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Leksell Gamma Knife® Radiosurgery Bibliography

Vestibular Schwannoma

2012–2020

≥ 30 patient cohorts

[1] Stereotactic Radiosurgery for Vestibular Schwannomas: Tumor Control Probability Analyses and Recommended Reporting Standards.

Int J Radiat Oncol Biol Phys. 2020 Dec 26. pii: S0360-3016(20)34541-7. Soltys SG, Milano MT, Xue J, Tome WA, Yorke E, Sheehan J, Ding GX, Kirkpatrick JP, Ma L, Sahgal A, Solberg T, Adler J, Grimm J, El Naqa I
PMID: 33375955 DOI: 10.1016/j.ijrobp.2020.11.019

PURPOSE: We sought to investigate the tumor control probability (TCP) of vestibular schwannomas after single-fraction stereotactic radiosurgery (SRS) or hypofractionated SRS over 2 to 5 fractions (fSRS). **METHODS AND MATERIALS:** Studies (PubMed indexed from 1993-2017) were eligible for data extraction if they contained dosimetric details of SRS/fSRS correlated with local tumor control. The rate of tumor control at 5 years (or at 3 years if 5-year data were not available) were collated. Poisson modeling estimated the TCP per equivalent dose in 2 Gy per fraction (EQD2) and in 1, 3, and 5 fractions. **RESULTS:** Data were extracted from 35 publications containing a total of 5162 patients. TCP modeling was limited by the absence of analyzable data of <11 Gy in a single-fraction, variability in definition of "tumor control," and by lack of significant increase in TCP for doses >12 Gy. Using linear-quadratic-based dose conversion, the 3- to 5-year TCP was estimated at 95% at an EQD2 of 25 Gy, corresponding to 1-, 3-, and 5-fraction doses of 13.8 Gy, 19.2 Gy, and 21.5 Gy, respectively. Single-fraction doses of 10 Gy, 11 Gy, 12 Gy, and 13 Gy predicted a TCP of 85.0%, 88.4%, 91.2%, and 93.5%, respectively. For fSRS, 18 Gy in 3 fractions (EQD2 of 23.0 Gy) and 25 Gy in 5 fractions (EQD2 of 30.2 Gy) corresponded to TCP of 93.6% and 97.2%. Overall, the quality of dosimetric reporting was poor; recommended reporting guidelines are presented. **CONCLUSIONS:** With current typical SRS doses of 12 Gy in 1 fraction, 18 Gy in 3 fractions, and 25 Gy in 5 fractions, 3- to 5-year TCP exceeds 91%. To improve pooled data analyses to optimize treatment outcomes for patients with vestibular schwannoma, future reports of SRS should include complete dosimetric details with well-defined tumor control and toxicity endpoints.

[2] Long-term Outcomes of Gamma Knife Radiosurgery for Treating Vestibular Schwannoma With a Lower Prescription Dose of 12 Gy Compared With Higher Dose Treatment.

Otol Neurotol. 2020 Dec;41(10):e1314-e1320. Kawashima M, Hasegawa H, Shin M, Takahashi W, Shinya Y, Iwasaki S, Kashio A, Nakatomi H, Saito N
PMID: 33492807 DOI: 10.1097/MAO.0000000000002885

OBJECTIVE: Gamma knife radiosurgery (GKRS) is commonly used to treat vestibular schwannomas (VSs). The risk of complications from GKRS decreases at lower doses, but it is unknown if long-term tumor control is negatively affected by dose reduction. **STUDY DESIGN:** This was a retrospective case review and analysis of patient data. **SETTING:** Tertiary referral center. **PATIENTS:** Patients with VSs who underwent GKRS between 1990 and 2007 at the authors' institution. **INTERVENTION(S):** The subjects were divided into two cohorts based on the prescribed doses of radiation received: a 12 Gy cohort (96 patients) with a follow-up period of 124 months and a >12 Gy cohort (118 patients) with a follow-up period of 143 months. **MAIN OUTCOME MEASURES:** Tumor control rates at 10 to 15 years, frequency of facial and trigeminal nerve complications, and hearing function. **RESULTS:** The 10 to 15-year tumor control rates were 95% in the 12 Gy cohort and 88% in the > 12 Gy cohort, but the differences were not significant. Compared with the >12 Gy cohort, facial and trigeminal nerve deficits occurred significantly less frequently in the 12 Gy cohort, with the 10-year cumulative, permanent deficit-free rates being 2% and 0%, respectively. Multivariate analyses revealed that treatment doses exceeding 12 Gy were associated with a significantly higher risk for cranial nerve deficits. The percentage of subjects retaining pure-tone average \leq 50 dB at the final follow-up did not significantly differ between the cohorts (12 Gy cohort, 30% and >12 Gy cohort, 33%; $p = 0.823$). **CONCLUSIONS:** Dose reduction to 12 Gy for GKRS to treat VSs decreased facial and trigeminal nerve complications without worsening tumor control rates.

[3] Evolving Role of Non-Total Resection in Management of Acoustic Neuroma in the Gamma Knife Era.

Otol Neurotol. 2020 Dec;41(10):e1354-e1359. Luryi AL, Kveton JF, Babu S, Bojrab DI, Michaelides EM, Schutt CA
PMID: 33492813 DOI: 10.1097/MAO.0000000000002904

OBJECTIVE: To examine patients with residual tumor after vestibular schwannoma (VS) resection with focus on need for further therapy, including stereotactic radiosurgery (SRS) and revision surgery. **STUDY DESIGN AND SETTING:** Retrospective review at two tertiary otology referral centers. **PATIENTS AND INTERVENTION:** Patients undergoing primary surgery for VS from 2007 to 2017. **MAIN OUTCOME MEASURE:** Degree of resection and need for further treatment. **RESULTS:** Of 289 patients undergoing surgery, 38 (13.1%) underwent subtotal resections (<95% of tumor resected) and 77 (26.6%) underwent near-total resections (>=95% but <100%). Patients with any residual tumor had larger tumors preoperatively (mean estimated volume 6.3 cm versus 2.1 cm, $p < 0.0005$) but were otherwise clinically and demographically similar to the population as a whole. Further treatment (surgery or SRS) was needed in 4.6, 14.3, and 50.0% of patients after gross total, near-total, and subtotal resections, respectively ($p < 0.0005$). Patients undergoing additional therapy had larger residual tumors (median post- to preoperative estimated volume ratio 0.09 versus 0.01, $p < 0.0005$). Patients undergoing subtotal and near-total resections had poorer facial function at ultimate follow up than those undergoing gross total resections ($p = 0.001$), likely due to larger tumors and more difficult resections. Literature review revealed higher rates of gross total resection as well as facial palsy in the pre-SRS era. **CONCLUSION:** Residual tumor following VS resection is more common today than in the pre-SRS era. Availability of SRS may encourage leaving residual tumor intraoperatively to preserve neural structures. Current surgical strategies decrease surgical morbidity but necessitate further treatment in over 10% of cases.

[4] Equivalent efficacy and safety of radiosurgery for cystic and solid vestibular schwannomas: A systematic review.

World Neurosurg. 2020 Nov 16. pii: S1878-8750(20)32415-3. Massaad E, Hamidi N, Goetz J, Padmanaban V, Mau C, Tsang D, de Moraes FY, Chung C, Zacharia BE, Mansouri A
PMID: 33212274 DOI: 10.1016/j.wneu.2020.11.040

BACKGROUND: Cystic vestibular schwannomas (VS) are associated with unpredictable growth behavior and potentially worse surgical outcomes compared to their solid counterpart. Growth control and potential adverse effects of radiosurgery for cystic VS has created concerns surrounding this modality. **PURPOSE:** To compare the treatment efficacy and safety profile of radiosurgery between cystic and solid VS through a systematic review **MATERIALS AND METHODS:** PubMed, EMBASE, Web of Science, and Cochrane were searched for related terms and studies reporting radiosurgical outcomes of cystic and solid VS. A meta-analysis was performed to compare the rates of tumor control. Random-effect models with generic inverse variance method was used to calculate overall pooled estimates. Study quality was assessed with the Newcastle Ottawa Criteria (NOS). **RESULTS:** 2,989 studies were retrieved and 6 including 1,358 VS (79.89% solid; 20.11% cystic, median follow-up range 31.8-150 months) were selected. The median maximal dose was 25 Gy (range, 13-36 Gy) and the median marginal tumor dose was 12 Gy (10-18 Gy). There was no difference between cystic and solid VS (RR, 1.02; 95% CI, 0.94-1.10; $p=0.69$; $I(2)=78%$). Transient enlargement of cystic tumors may be associated with trigeminal or facial neuropathy. **CONCLUSION:** The evidence collected by this study suggests that radiosurgery for cystic VS exhibits effective tumor control probabilities similar to solid VS. Consensus definitions and standard criteria are needed in the future to better understand the patterns of tumor growth and response to treatment following radiosurgery for cystic VS, as well as long-term neurological and functional outcomes.

[5] Prediction of Pseudoprogression and Long-term Outcome of Vestibular Schwannoma after Gamma Knife Radiosurgery based on Preradiosurgical MR Radiomics.

Radiother Oncol. 2020 Nov 5. pii: S0167-8140(20)30888-4.
Yang HC, Wu CC, Lee CC, Huang HE, Lee WK, Chung WY, Wu HM, Guo WY, Wu YT, Lu CF
PMID: 33161011 DOI: 10.1016/j.radonc.2020.10.041

BACKGROUND AND PURPOSE: Gamma Knife radiosurgery (GKRS) is a safe and effective treatment modality with a long-term tumor control rate over 90% for vestibular schwannoma (VS). However, numerous tumors may undergo a transient pseudoprogression during 6 to 18 months after GKRS followed by a long-term volume reduction. The aim of this study is to determine whether the radiomics analysis based on preradiosurgical MRI data could predict the pseudoprogression and long-term outcome of VS after GKRS. **MATERIALS AND METHODS:** A longitudinal dataset of patients with VS treated by single GKRS were retrospectively collected. Overall 336 patients with no previous craniotomy for tumor removal and a median of 65-month follow-up period after radiosurgery were finally included in this study. In total 1763 radiomic features were extracted from the multiparametric MRI data before GKRS followed by the machine-learning classification. **RESULTS:** We constructed a two-level machine-learning model to predict the long-term outcome and the occurrence of transient pseudoprogression after GKRS separately. The prediction of long-term outcome achieved an accuracy of 88.4% based on five radiomic features describing the variation of T2-weighted intensity and inhomogeneity of contrast enhancement in tumor. The prediction of transient pseudoprogression achieved an accuracy of 85.0% based on another five radiomic features associated with the inhomogeneous hypointensity pattern of contrast enhancement and the variation of T2-weighted intensity. **CONCLUSION:** The proposed machine-learning model based on the preradiosurgical MR radiomics provides a potential to predict the pseudoprogression and long-term outcome of VS after GKRS, which can benefit the treatment strategy in clinical practice.

[6] Fundal Fluid Cap Is Associated With Hearing Preservation in the Radiosurgical Treatment of Vestibular Schwannoma.

Otol Neurotol. 2020 Oct 12.
Bojrab DI 2nd, Fritz CG, Lin KF, Schutt CA, Hong RS, Babu SC, Chen PY, Maitz A, Bojrab DI
PMID: 33055496 DOI: 10.1097/MAO.0000000000002837

OBJECTIVE: To evaluate the relationship between fundal fluid and hearing outcomes after treatment of vestibular schwannoma (VS) with Gamma Knife radiosurgery (GKRS). **STUDY DESIGN:** Retrospective case series. **SETTING:** Tertiary neurotology referral center. **PATIENTS:** Patients treated with GKRS for vestibular schwannoma between March 2007 and March 2017 were considered for this study. Exclusion criteria included pretreatment pure-tone average (PTA) >90 dB, neurofibromatosis type II, history of previous surgical resection, and follow-up less than 1 year. **MAIN OUTCOME MEASURE(S):** Hearing function was assessed both by preservation of serviceable hearing and by preservation of baseline hearing (≤ 20 dB change in PTA) after GKRS. Hearing preservation comparisons were made between groups of patients with and without a fundal fluid cap. **RESULTS:** Patients with a fundal cap had significantly higher rates of baseline hearing preservation (≤ 20 dB change in PTA) according to Kaplan-Meier survival analysis of all 106 patients ($p = 0.006$). By the 3rd year posttreatment, 70.9% of patients with a fundal cap had maintained a ≤ 20 dB change in PTA, while only 43.6% of patients without a fundal fluid cap achieved this outcome ($p = 0.004$). **CONCLUSIONS:** Fundal fluid present on pretreatment magnetic resonance imaging is predictive of improved baseline hearing preservation rates in patients undergoing GKRS for vestibular schwannoma when considering all patients with PTA ≤ 90 dB. Fundal fluid cap presence may serve as a favorable prognostic indicator to help set hearing expectations and guide patient selection efforts.

[7] Gamma Knife Radiosurgery does not alter the copy number aberration profile in sporadic vestibular schwannoma.

J Neurooncol. 2020 Sep 27. pii: 10.1007/s11060-020-03631-4.
Loge Havik A, Bruland O, Dhayalan D, Lund-Johansen M, Knappskog PM
PMID: 32980934 DOI: 10.1007/s11060-020-03631-4

INTRODUCTION: Ionizing radiation is a known etiologic factor in tumorigenesis and its role in inducing malignancy in the treatment of vestibular schwannoma has been debated. The purpose of this study was to identify a copy number aberration (CNA) profile or specific CNAs associated with radiation exposure which could either implicate an increased risk of malignancy or elucidate a mechanism of treatment resistance. **METHODS:** 55 sporadic VS, including 18 treated with Gamma Knife Radiosurgery (GKRS), were subjected to DNA whole-genome microarray and/or whole-exome sequencing. CNAs were called and statistical tests were performed to identify any association with radiation exposure. Hierarchical clustering was used to identify CNA profiles associated with radiation exposure. **RESULTS:** A median of 7 (0-58) CNAs were identified across the 55 VS. Chromosome 22 aberration was the only recurrent event. A median aberrant cell fraction of 0.59 (0.25-0.94) was observed, indicating several genetic clones in VS. No CNA or CNA profile was associated with GKRS. **CONCLUSION:** GKRS is not associated with an increase in CNAs or alteration of the CNA profile in VS, lending support to its low risk. This also implies that there is no major issue with GKRS treatment failure being due to CNAs. In agreement with previous studies, chromosome 22 aberration is the only recurrent CNA. VS consist of several genetic clones, addressing the need for further studies on the composition of cells in this tumor.

[8] Gamma knife surgery in the treatment of intracanalicular vestibular schwannomas.

Acta neurologica Scandinavica. 2020;141(5):415-422
Dzierzecki S, Turek G, Czapski B, Dyttus-Cebulok K, Tomasiuk R, Kaczor S, Zabek M
PMID: 31922606 DOI: 10.1111/ane.13220

OBJECTIVE: According to the literature, gamma knife surgery (GKS) is a promising method for intracanalicular vestibular schwannoma (IVS) management, providing excellent tumor growth control rates (91%-100%) and good hearing preservation rates (41%-76%), but this evidence originates primarily from a small series of patients. The aim of this study was to present the outcomes of GKS in the largest group of patients with IVS studied to date, with particular emphasis on the long-term outcomes of treatment. **METHODS:** The study included 136 consecutive patients with unilateral IVS, who underwent GKS in 2011-2015. Mean age of the patients was 54 +/- 12.6 years. All patients were operated on with a 192-source cobalt-60 gamma knife unit. All patients had complete follow-up documentation and the mean duration of the follow-up was 52 +/- 13.8 months (6-83 months). Neurological status (facial and trigeminal nerve), hearing and instability/dizziness presence were determined prior to GKS, immediately after the procedure, and during the follow-up visits. **RESULTS:** Tumor growth control was obtained in 124/136 (~91.2%) patients. Hearing improvement was observed in 32/136 (23.5%) patients, and there was a distinct cluster of 9 patients (6.6%) regaining serviceable hearing after GKS, whereas in 36 patients (26.5%) was stable. Four patients developed facial nerve dysfunction, including 3 periodic hemifacial spasm and 1 partial paresis, which resolved spontaneously within 12 months of GKS. None of the operated patients showed new, debilitating neurological deficits, including trigeminal sensory disturbances or hydrocephalus. **CONCLUSIONS:** GKS is a highly effective treatment for IVS, associated with low morbidity and good tumor growth control.

[9] Prediction of transient tumor enlargement using MRI tumor texture after radiosurgery on vestibular schwannoma.

