EAONO position statement on Vestibular Schwannoma: Imaging Assessment Question: How should growth of Vestibular Schwannoma be defined?

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The relevance of defining the growth of vestibular schwannoma (VS) is that any significant VS growth may impact treatment strategy. A conservative treatment strategy is often proposed as a primary treatment option in the management of VS. Several authors have demonstrated that a significant proportion of VSs do not grow, and those that do, usually grow slowly. Surgical and/or radiosurgical treatment options may be offered to the patient according to the VS growth. Therefore, defining the VS growth is a determinant in managing treatment strategies. A comprehensive literature search was performed to examine the definition of tumor growth for VS. The literature review was conducted using PubMed and Embase databases dated back to 20 years (1995–2015) and was updated until February 2015. VS growth should be measured on contrast-enhanced T1-weighted images. Although there the overall quality of the present studies is low, all highlight a significant VS growth of >2 mm, and/or 1.2 cm³, and/or 20% change in volume, and/or the square of the product of the 2 orthogonal diameters. We suggest that VS growth should instead change management strategies when a 3-mm increase in diameter on two consecutive MRI scans are performed 1 year apart.

KEYWORDS: Vestibular Schwannoma, growth rate, natural history, imaging assessment

MATERIALS and METHODS
As part of the Vestibular Schwannoma Project conducted by the European Academy of Otology & Neuro-Otology (EAONO), a comprehensive literature search was conducted to examine the definition of tumor growth for vestibular schwannoma (VS).

The literature review was conducted on the databases Pubmed and Embase dated back to 20 years (1995-2015) and was updated until February 2015.

A PubMed search using the key words “Natural history,” “vestibular schwannoma,” “acoustic neuroma,” and “tumor growth” alone and in combination was performed: This query identified 680 papers in the last 20 years, between 1995 and 2015.

Search syntax

Inclusion and exclusion criteria

a) Article titles and abstracts were screened according to the following criteria:
b) Clinical articles reporting original data, thereby excluding reviews and case reports
c) Data only from adult patients

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d) Series using conservative management; microsurgery, radiosurgery, or fractioned stereotactic radiotherapy; and single and/or combined treatment for solitary VS

e) More than 50 patients included

f) Quantitative assessment of VS growth as one of the primary study end-points

g) Mean follow-up of at least 3 years

h) Studies in which the reported data included patients with neurofibromatosis type 2; if these data could not be separately identified from the reported data for patients with VS, the articles were excluded.

After the initial search, 763 articles were obtained, but 721 did not meet one or more of the inclusion criteria and hence were discarded. The remaining 41 articles were reviewed for methodology and scored using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system [1].

## RESULTS

### The question: How should growth of VS be defined?

### INTRODUCTION

The relevance of defining the growth of VS is that any significant VS growth may impact the treatment strategy. A conservative treatment strategy is often proposed as a primary treatment option in the management of VS. Several authors have demonstrated that a significant proportion of VS do not grow, and those that do, usually grow slowly. Surgical and/or radiosurgical treatment options may be offered to the patient according to VS growth. Therefore, the definition of VS growth is a determinant in managing treatment strategies.

### Evidence

The reviewed articles selected to find an answer how should VS growth be defined comprised 2 meta-analysis, 6 cohort studies, and 33 case series. The mean number of patients included for the clinical series was 215 (50-2500).

### Literature review

| AUTHOR | YEAR | STUDY | n | METHOD | VS GROWTH RATE | VS GROWTH CHANGING STRATEGY | GRADE | GRADE | GRADE |
|--------|------|-------|---|--------|----------------|-----------------------------|-------|-------|-------|
| Jethanament et al. [2] | 2015 | Case series | 94 | 2 | 1 | 1.14 | Low | Weak | |
| Hougaard et al. [3] | 2014 | Case series | 72 | 2 | 1-2 | 3 | Moderate | Weak | 1 |
| Jeltema et al. [4] | 2014 | Case series | 55 | 4 | | | Very low | Weak | |
| Tang et al. [5] | 2014 | Case series | 88 | 2,3,4 | 91.4 mm for 1D, 7 mm2 for 2D, and 133.3 mm 3 for 3D | Low | Weak | |
| Niu et al. [6] | 2014 | Case series | 58 | 4 | 20% | Low | Weak | |
| Nikopoulos et al. [7] | 2013 | Meta-analysis | | | 1-2 | 2-4 | Moderate | Weak | |
| González-Orús Álvarez-Moruo et al. [8] | 2013 | Case series | 73 | 2 | 2 | 2 | Low | Weak | |
| Stangerup and Caye-Thomasen [9] | 2012 | Case series prospective | 2500 | 1 | 3 | 3 | Moderate | Weak | 2 |
| Varughese et al. [10] | 2012 | Case series prospective | 178 | 4 | 1 | 5.22 years VDT | Low | Weak | |
| Moffat et al. [11] | 2012 | Case series | 381 | 2 | 2 | Low | Weak | |
| Kim et al. [12] | 2012 | Case series | 60 | 4 | 20% | Low | Weak | |
| Breivik et al. [13] | 2012 | Case series | 193 | 1 | >2 | >2 | Moderate | Weak | |
| Sughrue et al. [14] | 2011 | Case series prospective | 59 | 2 | 2.5 | 2.5 | Low | Weak | 3 |
| Eljamel et al. [15] | 2011 | Case series | 53 | 1,3 | 2 | Very Low | Weak | |
| Varughese et al. [16] | 2010 | Case series | 139 | 3 | | Low | Weak | |
| Agrawal et al. [17] | 2010 | Case series | 180 | 1,4,1 | | Moderate | Weak | |
| Suryanarayanan et al. [18] | 2010 | Case series | 286 | 1.1 (range 0 to 15/y) | | Low | Weak | |
| Whitehouse, et al. [19] | 2010 | Case series | 88 | 2 | 1.24 (range -4.7 to 14 mm/y) | Low | Weak | |
| Bakkouri et al. [20] | 2009 | Case series | 325 | 1 | 1-2 | 3 | Low | Weak | |
| Artz et al. [21] | 2009 | Case series | 234 | 2 | | Low | Weak | |
| Van de Landergerg et al. [22] remark 5 | 2008 | Case series | 68 | 4 | 19.7 % volume change | Moderate | Weak | |

