa approaches. For small intracanalicular tumors, the middle fossa approach is a feasible option(24, 65). Del Monte *et al*. reported 73% hearing preservation and 93% good facial nerve outcomes after the MF approach for tumors less than 2 cm(100). In general, MF approach is better for hearing preservation while the rates for facial nerve dysfunction are worse(83, 101-104). The retrosigmoid approach is reserved for tumors with minimal extension into the IAC (less than one-half of the proximal IAC) with a predominantly cerebellopontine angle component(104). The comparative data between the MF and RS approaches show that while the rates for hearing preservation

are approximately 52% and 36% respectively, the facial dysfunction rates contrast at 16% and 5% depending on the size of the tumour (less than 1.5 cm and between 1.5-3 cm)(101).

Adjuncts to safer surgery

Intraoperative neuromonitoring (IONM) has improved functional outcomes in VS surgery. The most commonly used techniques are electromyography (EMG) of the seventh nerve and brainstem auditory evoked potentials (BAEP) for the eighth nerve(105). Multiple studies suggest that the use of IONM for the facial nerve leads to better nerve function outcomes. From anatomical preservation, the role of EMG of the facial nerve has expanded to predicting outcomes after surgery. Post resection stimulation thresholds, response amplitude and tonic/train activity on continuous EMG monitoring can be reliably used to predict good facial function post operative(106).

Eighth nerve monitoring techniques are still evolving. The use of BAEP is marred by the data averaging required and delay issues limit usefulness. Newer BAEP techniques have been reported to be more effective in this regard(89). Direct cochlear nerve monitoring is developing as a more effective alternative. There are isolated reports of cochlear nerve monitoring being very useful in hearing preservation surgeries(107, 108). Presently, it is not used extensively due to technical difficulties including probe size, difficulty in accessing the proximal part of the nerve in the beginning of surgery and variability in measurements and difficulty of interpretation.

Although observation and RS are presently the main treatment strategies for small vestibular schwannomas, MS definitely has a role to play in a selected subgroup of patients. With advances in monitoring techniques, MS can remain a viable, safe option for management of small VS.

VS population is heterogeneous

Obtaining an onco-functinoal fleece in different patient spectrum of VS is not a generalised approach. Especially in an asymptomatic patient, the management decision for the tumour has to consider multiple factors including age, comorbidities, tumour size and morphology, expected functional outcomes and patient preference. There are strong preoperative parameters that determine the chances of maintenance of the dual goal. Hence, one size fits all approach cannot be applied to even Koos grade I and II VS. Because of the wide variation in the tumour extent inside IAC and cistern, variable hearing status in different subgroups, preoperative evaluation of the individual risk at the time of decision-making process is a difficult task. A young patient is found to be at an advantage of better hearing preservation compared to the older population. The reasons may be fragility of older nerve, its blood supply, ongoing presbycusis.

Management options for cystic VS

Cystic VS (described variously as more than 50% or two-thirds of the tumour showing a cyst component) have the potential for rapid growth and are considered to be an indication for MS(109-111). However, the functional outcomes for surgery in these tumors is also worse and this is attributed to the poor plane between the cyst walls and the surrounding neurovascular structures(112). Management decision for these tumors is complicated by the fact that these tumors can respond adversely to RS(113). RS can cause cyst expansion, hemorrhage and neuropathies(114). Even if the cystic tumour has regressed after RS, sustained follow-up is required as these tumors can show expansion later.

Radio surgical reports on the management of cystic VS has ranged from overtly pessimistic to very favourable outcomes. The literature till last century considered cystic composition a negative prognostic marker while the later long term follow up reports mentioned that cystic tumors are better responder with early volumetric reduction compared to the solid component. It needs to be emphasised here that cysts (especially macrocysts) need to be differentiated from occasional arachnoid cap around the tumor(113). An arachnoid cap is an entrapped CSF loculation that does not respond to radiosurgery while cystic tumor shows volumetric reduction of the tumor.