Med Phys. 2020 Apr;47(4):1692-1701.
Langenhuizen PPJH, Sebregts SHP, Zinger S, Leenstra S, Verheul JB, de With PHN
PMID: 31975523 DOI: 10.1002/mp.14042

PURPOSE: Vestibular schwannomas (VSs) are uncommon benign brain tumors,

generally treated using Gamma Knife radiosurgery (GKRS). However, due to the possible adverse effect of transient tumor enlargement (TTE), large VS tumors are often surgically removed instead of treated radiosurgically. Since microsurgery is highly invasive and results in a significant increased risk of complications, GKRS is generally preferred. Therefore, prediction of TTE for large VS tumors can improve overall VS treatment and enable physicians to select the most optimal treatment strategy on an individual basis. Currently, there are no clinical factors known to be predictive for TTE. In this research, we aim at predicting TTE following GKRS using texture features extracted from MRI scans. **METHODS:** We analyzed clinical data of patients with VSs treated at our Gamma Knife center. The data was collected prospectively and included patient- and treatment-related characteristics and MRI scans obtained at day of treatment and at follow-up visits, 6, 12, 24 and 36 months after treatment. The correlations of the patient- and treatment-related characteristics to TTE were investigated using statistical tests. From the treatment scans, we extracted the following MRI image features: first-order statistics, Minkowski functionals (MFs), and three-dimensional gray-level co-occurrence matrices (GLCMs). These features were applied in a machine learning environment for classification of TTE, using support vector machines. **RESULTS:** In a clinical data set, containing 61 patients presenting obvious non-TTE and 38 patients presenting obvious TTE, we determined that patient- and treatment-related characteristics do not show any correlation to TTE. Furthermore, first-order statistical MRI features and MFs did not significantly show prognostic values using support vector machine classification. However, utilizing a set of 4 GLCM features, we achieved a sensitivity of 0.82 and a specificity of 0.69, showing their prognostic value of TTE. Moreover, these results increased for larger tumor volumes obtaining a sensitivity of 0.77 and a specificity of 0.89 for tumors larger than 6 cm³. **CONCLUSIONS:** The results found in this research clearly show that MRI tumor texture provides information that can be employed for predicting TTE. This can form a basis for individual VS treatment selection, further improving overall treatment results. Particularly in patients with large VSs, where the phenomenon of TTE is most relevant and our predictive model performs best, these findings can be implemented in a clinical workflow such that for each patient, the most optimal treatment strategy can be determined.

[10] Is There a Need for a 6-Month Postradiosurgery Magnetic Resonance Imaging in the Treatment of Vestibular Schwannoma?

Neurosurgery. 2020;86(2):250-256

Perry A, Graffeo CS, Carlstrom LP, Hughes JD, Peris-Celda M, Cray NM, Pollock BE, Link MJ

PMID: 30980077 DOI: 10.1093/neuros/nyz052

BACKGROUND: Stereotactic radiosurgery (SRS) is a common treatment modality for vestibular schwannoma (VS), with a role in primary and recurrent/progressive algorithms. At our institution, routine magnetic resonance imaging (MRI) is obtained at 6 and 12 mo following SRS for VS. **OBJECTIVE:** To analyze the safety and financial impact of eliminating the 6-mo post-SRS MRI in asymptomatic VS patients. **METHODS:** A prospectively maintained SRS database was retrospectively reviewed for VS patients with 1 yr of post-treatment follow-up, 2005 to 2015. Decisions at 6-mo MRI were binarily categorized as routine follow-up vs clinical action-defined as a clinical visit, additional imaging, or an operation as a direct result of the 6-mo study. **RESULTS:** A total of 296 patients met screening criteria, of whom 53 were excluded for incomplete follow-up and 8 for NF-2. Nine were reimaged prior to 6 mo due to clinical symptoms. Routine 6-mo post-SRS MRI was completed by 226 patients (76% of screened cohort), following from which zero instances of clinical action occurred. When scaled using national insurance database-derived financials-which estimated the mean per-study charge for MRI of the brain with and without contrast at \$1767-the potential annualized national charge reduction was approximated as \$1 611 504. **CONCLUSION:** For clinically stable VS, 6-mo post-SRS MRI does not contribute significantly to management. We recommend omitting routine MRI before 12 mo, in patients without new or progressive neurological symptoms. If extrapolated nationally to the more than 100 active SRS centers, thousands of patients would be spared

an inconvenient, nonindicated study, and national savings in health care dollars would be on the order of millions annually.

[11] Factors Associated With Facial Nerve Paresis Following Gamma Knife for Vestibular Schwannoma.

Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 2020;41(1):e83-e88

Lerner DK, Lee D, Naples JG, Brant JA, Bigelow D, Alonso-Basanta M, Ruckenstein MJ

PMID: 31743296 DOI: 10.1097/MAO.0000000000002401

OBJECTIVE: Evaluate the incidence of and potential contributory factors to facial nerve paresis and other cranial neuropathies (CN) following stereotactic radiosurgery with Gamma Knife (GK) for primary treatment of vestibular schwannoma (VS). **STUDY DESIGN:** Retrospective chart review. **SETTING:** Tertiary referral center. **PATIENTS:** Charts were reviewed for all adult patients receiving primary GK treatment for unilateral VS between 2005 and 2013. Patients with NF2 or previous surgery were excluded from analysis. **INTERVENTION:** GK radiosurgery. **MAIN OUTCOME MEASURES:** The incidence of new-onset facial nerve paresis after primary GK treatment of VS was evaluated. Secondary endpoints included other cranial neuropathies. **RESULTS:** One hundred thirty-three patients with VS received primary GK therapy. Posttreatment CN developed in 33 patients (24.8%). Twelve patients (9.0%) experienced trigeminal paresthesia, 11 (8.3%) developed sudden sensorineural hearing loss (SSNHL) requiring steroids, and seven (5.3%) demonstrated facial paresis. The mean maximum cochlear dose was 15.49 Gy in patients with facial paresis compared with 12.42 Gy in subjects without facial paresis ($p = 0.032$). Subjects with facial paresis were more likely to have a lateral tumor without fundal fluid on magnetic resonance imaging (MRI) (71%) compared with subjects without facial paresis (43%). **CONCLUSIONS:** In the treatment of VS with primary GK, maximum cochlear dose was significantly associated with facial paresis. Laterally extending tumors without fundal fluid on MRI experienced higher rates of facial paresis. These factors should be considered during GK treatment planning for VS.

2019

[12] Treatment Outcomes and Dose Rate Effects Following Gamma Knife Stereotactic Radiosurgery for Vestibular Schwannomas.

Neurosurgery. 2019;85(6):E1084-E1094

Smith DR, Saadatmand HJ, Wu CC, Black PJ, Wu YR, Lesser J, Horan M, Isaacson SR, Wang TJC, Sisti MB

PMID: 31270543 DOI: 10.1093/neuros/nyz229

BACKGROUND: Gamma Knife radiosurgery (GKRS; Elekta AB) remains a well-established treatment modality for vestibular schwannomas. Despite highly effective tumor control, further research is needed toward optimizing long-term functional outcomes. Whereas dose-rate effects may impact post-treatment toxicities given tissue dose-response relationships, potential effects remain largely unexplored. **OBJECTIVE:** To evaluate treatment outcomes and potential dose-rate effects following definitive GKRS for vestibular schwannomas. **METHODS:** We retrospectively reviewed 419 patients treated at our institution between 1998 and 2015, characterizing baseline demographics, pretreatment symptoms, and GKRS parameters. The cohort was divided into 2 dose-rate groups based on the median value (2.675 Gy/min). Outcomes included clinical tumor control, radiographic progression-free survival, serviceable hearing preservation, hearing loss, and facial nerve dysfunction (FND). Prognostic factors were assessed using Cox regression. **RESULTS:** The study cohort included 227 patients with available follow-up. Following GKRS 2-yr and 4-yr clinical tumor control rates were 98% (95% CI: 95.6%-100%) and 96% (95% CI: 91.4%-99.6%), respectively. Among

177 patients with available radiographic follow-up, 2-yr and 4-yr radiographic progression-free survival rates were 97% (95% CI: 94.0%-100.0%) and 88% (95% CI: 81.2%-95.0%). The serviceable hearing preservation rate was 72.2% among patients with baseline Gardner-Robertson class I/II hearing and post-treatment audiological evaluations. Most patients experienced effective relief from prior headaches (94.7%), tinnitus (83.7%), balance issues (62.7%), FND (90.0%), and trigeminal nerve dysfunction (79.2%), but not hearing loss (1.0%). Whereas GKRS provided effective tumor control independently of dose rate, GKRS patients exposed to lower dose rates experienced significantly better freedom from post-treatment hearing loss and FND (P = .044). **CONCLUSION:** Whereas GKRS provides excellent tumor control and effective symptomatic relief for vestibular schwannomas, dose-rate effects may impact post-treatment functional outcomes. Further research remains warranted.

[13] Long term results of primary radiosurgery for vestibular schwannomas.

Journal of neuro-oncology. 2019;145(2):247-255

Johnson S, Kano H, Faramand A, Pease M, Nakamura A, Hassib M, Spencer D, Sisterson N, Faraji AH, Arai Y, Monaco E, Niranjana A, Flickinger JC, Lunsford LD
PMID: 31535315 DOI: 10.1007/s11060-019-03290-0

BACKGROUND: Stereotactic radiosurgery (SRS) has become a primary option for management for both newly diagnosed vestibular schwannomas (VS), as well as VS that enlarge after initial observation. **METHODS:** A retrospective review of our prospectively maintained data base found 871 patients who underwent Gamma knife(R) SRS as their initial (primary) management between 1987 and 2008. Follow-up ranged from 1-25 years (median = 5.2 years) Median tumor volume was 0.9 cc (0.02-36) and median margin dose was 13 Gy (12-25). **RESULTS:** Progression free survival (PFS) after SRS was 97% at 3 years, 95% at 5 years, and 94% at 10 years. Freedom from delayed surgical resection was found in 98.7% of patients. Smaller tumor volume was significantly associated with improved PFS. There were 326 patients with serviceable hearing (Gardner-Robertson 1 or 2) at the time of SRS with audiological follow-up of ≥ 1 year. Serviceable hearing preservation rates after SRS were 89.8% at 1 year, 76.9% at 3 years, 68.4% at 5 years, 62.5% at 7 years, and 51.4% at 10 years. Factors associated with improved serviceable hearing preservation included younger age, Gardner-Robertson grade 1 at SRS, and absence of subjective complaints of dysequilibrium or vertigo (vestibulopathy). Fifty-one patients (5.8%) developed trigeminal neuropathy. Fourteen (1.6%) developed a transient House-Brackmann grade 2 or 3 facial neuropathy.

CONCLUSIONS: In this report with extended follow-up, primary SRS achieved tumor growth control in 94% of patients. Optimization of long-term cranial nerve outcomes remains an important achievement of this management strategy for VS.

[14] Repeat Stereotactic Radiosurgery for Progressive or Recurrent Vestibular Schwannomas.

Neurosurgery. 2019;85(4):535-542

Iorio-Morin C, Liscak R, Vladyka V, Kano H, Jacobs RC, Lunsford LD, Cohen-Inbar O, Sheehan J, Emad R, Karim KA, El-Shehaby A, Reda WA, Lee CC, Pai FY, Wolf A, Kondziolka D, Grills I, Lee KC, Mathieu D
PMID: 30189018 DOI: 10.1093/neuros/nyy416

BACKGROUND: Stereotactic radiosurgery (SRS) is a highly effective management approach for patients with vestibular schwannomas (VS), with 10-yr control rates up 98%. When it fails, however, few data are available to guide management.

OBJECTIVE: To perform a retrospective analysis of patients who underwent 2 SRS procedures on the same VS to assess the safety and efficacy of this practice. **METHODS:** This study was opened to centers of the International Gamma Knife Research Foundation (IGKRF). Data collected included patient characteristics, clinical symptoms at the time of SRS, radiosurgery dosimetric data, imaging response, clinical evolution, and survival. Actuarial analyses of tumor responses were performed. **RESULTS:** Seventy-six patients from 8 IGKRF centers were identified. Median follow-up from the second SRS was 51.7 mo. Progression after the first SRS occurred at a median of 43 mo. Repeat SRS was performed using a median dose of 12 Gy. Actuarial tumor control rates at 2, 5,

and 10 yr following the second SRS were 98.6%, 92.2%, and 92.2%, respectively. Useful hearing was present in 30%, 8%, and 5% of patients at first SRS, second SRS, and last follow-up, respectively. Seventy-five percent of patients reported stable or improved symptoms following the second SRS. Worsening of facial nerve function attributable to SRS occurred in 7% of cases. There were no reports of radionecrosis, radiation-associated edema requiring corticosteroids, radiation-related neoplasia, or death attributable to the repeat SRS procedure.

CONCLUSION: Patients with progressing VS after radiosurgery can be safely and effectively managed using a second SRS procedure.

[15] Predicting hearing outcomes before primary radiosurgery for vestibular schwannomas.

Journal of neurosurgery. 2019;:1-7

Johnson S, Kano H, Faramand A, Niranjana A, Flickinger JC, Lunsford LD
PMID: 31491764 DOI: 10.3171/2019.5.JNS182765

OBJECTIVE: Optimizing outcomes in the management of patients with vestibular schwannomas (VSs) requires consideration of the patient's goals. Earlier recognition of VS by imaging has led to an evolution in management. Stereotactic radiosurgery (SRS) has emerged as a frequently used strategy designed to reduce management risks, obtain long-term tumor control, and preserve current neurological function. The authors analyzed features that impact hearing preservation rates in patients with serviceable hearing prior to SRS. **METHODS:** The study included 307 patients who had serviceable hearing (Gardner-Robertson hearing scale [GR] grade 1 or 2, speech discrimination score $\geq 50\%$, pure tone average ≤ 50 dB) at the time of SRS. The authors evaluated parameters that included age, tumor volume, hearing status, disequilibrium, tinnitus, Koos class, sex, and tumor margin dose. The Pittsburgh Hearing Prediction Score (PHPS) was evaluated as a method to predict long-term hearing outcomes in these cases.

RESULTS: At a median of 7.6 years after SRS (range 1-23 years), tumor control was achieved in 95% of patients. The overall serviceable hearing preservation rate was 77.8% at 3 years, 68.8% at 5 years, and 51.8% at 10 years. The PHPS assigns a total of 5 points based on patient age (1 point if < 45 years, 2 points if 45-59 years, and 3 points if ≥ 60 years), tumor volume (0 points if < 1.2 cm³, 1 point if ≥ 1.2 cm³), and GR grade (0 points if grade 1 hearing, 1 point if grade 2 hearing). The serviceable hearing preservation rate was 92.3% at 10 years in patients whose score total was 1. In contrast, none of the patients whose PHPS was 5 maintained serviceable hearing at 10 years ($p < 0.001$). **CONCLUSIONS:** SRS resulted in a high rate of long-term tumor control and cranial nerve preservation. The PHPS helped to predict long-term hearing preservation rates in patients who underwent SRS when they still had serviceable hearing. The best long-term hearing preservation rates were found in younger patients with smaller tumor volumes.

[16] Vestibular Schwannoma Tumor Size Is Associated With Acute Vestibular Symptoms After Gamma Knife Therapy.

Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 2019;40(8):1088-1093

Lee DY, Lerner DK, Naples JG, Brant JA, Bigelow DC, Lee JYK, Alonso-Basanta M, Ruckenstein MJ

PMID: 31335798 DOI: 10.1097/MAO.0000000000002312

OBJECTIVE: To assess how pretreatment vestibular schwannoma (VS) tumor characteristics are associated with vestibular symptoms after gamma knife (GK) surgery. **STUDY DESIGN:** Retrospective chart review of patients undergoing GK treatment for VS at our institution from 2005 to 2018. **SETTING:** Academic tertiary referral center. **PATIENTS:** Patients receiving primary GK surgery for vestibular schwannomas with at least 6 months of follow up. Patients with neurofibromatosis 2 or previous surgery were excluded. **MAIN OUTCOME MEASURES:** The presence of posttreatment vestibular symptoms within 6 months after GK. Clinical records were assessed for pretreatment tumor, patient, and treatment characteristics that impacted posttreatment symptoms. **RESULTS:** All patients received radiation doses between 12 and 13 Gy. Of 115 patients, the average

age was 60. Thirty-seven (32%) patients developed vestibular symptoms within 6 months post-GK, and 18 patients were referred for vestibular rehabilitation. Ten of 13 patients undergoing vestibular rehabilitation reported improvement. Overall, 112 patients had tumor measurements. Pretreatment tumors were significantly smaller for patients with acute vestibular symptoms (mean 1.43 cm versus 1.71 cm, $p = 0.007$). On multivariate analysis, smaller tumor size ($p = 0.009$, odds ratio [OR] = 0.29, 95% confidence interval [CI] [0.12-0.73]) was significantly associated with vestibular symptoms within 6 months of GK. Patients with tumors less than 1.6 cm were more likely to receive referrals for vestibular rehabilitation within 6 months posttreatment (25% versus 9.4%, $p = 0.026$, OR = 3.22, 95% CI [1.00, 11.32]).

CONCLUSIONS: Smaller vestibular schwannomas were significantly associated with higher rates of post-GK vestibular symptoms. Pretreatment tumor size may be used to counsel patients on the likelihood of post-GK vestibular symptoms and vestibular rehabilitation.

[17] Long-term follow-up results of stereotactic radiosurgery for vestibular schwannomas larger than 8 cc.

