

CONGRESS OF NEUROLOGICAL SURGEONS SYSTEMATIC REVIEW AND EVIDENCE-BASED GUIDELINES UPDATE FOR THE ROLE OF IMAGING IN THE MANAGEMENT OF PATIENTS WITH VESTIBULAR SCHWANNOMAS

Sponsored by: Congress of Neurological Surgeons (CNS) and the Section on Tumors

Endorsement: Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS)

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Keywords: Vestibular schwannoma; acoustic neuroma; guidelines; neuroimaging; magnetic resonance imaging; surveillance; stereotactic radiosurgery; diffusion tensor tractography

Running Title: Vestibular Schwannoma Imaging Guidelines

Abbreviations: Vestibular schwannoma (VS); cerebellopontine angle (CPA); stereotactic radiosurgery (SRS); Congress of Neurological Surgeons (CNS)

ABSTRACT

Background: Imaging is a critical aspect of vestibular schwannoma (VS) management, influencing essentially every aspect of care including diagnosis, surveillance, treatment decision-making, and follow-up after either resection or stereotactic radiosurgery (SRS). Despite this, treatment protocols are heterogeneous, and frequently based on historical practices, or low-quality evidence.

Objective: To update evidence-based guidelines for the use of imaging in the clinical management of patients with VS published by the Congress of Neurological Surgeons (CNS) in 2018.

Methods: Systematic review of the literature published from 1/1/2015 to 12/31/2022 regarding imaging protocols for VS management. Salient questions were identified by a writing group of diverse individuals with topic-specific expertise. Questions were validated by the CNS Guidelines Committee. Following systematic review, literature tables and summary statements pertinent to the study questions were generated by the writing group, which underwent subsequent evaluation and revision by the task force prior to formalization.

Results: Seven questions were formulated; adequate literature was identified to formulate updated recommendations for 6 of these. Search strategy identified 1143 unique records, of which 109 underwent full-text review, and 57 were included in the current study. Most studies provided level III evidence, with rare level II studies noted, yielding level III recommendations.

Conclusion: The current evidence base for imaging protocols in VS clinical management is broad, diverse, low-certainty, and low-quality. This in part reflects a heterogeneous disease, although variability in treatment philosophies may also influence local decision-making. Key areas for future study include the clinical utility of advanced imaging techniques, and head-to-head comparisons of imaging protocols for patients in common initial VS management pathways (e.g., observation, resection, or SRS).

RECOMMENDATIONS

Questions and Recommendations from the Prior Version of These Guidelines Without Change:

Prior Question: Do cystic VSs behave differently than their solid counterparts?

Prior Recommendation (Level III): Adults with cystic VSs should be counseled that their tumors may more often be associated with rapid growth, lower rates of complete resection, and facial nerve outcomes that may be inferior in the immediate postoperative period but similar to non-cystic schwannomas over time.

Prior Question: Should the extent of lateral internal auditory canal (IAC) involvement be considered by treating physicians?

Prior Recommendation (Level III): The degree of lateral IAC involvement by tumor adversely affects facial nerve and hearing outcomes and should be emphasized when interpreting imaging for preoperative planning.

Prior Question: How should patients with neurofibromatosis type 2 (NF2) and VS be imaged and over what follow-up period?

Prior Recommendation (Level III): In general, VSs associated with NF2 should be imaged (similar to sporadic schwannomas) with the following caveats:

1. More frequent imaging may be adopted in NF2 patients because of a more variable growth rate for VSs, and annual imaging may ensue once the growth rate is established.
2. In NF2 patients with bilateral VSs, growth rate of a vestibular schwannoma may increase after resection of the contralateral tumor, and therefore, more frequent imaging may be indicated, based on the non-operated tumor's historical rate of growth.
3. Careful consideration should be given to whether contrast is necessary in follow-up studies or if high-resolution T2 (including CISS or FIESTA-type sequences) MRI may adequately characterize changes in lesion size instead.

Questions and Recommendations from the Prior Version of These Guidelines that are Updated:

Prior Question: What sequences should be obtained on MRI to evaluate VSs before and after surgery?

New Question 1: *In patients presenting with unilateral hearing loss is non-enhanced MRI, as compared to gadolinium-enhanced MRI, sufficiently sensitive to assess for the diagnosis of VS?*

Recommendation (Level III): *Non-contrasted, high-resolution MRI can be utilized as a cost-effective alternative to gadolinium-enhanced MRI when screening patients for VS. Further, it is suggested that the MRI sequences for the assessment of acute unilateral sensorineural hearing loss should include coronal T2, axial T1, and high-contrast T2, ideally in axial and coronal planes.*

New Question 2: *In patients with sporadic VS undergoing initial observation, are high-contrast T2 sequences (CISS/FIESTA-C), as compared to gadolinium-enhanced studies, sufficiently sensitive for surveillance of interval growth?*

Recommendation (Level III): *The use of high-resolution T2 imaging without enhanced T1 imaging in follow-up of observed VS is suggested, with enhanced T1 studies considered for instances of equivocal growth, or lesions suspected to be high-risk for phenotypically aggressive behavior.*

Prior Question: What is the expected growth rate of VSs on MRI, and how often should they be imaged if a “watch and wait” philosophy is pursued?

New Question 3: *In patients with sporadic VS undergoing initial observation, is a follow-up MRI at 2 years, as compared to a follow-up MRI at 1 year, associated with an increased risk of clinical decompensation requiring urgent/emergent intervention?*

Recommendation (Level III): *It is suggested that close early imaging follow-up, with annual studies for at least 3 years after diagnosis, followed by interval imaging at least every 3-5 years, with specific plans tailored to the patient-specific parameters (e.g., age, tumor size, prior growth), and the comfort levels of the patient and multidisciplinary treatment team be used in patients with sporadic VS undergoing initial observation.*

Prior Question: Is there a role for advanced imaging for facial nerve detection preoperatively (eg, CISS/FIESTA or DTI imaging)?

New Question 4: *In patients with sporadic VS undergoing preoperative planning for microsurgical resection, is high-field MRI (7T), as compared to routine MRI (1.5T and 3T), able to reliably determine the position of the facial nerve with respect to the tumor?*

Recommendation: *At present, there is insufficient evidence to determine the relative benefits of high-field versus standard-field MRI for determination of the position of the facial nerve with respect to the tumor.*

New Question 5: *In patients with sporadic VS undergoing preoperative planning for microsurgical resection, is MRI with fiber tractography, as compared to routine MRI (1.5T and 3T), able to reliably determine the position of the facial nerve with respect to the tumor?*

Recommendation (Level II): *Preoperative fiber tractography is recommended, when feasible, to assist in determining the location of the facial nerve with respect to the tumor, yet additional research is necessary to better elucidate whether this additional neuroanatomic information confers an improved long-term outcome.*

Prior Question: How long should VSs be imaged after surgery, including after gross total, near total, and subtotal resection?

New Question 6: *In patients with sporadic VS who undergo primary microsurgical resection, is early postoperative MRI (during the same hospitalization), as compared to delayed postoperative MRI at 3 months, less accurate and reliable in the detection of postoperative residual tumor?*

Recommendation (Level III): *While there is no evidence to suggest an advantage of early versus late initial postoperative imaging, it is suggested that initial imaging at ≥ 3 months after surgery, with follow-up imaging at closer intervals for STR/NTR (e.g., 3, 12, and 24 months), and longer intervals after GTR (e.g., 6, 18, and 36 months) is reasonable.*

Question and Recommendation that is New:

New Question 7: *In patients with sporadic VS who undergo primary SRS, is initial interval imaging at ≥ 24 months, as compared to initial interval imaging at ≤ 12 months, associated with increased incidence of tumor-directed clinical action, defined as a neurosurgical intervention that is undertaken strictly as a consequence of the imaging study and not due to patient symptoms, including repeat irradiation, surgical resection, treatment of ventriculomegaly with CSF diversion, or initiation of a VS disease-directed medical therapy?*

Recommendation (Level III): *Post-radiosurgery imaging is suggested at 12, 24, and 36 months, and deferral of retreatment is suggested until progression is noted on 3 consecutive imaging studies, absent concerning parallel changes in clinical symptoms.*

INTRODUCTION

VS is a benign neoplasm arising from the myelinating Schwann cells of the superior or inferior vestibular nerve, with an estimated annual incidence rate of 1.52 per 100,000 population.¹ Although uncommon, VS account for the majority of cerebellopontine angle (CPA) lesions and are the most common nerve sheath tumors overall. Although VS are pathologically benign, their posterior fossa location and propensity for growth over time predispose patients to a wide swath of disease morbidities, including hearing loss, vertigo, imbalance, hydrocephalus, and potentially death.²

Common VS management strategies include observation with radiographic surveillance, microsurgical resection, or stereotactic radiosurgery (SRS), with decision-making highly individualized, and modulated by the specific parameters of a given tumor, patient, or practice.³⁻⁷ Given the breadth of treatment pathways, as well as intrinsic disease heterogeneity, and the range of attendant risks and benefits associated with various management strategies, contemporary clinical practices vary considerably between centers and individual surgeons. Considering this diversity, the Congress of Neurological Surgeons (CNS) Guidelines Taskforce has published guidelines detailing best-practice recommendations covering most aspects of VS clinical care.⁸⁻¹⁶

Imaging is a foundational aspect of VS management that influences decision-making at essentially all phases-of-care, including initial diagnosis, surveillance, treatment planning, and post-treatment follow-up after either resection or SRS. The current study represents an update to the preceding CNS Guidelines for the role of imaging in the diagnosis and management of patients with VS, covering additions to the literature since the publication of those recommendations, 2015-2022.⁸ In addition to providing a general scientific update regarding primary clinical neuroimaging in VS, we also sought to partially tailor our study questions to the increasingly urgent need for efficiency in the delivery of advanced cranial care.