Factors determining the quality of life

These are increasingly being recognised as barometers of successful management. Klersy *et al*. found that the Qol as measured by the Short Form 36 (SF-36) questionnaire in patients

with small VS on conservative management was the same as the general population(115). There are studies which show QoL worsening after any surgical procedure for VS and claim that on some metrics, patients undergoing RS perform better than those after MS(116). Link *et al* found that patients undergoing subtotal resection have a worse QoL than those who undergo gross total resection and attributed it to the patient feeling better with the knowledge that the entire tumour was taken out. Most studies have found no difference in QoL parameters between any of the three treatment arms for small VS(117). Carlson *et al*. maintained that just the diagnosis of VS itself impacted QoL while the differences in outcomes following the different treatment arms are small(118). Other studies also maintain that the QoL across observation or intervention remains the same(119).

A sensorineural hearing loss (SNHL) is associated with poor understanding of speech and sound localisation. For normal life, binaural hearing is critical especially for people in certain occupations such as singers, musicians, military personnel, and law enforcement. Additionally, VS with hearing loss in only functional ear is devastating. However, hearing preservation is only one of the many factors that determine the functional quality of life. Other disease and treatment related factors such as vertigo, tinnitus, facial paresis, trigeminal sensory and motor neuropathy, and hearing in the contralateral ear are equally important which needs to be evaluated while counselling these patients. Contrary to the popular belief, vertigo, headache, and tinnitus are the factors that determine the Functional quality of life of a patient of VS(120). Hearing status is not that bothersome if the other ear is functional. On a personal note, clinician should not forget the patients' expectations and their personal experience with different treatment modalities. Current strategies favour a trend towards maximising functional outcome sometimes at the cost of tumour control. Many radio surgeons underdose the lateral most component of tumor inside IAC, to spare cochlea. surgical centers also operate with a planned partial resection under strict neuro monitoring. Though these approaches have shown promising results in short term, they remain at risk of poorer tumor control and recurrence in the long term.

Future Directions

The key issues for the future investigations to understand the pattern of hearing loss among patients of VS lie in high quality comparative long term analysis of hearing preservation between different modalities of treatment and conservative strategy. Only a well-designed prospective randomised study with long term follow up may answer this question. On a practical note, it is unlikely to conduct such a study.

Audiological rehabilitation involves routing of sound to the contralateral good ear either surgically through bone conduction or via a hearing aid system. Cochlear nerve implantation is a promising tool that has a much better probability of achieving binaural hearing, and speech recognition. It demands anatomically intact cochlear nerve. At present insurance companies do not cover cochlear nerve implantation for single side deafness. However, they have a promising role in the near future.

Conclusion

At present, there is no class I evidence to guide management of patient cohort of small VS with preserved hearing. In the absence of any well-designed long term randomized control trial, the controversy between observation, microsurgery, and radiosurgery is going to prevail. Till then, we need to bargain treatment outcomes with the possible complications of the natural history of incidentally detected small VS. In the long term, the chances of maintenance of serviceable hearing are remote by any possible strategy and treatment option is a Sophie's choice.

Treatment needs to be catered to the patients age, extent of hearing loss, nonaudiological symptoms, and expectations. In present era, patients are better informed and demand excellent care at par with the reference centers. The onus of acceptable outcome is shared by surgeons and patients' to variable extent, however with changing landscape many a times patients are more considereate to non surgical options than the surgeon. Consistent and durable hearing preservation in sporadic VS remains an elusive goal. Most of the patients remain at risk of losing functional hearing either as a result of diseases or the

treatment. The subgroup with the highest chances of long-term functional preservation with proactive GKRS is of young patient (<50 years age) with Koos grade I VS, serviceable hearing loss (GR 1 or 2), differential PTA between two ears of 10 dB or less, tumour location near cistern with minimal intracanalicular tumor extension (Ohata Class D or E), presenting symptom other than hearing loss, and absence of tinnitus at the time of presentation. The risk of losing serviceable hearing is upfront with surgery, while it's a time bound progressive phenomenon in observation or radiosurgery. In the short term (up to 10 years), the chances of maintaining useful hearing are high with observation or SRS. In the long term, microsurgery may provide the best possible hearing outcome, if there is no insult and loss with upfront surgery. The patient needs to be counselled for both short- and long-term risk of loss of serviceable hearing, as most of these patients are in 40s or 60s of their age and expected to live longer.

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