Acta neurochirurgica. 2019;161(7):1457-1465

Watanabe S, Yamamoto M, Kawabe T, Koiso T, Aiyama H, Kasuya H, Barfod BE
PMID: 31127373 DOI: 10.1007/s00701-019-03951-z

BACKGROUND: Accumulated stereotactic radiosurgery (SRS) experience for large vestibular schwannomas (VSs) based on over 5 years of follow-up are as yet insufficient, and chronological volume changes have not been documented. **METHOD:** Among 402 patients treated between 1990 and 2015, tumor volumes exceeded 8 cc in 30 patients. We studied 19 patients with follow-up for more than 36 post-SRS months or until an event. Median tumor volume was 11.5 cc (range; 8.0 to 30.6). The target volume was basically covered with 12.0 Gy. **RESULTS:** The median magnetic resonance imaging and clinical follow-up periods were both 98 months (range 49 to 204). Tumor shrinkage was documented in 13 patients (72%), no change in 2 (11%), and growth in the other 3 (17%). Therefore, the crude growth control rate was 83%. All three patients with tumor enlargement needed salvage treatment. Thus, the crude clinical control rate was 84%. Actuarial further procedure-free rates were 91%, 83% and 76%, at the 60th, 120th, and 180th post-SRS month. Among six patients followed chronologically, transient tumor expansion was observed in three (43%) and two cystic VSs showed rapid tumor growth. Transient trigeminal neuropathy occurred in two patients (11%). No patients experienced facial nerve palsy. None of the six patients with useful hearing pre-SRS maintained serviceable hearing. Ventricular-peritoneal shunt placement was required in three patients. **CONCLUSIONS:** Long-term tumor control with SRS was moderately acceptable in large VSs. In terms of functional outcome, trigeminal neuropathies and facial palsies were rare. However, hearing preservation remains a challenge. In the long term, chronological tumor volumes were generally decreased after SRS. However, caution is required regarding rapid increases in tumor size, especially for cystic type VSs. Further studies are needed to optimize clinical positioning of SRS for large VSs.

[18] Effect of Gamma Knife Radiosurgery on Vestibular Schwannoma with Serviceable Hearing: A Single-Center Indian Study.

World neurosurgery. 2019;127:e114-e123

A R P, Yeole U, Arimappamagan A, Rao KVLN, Bhat DI, Dwarakanath S, Govindswamy B, Somanna S

PMID: 30862586 DOI: 10.1016/j.wneu.2019.02.169

OBJECTIVE: Gamma Knife radiosurgery (GKRS) is an established treatment modality for vestibular schwannomas (VSs). The tumor control and hearing preservation rates suggest that GKRS is a good alternative treatment for small- and medium-size VS. Data are lacking from India regarding GKRS for VSs. Our aim was to find the hearing preservation and tumor control rates and the factors contributing to these. **METHODS:** In a retrospective 9-year study period, 87 patients had undergone GKRS for unilateral VS with Gardner-Robertson (GR) class I or II serviceable hearing. All 87 had been evaluated with magnetic resonance imaging and audiometry before GKRS and during follow-up to assess for the

factors influencing tumor control and hearing preservation. **RESULTS:** Of the 87 patients, 77 with a minimum follow-up of 2 years and magnetic resonance imaging and audiometry evaluations available were included in the present study. The median follow-up period was 30 months. The tumor control rate and hearing preservation rate was 96.1% and 79.2%, respectively. Hearing preservation was not affected by the tumor volume. However, age >40 years, pre-GKRS pure tone average <30 decibels, speech discrimination score >85%, pre-GKRS Gardner-Robertson grade I hearing, mean cochlear dose <4 Gy, and pre-GKRS Ohata class of laterality C, D, E were significant on univariate analysis. The multivariate analysis revealed that age >40 years ($P = 0.017$), pre-GKRS pure tone average <30 decibels ($P = 0.002$), and Gardner-Robertson class I ($P = 0.001$) were significant factors. No patient developed cranial nerve dysfunction, hydrocephalus, or malignant degeneration. **CONCLUSION:** For most patients with small VSs, GKRS will be an effective alternative treatment to microsurgery with retained serviceable hearing and good tumor control.

[19] Predictive Factors of Early Postoperative and Long-Term Facial Nerve Function After Large Vestibular Schwannoma Surgery.

World neurosurgery. 2019;127:e599-e608

Troude L, Boucekine M, Montava M, Lavielle JP, Regis JM, Roche PH
PMID: 30930324 DOI: 10.1016/j.wneu.2019.03.218

OBJECTIVE: The preservation of acceptable facial nerve (FN) function after surgery is the key concern for most patients with vestibular schwannomas (VS). To assess predictive factors of early postoperative and long-term FN function in patients harboring large VS operated with a FN-sparing technique. **METHODS:** Single-center retrospective cohort study with 169 consecutive large VS operated on between January 2003 and May 2015. Clinical, radiologic, and intraoperative factors were assessed according to FN function. **RESULTS:** At last follow-up examination, among the 145 patients without preoperative FN palsy, FN function was good (House-Brackmann [HB] grades I or II) in 84% and moderate (HB grade III) in 15% of patients. Only 1 patient presented with poor HB grade IV function. Multivariate logistic regression model showed the mean preoperative VS extrameatal diameter as being an independent predictor of an unfavorable initial FN outcome (odds ratio [OR], 1.062; $P = 0.038$). Surgical anatomic preservation of the cochlear nerve was associated with better FN outcomes (OR, 0.237; $P = 0.012$). A history of previous surgery seemed to be related to long-term impaired FN function (OR, 71.405; $P = 0.042$), as well as early postoperative FN function (OR, 19.068; $P = 0.000$). No correlation was found between a history of previous Gamma Knife surgery treatment ($P = 0.225$) or the extent of resection ($P = 0.438$) and impaired FN outcomes. History of previous surgery was identified as an unfavorable predictive recovery factor of impaired postoperative FN function ($P = 0.034$). **CONCLUSIONS:** As long as the extent of resection or additional Gamma Knife surgery have not been identified as predictive risk factors of postoperative FN palsy, we suggest that optimal resection is the main option for patients harboring large VS.

[20] Impact of pretreatment growth on Tumor control for vestibular schwannomas following gamma knife.

The Laryngoscope. 2019;129(3):743-747

Chang J, Breshears JD, Molinaro AM, Sneed PK, McDermott MW, Theodosopoulos PV, Tward AD

PMID: 30408172 DOI: 10.1002/lary.27427

OBJECTIVES/HYPOTHESIS: To determine if volumetric growth prior to gamma knife (GK) radiosurgery predicts long-term tumor control. **STUDY DESIGN:** Retrospective cohort study. **METHODS:** Sporadic vestibular schwannomas (VS) treated with GK between 2002 and 2014 at a single tertiary care center were identified. Patients were included if they had over 6 months of pretreatment observation and over 1.5 years of posttreatment follow-up. Volumetric tumor analysis was performed on T1 postcontrast imaging. Pretreatment and posttreatment volume change was calculated. Tumors with over 20% volume increase were classified as growing. **RESULTS:** There were 62 patients included

in this study; 48 had pretreatment growth and 14 had no pretreatment growth. Median tumor volume was 0.58 +/- 1.8 cm³ and median follow-up was 3.3 +/- 2.0 years. For tumors with and without pretreatment growth, salvage treatment rates were 2% and 7% (P = .35), and posttreatment radiologic stability rates were 73% and 86%, respectively (P = .33). Median pretreatment growth was 27 +/- 33% per year for tumors with posttreatment radiographic growth and 18 +/- 26% per year for tumors without posttreatment radiographic growth (P = .99). **CONCLUSIONS:** Pretreatment growth was not associated with increased salvage treatment or posttreatment radiographic progression rates in VS following GK. **LEVEL OF EVIDENCE:** 4 Laryngoscope, 129:743-747, 2019.

[21] Long-Term Tumor Control Rates Following Gamma Knife Radiosurgery for Acoustic Neuroma.

World neurosurgery. 2019;122:366-371

Tucker DW, Gogia AS, Donoho DA, Yim B, Yu C, Fredrickson VL, Chang EL, Freidman RA, Zada G, Giannotta SL
PMID: 30447465 DOI: 10.1016/j.wneu.2018.11.009

BACKGROUND: Acoustic neuromas (ANs) are benign intracranial tumors that arise from myelin-forming Schwann cells surrounding the vestibular branch of the vestibulocochlear nerve (cranial nerve VIII). Treatment options for AN include observation, radiosurgery, and microsurgical resection. Gamma Knife radiosurgery (GKRS) for AN has well-documented short-term safety and efficacy for carefully selected patients. Recent innovations in GKRS technology may improve long-term outcomes. The aim of this study was to report long-term tumor control and complication rates after GKRS for sporadic AN. **METHODS:** A retrospective review was performed of patients with sporadic ANs at Keck Hospital of USC who underwent GKRS from 1995 to 2015 with a minimum follow-up of 12 months. **RESULTS:** Median age at treatment was 63.7 years (range, 19.4-84.2 years). Median follow-up time was 69 months. Median tumor diameter was 17.5 mm (range, 5.0-29.0 mm), and median treatment volume was 2.41 cm³ (range, 0.09-12.8 cm³). Median prescribed dose was 12.50 Gy. Tumor control was achieved in 51 (98.1%) patients over the follow-up period (12-192 months). One patient experienced tumor progression at 22 months after GKRS, requiring surgical intervention, which ultimately resulted in remission. Complications included hearing loss (17.3%), worsened balance/ataxia (7.7%), and hydrocephalus (1.92%). **CONCLUSIONS:** Patients undergoing GKRS for sporadic ANs had high rates of tumor control over a median follow-up time of >5 years. Improvements in radiosurgery treatment planning were seen in the most recent cohort of patients. GKRS is a safe and effective modality for treating sporadic ANs in selected patients.

[22] Local Tumor Control and Clinical Symptoms After Gamma Knife Radiosurgery for Residual and Recurrent Vestibular Schwannomas.

World neurosurgery. 2019;122:e1240-e1246

Suero Molina E, van Eck ATCJ, Sauerland C, Schipmann S, Horstmann G, Stummer W, Brokinkel B

PMID: 30447443 DOI: 10.1016/j.wneu.2018.11.022

BACKGROUND: The use of Gamma Knife radiosurgery (GKRS) for recurrent or residual vestibular schwannoma (VS) after microsurgery (MS) has been investigated in several retrospective studies. The purpose of this study was to identify potential risk factors for both neurologic deterioration and tumor progression after GKRS for previously operated VSs in a prospective setting. **METHODS:** Patients who underwent GKRS for previously operated and histopathologically confirmed VS between 1998 and 2015 were prospectively followed-up. Risk factors for therapy side effects and predictors for tumor control were investigated in uni- and multivariate analyses. **RESULTS:** A total of 160 individuals with a median age of 55 years were included. Median tumor volume prior to GKRS was 1.40 cm³ (range, 0.06-35.80 cm³). After a median follow-up of 36 months, hearing and facial nerve function were serviceable (modified Gardner-Robertson and House-Brackmann grades I and II) in 7 (5%) and 82 (55%) patients, respectively. Deterioration to a nonserviceable facial nerve function after GKRS was found in 3% (3/89) and tended to increase with rising tumor

volume (odds ratio, 1.65 per cm³; 95% confidence interval, 1.00-2.71; P = 0.051). Median tumor volume prior to GKRS was higher in patients with radiologic (P = 0.020) or clinical tumor progression (P < 0.001). Critical tumor volume prior to GKRS to predict clinical and radiologic tumor progression was 1.30 cm³ (P < 0.001) and 3.30 cm³ (P = 0.019), respectively. However, in multivariate analyses, none of the analyzed variables were found to independently predict tumor progression. **CONCLUSIONS:** Intended submaximal resection followed by GKRS is a viable treatment for VS. Because tumor remnant size after MS is an important predictor for recurrence after adjuvant GKRS, both brainstem and cerebellar decompression and maximal safely achievable resection should remain major goals of microsurgery.

[23] Temporal Dynamics of Pseudoprogession After Gamma Knife Radiosurgery for Vestibular Schwannomas-A Retrospective Volumetric Study.

Neurosurgery. 2019;84(1):123-131

Breshears JD, Chang J, Molinaro AM, Sneed PK, McDermott MW, Tward A, Theodosopoulos PV

PMID: 29518221 DOI: 10.1093/neuros/nyy019

BACKGROUND: The optimal observation interval after the radiosurgical treatment of a sporadic vestibular schwannoma, prior to salvage intervention, is unknown. **OBJECTIVE:** To determine an optimal postradiosurgical treatment interval for differentiating between pseudoprogession and true tumor growth by analyzing serial volumetric data. **METHODS:** This single-institution retrospective study included all sporadic vestibular schwannomas treated with Gamma Knife radiosurgery (Eketa AB, Stockholm, Sweden; 12-13 Gy) from 2002 to 2014. Volumetric analysis was performed on all available pre- and posttreatment magnetic resonance imaging scans. Tumors were classified as "stable/decreasing," "transient enlargement", or "persistent growth" after treatment, based on incrementally increasing follow-up durations. **RESULTS:** A total of 118 patients included in the study had a median treatment tumor volume of 0.74 cm³ (interquartile range [IQR] = 0.34-1.77 cm³) and a median follow-up of 4.1 yr (IQR = 2.6-6.0 yr). Transient tumor enlargement was observed in 44% of patients, beginning at a median of 1 yr (IQR = 0.6-1.4 yr) posttreatment, with 90% reaching peak volume within 3.5 yr, posttreatment. Volumetric enlargement resolved at a median of 2.4 yr (IQR 1.9-3.6 yr), with 90% of cases resolved at 6.9 yr. Increasing follow-up revealed that many of the tumors initially enlarging 1 to 3 yr after stereotactic radiosurgery ultimately begin to shrink on longer follow-up (45% by 4 yr, 77% by 6 yr). **CONCLUSION:** Tumor enlargement within approximately 3.5 yr of treatment should not be used as a sole criterion for salvage treatment. Patient symptoms and tumor size must be considered, and giving tumors a chance to regress before opting for salvage treatment may be worthwhile.

2018

[24] Long-term results of Gamma-knife stereotactic radiosurgery for vestibular schwannomas in patients with type 2 neurofibromatosis.

Neuro-Chirurgie. 2018;64(5):355-363

Spatola G, Carron R, Delsanti C, Thomassin JM, Roche PH, Regis J

PMID: 27527622 DOI: 10.1016/j.neuchi.2016.03.005

INTRODUCTION: The aim of this study was to analyze the long-term results of Gamma-knife radiosurgery treatment of vestibular schwannomas in type 2 neurofibromatosis patients. **MATERIALS AND METHODS:** A cohort of 129 treatments for vestibular schwannomas in 103 patients was selected from a prospectively-maintained clinical database. Tumor control was assessed by volumetric analysis of the tumor at the last follow-up. Any need of a further procedure such as microsurgical removal or second treatment was regarded as a failure of tumor control. Hearing function was assessed based on Gardner-Robertson classification. Progression-free survival and functional hearing

preservation rates were estimated using the Kaplan-Meier method. **RESULTS:** The median age at treatment was 34 years with no gender predominance. The median tumor volume was 1.5cm³. At a median clinical follow-up of 5.9 years, five patients had died, four underwent a second radiosurgical procedure and eight underwent microsurgical resection. Progression-free survival was 88 and 75% respectively at 5 and 10 years. Hearing was considered serviceable in 70 ears and remained functional in 28 ears. Kaplan-Meier estimates for 5 and 10 years functional hearing was 47 and 34%, respectively. Three patients developed new facial nerve palsy after radiosurgery at 15 days, 6 and 19 months respectively and only one partially recovered. Five patients complained of a subjective instability worsening. Four cases developed trigeminal neuropathy. No predictive factors were found to be statistically correlated with a better hearing outcome or an improved tumor growth control. **CONCLUSION:** Results prove less satisfying than in sporadic unilateral schwannomas. However, the lower rate of mortality and morbidity compared with microsurgical resection may support a proactive role of Gamma-knife in this pathology.

[25] Influence of pretreatment growth rate on Gamma Knife treatment response for vestibular schwannoma: a volumetric analysis.