METHODOLOGY

The guidelines task force initiated a systematic review of the literature published after the last search date in the first version of this guideline to update the evidence-based information relevant to the treatment of patients with VSs. Through objective evaluation of the evidence and transparency in the process of making recommendations, this evidence-based clinical practice guideline was developed for the diagnosis and treatment of adult patients with functioning pituitary adenomas. These guidelines are developed for educational purposes to assist practitioners in their clinical decision-making processes. Additional information about the methods utilized in this systematic review is provided below.

Literature Search

Under the supervision of a research librarian and using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines, we queried the Ovid Medline and Embase peer-reviewed databases for articles pertinent to clinical imaging protocols for VS management (for full search strategy, please see Supplement 1; for PRISMA flow diagram, see Figure 1). Initial search identified 1143 candidate citations, which were subject to title and abstract review in duplicate by 2 study investigators (CSG, WS). All articles identified as potentially meeting study criteria (n=109) underwent full-text review for confirmation of eligibility, with ambiguities in application of study criteria resolved by deferral to a senior investigator (IFD).

Study Selection and Eligibility

Prior to completing the formal systematic literature review, objective inclusion and exclusion criteria were collaboratively defined by the study writing group. Finalized criteria were ratified by the writing group prior to initiation of the literature search, in order to minimize the risk of bias. The final, standardized criteria were applied to the assessment of all pertinent articles, including those identified outside the primary search, via bibliography review, investigator contribution, or any other mechanism. Articles were considered eligible for inclusion in the formulation of these evidence-based clinical practice guidelines if they adhered to the following conditions:

Inclusion Criteria:

- *Was published in an English-language peer-reviewed publication during the study sampling frame, 1/1/2015-12/31/2021*
- *Was a full article reporting primary, quantitative data from original clinical research*
- *Reported a minimum sample size of 5 patients*
- *Investigated patients with sporadic VS*

Exclusion Criteria:

- *Non-human, cadaver, or in vitro analyses*
- *Incomplete, non-peer-reviewed citations (e.g., meeting abstracts)*
- *Qualitative analyses (e.g., review articles, historical articles, editorials, letters, commentaries)*
- *Meta-research (e.g., prior systematic reviews, meta-analyses, society guidelines)*

Previously published systematic reviews, meta-analyses, or guidelines were not considered evidence for inclusion in the study results, but were subject to bibliographic review, in order to optimize capture of candidate citations.

These assessments for the included articles in turn informed the evidence levels assigned to the associated recommendations. Level-setting for the study recommendations was benchmarked to the highest-quality publication included within the manuscripts for a given question.

Following initial assessment of all included articles and determination that the current study would be restricted to a qualitative systematic review without meta-analysis, formal risk-of-bias including Egger's and Begg's tests or the creation of funnel plots was deferred. Qualitative assessment for risk-of-bias was conducted by determining the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) criteria for all included studies, which were deemed to be of good quality to answer the PICO questions.¹⁷

Rating Quality of Evidence

The quality of evidence was rated using an evidence hierarchy for each of four different study types; therapeutic, prognostic, diagnostic, and decision modeling. These hierarchies are shown in Appendix II: Rating Evidence Quality. Additional information regarding the hierarchy classification of evidence can be located here: <https://www.cns.org/guidelines/guideline-procedures-policies/guideline-development-methodology>.

Revision Plans

In accordance with the Institute of Medicine's standards for developing clinical practice guidelines and criteria specified by the National Guideline Clearinghouse, the task force will monitor related publications following the release of this document and will revise the entire document and/or specific sections "if new evidence shows that a recommended intervention causes previously unknown substantial harm; that a new intervention is significantly superior to a previously recommended intervention from an efficacy or harms perspective; or that a recommendation can be applied to new populations."¹⁸ In addition, the task force will confirm within five years from the date of publication that the content reflects current clinical practice and the available technologies for the evaluation and treatment for patients with perioperative spinal disease.

SUMMARY OF PREVIOUS GUIDELINES

The preceding CNS Guidelines regarding the role of imaging in VS management tackled 7 key clinical questions, with partial overlap regarding the current study.⁸ They addressed optimal MRI sequences for

before and after VS resection; the role of advanced imaging (e.g., CISS/FIESTA, DTI) prior to VS resection; expected VS growth rates and timing for surveillance under “watch and wait” management strategies; imaging behavior of cystic vs. solid VS components; the influence of VS within the lateral auditory canal (IAC) on treatment decision-making and counseling; imaging protocols for patients with neurofibromatosis type 2 (NF2); and postoperative imaging protocols and duration, as modulated by extent-of-resection. The authors made level III recommendations for most questions, which emphasized the importance of both enhanced and high-resolution T2-weighted imaging; the potential utility of T2 imaging for preoperative facial nerve localization; close follow-up imaging in the early observation and/or post-treatment period, generally lasting at least 5 years; the impact of lateral IAC tumor on adverse facial nerve and hearing outcomes; and the importance of a thoughtful and aggressive stance towards imaging patients with NF2 in follow-up. Of note, given the general nature of the questions addressed by these guidelines, and the relatively short interval, we emphasized in the current update novel questions that interrogated more detailed or nuanced aspects of imaging in VS management.

RESULTS

Following full-text review and deliberation, of 109 articles, 52 were excluded for failing to meet criteria, reporting inadequate data, or not being relevant to the study questions. In total, 57 articles were identified as meeting all study criteria and were included to formulate our recommendations in response to the study questions. For each of the 7 questions, we included 11, 4, 14, 0, 15, 5, and 8 manuscripts. The overarching population for the study questions was patients with sporadic VS; however, this was modulated by the specific parameters under assessment with each question, as detailed below (e.g., timing for imaging after primary SRS is salient only to those patients who underwent primary SRS, *among patients with sporadic VS*).

Question 1

In patients presenting with unilateral hearing loss is non-enhanced MRI, as compared to gadolinium-enhanced MRI, sufficiently sensitive to assess for the diagnosis of VS?

Target Population

All individuals presenting to medical attention with unilateral hearing loss that is spontaneous in nature and not referable to an obvious underlying diagnosis, such as trauma.

Recommendation (Level III): *Non-contrasted, high-resolution MRI can be utilized as a cost-effective alternative to gadolinium-enhanced MRI when screening patients for VS. Further, it is suggested that the*

MRI sequences for the assessment of acute unilateral sensorineural hearing loss should include coronal T2, axial T1, and high-contrast T2, ideally in axial and coronal planes.

Results of Individual Studies, Discussion of Study Limitations, and Risk of Bias

Following full-text review, 2 studies meeting criteria were considered pertinent to the question (Appendix IV, Table 1).^{19,20} These studies specifically assessed the role of non-enhanced MRI in the setting of sudden sensorineural hearing loss (SSNHL). Both employed cohort-type study designs, with large samples of patients screened radiographically after presenting with SSNHL. In one cohort study of 499 individuals presenting with unilateral SSNHL, the overall incidence of VS was observed at 3% (n=15).¹⁹ Lesions were ipsilateral to the SSNHL in all cases, and non-enhanced sequences were deemed sufficient for identification of the tumor itself. In another cohort study of 1249 individuals with unilateral SSNHL, the VS incidence was observed at 1.12% (n=14).²⁰ This study also assessed cost effectiveness, with significant savings observed in association with protocols omitting enhanced sequences. In both studies, MRI sequences including routine T1/T2 and high-contrast T2 (e.g., CISS/FIESTA) were identified as instrumental in establishing the VS diagnosis without gadolinium enhancement.

Synthesis

While gadolinium-enhanced MRI is the gold standard imaging modality for diagnosing VS, non-contrast, high-resolution MRI has the sensitivity to be utilized as a cost-effective screening tool. *Further, it is suggested that the MRI sequences for the assessment of acute unilateral sensorineural hearing loss should include coronal T2, axial T1, and high-contrast T2, ideally in axial and coronal planes.*

Question 2

In patients with sporadic VS undergoing initial observation, are high-contrast T2 sequences (CISS/FIESTA-C), as compared to gadolinium-enhanced studies, sufficiently sensitive for surveillance of interval growth?

Target Population

Patients with new radiographic findings consistent with sporadic (e.g., unilateral) VS, whose initial management recommendation is observation with radiographic follow-up.

Recommendation (Level III): *The use of high-resolution T2 imaging without enhanced T1 imaging in follow-up of observed VS is suggested, with enhanced T1 studies considered for instances of equivocal growth, or lesions suspected to be high-risk for phenotypically aggressive behavior.*

Results of Individual Studies, Discussion of Study Limitations, and Risk of Bias

Following full-text review, 4 studies meeting criteria were considered pertinent to the question (Appendix IV, Table 2).²¹⁻²⁴ These publications addressed the study question directly, allowing summative conclusions to be drawn with minimal extrapolation or indirect inference. All studies were retrospective, observational, and assessed the accuracy of high-contrast T2 sequences in measuring VS size and change-in-size, as compared to enhanced T1 sequences. Two additional studies included cost analyses; one assessed routine T2 in addition to high-contrast FIESTA/CISS imaging. Key study statistics also included accuracy and reliability testing between sequences for a single study; across imaging studies for each sequence under evaluation; and between raters, who were neuroradiologists in almost all studies. Overall, these assessments demonstrated high levels of accuracy and reliability for high-contrast T2 sequences, which were more robust when comparable to enhanced T1 sequences than were routine T2 sequences—observations that were noted both at time-of-diagnosis and in follow-up. Those studies incorporating economic analyses indicated that both costs and charges would be significantly lowered by surveillance protocols for observed VS that eliminate enhanced sequences. Of note, the role of high-contrast T2 imaging in the setting of recurrent/residual VS was not addressed by this study question.

Synthesis

Routine T2 sequences are highly specific and sensitive for detecting growth in observed VS, but may be inferior to enhanced T1 sequences. High-resolution T2 sequences such as CISS and FIESTA appear to provide equivalent accuracy, specificity, and sensitivity in detecting growth of observed VS, and are associated with significant cost savings. *The use of high-resolution T2 imaging without enhanced T1 imaging in follow-up of observed VS is suggested, with enhanced T1 studies considered for instances of equivocal growth, or lesions suspected to be high-risk for phenotypically aggressive behavior.*

Question 3

In patients with sporadic VS undergoing initial observation, is a follow-up MRI at 2 years, as compared to a follow-up MRI at 1 year, associated with an increased risk of clinical decompensation requiring urgent/emergent intervention?