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Somers et al. Frequency of MRI scanning for VS schwannoma
The mean VS growth was calculated according to the maximal diameter in the CPA, maximal total diameter, mean of 2 measurements and volume changes in 7, 14, 7, and 8 studies, respectively. Once the VS reaches 2 cm in intracranial diameter, it is likely to continue growing.

The mean VS growth was 1.75±0.83 mm/year but ranged from −13–+18 mm/year. In 3 studies reporting volume change measurements, 20% of volume change was considered to be significant growth. A minimum of 2 mm/year of VS growth was considered to be significant for changing management strategies. When considering VS...
growth that changed management strategies, values retained were 3 mm, 2.5, and 2 mm of VS growth per year in 4, 1, and 2 articles, respectively.

Although there is an overall low quality of the present studies, all highlight a significant VS growth >2 mm, and/or 1.2 cm³, and/or 20% change in volume, and/or the square of the product of the 2 orthogonal diameters.

Following the GRADE system, 29 articles were considered to have a “low” level of evidence for being observational studies. Furthermore, 4 observational studies were down-graded to “very low” evidence for possible confounding factors. Finally, the 2 meta-analysis and 6 good quality observational studies were graded as “moderate” evidence.

CONCLUSION
VS growth should be measured on contrast-enhanced T1 weighted images.

Although there is an overall low quality of the present studies, all highlight a significant VS growth >2 mm, and/or 1.2 cm³, and/or 20% change in volume, and/or the square of the product of the 2 orthogonal diameters. We suggest that VS growth should instead change management strategies when there is a 3-mm increase in the diameter on two consecutive MRI scans 1 year apart.

Remarks
Most of the available evidence for VS growth comes from retrospective case series. The follow-up period in these series is quite heterogeneous. The VS growth rate should be assessed by VS growth per year in further prospective designed studies.

Position EAONO
- There is no high-quality evidence of the definition of VS growth. Future studies should try to overcome the present limitations in the study design to provide VS growth rate per year.
- Nevertheless, the consistency of results across different studies allows for a “moderate” recommendation to consider a significant VS growth of >2 mm, and/or 1.2 cm³, 20% volume, with VS growth rate >3 mm/year as a sign of evolution requiring a change in the treatment strategy.
- The optimal method of measuring VS volumes continues to be debated.
- In literature, the most common method used clinically is to measure the maximum diameter of the tumor, sometimes excluding the dimensions of the intracanalicular component but often including the intracanalicular component.
- The mean growth rate for all tumors, when growing, varies between 1 and 2 mm/year (1.75±0.83 mm/year) and between 2 and 4 mm/year for only those that grow.
- There are various patterns of growth, and a tumor that grows may stop growing and vice versa. Nevertheless, the first years of observation may give a good estimate of the pattern of growth. Some cases can exhibit significant regression or exceptional growth.
- Clinicians should seek to instigate national tumor registries in their countries and a common data set to facilitate international cooperation.
- The 2-mm cut-off should be recommended to avoid the effect of MRI slice thickness and partial volume effects. Tumor shrinkage was defined as tumor-size reduction in any plane by at least 2 mm.
- VS growth rate >3 mm/year should be considered a sign of evolution requiring a change in the treatment strategy.

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Editor’s Note:
The EAONO Project on guidelines of Otology and Neurotology was initiated by Franco Trabalzini and the Working Groups began working in 2011. Since then a considerable work has been issued to produce the first Consensus Documents.

The working Group on Vestibular Schwannoma have esteemed members from dedicated centers all over Europe. I wish to express my thanks to the working group leaders Miguel Arestegui and Jacques Magnan for their great effort as well as to all the other active members of the group.

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This study is very much respected by the Editorial of the Journal in this regard.

Prof. Dr. O. Nuri Ozgirgin
Editor in Chief

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