Journal of neurosurgery. 2018;:1-8

Langenhuizen PPJH, Zinger S, Hanssens PEJ, Kunst HPM, Mulder JJS, Leenstra S, de With PHN, Verheul JB

PMID: 30497177 DOI: 10.3171/2018.6.JNS18516

OBJECTIVE: The aim of this study was to gain insight into the influence of the pretreatment growth rate on the volumetric tumor response and tumor control rates after Gamma Knife radiosurgery (GKRS) for incidental vestibular schwannoma (VS). **METHODS:** SAll patients treated with GKRS at the Gamma Knife Center, ETZ Hospital, who exhibited a confirmed radiological progression of their VS after an initial observation period were included. Pre- and posttreatment MRI scans were volumetrically evaluated, and the volume doubling times (VDTs) prior to treatment were calculated. Posttreatment volumes were used to create an objective mathematical failure definition: 2 consecutive significant increases in tumor volume among 3 consecutive follow-up MRI scans. Spearman correlation, Kaplan-Meier survival analysis, and Cox proportional hazards regression analysis were used to determine the influence of the VDT on the volumetric treatment response. **RESULTS:** The resulting patient cohort contained 311 patients in whom the VDT was calculated. This cohort had a median follow-up time of 60 months after GKRS. Of these 311 patients, 35 experienced loss of tumor control after GKRS. The pretreatment growth rate and the relative volume changes, calculated at 6 months and 1, 2, and 3 years following treatment, showed no statistically significant correlation. Kaplan-Meier analysis revealed that slow-growing tumors, with a VDT equal to or longer than the median VDT of 15 months, had calculated 5- and 10-year control rates of 97.3% and 86.0%, respectively, whereas fast-growing tumors, with a VDT less than the median growth rate, had control rates of 85.5% and 67.6%, respectively (log-rank, $p = 0.001$). The influence of the VDT on tumor control was also determined by employing the Cox regression analysis. The resulting model presented a significant ($p = 0.045$) effect of the VDT on the hazard rates of loss of tumor control. **CONCLUSIONS:** SBy employing a unique, large database with long follow-up times, the authors were able to accurately investigate the influence of the pretreatment VS growth rate on the volumetric GKRS treatment response. The authors have found a predictive model that illustrates the negative influence of the pretreatment VS growth rate on the efficacy of radiosurgery treatment. The resulting tumor control rates confirm the high efficacy of GKRS for slow-growing VS. However, fast-growing tumors showed significantly lower control rates. For these cases, different treatment strategies may be considered.

[26] CT versus MR Imaging in Estimating Cochlear Radiation Dose during Gamma Knife Surgery for Vestibular Schwannomas.

AJNR. American journal of neuroradiology. 2018;39(10):1907-1911

Faramand AM, Kano H, Johnson S, Niranjana A, Flickinger JC, Lunsford LD

PMID: 30213806 DOI: 10.3174/ajnr.A5808

BACKGROUND AND PURPOSE: Leksell stereotactic radiosurgery is an effective option for patients with vestibular schwannomas. Some centers use a combination of stereotactic CT fused with stereotactic MR imaging to achieve an optimal target definition as well as minimize the radiation dose delivered to adjacent structures that correlate with hearing outcomes. The present prospective study was designed to determine whether there is cochlear dose variability between MR imaging and CT. **MATERIALS AND METHODS:** Fifty consecutive patients underwent stereotactic radiosurgery for vestibular schwannomas. Dose-planning was performed using high-definition fused stereotactic MR imaging and stereotactic CT images. The 3D cochlear volume was determined by delineating the cochlea on both CT and T2-weighted MR imaging. The mean radiation dose, maximum dose, and 3- and 4.20-Gy cochlear volumes were identified using standard Leksell Gamma Knife software. **RESULTS:** The median mean radiation dose delivered to the cochlea was 3.50 Gy (range, 1.20-6.80 Gy) on CT and 3.40 Gy (range, 1-6.70 Gy) on MR imaging (concordance correlation coefficient = 0.86, $r(2) = 0.9$, $P < / = .001$). The median maximum dose delivered to the cochlea was 6.7 Gy on CT and 6.6 Gy on MR imaging (concordance correlation coefficient = 0.89, $r(2) = 0.90$, $P < / = .001$). Dose-volume histograms generated from CT and MR imaging demonstrated a strong level of correlation in estimating the 3- and 4.20-Gy volumes (concordance correlation coefficient = 0.81, $r(2) = 0.82$, $P < / = .001$ and concordance correlation coefficient = 0.87, $r(2) = 0.89$, $P < / = .001$). **CONCLUSIONS:** Both MR imaging and CT provide similar cochlear dose parameters. Despite the reported superiority of CT in identifying bony structures, high-definition MR imaging alone is sufficient to identify the radiation doses delivered to the cochlea.

[27] Adjunctive Gamma Knife Surgery or Wait and Scan Policy After Optimal Resection of Large Vestibular Schwannomas: Clinical and Radiologic Outcomes.

World neurosurgery. 2018;118:e895-e905

Troude L, Boucekine M, Montava M, Lavielle JP, Regis JM, Roche PH

PMID: 30031182 DOI: 10.1016/j.wneu.2018.07.093

OBJECTIVES: Patients with large vestibular schwannomas (VSs) will require surgical treatment owing to the potential consequences of long tract and cranial nerve compression. We assessed the long-term clinical and radiologic outcomes of patients harboring large VSs treated with a facial nerve (FN)-sparing technique. **METHODS:** We performed a single-center retrospective cohort study of 169 consecutive large VSs treated surgically from January 2003 to May 2015. The postoperative volume of the tumor residue was assessed using thin-slice magnetic resonance imaging 6 months after surgery. Postoperatively, the patients were allocated to a wait and rescan (W&reS) or an upfront gamma knife surgery (GKS) policy. **RESULTS:** At the last follow-up examination, FN function was good (House-Brackmann grade I or II) in 84% of the patients. Of the 169 patients, 11% had undergone gross total resection, 59% near total, 21% subtotal, and 9% partial resection. In the 143 patients without gross total resection, the overall median tumor residue volume was 0.39 cm³. Of these 143 patients, 66 had been allocated to the W&reS policy and 77 to upfront GKS. Overall tumor control was achieved in 83% of cases, with a mean follow-up of 62 months. Of the 27 growing residues, 17 required salvage treatment (11% failure rate). The 1-, 5-, and 7-year progression-free survival rate was 95%, 82%, and 76% in the W&reS group and 99%, 81%, and 78% in the GKS group, respectively ($P = 0.57$). **CONCLUSIONS:** Functional nerve-sparing resection provides satisfactory FN preservation. The low probability of long-term regrowth of small remnants is an argument for a W&reS protocol. GKS is a legitimate option for salvage treatment.

[28] Retreatment of vestibular schwannoma with Gamma Knife radiosurgery: clinical outcome, tumor control, and review of literature.

Journal of neurosurgery. 2018;129(1):137-145

Fu VX, Verheul JB, Beute GN, Leenstra S, Kunst HPM, Mulder JJS, Hanssens PEJ

PMID: 28984523 DOI: 10.3171/2017.3.JNS162033

OBJECTIVE: Gamma Knife radiosurgery (GKRS) has become an accepted

treatment for vestibular schwannoma, with a high rate of tumor control and good clinical outcome. In a small number of cases, additional treatment is needed. This retrospective study examines the clinical outcome, reproducibility of volumetric response patterns, and tumor control rate after administering a second GKRS to treat vestibular schwannomas. **METHODS:** A total of 38 patients were included: 28 patients underwent a radiosurgical procedure as the initial treatment (Group 1), and 10 patients underwent microsurgical resection with adjuvant radiosurgery on the tumor remnant as the initial treatment (Group 2). The indication for a second GKRS treatment was growth observed on follow-up imaging. The median margin dose was 11.0 Gy for the first procedure and 11.5 Gy for the second procedure. Tumor control after retreatment was assessed through volumetric analysis. Clinical outcome was assessed through medical chart review. **RESULTS:** Median tumor volume at retreatment was 3.6 cm³, with a median treatment interval of 49 months. All patients showed tumor control in a median follow-up period of 75 months after the second radiosurgical procedure. Volumetric tumor response after the second procedure did not correspond to response after the first procedure. After retreatment, persisting House-Brackmann Grade II facial nerve dysfunction was observed in 3 patients (7.9%), facial spasms in 5 patients (13%), and trigeminal nerve hypesthesia in 3 patients (7.9%). Hearing preservation was not evaluated because of the small number of patients with serviceable hearing at the second procedure. **CONCLUSIONS:** Repeat GKRS after a failed first treatment appears to be an effective strategy in terms of tumor control. The volumetric response after a repeat procedure could not be predicted by the volumetric response observed after first treatment. This justifies considering repeat GKRS even for tumors that do not show any volumetric response and show continuous growth after first treatment. An increased risk of mild facial and trigeminal nerve dysfunction was observed after the second treatment compared with the first treatment.

[29] Preserved Cochlear CISS Signal is a Predictor for Hearing Preservation in Patients Treated for Vestibular Schwannoma With Stereotactic Radiosurgery.

Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 2018;39(5):628-631

Prabhu V, Kondziolka D, Hill TC, Benjamin CG, Shinseki MS, Golfinos JG, Roland JT Jr, Fatterpekar GM

PMID: 29561382 DOI: 10.1097/MAO.0000000000001762

BACKGROUND: Hearing preservation is a goal for many patients with vestibular schwannoma. We examined pretreatment magnetic resonance imaging (MRI) and posttreatment hearing outcome after stereotactic radiosurgery. **METHODS:** From 2004 to 2014, a cohort of 125 consecutive patients with vestibular schwannoma (VS) treated via stereotactic radiosurgery (SRS) were retrospectively reviewed. MRIs containing three-dimensional constructive interference in steady state or equivalent within 1 year before treatment were classified by two radiologists for pretreatment characteristics. "Good" hearing was defined as American Academy of Otolaryngology-Head and Neck Surgery class A. Poor hearing outcome was defined as loss of good pretreatment hearing after stereotactic radiosurgery. **RESULTS:** Sixty-one patients met criteria for inclusion. Most had tumors in the distal internal auditory canal (55%), separated from the brainstem (63%), oval shape (64%) without cysts (86%), and median volume of 0.85 +/- 0.55 cm. Pretreatment audiograms were performed a median of 108 +/- 173 days before stereotactic radiosurgery; 38% had good pretreatment hearing. Smaller tumor volume ($p < 0.005$) was the only variable associated with good pretreatment hearing. 49 (80%) patients had posttreatment audiometry, with median follow-up of 197 +/- 247 days. Asymmetrically decreased pretreatment cochlear CISS signal on the side of the VS was the only variable associated with poor hearing outcome ($p = 0.001$). Inter-rater agreement on cochlear three-dimensional constructive interference in steady state preservation was 91%. **CONCLUSIONS:** Decreased cochlear CISS signal may indicate a tumor's association with the cochlear neurovascular bundle, influencing endolymph protein concentration and creating an inability to preserve hearing. This important MRI characteristic can influence planning, counseling, and patient selection for vestibular schwannoma treatment.

[30] Place of Gamma Knife Stereotactic Radiosurgery in Grade 4 Vestibular Schwannoma Based on Case Series of 86 Patients with Long-Term Follow-Up.

World neurosurgery. 2018;114:e1192-e1198

Lefranc M, Da Roz LM, Balossier A, Thomassin JM, Roche PH, Regis J
PMID: 29614352 DOI: 10.1016/j.wneu.2018.03.175

INTRODUCTION: Grade IV vestibular schwannoma (Koos classification) is generally considered to be an indication for microsurgical resection or combined radiosurgery-microsurgery. However, the place of Gamma Knife stereotactic surgery (GK-SRS), either as first-line treatment or when progression of residual tumor compresses the brainstem, has not been clearly evaluated. This article reports the results of a large case series of patients with grade 4 vestibular schwannoma treated by GK-SRS. **MATERIAL AND METHOD:** All consecutive patients with grade IV vestibular schwannoma treated by GK-SRS in our department between 1996 and 2011 with a minimum follow-up of 3 years were included in this study. **RESULTS:** 86 patients were treated by GK-SRS with a minimum follow-up of 3 years. Mean follow-up was 6.2 years (3-16 years). The mean age of the patients at the time of GK-SRS was 54.6 years (range: 23-84) and the sex ratio was 0.6. At the time of radiosurgery, no patient presented brainstem dysfunction prior to GK-SRS. 38 patients had functional hearing before treatment. One patient presented mild trigeminal neuralgia before GK-SRS. Tumor control with no clinical deterioration was obtained in 78 patients (90.7%). No radiation-induced brainstem or cranial nerve toxicity was observed in any of these patients. Functional hearing was maintained in 25 patients. 8 (9.3%) patients presented tumor growth and required microsurgical resection in 7 cases and ventricular shunt in 1 case. **CONCLUSION:** On the basis of this large series, GK-SRS appears to be a safe and effective treatment option for grade IV vestibular schwannoma for patients with no signs of brainstem dysfunction.

[31] Long-term hearing outcomes after gamma knife surgery in patients with vestibular schwannoma with hearing preservation: evaluation in 92 patients with serial audiograms.

Journal of neuro-oncology. 2018;138(2):283-290

Hasegawa T, Kato T, Yamamoto T, Naito T, Kato N, Torii J, Ishii K

PMID: 29667085 DOI: 10.1007/s11060-018-2784-x

The treatment strategy for patients with vestibular schwannoma (VS) is controversial, and data concerning the long-term hearing outcomes > 5 years after gamma knife surgery (GKS) are limited. The long-term hearing outcomes after GKS were evaluated in VS patients with hearing preservation. Ninety-two VS patients with a pure tone average (PTA) \leq 50 dB were evaluated. The median age was 54 years; the median tumor volume was 1.5 cm³. The tumors were treated with a median margin dose of 12 Gy and a median mean cochlear dose of 4.0 Gy. At the time of GKS, 65 patients retained a PTA of 0-30 dB, and 27 had a PTA of 31-50 dB. The median follow-up period was 106 months. At the final follow-up, 2 (2%) developed tumor progression. During the median audiogram follow-up of 83 months, the PTA was \leq 30 dB in 22 patients (24%) and 31-50 dB in 27 patients (29%); 43 patients (47%) worsened to a PTA > 50 dB. Hearing preservation rates were 66, 57, and 44% at 3, 5, and 10 years, respectively. In multivariate analysis, the mean cochlear dose ($P < 0.001$) and pre-GKS PTA ($P = 0.045$) were significant for hearing preservation. GKS was an effective treatment option for VS patients with a PTA \leq 50 dB. As a lower cochlear dose and better pre-GKS PTA contributed to long-term hearing preservation, prophylactic GKS before hearing deterioration or tumor growth would be a treatment of choice if patients provided informed consent.

[32] Gamma Knife radiosurgery for large vestibular schwannomas greater than 3 cm in diameter.

Journal of neurosurgery. 2018;128(5):1380-1387

Huang CW, Tu HT, Chuang CY, Chang CS, Chou HH, Lee MT, Huang CF

PMID: 28707997 DOI: 10.3171/2016.12.JNS161530

OBJECTIVE: Stereotactic radiosurgery (SRS) is an important alternative management option for patients with small- and medium-sized vestibular

schwannomas (VSs). Its use in the treatment of large tumors, however, is still being debated. The authors reviewed their recent experience to assess the potential role of SRS in larger-sized VSs. **METHODS:** Between 2000 and 2014, 35 patients with large VSs, defined as having both a single dimension > 3 cm and a volume > 10 cm³, underwent Gamma Knife radiosurgery (GKRS). Nine patients (25.7%) had previously undergone resection. The median total volume covered in this group of patients was 14.8 cm³ (range 10.3-24.5 cm³). The median tumor margin dose was 11 Gy (range 10-12 Gy). **RESULTS:** The median follow-up duration was 48 months (range 6-156 months). All 35 patients had regular MRI follow-up examinations. Twenty tumors (57.1%) had a volume reduction of greater than 50%, 5 (14.3%) had a volume reduction of 15%-50%, 5 (14.3%) were stable in size (volume change < 15%), and 5 (14.3%) had larger volumes (all of these lesions were eventually resected). Four patients (11.4%) underwent resection within 9 months to 6 years because of progressive symptoms. One patient (2.9%) had open surgery for new-onset intractable trigeminal neuralgia at 48 months after GKRS. Two patients (5.7%) who developed a symptomatic cyst underwent placement of a cystoperitoneal shunt. Eight (66%) of 12 patients with pre-GKRS trigeminal sensory dysfunction had hypoesthesia relief. One hemifacial spasm completely resolved 3 years after treatment. Seven patients with facial weakness experienced no deterioration after GKRS. Two of 3 patients with serviceable hearing before GKRS deteriorated while 1 patient retained the same level of hearing. Two patients improved from severe hearing loss to pure tone audiometry less than 50 dB. The authors found borderline statistical significance for post-GKRS tumor enlargement for later resection ($p = 0.05$, HR 9.97, CI 0.99-100.00). A tumor volume ≥ 15 cm³ was a significant factor predictive of GKRS failure ($p = 0.005$). No difference in outcome was observed based on indication for GKRS ($p = 0.0761$). **CONCLUSIONS:** Although microsurgical resection remains the primary management choice in patients with VSs, most VSs that are defined as having both a single dimension > 3 cm and a volume > 10 cm³ and tolerable mass effect can be managed satisfactorily with GKRS. Tumor volume ≥ 15 cm³ is a significant factor predicting poor tumor control following GKRS.

[33] Long-term outcome after Gamma Knife radiosurgery for acoustic neuroma of all Koos grades: a single-center study.