Target Population

Patients with new radiographic findings consistent with sporadic (e.g., unilateral) VS, whose initial management recommendation is observation with radiographic follow-up.

Recommendation (Level III): *It is suggested that close early imaging follow-up, with annual studies for at least 3 years after diagnosis, followed by interval imaging at least every 3-5 years, with specific plans tailored to the patient-specific parameters (e.g., age, tumor size, prior growth), and the comfort levels of the patient and multidisciplinary treatment team be used in patients with sporadic VS undergoing initial observation.*

Results of Individual Studies, Discussion of Study Limitations, and Risk of Bias

Following full-text review, 12 studies meeting criteria were considered pertinent to the question (Appendix IV, Table 3).²⁵⁻³⁶ The specific endpoint of early decompensation was not reported by any prior study; however, all studies reported their institutional protocol for follow-up among observed VS, generally with detailed information regarding timing of progression and subsequent treatment recommendations. Protocols for follow-up imaging of observed VS are highly heterogeneous between centers, with variability clustered around two parameters: Timing of follow-up, and clinical action following tumor growth.

Most centers defined growth as ≥ 2 mm change in size of nodular tumor; some centers also incorporate volumetric analysis. The shortest follow-up interval for newly diagnosed sporadic VS was 3 months; the longest was 24 months; the most common protocol was 12 months. Subsequent imaging protocols were even more diverse than the initial follow-up imaging protocols. The most frequent imaging protocol was every 3 months for a year, then every six months for a year, then annually for 10 years; the least frequent imaging protocol included follow-up at 1, 3, 5, and 10 years; most protocols involved annual imaging for 3-5 years, followed by larger intervals for another 3-5 years, and infrequent imaging after 10 years.

Where interval growth was observed, treatment protocols again varied widely. Most centers offered treatment, with determination for SRS versus resection governed by a variety of patient-, surgeon- and institution-specific considerations. Some centers offered on-going observation until at least two instances of interval growth were observed—in particular for patients presenting at more advanced ages, or with tumors confined to the IAC. A large minority of patients underwent treatment within 3 years of initial observation in most series, with by-study incidences ranging from 30-70%. Some patients elected to observe until serial progression was observed; the rate of subsequent growth following initial growth was directly assessed by Carlson et al., who noted sustained growth in only 7% of patients at 1 year after initial growth, with annual incidence rates for sustained growth increasing to 33%, 46%, 56%, and 59%, and 2-, 3-, 4-, and 5-year intervals after initial growth was documented (e.g., >40% of tumors did not demonstrate sustained growth in 5 years of subsequent follow-up after initial documentation of tumor growth).

Synthesis

Imaging protocols for initially observed sporadic VS are highly variable. Early growth within 3 years of diagnosis appears to occur in a large minority of patients, but is not always associated with sustained growth if intervention is not indicated. Among studies that performed early follow-up imaging at 6 months, initial tumor expansion was associated with further growth on subsequent studies. The conditional probability of new growth after 5 years of freedom-from-growth appears to be <2%. Risk factors for sustained growth appear to include larger cisternal components, rapid initial growth rates, and young patient age. *It is suggested that close early imaging follow-up, with annual studies for at least 3 years after diagnosis, followed by interval imaging at least every 3-5 years, with specific plans tailored to the patient-specific parameters (e.g., age, tumor size, prior growth), and the comfort levels of the patient and multidisciplinary treatment team.* Sustained growth is not universally observed, and many patients may benefit from on-going radiographic surveillance following initial observation of tumor expansion, if reliable follow-up is anticipated.

Question 4

In patients with sporadic VS undergoing preoperative planning for microsurgical resection, is high-field MRI (7T), as compared to routine MRI (1.5T and 3T), able to reliably determine the position of the facial nerve with respect to the tumor?

Target Population

Patients with sporadic VS undergoing preoperative planning for microsurgical resection.

Recommendation: *At present, there is insufficient evidence to determine the relative benefits of high-field versus standard-field MRI for determination of the position of the facial nerve with respect to the tumor.*

Results of Individual Studies, Discussion of Study Limitations, and Risk of Bias

The literature search did not provide qualifying manuscripts to address this question (Appendix IV, Table 4). Thus, there is insufficient evidence to determine the relative benefits of high-field MRI versus standard-field MRI for the assessment of the position of the facial nerve with respect to the tumor.

Question 5

In patients with sporadic VS undergoing preoperative planning for microsurgical resection, is MRI with fiber tractography, as compared to routine MRI (1.5T and 3T), able to reliably determine the position of the facial nerve with respect to the tumor?

Target Population

Patients with sporadic VS undergoing treatment with primary microsurgical resection, whose preoperative/perioperative assessment included MRI with fiber tractography for determination of facial nerve positioning, relative to the tumor.

Recommendation (Level II): Preoperative fiber tractography is recommended, when feasible, to assist in determining the location of the facial nerve with respect to the tumor, yet additional research is necessary to better elucidate whether this additional neuroanatomic information confers an improved long-term outcome.

Results of Individual Studies, Discussion of Study Limitations, and Risk of Bias

Following full-text review, 15 studies meeting criteria were considered pertinent to the question (Appendix IV, Table 5).³⁷⁻⁵¹ No study specifically compared tractography with routine MRI for facial nerve localization purposes in the setting of VS, with the poor reliability of conventional imaging cited as the underlying explanation for those methodological decisions. One study reported by Hilly et al. included data from normal controls with comparative analysis of tractography and routine T1/T2 sequences for facial nerve localization in the CPA and IAC, with results that generalize poorly to the VS setting. All results assessing tractography in patients with VS specifically addressed the question of whether facial nerve localization was reliable with tractography; with most studies additionally providing intraoperative confirmation that the tractographic results were also valid. Reliability and validity were both strong across numerous studies, with successful nerve imaging and accurate nerve localization confirmed in >90% of patients.

Samala et al. reported a randomized study of 86 patients with large (>3cm) VS undergoing primary resection, who were allocated to treatment with or without preoperative DTI.³⁷ In their analysis, DTI appeared to provide significantly improved anatomic and functional facial nerve outcomes, although the relatively low rate of favorable facial nerve outcomes noted in the control group, relative to prior reports from numerous centers, calls into question the generalizability of their results.⁵²⁻⁵⁴ Outcomes data were otherwise quite limited, descriptive in nature, and restricted to small samples. Taken together, these results indicate that tractography is a reliable and valid tool for preoperative facial nerve localization

before VS resection; however, data on the meaningful clinical impact of this information is limited and subject to guarded interpretation.

Synthesis

MRI with fiber tractography appears to reliably localize the facial nerve with respect to the tumor in the great majority of cases, with some variance by technique. Data on the relationship between nerve localization and long-term facial nerve outcomes is promising but limited, and no definitive benefit has been confirmed at present. Consideration for preoperative fiber tractography is suggested where possible, as well as on-going research to better determine whether the additional neuroanatomic information it provides leads to improved outcomes in large samples of patients followed prospectively

Question 6

In patients with sporadic VS who undergo primary microsurgical resection, is early postoperative MRI (during the same hospitalization), as compared to delayed postoperative MRI at 3 months, less accurate and reliable in the detection of postoperative residual tumor?

Target Population

Patients with sporadic VS being treated with primary microsurgical resection.

Recommendation (Level III): *While there is no evidence to suggest an advantage of early versus late initial postoperative imaging, it is suggested that initial imaging at ≥ 3 months after surgery, with follow-up imaging at closer intervals for STR/NTR (e.g., 3, 12, and 24 months), and longer intervals after GTR (e.g., 6, 18, and 36 months) is reasonable.*

Results of Individual Studies, Discussion of Study Limitations, and Risk of Bias

Following full-text review, 5 studies meeting criteria were considered pertinent to the question (Appendix IV, Table 6).⁵⁵⁻⁵⁹ No study directly addressed the reliability, validity, or other test parameters of MRI in the assessment of extent-of-resection at early (immediate postoperative) versus delayed (≥ 3 month) timepoints. Institutional protocols for postoperative imaging after VS resection are highly variable. Initial imaging is performed by most centers either during the same hospitalization or at a 3-month postoperative visit; however, some centers delay imaging up to 6 or 12 months. Once baseline postoperative extent-of-resection has been established, further follow-up protocols are more consistent, and typically involve annual imaging for at least 3-5 years, which may be individualized in accordance with pertinent radiographic findings. Although most centers delay post-resection SRS until radiographic progression is

confirmed, some centers proceed directly to up-front SRS in the setting of initial STR. Imaging protocols in this context are more aligned with post-SRS protocols, rather than post-resection protocols.

Synthesis

There is no evidence to suggest an advantage with regard to early (immediate postoperative) or delayed (≥ 3 months) initial postoperative MRI to assess radiographic extent-of-resection. Initial follow-up imaging after 0 or 3 months is completed at 1 year by almost all centers, and no centers report retreatment on the basis of radiographic findings sooner than 12 months after surgery. Subsequent imaging protocols are heterogeneous and range from annual studies to every 5 years. Volume of residuum appears to predict risk of recurrence. Initial postoperative imaging is suggested at ≥ 3 months, with follow-up imaging at closer intervals for STR/NTR (e.g., 3, 12, and 24 months), and longer intervals after GTR (e.g., 6, 18, and 36 months).

Question 7

In patients with sporadic VS who undergo primary SRS, is initial interval imaging at ≥ 24 months, as compared to initial interval imaging at ≤ 12 months, associated with increased incidence of tumor-directed clinical action, defined as a neurosurgical intervention that is undertaken strictly as a consequence of the imaging study and not due to patient symptoms, including repeat irradiation, surgical resection, treatment of ventriculomegaly with CSF diversion, or initiation of a VS disease-directed medical therapy?

Target Population

Patients with sporadic VS being treated with primary SRS.