Journal of neurosurgery. 2018;:1-10

Frischer JM, Gruber E, Schoffmann V, Ertl A, Hoftberger R, Mallouhi A, Wolfsberger S, Arnoldner C, Eisner W, Knosp E, Kitz K, Gatterbauer B
PMID: 29498575 DOI: 10.3171/2017.8.JNS171281

OBJECTIVE: The authors present long-term follow-up data on patients treated with Gamma Knife radiosurgery (GKRS) for acoustic neuroma. **METHODS:** Six hundred eighteen patients were radiosurgically treated for acoustic neuroma between 1992 and 2016 at the Department of Neurosurgery, Medical University Vienna. Patients with neurofibromatosis and patients treated too recently to attain 1 year of follow-up were excluded from this retrospective study. Thus, data on 557 patients with spontaneous acoustic neuroma of any Koos grade are presented, as are long-term follow-up data on 426 patients with a minimum follow-up of 2 years. Patients were assessed according to the Gardner-Robertson (GR) hearing scale and the House-Brackmann facial nerve function scale, both prior to GKRS and at the times of follow-up. **RESULTS:** Four hundred fifty-two patients (81%) were treated with radiosurgery alone and 105 patients (19%) with combined microsurgery-radiosurgery. While the combined treatment was especially favored before 2002, the percentage of cases treated with radiosurgery alone has significantly increased since then. The overall complication rate after GKRS was low and has declined significantly in the last decade. The risk of developing hydrocephalus after GKRS increased with tumor size. One case (0.2%) of malignant transformation after GKRS was diagnosed. Radiological tumor control rates of 92%, 91%, and 91% at 5, 10, and 15 years after GKRS, regardless of the Koos grade or pretreatment, were observed. The overall tumor control rate without the need for additional treatment was even higher at 98%. At the last follow-up, functional hearing was preserved in 55% of patients who had been classified with GR hearing class I or II prior to GKRS. Hearing preservation

rates of 53%, 34%, and 34% at 5, 10, and 15 years after GKRS were observed. The multivariate regression model revealed that the GR hearing class prior to GKRS and the median dose to the cochlea were independent predictors of the GR class at follow-up. **CONCLUSIONS:** In small to medium-sized spontaneous acoustic neuromas, radiosurgery should be recognized as the primary treatment at an early stage. Although minimizing the cochlear dose seems beneficial for hearing preservation, the authors, like others before, do not recommend undertreating intracanalicular tumors in favor of low cochlear doses. For larger acoustic neuromas, radiosurgery remains a reliable management option with tumor control rates similar to those for smaller acoustic neuromas; however, careful patient selection and counseling are recommended given the higher risk of side effects. Microsurgery must be considered in acoustic neuromas with significant brainstem compression or hydrocephalus.

[34] Factors affecting hearing deterioration in vestibular schwannoma patients treated with gamma knife radiosurgery: the Asan Medical Center experience.

Acta oto-laryngologica. 2018;138(2):96-104

Park MJ, Park HJ, Chung JW, Lee DH, Cho YH, Choi YJ, Ahn JH
PMID: 29069961 DOI: 10.1080/00016489.2017.1386800

OBJECTIVES: To investigate the changes in hearing and to determine factors predicting hearing deterioration in patients with vestibular schwannoma (VS) who undergo gamma knife radiosurgery (GKRS). **DESIGN:** A retrospective review of medical records in patients diagnosed with VS and initially treated with GKRS at a tertiary care medical center between 1995 and 2015 was performed. Tumor factors (location, volume), parameters related to irradiation to the tumor and cochlea, and distance between the tumor and cochlea were reviewed. **RESULTS:** Fifty-six patients were included in the final analysis with a mean observation period following GKRS as 24.4 +/- 27.8 months. Prior to GKRS, the average pure tone threshold at 500, 1k, 2k, and 4k Hz (PTA4) was 51.0 +/- 29.7 dB HL. After GKRS, the mean PTA4 was 71.6 +/- 33.3 dB HL. Significant independent odds ratios for hearing deterioration were 8.5 for extracanalicular tumors, 18.8 for more than 10 shots in GKRS, and 12.2 for a distance between the tumor center and cochlea modiolus less than 20 mm. **CONCLUSIONS:** A significant hearing deterioration was shown in 2 years after GKRS. Tumor location, number of radiation shots, and distance between the tumor and cochlea affected hearing level after GKRS.

2017

[35] Predictive Factors of Unfavorable Events After Gamma Knife Radiosurgery for Vestibular Schwannoma.

World neurosurgery. 2017;107:175-184

Kim JH, Jung HH, Chang JH, Chang JW, Park YG, Chang WS
PMID: 28826715 DOI: 10.1016/j.wneu.2017.07.139

OBJECTIVE: Gamma Knife radiosurgery (GKS) for the treatment of vestibular schwannoma (VS) introduces risks to the facial nerve and auditory perception and may involve post-treatment complications such as pseudoproliferation, hydrocephalus, and other cranial neuropathies. This study of patients with VS who underwent GKS investigated radiosurgical results, focusing on post-treatment complications and identifying the factors that predict such complications.

METHODS: We undertook a retrospective review of all VS patients treated with the Perfexion Leksell Gamma Knife between November 2007 and October 2010 at our institution. Patients who underwent at least 12 months of clinical and radiologic assessments before and after GKS were included. **RESULTS:** All 235 patients were included in the analyses reported here. The 5-year serviceable hearing and facial nerve preservation values were 73.9% and 94.3%, respectively. Following GKS, 43 patients (18.30%) showed pseudoproliferation, 15 (6.38%) exhibited hydrocephalus, 22 (9.36%) showed trigeminal neuropathy, 14 (5.96%) showed vertigo, and 25 (10.64%) showed facial myokymia. According

to multivariate analysis, solid tumor nature was significantly associated with pseudoprogression and patient age was significantly associated with hydrocephalus. Patients receiving margin doses ≥ 13 Gy had a significantly higher probability of loss of serviceable hearing. Patients with smaller tumors had a trigeminal nerve preservation rate comparable with patients harboring larger tumors. Patients receiving margin doses < 13 Gy or older patients had a significantly higher probability of vestibular nerve dysfunction. **CONCLUSIONS:** Further prospective studies should be designed to provide further insight into the exact relationship between the predictive factors we investigated and post-treatment complications.

[36] Cystic Vestibular Schwannomas Respond Best to Radiosurgery.

Neurosurgery. 2017;81(3):490-497

Bowden G, Cavaleri J, Monaco E III, Niranjan A, Flickinger J, Lunsford LD
PMID: 28368501 DOI: 10.1093/neuros/nyx027

BACKGROUND: Vestibular schwannomas (VS) have a well-documented response to Gamma Knife(R) (Elekta AB, Stockholm, Sweden) Stereotactic radiosurgery (SRS). However, there are limited data available regarding the volumetric response of cystic tumors. **OBJECTIVE:** This report correlates the radiographic appearance of VS before radiosurgery with the delayed volumetric response. **METHODS:** This study reviewed our SRS experience with 219 VS patients between 2003 and 2013. Patients were treatment naive and had a significant extracanalicular tumor volume. Magnetic resonance imaging at the time of SRS identified 42 contrast-enhancing macrocystic tumors, 45 contrast-enhancing microcystic tumors, and 132 homogeneously enhancing tumors with no intratumoral cyst formation. The median follow-up was 49.1 months. The median tumor volume was 2.6 cm³ (0.70-16.1 cm³) and the median dose was 12.5 Gy (11-13 Gy).

RESULTS: The actuarial tumor control rate was 99.4% at 2 years and 96.4% at 5 years. A volumetric reduction of $>20\%$ occurred in 85.4% of macrocystic tumors, 76.1% of microcystic tumors, and 62.8% of homogeneously enhancing VS. The median volume decrease per year for macrocystic, microcystic, and homogenous tumors was 17.2%, 7.5%, and 7.9% per year respectively ($P < .001$). A 2:1 blinded volumetric case match showed a significant size reduction in macrocystic tumors compared to noncystic tumors ($P = .007$). Serviceable hearing was maintained in 61.5% of patients that had Gardner-Robertson grade I-II hearing before treatment. Surgical resection or repeat radiosurgery was performed in 8 patients (3.6%) who had sustained tumor progression. **CONCLUSION:** SRS provided VS tumor control in $>95\%$ of patients, regardless of radiographic characteristics. Tumor volume regression was most evident in patients with cystic tumors.

[37] Outcome of hearing preservation related to tumor morphologic analysis in acoustic neuromas treated by gamma knife radiosurgery.

Radiation oncology (London, England). 2017;12(1):134

Pan SY, Liu SA, Sun MH, Tsou HK, Lee SD, Chen YJ, Sheehan J, Sheu ML, Pan HC
PMID: 28810890 DOI: 10.1186/s13014-017-0875-z

BACKGROUND: Gamma Knife radiosurgery (GKRS) is an important part of the neurosurgical armamentarium in the treatment of acoustic neuromas. However, the treatment outcome related to the morphology of the tumor has not been rigorously studied. In this cohort, we evaluated the morphological features of the tumor in the tumor response and neurological outcomes after GKRS. **MATERIAL AND METHODS:** From July 2003 to December 2008, there were 93 cases of acoustic neuromas treated upfront with GKRS with 64 cases with serviceable hearing and 29 cases without serviceable hearing to fulfill the margin dose of 12Gy with at least follow up 5 years. **RESULTS:** The duration of symptom before GKRS in serviceable /no serviceable hearing was 7.9 +/- 1.2 and 15.3 +/- 3.1 months ($p < 0.001$) and associated no-hearing symptom was 70% and 35%, respectively ($p < 0.001$). There was 81.2% of hearing preservation after GKRS in serviceable hearing group including 27 cases of pear type (84%), 14 of linear type (70%), and 9 cases of sphere type (90%) ($p < 0.01$); however, there was no case of hearing improvement in the no-serviceable hearing group (0 of 29). There were 85% of patients with decreased tinnitus in serviceable hearing groups as

compared to 61.5% of patients in no serviceable hearing group ($p < 0.05$). In multivariate analysis, the tumor morphology was highly correlated to hearing preservation rate ($p < 0.01$). **CONCLUSION:** In the limited case of this cohort, we found that the tumor morphology and timing of treatment was highly correlated to the rate of hearing preservation. The sphere type of tumor morphology was associated with the best chance of hearing preservation.

[38] Pretreatment growth rate as a predictor of tumor control following Gamma Knife radiosurgery for sporadic vestibular schwannoma.

Journal of neurosurgery. 2017;127(2):380-387

Marston AP, Jacob JT, Carlson ML, Pollock BE, Driscoll CLW, Link MJ
PMID: 27885952 DOI: 10.3171/2016.5.JNS153013

OBJECTIVE: Over the last 30 years, stereotactic radiosurgery (SRS) has become an established noninvasive treatment alternative for small- to medium-sized vestibular schwannoma (VS). This study aims to further define long-term SRS tumor control in patients with documented pretreatment tumor growth for whom conservative observation failed. **METHODS:** A prospective clinical database was queried, and patients with sporadic VS who elected initial observation and subsequently underwent SRS after documented tumor growth between 2004 and 2014 were identified. Posttreatment tumor growth or shrinkage was determined by a ≥ 2 -mm increase or decrease in maximum linear dimension, respectively.

RESULTS: Sixty-eight patients met study inclusion criteria. The median pre- and posttreatment observation periods were 16 and 43.5 months, respectively. The median dose to the tumor margin was 13 Gy (range 12-14 Gy), and the median maximum dose was 26 Gy (range 24-28 Gy). At the time of treatment, 59 tumors exhibited extracanalicular (EC) extension, and 9 were intracanalicular (IC). Of the 59 EC VSs, 50 (85%) remained stable or decreased in size following treatment, and 9 (15%) enlarged by > 2 mm. Among EC tumors, the median pretreatment tumor growth rate was 2.08 mm/year for tumors that decreased or were stable, compared with 3.26 mm/year for tumors that grew following SRS ($p = 0.009$). Patients who demonstrated a pretreatment growth rate of < 2.5 mm/year exhibited a 97% tumor control rate, compared with 69% for those demonstrating ≥ 2.5 mm/year of growth prior to SRS ($p = 0.007$). No other analyzed variables were found to predict tumor growth following SRS. **CONCLUSIONS:** Overall, SRS administered using a marginal dose between 12-14 Gy is highly effective in treating VSs in which initial observation fails. Tumor control is achieved in 97% of VSs that exhibit slow (< 2.5 mm/year) pretreatment growth; however, SRS is less successful in treating tumors exhibiting rapid growth (≥ 2.5 mm/year).

[39] Preserving normal facial nerve function and improving hearing outcome in large vestibular schwannomas with a combined approach: planned subtotal resection followed by gamma knife radiosurgery.

Acta neurochirurgica. 2017;159(7):1197-1211

Daniel RT, Tuleasca C, George M, Pralong E, Schiappacasse L, Zeverino M, Maire R, Levivier M

PMID: 28516364 DOI: 10.1007/s00701-017-3194-0

OBJECTIVE: To perform planned subtotal resection followed by gamma knife surgery (GKRS) in a series of patients with large vestibular schwannoma (VS), aiming at an optimal functional outcome for facial and cochlear nerves. **METHODS:** Patient characteristics, surgical and dosimetric features, and outcome were collected prospectively at the time of treatment and during the follow-up. **RESULTS:** A consecutive series of 32 patients was treated between July 2010 and June 2016. Mean follow-up after surgery was 29 months (median 24, range 4-78). Mean presurgical tumor volume was 12.5 cm³ (range 1.47-34.9). Postoperative status showed normal facial nerve function (House-Brackmann I) in all patients. In a subgroup of 17 patients with serviceable hearing before surgery and in which cochlear nerve preservation was attempted at surgery, 16 (94.1%) retained serviceable hearing. Among them, 13 had normal hearing (Gardner-Robertson class 1) before surgery, and 10 (76.9%) retained normal hearing after surgery. Mean duration between surgery and GKRS was 6.3 months (range 3.8-13.9). Mean tumor volume at GKRS was 3.5 cm³ (range 0.5-12.8), corresponding to mean residual

volume of 29.4% (range 6-46.7) of the preoperative volume. Mean marginal dose was 12 Gy (range 11-12). Mean follow-up after GKRS was 24 months (range 3-60). Following GKRS, there were no new neurological deficits, with facial and hearing functions remaining identical to those after surgery in all patients. Three patients presented with continuous growth after GKRS, were considered failures, and benefited from the same combined approach a second time. **CONCLUSION:** Our data suggest that large VS management, with planned subtotal resection followed by GKRS, might yield an excellent clinical outcome, allowing the normal facial nerve and a high level of cochlear nerve functions to be retained. Our functional results with this approach in large VS are comparable with those obtained with GKRS alone in small- and medium-sized VS. Longer term follow-up is necessary to fully evaluate this approach, especially regarding tumor control.

[40] Gamma Knife Radiosurgery for Vestibular Schwannomas and Quality of Life Evaluation.

Stereotactic and functional neurosurgery. 2017;95(3):166-173

Berkowitz O, Han YY, Talbot EO, Iyer AK, Kano H, Kondziolka D, Brown MA, Lunsford LD

PMID: 28531896 DOI: 10.1159/000472156

BACKGROUND: Further investigation is needed to look at the impact of vestibular schwannoma (VS) on the health-related quality of life (QOL) of participants who undergo Gamma Knife(R) radiosurgery (GKRS). **OBJECTIVES:** Investigators compared the QOL for VS participants to reported US population norms in order to evaluate disease burden and long-term QOL several years after GKRS. **METHODS:** This cross-sectional study surveyed participants to assess hearing status, tinnitus, imbalance, vertigo, as well as the Short-Form 36-item Health Questionnaire (SF-36). The data were normalized, age adjusted, and functional status was correlated to determine clinically significant differences. **RESULTS:** A total of 353 participants who underwent GKRS between 1997 and 2007 were included in this study with a median postoperative period of 5 years. SF-36 scores were very similar to population norms, and age-adjusted scores for participants followed the US population curve. Frequent vertigo and balance problems had the largest statistically and clinically significant effect on physical and mental component summary scores followed by nonuseful hearing in the tumor ear. **CONCLUSIONS:** Participants reported a good long-term QOL that was very similar to the QOL of US population norms. Of the common VS symptoms, vertigo had the greatest impact on QOL followed by imbalance and then hearing loss.

[41] Stereotactic radiosurgery for recurrent vestibular schwannoma after previous resection.

Journal of neurosurgery. 2017;126(5):1506-1513

Huang MJ, Kano H, Mousavi SH, Niranjana A, Monaco EA 3rd, Arai Y, Flickinger JC, Lunsford LD

PMID: 27471891 DOI: 10.3171/2016.5.JNS1645

OBJECTIVE: The goal of this retrospective cohort study was to assess long-term outcomes in patients with vestibular schwannoma (VS) who underwent stereotactic radiosurgery (SRS) after initial microsurgical resection. **METHODS:** From the authors' database of 1770 patients with VS, the authors retrospectively analyzed data from 173 Gamma Knife SRS procedures for VS after 1 (128 procedures) or multiple (45 procedures) microsurgical resections. The median length of the interval between the last resection and SRS was 42 months (range 2-329 months). The median length of clinical follow-up was 74 months (range 6-285 months). Progression-free survival after SRS was determined with Kaplan-Meier analysis. **RESULTS:** At the time of SRS, the hearing of 161 patients (93%) was Gardner-Robertson Class V, and 81 patients (47%) had facial neuropathy (i.e., facial function with House-Brackmann [HB] grades of III-VI), 87 (50%) had trigeminal neuropathy, and 71 (41%) reported imbalance or disequilibrium disorders. The median tumor volume was 2.7 cm³ (range 0.2-21.6 cm³), and the median dose to the tumor margin was 13 Gy (range 11-20 Gy). Radiosurgery controlled growth of 163 (94%) tumors. Progression-free survival after SRS was 97% at 3 years, 95% at 5 years,

and 90% at 10 years. Four patients with delayed tumor progression underwent repeat SRS at a median of 35 months (range 23-64 months) after the first SRS. Four patients (2.3%) with tumor progression underwent repeat resection at a median of 25 months (range 19-33 months). Among the patients with any facial dysfunction (indicated by HB grades of II-VI), 19% had improvement in this condition after SRS, and 5.5% with some facial function (indicated by HB grades of I-V) developed more facial weakness. Among patients with trigeminal neuropathy, 20% had improvement in this condition, and 5.8% developed or had worsened trigeminal neuropathy after SRS. **CONCLUSIONS:** Stereotactic radiosurgery offered a safe and effective long-term management strategy for VS patients whose tumors remained or recurred after initial microsurgery.

[42] Gamma Knife Radiosurgery for Residual and Recurrent Vestibular Schwannomas After Previous Surgery: Clinical Results in a Series of 90 Patients and Review of the Literature.

World neurosurgery. 2017;98:60-72

Bailo M, Boari N, Gagliardi F, Franzin A, Piloni M, Spina A, Gemma M, Vecchio AD, Bolognesi A, Mortini P

PMID: 27777157 DOI: 10.1016/j.wneu.2016.10.066

OBJECTIVE: Complete removal of vestibular schwannomas (VS) is not always achievable without any risk of disabling postoperative complications, especially in terms of facial nerve function. Moreover, even after gross total removal, a relevant rate of recurrence has been reported. The aim of this study is to validate Gamma Knife radiosurgery (GKRS) as an effective strategy to treat tumor regrowth after previous surgery. **METHODS:** Ninety patients treated with GKRS for VS after previous microsurgery were included in the present study. GKRS was performed at a median of 31 months (range, 4-174 months) postoperatively. Mean tumor volume was 3.35 cm³ (median, 2.5 cm³; range, 0.027-13 cm³) and median marginal dose was 13 Gy. **RESULTS:** At a mean follow-up of 77.2 months, tumor control was achieved in 90% of patients: 2 patients underwent repeated GKRS, and 7 patients underwent further microsurgery. Tumor shrinkage at last follow-up was recorded in 80.3% of cases. The complication rate was low and many consisted of a transient worsening of preexisting symptoms. The overall incidence of persisting facial nerve deficit and trigeminal nerve impairment was, in both cases, 3.3%. Two of 5 patients (40%) preserved functional hearing at last follow-up. One patient (1.1%) underwent ventriculoperitoneal shunting 12 months after GKRS. **CONCLUSIONS:** GKRS is a safe and effective treatment for growing residual and recurrent VSs, with tumor control obtained in 90% of cases and a low morbidity rate. Moreover, the possibility of treating patients with major medical comorbidities constitutes a significant advantage over repeated surgery.

[43] Low-Dose Gamma Knife Radiosurgery for Vestibular Schwannomas: Tumor Control and Cranial Nerve Function Preservation After 11 Gy.

Journal of neurological surgery. Part B, Skull base. 2017;78(1):2-10

Schumacher AJ, Lall RR, Lall RR, Nannek A III, Ayer A, Sejjal S, Liu BP, Marymont M, Lee P, Bendok BR, Kalapurakal JA, Chandler JP

PMID: 28180036 DOI: 10.1055/s-0036-1584231

OBJECTIVES: This study aims to report tumor control rates and cranial nerve function after low dose (11.0 Gy) Gamma knife radiosurgery (GKRS) in patients with vestibular schwannomas. **METHODS:** A retrospective chart review was performed on 30 consecutive patients with vestibular schwannomas treated from March 2004 to August 2010 with GKRS at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. The marginal dose for all patients was 11.0 Gy prescribed to the 50% isodose line. Median follow-up time was 42 months. The median treatment volume was 0.53 cm³. Hearing data were obtained from audiometry reports before and after radiosurgery. **RESULTS:** The actuarial progression free survival (PFS) based on freedom from surgery was 100% at 5 years. PFS based on freedom from persistent growth was 91% at 5 years. One patient experienced tumor progression requiring resection at 87 months. Serviceable hearing, defined as Gardner-Robertson score of I-II, was preserved in 50% of patients. On univariate and multivariate analyses, only higher mean and

maximum dose to the cochlea significantly decreased the proportion of patients with serviceable hearing. **CONCLUSION:** Vestibular schwannomas can be treated with low doses (11.0 Gy) of GKRS with good tumor control and cranial nerve preservation.

2016

[44] A matched cohort comparison of clinical outcomes following microsurgical resection or stereotactic radiosurgery for patients with small- and medium-sized vestibular schwannomas.

Journal of neurosurgery. 2016;125(6):1472-1482

Golfinos JG, Hill TC, Rokosh R, Choudhry O, Shinseki M, Mansouri A, Friedmann DR, Thomas Roland J Jr, Kondziolka D

PMID: 27035174 DOI: 10.3171/2015.12.JNS151857

OBJECTIVE: A randomized trial that compares clinical outcomes following microsurgery (MS) or stereotactic radiosurgery (SRS) for patients with small- and medium-sized vestibular schwannomas (VSs) is impractical, but would have important implications for clinical decision making. A matched cohort analysis was conducted to evaluate clinical outcomes in patients treated with MS or SRS. **METHODS:** The records of 399 VS patients who were cared for by 2 neurosurgeons and 1 neurotologist between 2001 and 2014 were evaluated. From this data set, 3 retrospective matched cohorts were created to compare hearing preservation (21 matched pairs), facial nerve preservation (83 matched pairs), intervention-free survival, and complication rates (85 matched pairs) between cases managed with SRS and patients managed with MS. Cases were matched for age at surgery (\pm 10 years) and lesion size (\pm 0.1 cm). To compare hearing outcomes, cases were additionally matched for preoperative Class A hearing according to the American Academy of Otolaryngology-Head and Neck Surgery guidelines. To compare facial nerve (i.e., cranial nerve [CN] VII) outcomes, cases were additionally matched for preoperative House-Brackmann (HB) score. Investigators who were not involved with patient care reviewed the clinical and imaging records. The reported outcomes were as assessed at the time of the last follow-up, unless otherwise stated. **RESULTS:** The preservation of preoperative Class A hearing status was achieved in 14.3% of MS cases compared with 42.9% of SRS cases (OR 4.5; $p < 0.05$) after an average follow-up interval of 43.7 months and 30.3 months, respectively. Serviceable hearing was preserved in 42.8% of MS cases compared with 85.7% of SRS cases (OR 8.0; $p < 0.01$) at a median follow-up interval of 35.7 and 19.0 months for MS and SRS, respectively. There was no difference in the need for subsequent intervention (2 MS patients and 2 SRS patients). **CONCLUSIONS:** At this high-volume center, VS resection or radiosurgery for tumors \leq 2.8 cm in diameter was associated with low overall morbidity. The need for subsequent intervention was the same in both groups. SRS was associated with improved hearing and facial preservation rates and reduced morbidity, but with a shorter average follow-up period. Facial function was excellent in both groups. Since patients were not randomly selected for surgery, different clinical outcomes may be of different value to individual patients. Both anticipated medical outcomes and patient goals remain the drivers of treatment decisions.

[45] Stereotactic radiosurgery for vestibular schwannomas: average 10-year follow-up results focusing on long-term hearing preservation.

Journal of neurosurgery. 2016;125(Suppl 1):64-72

Watanabe S, Yamamoto M, Kawabe T, Koiso T, Yamamoto T, Matsumura A, Kasuya H

PMID: 27903183 DOI: 10.3171/2016.7.GKS161494

OBJECTIVE: The aim of this study was to reappraise long-term treatment

outcomes of stereotactic radiosurgery (SRS) for vestibular schwannomas (VSs). The authors used a database that included patients who underwent SRS with a unique dose-planning technique, i.e., partial tumor coverage designed to avoid excess irradiation of the facial and cochlear nerves, focusing on tumor control and hearing preservation. Clinical factors associated with post-SRS tumor control and long-term hearing preservation were also analyzed. **METHODS:** This institutional review board-approved, retrospective cohort study used the authors' prospectively accumulated database. Among 207 patients who underwent Gamma Knife SRS for VSs between 1990 and 2005, 183 (who were followed up for at least 36 post-SRS months) were studied. The median tumor volume was 2.0 cm³ (range 0.05-26.2 cm³). The median prescribed dose at the tumor periphery was 12.0 Gy (range 8.8-15.0 Gy; 12.0 Gy was used in 171 patients [93%]), whereas tumor portions facing the facial and cochlear nerves were irradiated with 10.0 Gy. As a result, 72%-99% of each tumor was irradiated with the prescribed dose. The mean cochlear doses ranged from 2.3 to 5.7 Gy (median 4.1 Gy). **RESULTS:** The median durations of imaging and audiometric follow-up were 114 months (interquartile range 73-144 months) and 59 months (interquartile range 33-109 months), respectively. Tumor shrinkage was documented in 110 (61%), no change in 48 (27%), and enlargement in the other 22 (12%) patients. A further procedure (FP) was required in 15 (8%) patients. Thus, the tumor growth control rate was 88% and the clinical control rate (i.e., no need for an FP) was 92%. The cumulative FP-free rates were 96%, 93%, and 87% at the 60th, 120th, and 180th post-SRS month, respectively. Six (3%) patients experienced facial pain, and 2 developed transient facial palsy. Serviceable hearing was defined as a pure tone audiogram result better than 50 dB. Among the 66 patients with serviceable hearing before SRS who were followed up, hearing acuity was preserved in 23 (35%). Actuarial serviceable hearing preservation rates were 49%, 24%, and 12% at the 60th, 120th, and 180th post-SRS month, respectively. On univariable analysis, only cystic-type tumor (HR 3.36, 95% CI 1.18-9.36; $p = 0.02$) was shown to have a significantly unfavorable association with FP. Multivariable analysis followed by univariable analysis revealed that higher age (\geq 65 years: HR 2.66, 95% CI 1.16-5.92; $p = 0.02$), larger tumor volume (\geq 8 cm³): HR 5.36, 95% CI 1.20-17.4; $p = 0.03$), and higher cochlear dose (mean cochlear dose $>$ 4.2 Gy: HR 2.22, 95% CI 1.07-4.77; $p = 0.03$) were unfavorable factors for hearing preservation. **CONCLUSIONS:** Stereotactic radiosurgery achieved good long-term results in this series. Tumor control was acceptable, and there were few serious complications in patients with small- to medium-sized VSs. Unfortunately, hearing preservation was not satisfactory. However, the longer the observation period, the more important it becomes to compare post-SRS hearing decreases with the natural decline in untreated cases.

[46] Acute clinical adverse radiation effects after Gamma Knife surgery for vestibular schwannomas.

Journal of neurosurgery. 2016;125(Suppl 1):73-82

Tuleasca C, George M, Faouzi M, Schiappacasse L, Leroy HA, Zeverino M, Daniel RT, Maire R, Levivier M

PMID: 27903185 DOI: 10.3171/2016.7.GKS161496

OBJECTIVE: Vestibular schwannomas (VSs) represent a common indication of Gamma Knife surgery (GKS). While most studies focus on the long-term morbidity and adverse radiation effects (AREs), none describe the acute clinical AREs that might appear on a short-term basis. These types of events are investigated, and their incidence, type, and outcomes are reported in the present paper.

METHODS: The included patients were treated between July 2010 and March 2016, underwent at least 6 months of follow-up, and presented with a disabling symptom during the first 6 months after GKS that affected their quality of life. The timing of appearance, as well as the type of main symptom and outcome, were noted. The prescribed dose was 12 Gy at the margin. **RESULTS:** Thirty-five (22%) of 159 patients who fulfilled the inclusion criteria had acute clinical AREs. The mean followup period was 30 months (range 6-49.2 months). The mean time of appearance was 37.9 days (median 31 days; range 3-110 days). In patients with de novo symptoms, the more frequent symptoms were vertigo ($n = 4$; 11.4%) and gait

disturbance (n = 3; 8.6%). The exacerbation of a preexisting symptom was more frequently related to hearing loss (n = 10; 28.6%), followed by gait disturbance (n = 7; 20%) and vertigo (n = 3, 8.6%). In the univariate logistic regression analysis, the following factors were statistically significant: age (p = 0.002; odds ratio [OR] 0.96), hearing at baseline by Gardner-Robertson (GR) class (p = 0.006; OR 0.21), pure tone average at baseline (p = 0.006; OR 0.97), and Koos grade at baseline (with Koos Grade I used as a reference) (for Koos Grade II, OR 0.17 and p = 0.002; for Koos Grade III, OR 0.42 and p = 0.05). The following were not statistically significant but showed a tendency toward significance: the number of isocenters (p = 0.06; OR 0.94) and the maximal dose received by the cochlea (p = 0.07; OR 0.74). Fractional polynomial regression analysis showed a nonlinear relationship between the outcome and the radiation dose rate (minimum reached at a cutoff of 2.5 Gy/minute) and the maximal vestibular dose (maximum reached at a cutoff of 8 Gy), but the small sample size precludes a detailed analysis of the former. The clinical acute AREs disappeared in 32 (91.4%) patients during the first 6 months after appearance. Permanent and somewhat disabling morbidity was found in 3 cases (1.9% from the whole series): 1 each with complete hearing loss (GR Class I before and V after), hemifacial spasm (persistent but alleviated), and dysgeusia. **CONCLUSIONS:** Acute effects after radiosurgery for VS are not rare. They concern predominantly de novo vertigo and gait disturbance and the exacerbation of preexistent hearing loss. In de novo vestibular symptoms, a vestibular dose of more than 8 Gy is thought to play a role. In most cases, none of these effects are permanent, and they will ultimately improve or disappear with steroid therapy. Permanent AREs remain very rare.

[47] Gamma Knife Radiosurgery as Primary Treatment for Large Vestibular Schwannomas: Clinical Results at Long-Term Follow-Up in a Series of 59 Patients.

World neurosurgery. 2016;95:487-501

Bailo M, Boari N, Franzin A, Gagliardi F, Spina A, Del Vecchio A, Gemma M, Bolognesi A, Mortini P

PMID: 27535636 DOI: 10.1016/j.wneu.2016.07.117

BACKGROUND: Gamma Knife radiosurgery (GKRS) represents a well-accepted treatment for small-medium vestibular schwannomas (VS); however, its application in larger VS is still controversial. **METHODS:** Among the 523 patients treated at our institution for VS between 2001 and 2010, we included 59 patients with a VS larger than 25 mm, treated by GKRS as primary treatment, not affected by neurofibromatosis type 2, and with a clinical follow-up of at least 36 months. Five patients underwent ventriculoperitoneal shunt placement before radiosurgery. Clinical follow-up (mean, 79.4 months) was obtained in all patients. Patients' age ranged from 24 to 85 years (mean, 63.8 years). Mean tumor volume was 5.98 cm³ (maximum, 14.3 cm³) and median marginal dose was 13 Gy. A statistical analysis was performed to correlate clinical outcome with tumor radiologic features, dose-planning parameters, and patients' characteristics. **RESULTS:** Tumor control was achieved in 98.3% of cases. At last follow-up, 86.4% of VS showed volume reduction. Recorded complications were 3 cases (5.1%) of new permanent facial nerve deficit, 4 cases (6.8%) of new or worsened trigeminal impairment, and 10 new cases (18.5%) of hydrocephalus requiring ventriculoperitoneal shunt. Larger tumor size was significantly associated with a subsequent ventricular enlargement. Overall, functional hearing preservation rate was 31.3% (66.7% among patients with Gardner-Robertson I). **CONCLUSIONS:** Surgical resection remains the primary approach for large VS with symptomatic brainstem compression. GKRS can be considered a safe and effective option in particular in patients who are not good candidates for surgery.

[48] Surgical salvage of recurrent vestibular schwannoma following prior stereotactic radiosurgery.

The Laryngoscope. 2016;126(11):2580-2586

Wise SC, Carlson ML, Tveiten OV, Driscoll CL, Myrseth E, Lund-Johansen M, Link MJ

PMID: 27107262 DOI: 10.1002/lary.25943

OBJECTIVES/HYPOTHESIS: To evaluate outcomes of salvage surgery for vestibular schwannoma (VS) that failed primary stereotactic radiosurgery (SRS).