Recommendation (Level III): *Post-radiosurgery imaging is suggested at 12, 24, and 36 months, and deferral of retreatment is suggested until progression is noted on 3 consecutive imaging studies, absent concerning parallel changes in clinical symptoms.*

Results of Individual Studies, Discussion of Study Limitations, and Risk of Bias

Following full-text review, 5 studies meeting criteria were considered pertinent to the question (Appendix IV, Table 7).⁶⁰⁻⁶⁴ No study specifically addressed the question of SRS at ≤ 12 months versus ≥ 24 months. Perry et al. assessed the clinical utility and cost implication of initial imaging at 6 months, as compared to 12 months; they found that no clinical action was taken based on 6-month studies, absent clinical symptoms, and that significant cost savings without adverse clinical impact would be anticipated if the

early post-SRS MRI were eliminated.⁶⁰ Two other studies identified similar patterns, with no benefit identified in association with MRI before 12 months, and retreatment infrequently considered prior to confirmation of true progression rather than pseudoprogression, typically at 24-36 months after primary SRS. Breshears et al. reported long-term data on resolution of pseudoprogression, with initial volumetric expansion noted within 3.2 years and resolving as late as 6.9 years in 90% of tumors.⁶¹ Foudard et al. reported a high incidence of early tumor expansion in 63.5% within 12 months; however, only 7.7% of those patients had serial tumor growth on at least 3 consecutive MRIs, and they concluded that retreatment prior to year 6 post-SRS was not advised.⁶⁵

Synthesis

At present, no evidence specifically compares post-radiosurgery imaging at ≥ 24 months and ≤ 12 months. Imaging at ≤ 12 months does not appear to prompt clinical action, absent new symptoms potentially referable to changes in the tumor. Determination of radiosurgery treatment failure prior to 24-36 months is controversial. Routine post-radiosurgery imaging is suggested at 12, 24, and 36 months, and deferral of retreatment is suggested until progression

DISCUSSION

Imaging is a foundational component of VS management, influencing all areas of practice including initial diagnosis, preoperative planning, and surveillance during observation or after treatment with microsurgical resection or SRS. Contemporary evidence and associated recommendations regarding the use of neuroimaging in VS care is relatively low-quality, with most studies presenting level III data. At present, surveillance protocols between centers are highly heterogeneous, with variability noted in the preferred timing, MR sequences, and associated clinical actions following a significant change.

MRI with or without gadolinium is acceptable for the work-up of unilateral sensorineural hearing loss; however, once VS has been diagnosed, high-resolution T2 imaging may be relied upon for follow-up in the pre-treatment surveillance setting. Tractography appears to inform surgical planning in a reliable and valid fashion, although the impact on functional outcome is unclear. After primary microsurgical resection, an imaging baseline with contrast should be obtained, ideally in the 3-6 month timeframe, with annual imaging recommended over at least another 3-5 years of follow-up. For patients undergoing primary SRS, pseudoprogression is common, and early re-imaging does not appear to inform clinical action; correspondingly, we recommend annual imaging beginning at 12 month post-treatment, with retreatment reserved for patients who demonstrate serial volumetric expansion over multiple studies, or concerning associated clinical symptoms.

KEY ISSUES FOR FUTURE RESEARCH & CONCLUSIONS

Although these guidelines establish updated or new recommendations pertinent to numerous key areas of neuroimaging in VS management, we noted that several study questions have not been directly assessed by any clinical study in the past. Major deficiencies include data on the role of high-field MRI, adequately powered assessments of tractography as a perioperative tool, well-controlled radiographic assessment of postoperative imaging at various timepoints following resection, and additional outcome-oriented assessments of post-treatment imaging protocols in the setting of both resection and SRS. Robust data on the cost and quality-of-life impacts of various imaging protocols are also lacking, which represents a key target for future patient-centered study in VS imaging science.

Conflicts of Interest

All Guideline Task Force members were required to disclose all potential COIs prior to beginning work on the guideline, using the COI disclosure form of the AANS/CNS Joint Guidelines Review Committee. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination and participation on the task force. The CNS Guidelines Committee and Guideline Task Force Chair may approve nominations of task force members with possible conflicts and restrict the writing, reviewing, and/or voting privileges of that person to topics that are unrelated to the possible COIs. See Appendix V for a complete list of disclosures.

Disclosure of Funding

These evidence-based clinical practice guidelines were funded exclusively by the Congress of Neurological Surgeons, which received no funding from outside commercial sources to support the development of this document.

Disclaimer of Liability

This clinical systematic review and evidence-based guideline was developed by a physician volunteer task force as an educational tool that reflects the current state of knowledge at the time of completion. Each chapter is designed to provide an accurate review of the subject matter covered. This guideline is disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a competent physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines

must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

Acknowledgments

The guidelines task force would like to acknowledge the CNS Guidelines Committee for their contributions throughout the development of the guideline, the AANS/CNS Joint Guidelines Review Committee, as well as the contributions Trish Rehring, MPH, Director for Evidence-Based Practice Initiatives for the CNS, and Janet Waters, MLS, BSN, RN, for assistance with the literature searches. Throughout the review process, the reviewers and authors were blinded from one another. At this time the guidelines task force would like to acknowledge the following individual peer reviewers for their contributions: Patti Raksin, Tjoumakaris, Andrew Carlson, Neil Majmundar, Jeff Mullin and Koji Ebersole.

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Appendix I: Literature Searches

Ovid Medline

- 1 exp Magnetic Resonance Imaging/ 511451
- 2 (chemical shift imaging* or mr tomograph* or magnetic resonance tomograph* or magnetic resonance imag* or magnetization transfer contrast imaging* or nmr imaging* or nmr tomograph* or proton spin tomograph* or spin echo imaging* or zeugmatography* or fmri or MRI or MRIS or nmri imaging* or mr imaging*).ti,ab,kw. 494948
- 3 DIAGNOSTIC IMAGING*.mp. 1417905
- 4 screening imaging*.ti,ab,kw. 174
- 5 CISS.ti,ab,kw. 1036
- 6 FIESTA.ti,ab,kw. 373
- 7 'FAST IMAGING EMPLOYING STEADY-STATE ACQUISITION'.ti,ab,kw. 195
- 8 'CONSTRUCTIVE INTERFERENCE IN STEADY STATE'.ti,ab,kw. 298
- 9 Diffusion Tensor Imaging/ 12333
- 10 diffusion tensor imaging*.ti,ab,kw. 15641
- 11 TRACTOGRAPH*.mp. 6665
- 12 or/1-11 1898224
- 13 exp Neuroma, Acoustic/8763
- 14 ((vestib* or acoustic) adj3 (neuroma* or neurilemmoma* or neurilemoma* or neurinoma* or tumor* or tumour* or schwannoma*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 11046
- 15 (acoustic nerve cancer* or acoustic neurofibroma* or acusticus neurinoma* or auditory nerve neurinoma* or ear schwannoma* or angle tumor* or angle tumour* or cerebellopontine angle tumor* or neurinoma of the acoustic nerve or neurosensory deafness* or sensoryneural deafness* or sensory neural deafness*).ti,ab,kw. 1211
- 16 13 or 14 or 15 12489
- 17 limit 16 to english language 10469
- 18 Animals/ not Humans/ 4974929
- 19 17 not 18 10374
- 20 comment/ or editorial/ or letter/ or review/ or systematic review/ 5102112

21	19 not 20	8685	
22	exp adolescent/ or exp child/ or exp infant/	3849849	
23	exp Adult/	7797507	
24	22 not 23	2052582	
25	21 not 24	8366	
26	limit 25 to dt=20150101-20220522	2297	
27	in vitro techniques/	387712	
28	Culture Techniques/	47809	
29	Drug Evaluation, Preclinical/	54481	
30	Disease Models, Animal/	383220	
31	Xenograft Model Antitumor Assays/	44247	
32	26 not (27 or 28 or 29 or 30 or 31)	2275	
33	12 and 32	849	

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('nuclear magnetic resonance imaging'/exp OR 'magnetic resonance imaging':ti,ab,kw OR 'magnetic resonance tomography':ti,ab,kw OR 'magnetization transfer imaging':ti,ab,kw OR 'mr imaging':ti,ab,kw OR 'nmr imaging':ti,ab,kw OR 'chemical shift imaging':ti,ab,kw OR 'mr tomograph':ti,ab,kw OR 'magnetization transfer contrast imaging':ti,ab,kw OR 'nmr tomograph':ti,ab,kw OR 'proton spin tomography':ti,ab,kw OR 'spin echo imaging':ti,ab,kw OR zeugmatograph*:ti,ab,kw OR fmri:ti,ab,kw OR mri:ti,ab,kw OR mris:ti,ab,kw OR 'nmri imaging' OR 'magnetic resonance image':ti,ab,kw OR 'diagnostic imaging'/exp OR 'diagnostic imaging':ti,ab,kw OR 'screening imaging':ti,ab,kw OR ciss:ti,ab,kw OR fiesta:ti,ab,kw OR 'fast imaging employing steady state acquisition'/exp OR 'fast imaging employing steady state acquisition':ti,ab,kw OR 'constructive interference in steady state'/exp OR 'constructive interference in steady state':ti,ab,kw OR 'diffusion tensor imaging'/exp OR 'diffusion tensor imaging':ti,ab,kw OR 'magnetic resonance diffusion tensor imaging':ti,ab,kw OR 'tractography'/exp OR tractograph*:ti,ab,kw) AND ('acoustic nerve cancer':ti,ab,kw OR 'acoustic nerve neurinoma':ti,ab,kw OR 'acoustic nerve tumor':ti,ab,kw OR 'acoustic nerve tumour':ti,ab,kw OR 'acoustic neurofibroma':ti,ab,kw OR 'acusticus neurinoma':ti,ab,kw OR 'auditory nerve neurinoma':ti,ab,kw OR 'ear schwannoma':ti,ab,kw OR 'angle tumor':ti,ab,kw OR 'angle tumour':ti,ab,kw OR 'neurinoma of the acoustic nerve':ti,ab,kw OR 'neurosensory deafness':ti,ab,kw OR 'sensoryneural deafness':ti,ab,kw OR 'sensory neural deafness':ti,ab,kw OR ((vestib* OR acoustic) NEAR/3 (neuroma* OR neurilemmoma* OR neurilemoma* OR neurinoma* OR tumor* OR tumour* OR schwannoma*))) AND [english]/lim NOT ('animal'/exp NOT 'human'/exp) NOT ('juvenile'/exp NOT 'adult'/exp) NOT ('letter'/exp OR 'editorial'/exp OR 'conference paper'/exp OR 'review'/exp) NOT ('case report'/exp NOT 'case control study'/exp) NOT (('acoustic nerve cancer':ti,ab,kw OR 'acoustic nerve neurinoma':ti,ab,kw OR 'acoustic nerve tumor':ti,ab,kw OR 'acoustic nerve tumour':ti,ab,kw OR 'acoustic neurofibroma':ti,ab,kw OR 'acusticus neurinoma':ti,ab,kw OR 'auditory nerve neurinoma':ti,ab,kw OR 'ear schwannoma':ti,ab,kw OR 'angle