METHODS: Case-control study of 37 patients who underwent surgical resection of sporadic VS following prior SRS at two tertiary academic referral centers between 2003 and 2015. A cohort of nonirradiated control subjects, matched according to tumor size, age, and treatment center, were used as comparison. **RESULTS:** Thirty-seven patients were included. The median time from radiation to surgical salvage was 36 months (range 9.6-153 months). Following tumor progression after SRS, 18 (49%) patients underwent gross total resection, 10 (27%) underwent near-total resection, and nine (24%) underwent subtotal resection. Postoperative complications following salvage surgery included one (3%) case of stroke, four (11%) cases of cerebrospinal fluid leak, and two (5%) cases of meningitis. Twenty-seven (73%) patients had good postoperative facial nerve outcome (House-Brackmann Score I-II) at long-term follow-up. There were no cases of tumor recurrence or regrowth after a median length of 26 months following microsurgical salvage (range 3-114 months). The rate of satisfactory postoperative facial nerve function was not different between study and control subjects (73% vs. 76%; P = 0.8); however, less-than-complete resection was utilized more frequently among previously irradiated patients (P = 0.01). **CONCLUSION:** Microsurgical salvage of VS following primary radiation therapy is challenging. Less-than-complete resection is required in a greater percentage of patients to preserve facial nerve integrity and prevent neurological complications. Long-term follow-up is needed to determine the risk of delayed progression following incomplete tumor removal. **LEVEL OF EVIDENCE:** 3b. *Laryngoscope*, 126:2580-2586, 2016.

[49] Hearing Preservation after Low-dose Gamma Knife Radiosurgery of Vestibular Schwannomas.

Neurologia medico-chirurgica. 2016;56(4):186-92

Horiba A, Hayashi M, Chernov M, Kawamata T, Okada Y

PMID: 26876903 DOI: 10.2176/nmc.0a.2015-0212

The objective of the retrospective study was to evaluate the factors associated with hearing preservation after low-dose Gamma Knife radiosurgery (GKS) of vestibular schwannomas performed according to the modern standards. From January 2005 to September 2010, 141 consecutive patients underwent such treatment in Tokyo Women's Medical University. Mean marginal dose was 11.9 Gy (range, 11-12 Gy). The doses for the brain stem, cranial nerves (V, VII, and VIII), and cochlea were kept below 14 Gy, 12 Gy, and 4 Gy, respectively. Out of the total cohort, 102 cases with at least 24 months follow-up were analyzed. Within the median follow-up of 56 months (range, 24-99 months) the crude tumor growth control was 92% (94 cases), whereas its actuarial rate at 5 years was 93%. Out of 49 patients with serviceable hearing on the side of the tumor before GKS, 28 (57%) demonstrated its preservation at the time of the last follow-up. No one evaluated factor, namely Gardner-Robertson hearing class before irradiation, Koos tumor stage, extension of the intrameatal part of the neoplasm up to fundus, nerve of tumor origin, presence of cystic changes in the neoplasm, and cochlea dose demonstrated statistically significant association with preservation of the serviceable hearing after radiosurgery. In conclusion, GKS of vestibular schwannomas performed according to the modern standards of treatment permits to preserve serviceable hearing on the side of the tumor in more than half of the patients. The actual causes of hearing deterioration after radiosurgery remain unclear.

[50] Gamma Knife radiosurgery for vestibular schwannomas: evaluation of tumor control and its predictors in a large patient cohort in The Netherlands.

Journal of neurosurgery. 2016;124(6):1619-26

Klijn S, Verheul JB, Beute GN, Leenstra S, Mulder JJ, Kunst HP, Hanssens PE

PMID: 26430848 DOI: 10.3171/2015.4.JNS142415

OBJECTIVE: The authors of this study sought to assess tumor control and complication rates in a large cohort of patients who underwent Gamma Knife radiosurgery (GKRS) for vestibular schwannoma (VS) and to identify predictors of tumor control. **METHODS:** The records of 420 patients treated with GKRS for

VS with a median marginal dose of 11 Gy were retrospectively analyzed. Patients with neurofibromatosis Type 2 or who had undergone treatment for VS previously were excluded. The authors assessed tumor control and complication rates with chart review and used the Cox proportional hazards model to identify predictors of tumor control. Preservation of serviceable hearing, defined as Gardner-Robertson Class I-II, was evaluated in a subgroup of 71 patients with serviceable hearing at baseline and with available follow-up audiograms. **RESULTS:** The median VS tumor volume was 1.4 cm³, and the median length of follow-up was 5.1 years. Actuarial 5- and 10-year tumor control rates were 91.3% and 84.8%, respectively. Only tumor volume was a statistically significant predictor of tumor control rate. The tumor control rate decreased from 94.1% for tumors smaller than 0.5 cm³ to 80.7% for tumors larger than 6 cm³. Thirteen patients (3.1%) had new or increased permanent trigeminal nerve neuropathy, 4 (1.0%) had new or increased permanent facial weakness, and 5 (1.2%) exhibited new or increased hydrocephalus requiring a shunting procedure. Actuarial 3-year and 5-year hearing preservation rates were 65% and 42%, respectively. **CONCLUSIONS:** The 5-year actuarial tumor control rate of 91.3% in this cohort of patients with VS compared slightly unfavorably with the rates reported in other large studies, but the complication and hearing preservation rates in this study were similar to those reported previously. Various factors may contribute to the observed differences in reported outcomes. These factors include variations in treatment indication and in the definition of treatment failure, as well as a lack of standardization of terminology and of evaluation of complications. Last, differences in dosimetric variables may also be an explanatory factor.

[51] Predictors of Trigeminal Neuropathy After Radiosurgery for Vestibular Schwannomas.

International journal of radiation oncology, biology, physics. 2016;95(2):721-8
Senova S, Aggad M, Golmard JL, Hasboun D, Lamproglou I, Jenny C, Cornu P, Mazon JJ, Valery CA
PMID: 26960748 DOI: 10.1016/j.ijrobp.2016.01.012

PURPOSE: To analyze the relationship between dosimetric characteristics and symptoms related to trigeminal neuropathy (TN) observed after radiosurgery (RS) for vestibular schwannomas (VS); to propose guidelines to optimize planification in VS RS regarding TN preservation; and to detail the mechanism of TN impairment after VS RS. **METHODS AND MATERIALS:** One hundred seventy-nine patients treated between 2011 and 2013 for VS RS and without trigeminal impairment before RS were included in a retrospective study. Univariate and multivariate analyses were performed to determine predictors of TN among characteristics of the patients, the dosimetry, and the VS. **RESULTS:** There were 20 Koos grade 1, 99 grade 2, 57 grade 3, and 3 grade 4. Fourteen patients (7.8%) presented a transitory or permanent TN. Between the patients with and without TN after VS RS, there was no significant difference regarding dosimetry or VS volume itself. Significant differences (univariate analysis $P < .05$, Mann-Whitney test) were found for parameters related to the distal portion of the trigeminal nerve: total integrated dose, maximum dose, mean dose, volume of the Vth nerve (Volv), and volume of the Vth nerve receiving at least 11 Gy (VolVcist >11 Gy), but also for maximal dose to the Vth nerve nucleus and intra-axial portion (Dose maxVax). After multivariate analysis, the best model predicting TN included VolVcist >11 Gy ($P = .0045$), Dose maxVax ($P = .0006$), and Volv ($P = .0058$). The negative predictive value of this model was 97%. **CONCLUSIONS:** The parameters VolVcist >11 Gy, Dose maxVax, and Volv should be checked when designing dosimetry for VS RS.

[52] Early Radiosurgery Improves Hearing Preservation in Vestibular Schwannoma Patients With Normal Hearing at the Time of Diagnosis.

International journal of radiation oncology, biology, physics. 2016;95(2):729-34
Akpınar B, Mousavi SH, McDowell MM, Niranjana A, Faraji AH, Flickinger JC, Lunsford LD
PMID: 26975929 DOI: 10.1016/j.ijrobp.2016.01.019

PURPOSE: Vestibular schwannomas (VS) are increasingly diagnosed in patients with normal hearing because of advances in magnetic resonance imaging. We

sought to evaluate whether stereotactic radiosurgery (SRS) performed earlier after diagnosis improved long-term hearing preservation in this population. **METHODS AND MATERIALS:** We queried our quality assessment registry and found the records of 1134 acoustic neuroma patients who underwent SRS during a 15-year period (1997-2011). We identified 88 patients who had VS but normal hearing with no subjective hearing loss at the time of diagnosis. All patients were Gardner-Robertson (GR) class I at the time of SRS. Fifty-seven patients underwent early (≤ 2 years from diagnosis) SRS and 31 patients underwent late (> 2 years after diagnosis) SRS. At a median follow-up time of 75 months, we evaluated patient outcomes. **RESULTS:** Tumor control rates (decreased or stable in size) were similar in the early (95%) and late (90%) treatment groups ($P = .73$). Patients in the early treatment group retained serviceable (GR class I/II) hearing and normal (GR class I) hearing longer than did patients in the late treatment group (serviceable hearing, $P = .006$; normal hearing, $P < .0001$, respectively). At 5 years after SRS, an estimated 88% of the early treatment group retained serviceable hearing and 77% retained normal hearing, compared with 55% with serviceable hearing and 33% with normal hearing in the late treatment group. **CONCLUSIONS:** SRS within 2 years after diagnosis of VS in normal hearing patients resulted in improved retention of all hearing measures compared with later SRS.

[53] Safety and Efficacy of Gamma Knife Radiosurgery for the Management of Koos Grade 4 Vestibular Schwannomas.

Neurosurgery. 2016;78(4):521-30
Iorio-Morin C, AlSubaie F, Mathieu D
PMID: 26606668 DOI: 10.1227/NEU.0000000000001154

BACKGROUND: Gamma Knife radiosurgery (GKRS) is commonly used in treating small vestibular schwannomas; however, its use for larger vestibular schwannomas is still controversial. **OBJECTIVE:** To assess the long-term safety and efficacy of treating eligible Koos grade 4 vestibular schwannomas with GKRS. **METHODS:** We conducted a single-center, retrospective evaluation of patient undergoing GKRS for Koos grade 4 vestibular schwannomas. We evaluated clinical, imaging, and treatment characteristics and assessed treatment outcome. Inclusion criteria were tumor size of ≥ 4 cm and follow-up of at least 6 months. Patients with neurofibromatosis type 2 were excluded. Primary outcomes measured were tumor control rate, hearing and facial function preservation rate, and complications. All possible factors were analyzed to assess clinical significance. **RESULTS:** Sixty-eight patients met inclusion criteria. Median follow-up was 47 months (range, 6-125 months). Baseline hearing was serviceable in 60%. Median tumor volume at radiosurgery was 7.4 cm (range, 4-19 cm). The median marginal dose used was 12 Gy at the 50% isodose line. Actuarial tumor control rates were 95% and 92% at 2 and 10 years, respectively. Actuarial serviceable hearing preservation rates were 89% and 49% at 2 and 5 years, respectively. Facial nerve preservation was 100%. Clinical complications included balance disturbance (11%), facial pain (10%), facial numbness (5%), and tinnitus (10%). Most complications were mild and transient. Hydrocephalus occurred in 3 patients, requiring ventriculoperitoneal shunt insertion. Larger tumor size was significantly associated with persisting symptoms post-treatment. **CONCLUSION:** Patients with Koos grade 4 vestibular schwannomas and minimal symptoms can be treated safely and effectively with GKRS.

[54] Multisession Radiosurgery for Hearing Preservation.

Seminars in radiation oncology. 2016;26(2):105-11
Rashid A, Karam SD, Rashid B, Kim JH, Pang D, Jean W, Grimm J, Collins SP
PMID: 27000506 DOI: 10.1016/j.semradonc.2015.11.004
Clinically relevant dose-tolerance limits with reliable estimates of risk in 1-5 fractions for cochlea are still unknown. Timmermans limits from the October 2008 issue of *Seminars in Radiation Oncology* have served as the basis for clinical practice, augmented by updated constraints in TG-101 and QUANTEC, but the corresponding estimates of risk have not yet been well-reported. A total of 37 acoustic neuroma CyberKnife cases from Medstar Georgetown University Hospital treated in 3 or 5 fractions were combined with single-fraction Gamma Knife data

from the 69 cases in Timmer 2009 to form an aggregate dataset of 106 cochlea cases treated in 1-5 fractions. Probit dose-response modeling was performed in the DVH Evaluator software to estimate normal tissue complication probability. QUANTEC recommends keeping single-fraction maximum dose to the cochlea less than 14Gy to maintain less than 25% risk of serviceable hearing loss, and our 17.9% risk estimate for 14Gy in 1 fraction is within their predicted range. In 5 fractions, our estimate of the Timmerman 27.5Gy maximum cochlea dose limit was 17.4%. For cases in which lower risk is required, the Timmerman 12Gy in 1 fraction and the TG-101 limit of 25Gy in 5 fractions had an estimated risk level of 11.8% and 13.8%, respectively. High-risk and low-risk dose tolerance with risk estimates in 1-5 fractions are all presented.

2015

[55] Long-term Auditory Symptoms in Patients With Sporadic Vestibular Schwannoma: An International Cross-Sectional Study.

Neurosurgery. 2015;77(2):218-27; discussion 227

Tveiten OV, Carlson ML, Goplen F, Vassbotn F, Link MJ, Lund-Johansen M
PMID: 25850598 DOI: 10.1227/NEU.0000000000000760

BACKGROUND: There are limited data on the long-term auditory symptoms in patients with sporadic small- and medium-sized vestibular schwannoma (VS). The initial treatment strategy for VS is controversial. **OBJECTIVE:** To characterize auditory symptoms in a large cohort of patients with VS. **METHODS:** Patients with ≤ 3 cm VS who underwent primary microsurgery, gamma knife surgery, or observation between 1998 and 2008 at 2 independent hospitals were identified. Clinical data were extracted from existing VS databases. At a mean time of 7.7 years after initial treatment, patients were surveyed via mail with the use of the Hearing Handicap Inventory for Adults (HHIA) and the Tinnitus Handicap Inventory. **RESULTS:** The response rate was 79%; a total of 539 respondents were analyzed. Overall, the hearing prognosis was poor, because more than 75% of all patients had nonserviceable hearing at the last clinical follow-up. Good baseline hearing proved to be a strong predictor for maintained serviceable hearing. Treatment modality was independently associated with both audiometric outcome and HHIA results. Active treatment with microsurgery or gamma knife surgery did not appear to be protective, because patients who were observed had the greatest probability of durable hearing. Patients in the surgical series had the greatest hearing loss. Tinnitus Handicap Inventory results were less predictable. The only predictors of tinnitus handicap were age and HHIA score. **CONCLUSION:** The overall prognosis for hearing in sporadic VS is poor regardless of treatment strategy. Treatment modality was an independent predictor of hearing status; observation was associated with the highest rate of hearing preservation.

[56] Functional Preservation After Planned Partial Resection Followed by Gamma Knife Radiosurgery for Large Vestibular Schwannomas.

World neurosurgery. 2015;84(2):292-300

Iwai Y, Ishibashi K, Watanabe Y, Uemura G, Yamanaka K
PMID: 25790872 DOI: 10.1016/j.wneu.2015.03.012

OBJECTIVE: The treatment goal for vestibular schwannomas (VS) has been changed from total removal of the tumor to functional preservation with long-term tumor growth control. The small- to medium-sized VS can be treated by stereotactic radiosurgery, but large VS require surgical decompression for the relief of cerebellar dysfunction and increased intracranial pressure. We have been performing planned partial surgical resections followed by gamma knife radiosurgery (GKS) for large VS. Here, we evaluate a recent series of such cases from the standpoint of functional outcomes. **METHODS:** From January 2000 to May 2013, we treated 40 patients with large unilateral VS (maximum tumor diameter at least 25 mm) with planned partial tumor removal followed by GKS

for functional preservation. The median maximum diameter of the tumors was 32.5 mm (range 25-52 mm). All patients underwent surgery via the retrosigmoid approach, and tumors situated on the ventral and in the internal auditory canal intentionally were not removed, thus preserving cranial nerve functions. GKS was performed 1-12 months after surgical resection (median interval 3 months). The median tumor volume at GKS was 3.3 cm³ (range 0.4-10.4 cm³) and the median prescribed dose was 12 Gy (range 10-12 Gy). The median follow-up period after GKS was 65 months (18-156 months). **RESULTS:** At the final follow-up, facial nerve preservation (House-Brackmann grade I-II) was achieved in 38 patients (95%; House-Brackmann grade I: 92.5%, II: 2.5%). Among the 14 patients with preoperative pure tone average (PTA) less than 50 dB, 6 of them (42.9%) maintained PTA less than 50 dB at the last follow-up. Two patients improved from severe hearing loss to PTA less than 50 dB (1 patient after surgery and 1 patient one and half years after GKS). Five- and 10-year tumor growth control occurred in 86% of patients. Four patients (10%) required salvage surgery; the predictive factor was tumor volume greater than 6 cm³ at GKS (P = 0.01). **CONCLUSIONS:** Planned partial removal of large VS followed by GKS achieved a high rate of facial nerve and hearing preservation. To achieve long-term tumor growth control, the tumor volume at GKS after planned partial surgical resection should be smaller than 6 cm³. Our results revealed that patients with hearing preservation postoperatively have a chance of maintaining hearing function, even though the possibility exists of deterioration by long-term follow-up after surgical intervention and GKS. Furthermore, some patients with severe hearing loss before treatment have the chance of hearing improvement, even those with large VS.