tumor':ti,ab,kw OR 'angle tumour':ti,ab,kw OR 'neurinoma of the acoustic nerve':ti,ab,kw OR 'neurosensory deafness':ti,ab,kw OR 'sensoryneural deafness':ti,ab,kw OR 'sensory neural deafness':ti,ab,kw OR ((vestib* OR acoustic) NEAR/3 (neuroma* OR neurilemmoma* OR neurilemoma* OR neurinoma* OR tumor* OR tumour* OR schwannoma*)) AND [english]/lim NOT ('animal'/exp NOT 'human'/exp) NOT ('juvenile'/exp NOT 'adult'/exp) NOT ('letter'/exp OR 'editorial'/exp OR 'conference paper'/exp OR 'review'/exp) NOT ('case report'/exp NOT 'case control study'/exp) AND 'conference abstract'/it) AND [01-01-2015]/sd NOT ('preclinical study'/exp OR 'animal experiment'/de OR 'in vitro study'/exp)

Appendix II: Rating Evidence Quality

Classification of Evidence on Therapeutic Effectiveness and Levels of Recommendation

Class I Evidence Level I (or A) Recommendation	Evidence from one or more well-designed, randomized controlled clinical trial, including overviews of such trials.
Class II Evidence Level II (or B) Recommendation	Evidence from one or more well-designed comparative clinical studies, such as non-randomized cohort studies, case-control studies, and other comparable studies, including less well-designed randomized controlled trials.
Class III Evidence Level III (or C) Recommendation	Evidence from case series, comparative studies with historical controls, case reports, and expert opinion, as well as significantly flawed randomized controlled trials.

Classification of Evidence on Prognosis and Levels of Recommendation

Class I Evidence Level I (or A) Recommendation	All 5 technical criteria above are satisfied.
Class II Evidence Level II (or B) Recommendation	Four of five technical criteria are satisfied.
Class III Evidence Level III (or C) Recommendation	Everything else.

Classification of Evidence on Diagnosis and Levels of Recommendation

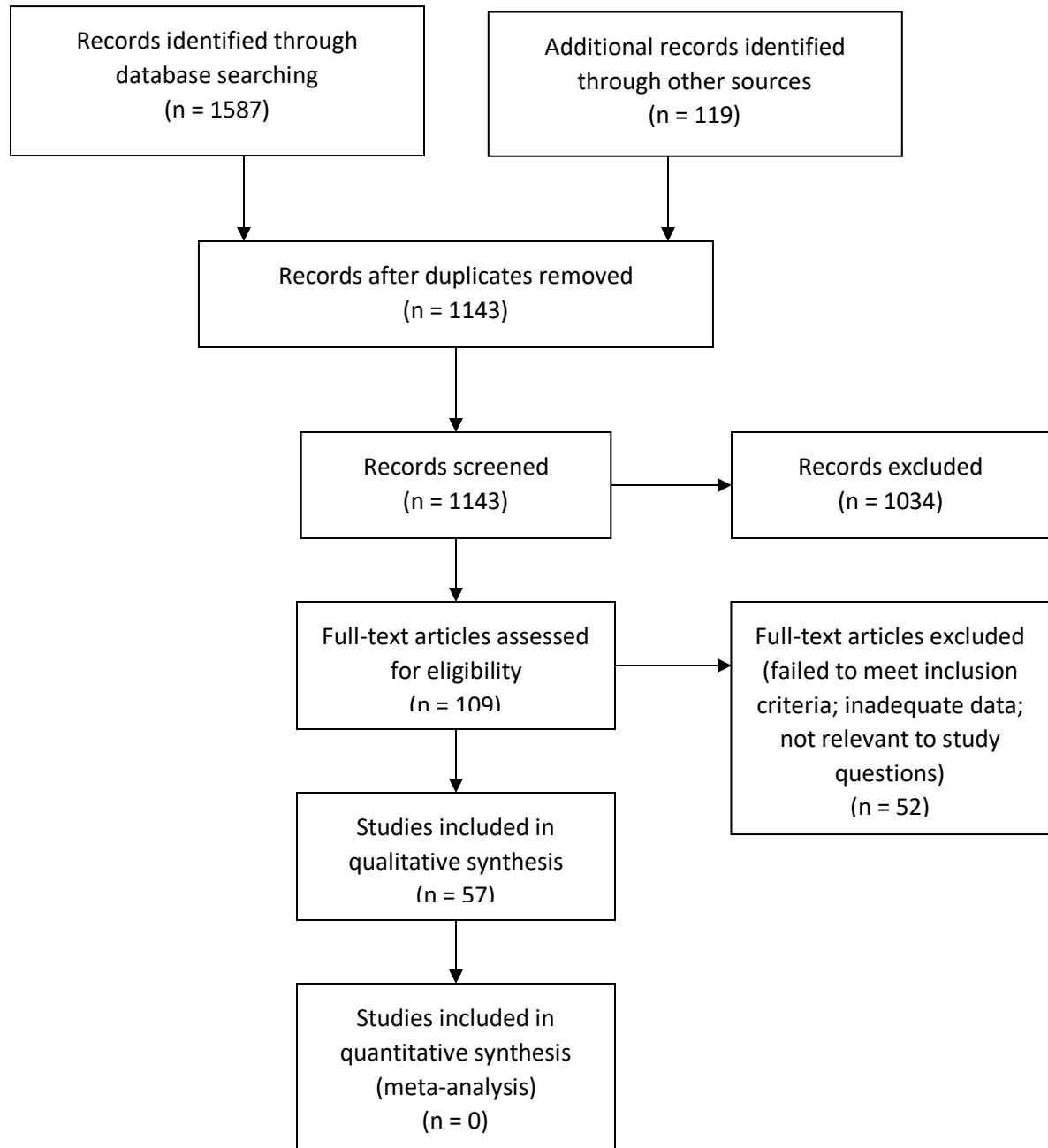
Class I Evidence Level I (or A) Recommendation	Evidence provided by one or more well-designed clinical studies of a <i>diverse</i> population using a “gold standard” reference test in a blinded evaluation appropriate for the diagnostic applications and enabling the assessment of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios.
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Class II Evidence Level II (or B) Recommendation	Evidence provided by one or more well-designed clinical studies of a <i>restricted</i> population using a “gold standard” reference test in a blinded evaluation appropriate for the diagnostic applications and enabling the assessment of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios.
Class III Evidence Level III (or C) Recommendation	Evidence provided by expert opinion or studies that do not meet the criteria for the delineation of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios.

Classification of Evidence on Clinical Assessment and Levels of Recommendation

Class I Evidence Level I (or A) Recommendation	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic > 0.60.
Class II Evidence Level II (or B) Recommendation	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic > 0.40.
Class III Evidence Level III (or C) Recommendation	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic < 0.40.

Appendix III: PRISMA Flowchart



Appendix IV. Evidence Tables

Table 1 – Screening imaging in unilateral hearing loss

Author (Year)	Study Description	Data Class	Conclusions
W. Yang (2020)	<u>Pt pop:</u> 1249 pts w/sudden sensorineural hearing loss (SSNHL) underwent MRI (1.5T or 3T) including coronal T2, axial T1, axial high-resolution T2	III	<u>Results:</u> 14 (1.12%) pts were found to have VS. Screening MRI found to be more cost-effective than auditory brainstem response (ABR) test <u>Authors Conclusions:</u> Noncontrast, high-resolution MRI was found to be a sensitive and more cost-effective screening tool for VS <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
T. Fujita(2019)	<u>Pt pop:</u> 499 pts w/SSNHL underwent MRI (1.5T or 3T) including coronal T2, axial T1, axial high-resolution T2; reviewed by experienced radiologists/otologists	III	<u>Results:</u> 15 (3%) pts exhibited tumors on the ipsilateral side of the SNHL <u>Authors Conclusions:</u> Noncontrast, high-resolution three-dimensional T2WI enables accurate evaluation of CN VII/VIII within the CP angle <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort

Table 2 – Surveillance imaging protocols

Author (Year)	Study Description	Data Class	Conclusions
S. Currie (2019)	<u>Pt pop:</u> 50 pts w/Vs who underwent initial radiographic observation and whose MRIs included enhanced T1 and high-resolution T2 sequences were retrospectively reviewed by 2 neuroradiologists, with attention to differences in VS measurements, inter-observer reliability, and potential cost savings for non-enhanced MRI protocols	III	<u>Results:</u> Mean VS diameter measurements were not significantly different on enhanced T1 sequences, as compared to high-resolution T2 sequences. Inter- and intra-observer reliability concordances were excellent (0.99; ≥ 0.98). Mean cost reduction of an unenhanced protocol was estimated at 37% <u>Authors Conclusions:</u> High-resolution T2 imaging provides comparable reliability to enhanced T1 sequences in follow-up assessment of observed VS, and is associated with a significant potential reduction in costs <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
D. H. Coelho (2018)	<u>Pt pop:</u> 50 randomly selected patients w/observed VS whose MRIs included both enhanced T1 and high-resolution T2 imaging underwent retrospective re-review by blinded neuroradiologists, with attention to VS measurement accuracy and correlation, inter-observer reliability, and differential costs and charges	II	<u>Results:</u> VS size measurements were highly correlated between sequences, with no significant difference in mean size estimates, and very high inter-observer reliability. Cost and charge savings of \$148 and \$1248 were estimated per patient per scan in an unenhanced protocol <u>Authors Conclusions:</u> High-resolution T2 imaging provides comparable reliability to

			enhanced T1 sequences in follow-up assessment of observed VS, and is associated with a significant potential reduction in costs and charges <u>Comments and Conclusions:</u> Class II achieved through blinded comparison of VS size measurements on enhanced T1 and high-resolution T2 images
M. Forgues (2018)	<u>Pt pop:</u> 26 VS patients with 107 MRIs were reviewed by 3 neuroradiologists, with T2 measurements compared to enhanced T1 measurements with respect to accuracy in detecting tumor growth	III	<u>Results:</u> T2 sequences detected growth observed on enhanced T1 sequences 88% of the time. Average measurement error between T2- and T1-weighted images was 1.27mm, or 10.4% of mean VS maximal diameter. T2 specificity was 88.2%; sensitivity was 77.8% <u>Authors Conclusions:</u> T2-weighted MRI is highly accurate, specific, and sensitive for detecting growth in observed VS, but is less specific and sensitive than enhanced T1 imaging, with an error of approximately 10% on routine linear measurements <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or validation cohort
K. Buch (2018)	<u>Pt pop:</u> 251 observed VS underwent retrospective MRI re-review, in order to analyze differences in enhanced T1 and high-resolution T2 sequences in	III	<u>Results:</u> No significant difference was observed in the measurements of VS made using enhanced T1 or high-resolution T2 images. Cystic and hemorrhagic

	the measurement of VS, or the detection of clinically significant radiographic changes during patient follow-up	components were better visualized on high-resolution T2 sequences <u>Authors Conclusions:</u> High-resolution T2 imaging provides comparable reliability to enhanced T1 sequences in follow-up assessment of observed VS <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
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Table 3 – Timing of imaging protocols for observed vestibular schwannoma

Author (Year)	Study Description	Data Class	Conclusions
D. Borsetto (2022)	<u>Pt pop:</u> 354 pts w/sporadic VS managed w/radiographic observation and at least 10 years of total radiographic follow-up and at least 5 years of initial freedom-from-growth underwent Bayesian analysis to determine conditional probability of late growth for patients without early growth	III	<u>Results:</u> Late growth was observed in 12 VS (3.4%) and not significantly associated with extra-canalicular disease. The yearly conditional probabilities of late growth at years 6, 7, 8, 9, and 10 were 2.28%, 1.35%, 0.8%, 0.47%, and 0.27%, respectively <u>Authors Conclusions:</u> Among VSs without observed growth in the first 5 years of radiographic surveillance, the conditional probability is approximately 2% or less, and continues to decrease over time. The authors recommend MRI surveillance at 6 months, then annually for 3 years, then twice at 2-year intervals, then one final scan at 3 years later, with no further imaging indicated if no growth observed over at least 10 years of follow-up <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort

J. P. Marinelli (2022)	<u>Pt pop:</u> 952 pts w/sporadic VS who underwent initial radiographic observation were assessed for volumetric tumor expansion	III	<u>Results:</u> 622 patients demonstrated $\geq 20\%$ volumetric growth, with growth-free survival rates at 1, 3, and 5 years of 66%, 30%, and 20%, respectively. Among 405 patients observed after initial growth, 210 continued to grow, w/subsequent growth-free survival rates at 1, 3, and 5 years of 77%, 37%, and 24%, respectively. Large VS volume or growth rate was significantly associated w/sustained growth. <u>Authors Conclusions:</u> Most observed VS appear to grow during early follow-up; however, initial growth does not reliably predict sustained growth, but larger tumors with rapid early expansion are the most likely to continue to progress <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
M. A. Hentschel (2021)	<u>Pt pop:</u> 1217 pts w/sporadic VS undergoing radiographic observation for at least 3 years after presentation were assessed with regard to risk factors for growth using multiple imputation, regression, and decision curve analysis techniques	III	<u>Results:</u> 653 pts demonstrated VS growth at follow-up (54%). Increased risk of VS growth was significantly associated w/imbalance, tinnitus, higher Koos grade, shorter symptomatic interval, and larger tumor diameter. More than half of observed VS demonstrated $\geq 2\text{mm}$ of linear

			growth within 3 years of diagnosis. <u>Authors Conclusions:</u> Larger size, higher grade, and more aggressive symptomatology may predict early growth <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
J. S. Kim (2021)	<u>Pt pop:</u> 118 pts w/sporadic VS undergoing initial observation were assessed for risk factors predicting tumor growth using survival analysis techniques	III	<u>Results:</u> 5-year cumulative incidence rate for VS growth was 41.3%. Increased risk of growth was associated with larger/cisternal tumors, and early hearing loss <u>Authors Conclusions:</u> Early VS growth occurs in a large minority of observed VS, in particular larger tumors, or those associated with rapid-onset early hearing loss <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort

H. Ruiz-Garcia (2021)	<u>Pt pop:</u> 243 pts w/sporadic VS initially managed with observation were assessed for predictors of radiographic tumor control and freedom-from-intervention	III	<u>Results:</u> Local control rates at 1, 5, and 10 years were 91%, 67%, and 58%, respectively. Larger tumors involving the CPA were significantly more likely to require treatment, in particular among younger patients <u>Authors Conclusions:</u> Although young patients w/larger VS are at increased risk of tumor growth requiring neurosurgical intervention, the majority of tumors did not demonstrate significant growth at 10 years <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
E. J. Patel (2021)	<u>Pt pop:</u> 13 sporadic, untreated VS that demonstrated spontaneous VS regression during observation, w/focused assessment of potential predictors of tumor regression	III	<u>Results:</u> Mean VS size reduction was 36%; 5 VS had a relative decrease of >40%, while 8 had <40% decrease, a difference that was not associated with differences in tumor size, regression rate, or audiometric parameters <u>Authors Conclusions:</u> Spontaneous VS regression is rare, with <4% incidence among sporadic VS, and occurs unpredictably in a relatively heterogenous patient population

			<u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
M. Kleijwegt (2020)	<u>Pt pop:</u> 836 pts w/sporadic VS who underwent initial radiographic surveillance with annual MRI	III	<u>Results:</u> 169 pts required neurosurgical intervention during observation (20%) at a mean of 2.19 years after diagnosis. Risk factors for intervention included short duration hearing loss, imbalance, extra-canalicular tumor extension, and cystic tumor architecture <u>Authors Conclusions:</u> A significant minority of pts w/ observed VS may require intervention during the early follow-up period. VS that are large, cystic, or associated with imbalance or rapid-onset hearing loss may be at increased risk of progression, requiring closer follow-up <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort

M. Sethi (2020)	<u>Pt pop:</u> 341 pts w/sporadic VS managed with initial observation and at least 5 years of follow-up, analyzed using conditional (e.g., Bayesian) probability techniques	III	<u>Results:</u> During the 5-year study period, 139 VS grew. Annual conditional probabilities of future growth, given no past growth, were 21%, 12%, 9%, 3%, and 2%. The conditional probability of growth was higher among extra-canalicular tumors in the first year alone <u>Authors Conclusions:</u> Most pts w/observed VS that fail observation will grow in the early follow-up period. VS that do not grow during the initial 4 years of observation have an estimated annual probability of <2% for future progression <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
M. Fieux (2020)	<u>Pt pop:</u> 336 pts w/sporadic VS (stage I or II) undergoing initial observation with annual MRI	III	<u>Results:</u> 125 VS progressed during the study period. Size at diagnosis (OR=2.6) and IAC filling (OR=7.7) were significantly associated with increased risk of VS growth <u>Authors Conclusions:</u> A large minority of observed VS demonstrate growth in early follow-up. Significant predictors of early growth included tumor size and IAC filling at time-of-diagnosis

			<u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
J. P. Marinelli (2020)	<u>Pt pop:</u> 85 sporadic VS with documented growth that underwent continued radiographic observation	III	<u>Results:</u> 40 pts demonstrated subsequent volumetric expansion at a median 1.7y; however, annual proportions of pts in the sample w/sustained freedom from subsequent growth were 93%, 67%, 54%, 44%, and 41% <u>Authors Conclusions:</u> Most VS w/observed growth did not demonstrate sustained volumetric tumor expansion over the ensuing 5 years of follow-up <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
R. J. Macielak (2019)	<u>Pt pop:</u> 361 pts w/sporadic VS, initially managed with MRI surveillance	III	<u>Results:</u> 172 VS grew during the during observation, 14 of which occurred ≥ 5 years after initial diagnosis. Among patients with delayed growth, the latest was observed at 11.1 years, and the fastest growth rate was 1.33mm/y <u>Authors Conclusions:</u> Delayed growth is uncommon, but occurs in at least 8% of pts with

			initially observed VS. Correspondingly, lifelong surveillance is likely required for these VS <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
S. D'Haese (2019)	<u>Pt pop:</u> 61 pts w/sporadic VS were managed w/initial observation via annual MRI	III	<u>Results:</u> VS growth prompting intervention was observed in 31 pts (56%), and in 87% of them this occurred within 3 years of diagnosis. Early and rapid growth were associated with larger VS size at time-of-diagnosis <u>Authors Conclusions:</u> Annual MRI is recommended for observed VS, in particular during the first 3 years after diagnosis. Patients with larger tumors on presentation are at increased risk of rapid or significant growth <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort

D. Borsetto (2019)	<u>Pt pop:</u> 112 pts w/sporadic VS age 70 years and over at diagnosis, managed with initial observation at 6 months and then annually for at least 3 years	III	<u>Results:</u> 32 pts had tumor growth; 26 received additional treatment; 6 underwent further observation. All growth was observed within 42 months of diagnosis. Extra-canalicular tumors were significantly more likely to grow <u>Authors Conclusions:</u> For pts ≥ 70 years w/sporadic VS undergoing initial surveillance, annual MRI is recommended for 3-4 years, after which consideration may be given to discontinuing further studies <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
Z. Schnurman (2019)	<u>Pt pop:</u> 212 pts w/sporadic VS undergoing initial observation had 699 MRIs obtained over 2-11 years of follow-up, which were re-reviewed with volumetric analysis	III	<u>Results:</u> 66% of VS demonstrated growth during follow-up, 33% were stable, 1% shrank. Rapid growth was noted in 30%. Mean follow-up interval was 25 months <u>Authors Conclusions:</u> Most VS demonstrate volumetric growth, with up to 30% demonstrating rapid early growth, while 34% did not grow or shrank. Growth, but not growth rate, was significantly associated with larger VS size at time-of-diagnosis

			<u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
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Table 4 – High-field MRI for preoperative assessment

Author (Year)	Study Description	Data Class	Conclusions
N/A	N/A	N/A	N/A

Table 5 – Tractography for preoperative assessment

Author (Year)	Study Description	Data Class	Conclusions
N. Ung (2021)	<u>Pt pop:</u> 11 pts w/sporadic VS, mean average max tumor diameter 2.82cm	III	<u>Results:</u> DTI was accurate in 90.9% (10/11) of patients. Post-op 72.7% (8/11) had HB score of I or II, 18.2% (2/11) had HB III, 1 had HB IV <u>Authors Conclusions:</u> DTI successfully and accurately localized VII in most patients <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
M. Castellaro (2020)	<u>Pt pop:</u> 5 pts w/sporadic VS (mean volume 854.4 mm ³) operated on via translabyrinthine approach. Multishell diffusion MRI was compared with the more standard single-shell diffusion MRI, and facial nerve tractography was performed using a probabilistic algorithm	III	<u>Results:</u> In the SS-MRI method, CNVII was able to be correctly visualized in 3/5 patients, in the MS-MRI technique, CNVII was able to correctly seen in 4/5 cases <u>Authors Conclusions:</u> Use of MS-dMRI protocol for a probabilistic tracking of FN course could be an aid for better presurgical planning of CNVII location as compared with SS-dMRI <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
T. Szmuda (2020)	<u>Pt pop:</u> 38 pts w/CPA tumor (32 VS, 5 meningioma, 1 epidermoid cyst) operated on via retrosigmoid approach (mean tumor diameter	II	<u>Results:</u> CNVII was correctly predicted in 81.6% of pts. Reliability of DTI-FT for CNVII location did not depend on tumor size. Shape of CNVII (compact shape) was the dominant component influencing accuracy (p=0.03)

	29.6 mm) had CNVII course simulated before surgery using StealthViz/transferred to Medtronic S7 neuronavigation and reconstructed by DTI-fibre tracking (DTI-FT)		<u>Authors Conclusions:</u> CNVII course can be predicted correctly in the majority of patients w/a CPA tumor, but far from the desired goal in neurosurgery <u>Comments and Conclusions:</u> Class II achieved through prospective analysis of reliability of CNVII localization by DTI-FT
L. Epprecht (2019)	<u>Pt pop:</u> 17 small CPA tumors (13 VS) are analyzed to localize CNVII using DTI super-resolution (SRR) vs. normal single plane DTI	III	<u>Results:</u> SRR increases separability of CN VII and VIII (16/17 vs. 0/17, p=0.008) <u>Authors Conclusions:</u> SRR improves resolution of VII and VIII in CPA compared w/single plane DTI in pts w/CPA pathologies that are small and non-operative <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
O. N. Churi (2019)	<u>Pt pop:</u> 40 pts w/CPA tumors (31 VS, 5 epidermoid, 2 meningioma, 2 trigeminal schwannoma) who underwent initial resection	III	<u>Results:</u> Accuracy of DTI as confirmed by intraoperative findings: CNVII (85%, 34/40), CNV (85%, 34/40), CNVIII (75%, 12/16) <u>Authors Conclusions:</u> DTI accurately localized CNVII and CNV in the majority of cases; localization of CNVIII was less successful and less accurate <u>Comments and Conclusions:</u> Class III data secondary to the retrospective

			nature of the analysis and lack of blinding or a validation cohort
R. Samala (2019)	<u>Pt pop:</u> 86 pts w/VS (>3cm) randomized to group 1 (DTI done pre-op and surgeon was informed of VII position) and group 2 (DTI not done)	II	<u>Results:</u> DTI group: Intraoperatively, CNVII was in the same location as seen on DTI in 39/40 patients (97.5%). CNVII was preserved anatomically and functionally in 36/40 (90%) Non-DTI group: VII was preserved anatomically/functionally in 29/46 (63%) (P= 0.002) <u>Authors Conclusions:</u> DTI visualization of CNVII may portend better outcomes w/regard to CNVII preservation after craniotomy for VS resection <u>Comments and Conclusions:</u> Class II achieved through randomization into two groups (with/without preoperative assessment of CNVII location on DTI) and prospective analysis
H. Li (2017)	<u>Pt pop:</u> 19 pts w/sporadic VS (mean tumor diameter 41mm) who underwent preoperative DTI	III	<u>Results:</u> Successful fiber tract localization occurred in 18/19 patients (95%). In 17/18 cases (94%) intra-operative navigation confirmed DTT localization. CNVII was located in the anterior middle part of the tumor in 7 cases <u>Authors Conclusions:</u> DTI was able to localize CNVII in most cases. When DTI did localize CNVII, the accuracy of that

			localization was validated intraoperatively <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
A. Zolal (2017)	<u>Pt pop:</u> Probabilistic non-tensor-based tractography was used in 21 pts w/large VS	III	<u>Results:</u> There was a 81% intra-operative correlation for CNVII, and 33% correlation w/CNVII <u>Authors Conclusions:</u> In the majority of cases, the position of CNVII, but not CNVIII, could be estimated using the probabilistic tractography <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
O. Hilly (2016)	<u>Pt pop:</u> 113 pts w/normal IAC/CPA anatomy were used to compare tractography using T1/T2 to determine the location of CNVII. A second group of 28 pts w/IAC/CPA tumors that were not treated surgically was used to evaluate location of the displaced CNVII. In 21 pts, preoperative localization of CNVII on MR-DTI imaging was compared with intraoperative findings	III	<u>Results:</u> CNVII was visualized on DTI imaging in 95% (20/21) cases. Concordance between intraoperative findings and tractography results was present in 90% of these patients (18/20). <u>Authors Conclusions:</u> CNVII tractography was found to be feasible and accurate in pts w/VS between 2 and 4.6 cm <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort

F. Song (2016)	<u>Pt pop:</u> 15 pts (mean tumor size 31.9 mm) w/preoperative DTI	III	<u>Results:</u> In 14/15 (92.9%) of pts the DTI location was concordant with intra-operative visualization. In those consistent cases, the location of CNVII was anterior (including upper, middle, lower) in 11/14 <u>Authors Conclusions:</u> DTI-FT is effective in localizing CNVII in pts w/VS <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
S. A. Borkar (2016)	<u>Pt pop:</u> 20 pts w/sporadic VS >3cm w/preoperative DTI	III	<u>Results:</u> In 16/18 cases the DTI location of CNVII corresponded to intra-operative findings <u>Authors Conclusions:</u> DTI can be used to reliably visualize CNVII <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
J. Ma (2016)	<u>Pt pop:</u> 9 pts w/sporadic VS >3cm	III	<u>Results:</u> In 8/9 cases (89%) CNVII was able to be visualized on DTI. And in 100% of these the location was confirmed intraoperatively <u>Authors Conclusions:</u> DTI was able to localize CNVII in most cases; in all cases where DTI localized CNVII, the accuracy of that localization was validated intraoperatively

			<u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
M. Yoshino (2015)	<u>Pt pop:</u> 22 pts w/Vs in whom VII and VIII could be identified during surgery	III	<u>Results:</u> Used to confirm location: DTI alone: CNVII 3/22 (13.6%), CNVIII 14/22 (63.6%) CE-FIESTA alone: CNVII 13/22 (63.6%), CNVIII 1/22 (4.5%) DTT + multifused CE-FIESTA: CNVII 14/22 (63.6%), CNVIII 14/22 (63.6%) <u>Authors Conclusions:</u> Using DTT and multifused CE-FIESTA, authors were able to increase the number of VS pts for whom location of CNVII and CNVIII nerves were able to be predicted <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
M. Yoshino (2015)	<u>Pt pop:</u> 11 pts w/sporadic VS (mean tumor size 27mm) w/preoperative DTT	III	<u>Results:</u> In 10/11 cases (91%) a visualized fiber tract was seen on DTT exiting the brainstem and entering IAC. In 3/11 (27%) the tract was confirmed to be CNVII intra-operatively, in 6/11 (55%) this was CNVIII <u>Authors Conclusions:</u> DTT allows for visualization of CNVII and CNVIII preoperatively, but is unable to predict between which nerve it is, or if findings represent noise

			<u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
P. H. Wei (2015)	<u>Pt pop:</u> 23 pts w/sporadic VS and preoperative DTT and CISS w/contrast	III	<u>Results:</u> DTT correctly identified CNVII as verified by intra-operative EMG 21/23 times (91.3%), even in cases where CNVII had become membranoid or when it was located between the capsule and tumor parenchyma <u>Authors Conclusions:</u> With a CNVII identification rate of 91.30%, DTT may be helpful in predicting the course of CNVII near a large VS, even in complex situations, such as a membranoid CNVII or a CNVII that traverses underneath the tumor capsule <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort

Table 6 – Timing of imaging protocols after vestibular schwannoma resection

Author (Year)	Study Description	Data Class	Conclusions
J. M. Gonzalez-Darder (2020)	<u>Pt pop:</u> 30 pts w/VS treated w/microsurgical resection, all via retrosigmoid craniotomy, with postoperative radiographic extent-of-resection assessed at 6 months by contrast-enhanced MRI	III	<u>Results:</u> Residual tumor was noted in 11 pts (36.7%), w/all residual volumes <0.5cm³. During annual follow-up over at least 6 years, only 1 pt had progression of residual; no pt w/o nodular enhancing residuum demonstrated postoperative tumor recurrence <u>Authors Conclusions:</u> Postoperative MRI at 6 months appears adequate for initial extent-of-resection assessment. Annual imaging is very sensitive for capturing recurrence and progression events in follow-up <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
M. Fieux (2020)	<u>Pt pop:</u> 135 pts w/ VS treated w/microsurgical resection and NTR or STR achieved (i.e., not GTR), followed w/annual contrast-enhanced MRI from 1 to 5 years after surgery, using volumetric analysis	III	<u>Results:</u> Progression was observed in 27 patients (23.3%), with a nearly 5-fold higher odds of progression observed after STR, as compared to NTR <u>Authors Conclusions:</u> Postoperative MRI at 12 months appears adequate for initial extent-of-resection assessment. Annual imaging is very sensitive for capturing recurrence and progression events in follow-up. Increased residual volume is

			associated with higher risk of progression after STR/NTR <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
J. D. Breshears (2020)	<u>Pt pop:</u> 66 pts w/VS treated w/microsurgical resection and STR achieved, followed w/contrast-enhanced MRI and volumetric analysis immediately after surgery, as well as at 6-months, and then 12-month intervals. Patients receiving up-front SRS (<12 months) were excluded	III	<u>Results:</u> Progression was noted in 22 patients (30%) at a median of 3.1 years. Residual tumor volume and residual disease within the IAC were significantly associated with progression (OR=2.0, OR=3.7, respectively) <u>Authors Conclusions:</u> Although pts were assessed at 0-, 6-, and 12-months, followed by annual updates, retreatment for disease progression prior to 24 months was rare <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort

M. E. Miller (2017)	<u>Pt pop:</u> 220 pts w/VS treated w/microsurgical resection	III	<u>Results:</u> 8 pts (4.1%) demonstrated radiographic progression, of whom 4 underwent retreatment. No patient was retreated at less than 1-2 years after resection; most were retreated at 5 and 10 years postoperatively <u>Authors Conclusions:</u> MRI surveillance after VS resection is recommended at 1, 5, and 10 years <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
Y. Tomita (2015)	<u>Pt pop:</u> 33 pts w/residual sporadic VS after STR	III	<u>Results:</u> At 3-year follow-up, growth had been observed in 10 of 33 VS after STR. Preoperative tumor volume was not related to postoperative tumor growth after STR; however, initial postoperative tumor volume was significantly associated with regrowth. No patient underwent repeat intervention during the 3-year initial postoperative follow-up period <u>Authors Conclusions:</u> Annual MRI surveillance is a safe and reasonable postoperative protocol for at least 3 years after surgery, w/no clinical action taken prior to 3 years

			<u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
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Table 7 – Timing of imaging protocols after vestibular schwannoma SRS

Author (Year)	Study Description	Data Class	Conclusions
O. Conlan (2022)	<u>Pt pop:</u> 159 pts w/sporadic VS treated w/initial SRS	III	<u>Results:</u> The mean time following SRS when regrowth began was 42 months, w/a mean growth rate of 0.48 mm/month; this growing rate was higher than the pre-SRS growth rate, but was not statistically significant ($p = 0.8$) <u>Authors Conclusions:</u> The authors did not identify any re-growth after the 6-year mark; thus, the 10-year period is reasonable, justifiable and supported by the presented data to stop w/further follow-up imaging <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
O. Fouard (2022)	<u>Pt pop:</u> 52 pts w/sporadic VS treated w/initial LINAC radiosurgery	III	<u>Results:</u> 1 tumor was stable, 26.9% had continuous shrinkage, transient tumor enlargement was observed in 63.5% (first peak at 6-12 months, late peak at 3-4 years), true progression suspected in 4 (7.7%). Only 1 patient required salvage radiotherapy <u>Authors Conclusions:</u> A significant tumor expansion observed on 3 sequential MRI scans after year 3 may suggest treatment failure. Long-term follow-up is therefore necessary and salvage treatment should be reserved until after year 6

			<u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
T. Ton (2021)	<u>Pt pop:</u> 42 pts w/sporadic VS (mean tumor size 16.9mm) treated w/initial SRS	III	<u>Results:</u> Prior to SRS the average growth rate was 0.26 mm/month, while post-SRS the growth rate was 0.05 mm/month and -0.16 mm/month at the time of the first scan (average time 11.0 months) and second scan (average time 22.3 months), respectively ($p < 0.001$) <u>Authors Conclusions:</u> Unless clinically indicated, MRI post-SRS at less than 1 year has no clinical value <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
E. Ermis (2021)	<u>Pt pop:</u> 53 pts w/sporadic VS treated with initial SRS (mean pre-SRS target volume 0.6 cm³)	III	<u>Results:</u> 1 pt had clinical/radiological progression at last f/u (55 months) and had salvage surgery. No other pt underwent salvage treatment. Two other pts had radiological progression at 24 and 36 months after SRS, but no clinical symptoms so they were not operated on <u>Authors Conclusions:</u> Advocate for presence of clinical deterioration as indication of salvage treatment in addition to progressive volume <u>Comments and Conclusions:</u> Class III data secondary to the retrospective

			nature of the analysis and lack of blinding or a validation cohort
A. Perry (2020)	<u>Pt pop:</u> 226 pts w/sporadic VS treated w/SRS, 91% without prior treatment (mean treatment volume 760 mm ³)	III	<u>Results:</u> 0% with clinical action occurring by 6 months and 12 months post-SRS <u>Authors Conclusions:</u> Six-month post-SRS MRI has no detectable impact on patient care. Imaging should be done 12 months post-GKRS, or if clinical symptoms arise or worsen <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
T. Hasegawa (2020)	<u>Pt pop:</u> 615 pts w/sporadic VS treated w/SRS, 82% without prior surgery	III	<u>Results:</u> 42 pts (7%) required salvage resection for tumor enlargement (mean 42 months post-SRS), 17 pts had clinical directed care post-SRS (Ommaya into cyst, surgical resection, VPS) due to clinical symptoms <u>Authors Conclusions:</u> Clinically directed care is not common post-SRS, particularly in the first 12-24 months. If it is required, it typically presents with a clinical symptom, and is uncommonly pursued based on radiographic findings alone <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
M. H. Khattab (2020)	<u>Pt pop:</u> 55 pts w/sporadic VS treated w/SRS	III	<u>Results:</u> 1 asymptomatic patient received a repeat dose of SRS at 30 months due to increased tumor size

			at 24 months. Another asymptomatic patient received a repeat dose of SRS at 31 months due to tumor progression <u>Authors Conclusions:</u> Repeat SRS, whether in a symptomatic or asymptomatic pt, was uncommon in this cohort <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort
J. D. Breshears (2019)	<u>Pt pop:</u> 118 pts w/sporadic VS treated w/SRS, 87% without prior surgical treatment (median treatment tumor volume of 0.73 cm³)	III	<u>Results:</u> 7 pts had salvage treatment after SRS (6 surgery, 1 repeat SRS) and all were related to tumor growth and/or clinical symptoms at median of 2.7 years following initial SRS <u>Authors Conclusions:</u> It can take as long as 6.9 yrs for 90% of tumors w/pseudoprogression to shrink back to treatment volume. Also, 90% had peaked in size by 3.5 yrs following SRS. Moreover, 90% of tumors w/pseudoprogression had begun enlarging by 3.2 yrs following SRS. Of those enlarging after the first year, 45% were regressing by 4 yrs, and 77% by 6 yrs post-treatment <u>Comments and Conclusions:</u> Class III data secondary to the retrospective nature of the analysis and lack of blinding or a validation cohort

Appendix V. Conflicts of Interest

Task Force Member	Disclosure
<i>Julie Honaker PhD, AuD</i>	Nothing to Disclose
<i>Ben Allen Strickland, MD</i>	Nothing to Disclose
<i>Eric J. Lehrer, MD</i>	Servier Pharmaceuticals, Novocure Inc.
<i>Sheryl Green, MBBCh</i>	Nothing to Disclose
<i>John P. Marinelli MD</i>	Medtronic
<i>Christopher S. Graffeo MD, MS</i>	Nothing to Disclose
<i>Isabelle M. Germano, MD, MBA</i>	Brianlab
<i>Mateo Ziu, MD</i>	Omniscient Neurotechnology America Ltd; GT Medical Technologies, Inc
<i>Walavan Sivakumar, MD</i>	Stryker Corporation
<i>Sherwin Tavakol, MD</i>	IRRAS USA, Inc.; Globus Medical, Inc.
<i>Lucas Paul Carlstrom, MD, PhD</i>	Kuros Biosciences USA, Inc
<i>Jamie J. Van Gompel, MD</i>	Medtronic, Cadence
<i>Ian Dunn, MD</i>	Nothing to Disclose
<i>Jeffrey J. Olson, MD</i>	Verastem, Inc., Research Grant American Cancer Society, Editorial Consultant; Azurity Pharmaceuticals, Inc.
<i>Ghazal S. Daher MD</i>	Nothing to Disclose
<i>Matthew L. Carlson, MD</i>	Cochlear Americas, Advanced Bionics, Stryker Corporation; IotaMotion, Inc.; Stryker Corporation
<i>Neil S. Patel, MD</i>	Cochlear Americas, Zeiss, Viridian Therapeutics, IotaMotion, Inc.
<i>Michael Sughrue, MD</i>	Omniscient Neurotechnology America Ltd
<i>Constantinos G. Hadjipanayis, MD, PhD</i>	Stryker Corporation; Integra LifeSciences Corporation; Omniscient Neurotechnology America Ltd
<i>Jeffrey Jacob, MD</i>	Stryker Corporation; KLS; Synthes