[57] Growth of Primary and Remnant Vestibular Schwannomas: A Three-Year Follow-Up Study.

World neurosurgery. 2015;83(6):937-44

Tomita Y, Tosaka M, Aihara M, Horiguchi K, Yoshimoto Y
PMID: 25701770 DOI: 10.1016/j.wneu.2015.02.005

OBJECTIVE: Vestibular schwannomas (VSs) are benign, slowly growing tumors. The management strategy, however, remains unclear for both primary VS and remnant VS after subtotal or partial resection. In this study, we analyzed the radiographical tumor growth to elucidate factors possibly predicting growth or regrowth of their tumors. **METHODS:** We retrospectively analyzed the data of 76 patients with diagnoses of VS at a single tertiary academic referral center. The primary VS group consisted of 43 patients with conservative management, and the remnant VS group included 33 patients with tumor remnant after surgery. All patients were followed up with serial magnetic resonance imaging without intervention. The primary end point in this study was significant tumor growth at the end of the 3-year follow-up period. **RESULTS:** Multivariate analysis revealed that remnant VS was less likely to grow than primary VS (odds ratio: 0.27, 95% confidence interval: 0.09-0.84). Tumor volume was correlated with tumor growth; larger tumors grew more frequently than small tumors in both primary and remnant VS groups with marginal (P = 0.05) and definite (P = 0.007) significance, respectively. The receiver operating characteristic curves plotted for tumor growth identified the optimum cutoff points of tumor volumes with greater sensitivity and specificity for remnant VS than for primary VS (sensitivity: 80% vs. 59%, specificity: 87% vs. 76%, respectively). **CONCLUSIONS:** Small remnant VS after surgery could be conservatively managed without additional treatment, and relatively large remnant VS should be followed up with close serial imaging or might be a possible candidate for radiosurgery during the early postoperative period.

[58] Hearing preservation up to 3 years after gamma knife radiosurgery for Gardner-Robertson class I patients with vestibular Schwannomas.

Neurosurgery. 2015;76(5):584-90; discussion 590-1

Mousavi SH, Kano H, Faraji AH, Gande A, Flickinger JC, Niranjana A, Monaco E 3rd, Lunsford LD
PMID: 25706519 DOI: 10.1227/NEU.0000000000000674

BACKGROUND: Vestibular schwannoma patients with Gardner-Robertson (GR) class I hearing seek to maintain high-level hearing whenever possible.

OBJECTIVE: To evaluate hearing outcomes at 2 to 3 years in GR class I patients who underwent Gamma Knife radiosurgery (GKRS). **METHODS:** Sixty-eight patients with GR class I hearing were identified between 2006 and 2009. Twenty-five patients had no subjective hearing loss (group A) and 43 patients reported subjective hearing loss (group B) before GKRS. The median tumor volume (1 cm) and tumor margin dose (12.5 Gy) were the same in both groups. **RESULTS:** Serviceable hearing retention rates (GR grade I or II) were 100% for group A compared with 81% at 1 year, 60% at 2 years, and 57% at 3 years after GKRS for group B patients. Group A patients had significantly higher rates of hearing preservation in either GR class I ($P < .001$) or GR class II ($P < .001$). Patients with a pure tone average (PTA) <15 dB before GKRS had significantly higher rates of preservation of GR class I or II hearing. **CONCLUSION:** At 2 to 3 years after GKRS, patients without subjective hearing loss or a PTA <15 dB had higher rates of grade I or II hearing preservation. Modification of the GR hearing classification into 2 groups of grade I hearing (group A, those with no subjective hearing loss and a PTA <15 dB; and group B, those with subjective hearing loss and a PTA >15 dB) may be useful to help predict hearing preservation rates at 2 to 3 years after GKRS.

[59] Modern Gamma Knife radiosurgery of vestibular schwannomas: treatment concept, volumetric tumor response, and functional results.

Neurosurg Rev. 2015 Apr;38(2):309-18; discussion 318.

Lipski SM, Hayashi M, Chernov M, Levivier M, Okada Y
PMID: 25519767 DOI: 10.1007/s10143-014-0601-3

The objective of the present study was longitudinal evaluation of the volumetric tumor response and functional results after Gamma Knife radiosurgery of vestibular schwannomas, performed according to the modern standards of treatment. From October 2003 to September 2007, 133 consecutive patients with vestibular schwannomas were treated according to the concept of robotic Gamma Knife microradiosurgery, which is based on precise irradiation of the lesion, sparing adjacent structures, and delivery of the high radiation energy to the target. Multiple small-sized isocenters located within the border of the neoplasm were applied. The mean marginal dose was 11.5 Gy (range, 11-12 Gy). In total, 126 cases with a minimum posttreatment follow-up of 2 years (range, 2-7 years; median, 4 years) were analyzed. Temporary enlargement was noted in 25% of tumors at 6 months after radiosurgery. At 3 years of follow-up, tumor shrinkage, stabilization, and increase in volume were marked in 73%, 23%, and 4% of cases, respectively. All progressing lesions spontaneously stabilized later on and did not require additional management. In 3% of patients, transitory impairment of the facial nerve function was marked; however, neither its permanent dysfunction nor trigeminal neuropathy attributed to radiosurgery was noted. Impairment of hearing compared to its pretreatment level was revealed in 4%, 12%, 13%, and 16% of patients at 6 months, 1 year, 2 years, and 3 years after radiosurgery, respectively, and this trend was statistically significant ($P = 0.0042$). Overall, 77% of patients with serviceable hearing before treatment preserved it 3 years thereafter. In conclusion, modern Gamma Knife radiosurgery provides effective and safe management of vestibular schwannomas. Nevertheless, possible temporary tumor enlargement, delay of its growth arrest, transient dysfunction of the cranial nerves, and gradual deterioration of hearing after irradiation should be always taken into consideration.

2014

[60] Gamma Knife radiosurgery following subtotal resection of vestibular schwannoma.

Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia. 2014;21(12):2077-82

Brokinkel B, Sauerland C, Holling M, Ewelt C, Horstmann G, van Eck AT, Stummer W

PMID: 25065850 DOI: 10.1016/j.jocn.2014.03.037

During treatment of large vestibular schwannomas, incomplete resection (IR) followed by Gamma Knife surgery (GKS; Elekta AB, Stockholm, Sweden) possibly offers tumor growth control and good clinical outcome, and is being discussed as an alternative to complete tumor removal with its inherent risks, especially for facial nerve function. However, available data for this concept are limited due to the small number of published studies. To analyze the effects of combined therapy in a larger cohort, we reviewed the currently available data. Six studies comprising 159 patients with a tumor diameter of at least 2 cm were included (median volume 19.95 cm³) in four studies, n=137). GKS was performed on average 6 months postoperatively with a mean marginal dose of 11.88 Gy (mean target volume 4.42 cm³, mean diameter 18.45 mm). Preoperatively facial nerve function was serviceable (House and Brackmann Grades I+II) in 158 of 159 patients (99.4%) and in 125 of 151 patients (82.8%, 95% confidence interval [CI] 76-88%) postoperatively. Hearing was serviceable in 29 of 151 patients (19.2%) preoperatively and in 16 of 79 patients postoperatively (20.2%, 95%CI 12-31%). Within a mean follow-up time of 50 months (range 12-102 months), facial nerve function and hearing after IR remained serviceable in 142 of 151 (94.0%, 95%CI 89-97%) and 15 of 129 patients (11.6%, 95%CI 7-18%). Tumor growth control was achieved in 149 of 159 patients (93.8%). Six patients were subjected to repeated therapy. Minimal complications were reported for microsurgery and GKS. Combined therapy was shown to be beneficial regarding both tumor control and adverse side effects among all analyzed studies.

[61] Gamma Knife radiosurgery for vestibular schwannoma: clinical results at long-term follow-up in a series of 379 patients.

Journal of neurosurgery. 2014;121 Suppl:123-42

Boari N, Bailo M, Gagliardi F, Franzin A, Gemma M, del Vecchio A, Bolognesi A, Picozzi P, Mortini P

PMID: 25434946 DOI: 10.3171/2014.8.GKS141506

OBJECTIVE: Since the 1990 s, Gamma Knife radiosurgery (GKRS) has become the first-line treatment option for small- to medium-size vestibular schwannomas (VSs), especially in patients without mass effect-related symptoms and with functional hearing. The aim of this study was to assess the safety and efficacy of GKRS, in terms of tumor control, hearing preservation, and complications, in a series of 379 consecutive patients treated for VS. **METHODS:** Of 523 patients treated at the authors' institution for VS between 2001 and 2010, the authors included 379 who underwent GKRS as the primary treatment. These patients were not affected by Type 2 neurofibromatosis and had clinical follow-up of at least 36 months. Clinical follow-up (mean and median 75.7 and 69.5 months, respectively) was performed for all patients, whereas audiometric and quantitative radiological follow-up examinations were obtained for only 153 and 219 patients, respectively. The patients' ages ranged from 23 to 85 years (mean 59 years). The mean tumor volume was 1.94 +/- 2.2 cm³ (median 1.2 cm³, range 0.013-14.3 cm³), and the median margin dose was 13 Gy (range 11-15 Gy). Parameters considered as determinants of the clinical outcome were long-term tumor control, hearing preservation, and complications. A statistical analysis was performed to correlate clinical outcomes with the radiological features of the tumor, dose-planning parameters, and patient characteristics. **RESULTS:** Control of the tumor with GKRS was achieved in 97.1% of the patients. In 82.7% of the patients, the tumor volume had decreased at the last follow-up, with a mean relative reduction of 34.1%. The rate of complications was very low, with most consisting of a transient worsening of preexisting symptoms. Patients who had vertigo, balance disorders, or facial or trigeminal impairment usually experienced a complete or at least significant symptom relief after treatment. However, no significant improvement was observed in patients previously reporting tinnitus. The overall rate of preservation of functional hearing at the long-term follow-up was 49%; in patients with hearing classified as Gardner-Robertson (GR) Class I, this value was 71% and reached 93% among cases of GR Class I hearing in patients younger than 55 years. **CONCLUSIONS:** Gamma Knife radiosurgery is a safe and effective treatment for VS, achieving tumor control in 97.1% of cases and resulting in a very low morbidity

rate. Younger GR Class I patients had a significantly higher probability of retaining functional hearing even at the 10-year follow-up; for this reason, the time between symptom onset, diagnosis, and treatment should be shortened to achieve better outcomes in functional hearing preservation.

[62] Radiosurgery as treatment for acoustic neuroma. Ten years' experience.

Acta otorinolaringologica espanola. 2014;65(6):327-31

Llopez Carratala I, Escorihuela Garcia V, Orts Alborch M, de Paula Vernetta C, Marco Algarra J

PMID: 24846561 DOI: 10.1016/j.otorri.2014.03.003

INTRODUCTION AND OBJECTIVE: The acoustic neuroma is a benign tumour that usually affects the vestibular portion of the vestibulocochlear nerve. It represents 8% of all intracranial tumours and 80% of those arising at the cerebellopontine angle. There are 3 treatment options: microsurgery (the technique of choice), radiosurgery and observation. The objective of the study was to evaluate the results and side effects obtained using radiosurgery as treatment for acoustic neuroma. **MATERIAL AND METHODS:** We performed a review of all patients treated with radiosurgery (Gamma Knife and linear accelerator) at doses of 1200-1300 cGy for unilateral acoustic neuroma in our hospital from January 1999 until January 2010. In all patients we evaluated the overall state, tumour growth control rate (tumour smaller or remaining the same size), the involvement of v and vii cranial nerves and central nervous system disorders. We also assessed follow-up time and changes in hearing thresholds after radiosurgery. **RESULTS:** From a total of 35 patients studied, with a mean age of 58.29 years and lacking statistically significant differences in gender, the tumour growth control rate was over 90%. The main reason for visit (65.71%) was unilateral and progressive hearing loss. After treatment, 34.28% of patients had hearing loss. The involvement of the cranial nerves (v-vii) was transitory in 100% of cases. Gamma Knife radiosurgery was administered in 82.85% of patients. **CONCLUSION:** Although microsurgery is the treatment of choice for acoustic neuroma, we consider radiosurgery as a valid alternative in selected patients (elderly, comorbidity, small tumour size and sensorineural hearing loss, among others).

[63] Long-term outcome of gamma knife radiosurgery for vestibular schwannoma.

Journal of neurological surgery. Part B, Skull base. 2014;75(4):273-8

Bir SC, Ambekar S, Bollam P, Nanda A

PMID: 25093151 DOI: 10.1055/s-0034-1371525

OBJECTIVE: We evaluated the long-term outcome of vestibular schwannoma (VS) treated with gamma knife radiosurgery (GKRS) as a primary treatment as well as an adjunct therapy. **MATERIALS AND METHODS:** We performed a retrospective review (2000-2012) of 82 patients with VS who received GKRS. Of 82 patients, 20 patients with prior resection received GKRS treatment as an adjunct therapy. The remainder of the patients (62) received GKRS as a primary treatment. **RESULTS:** GKRS for VS showed significant variations in tumor growth control (decreased in 44 patients [54%], arrested growth in 30 patients [36%], and increased tumor size in 8 patients [10%]). Progression-free survival rates after GKRS at 3, 5, and 10 years were 98%, 95%, and 95%, respectively. Hearing, facial nerve function, and Karnofsky performance scale were significantly improved after GKRS compared with pretreated status (79 versus 90). Two patients (2.5%) required resection again due to tumor progression and worsening of signs and symptoms. Conclusion Long-term follow-up demonstrated that GKRS offers a high rate of tumor control, preservation of multiple nerve functions, and a good quality of life in both new and recurrent patients with VS.

[64] Identifying predictors of early growth response and adverse radiation effects of vestibular schwannomas to radiosurgery.

PLoS one. 2014;9(10):e110823

Larjani S, Monsalves E, Pebdani H, Krischek B, Gentili F, Cusimano M, Laperriere N, Hayhurst C, Zadeh G

PMID: 25337892 DOI: 10.1371/journal.pone.0110823

PURPOSE: To determine whether pre-treatment growth rate of vestibular schwannomas (VS) predict response to radiosurgery. **METHODS:** A retrospective review of a prospectively maintained database of all VS patients treated with 12Gy prescription dose between September 2005 and June 2011 at our institution using the Leksell Model 4C Gamma Knife Unit was conducted. Patients who had a minimum of 12-months clinical and radiological assessment before and after radiosurgery were included in this study. Tumor growth rates were calculated using specific growth rate (SGR). Tumor volumes were measured on FIESTA-MRI scans using ITK-SNAP v2.2. **RESULTS:** Following radiosurgery, twenty-seven (42.9%) patients showed a significant decrease in volume after one year, twenty-nine (46.0%) stabilized, and seven (11.1%) continued to grow. There was no correlation between VS pre-treatment SGRs with post-treatment SGRs ($p = 0.34$), and incidence of adverse radiation effects (ARE). The reduction in tumors' SGRs after radiosurgery was proportional to pre-treatment SGRs, although this correlation was not statistically significant ($p = 0.19$). Analysis of risk factors revealed a positive correlation between post-treatment SGRs and incidence of non-auditory complications, most of which were attributed to ARE ($p = 0.047$). **CONCLUSION:** Pre-treatment growth rate of VS does not predict tumor response to radiosurgery or incidence of ARE. VS with higher SGRs post-radiosurgery are more likely to experience ARE.

[65] How to distinguish tumor growth from transient expansion of vestibular schwannomas following Gamma Knife radiosurgery.

Acta neurochirurgica. 2014;156(6):1121-3

Mindermann T, Schlegel I

PMID: 24682634 DOI: 10.1007/s00701-014-2063-3

BACKGROUND: Typically, vestibular schwannomas (VS) react to Gamma Knife radiosurgery (GKRS) with a transient increase of tumor volume owed to tumor swelling at about 6 months followed by a reduction of tumor volume owed to tumor shrinkage at about 18 months. It is important to distinguish this transient tumor expansion (TTE) from tumor growth. We undertook this study to see if there is a typical time interval in the follow-up of VS following GKRS, which may indicate tumor growth rather than TTE. **METHODS:** We retrospectively reviewed the patient charts of patients who underwent GKRS for unilateral sporadic VS at the Gamma Knife Center Zurich from 1994-2009 and who were treated by J. Siegfried or one of the authors (TM). Tumor progression was defined as an increase of tumor volume of $\geq 20\%$ as compared to the initial tumor volume at the earliest 2 years following GKRS. This time interval of ≥ 2 years was chosen in order to distinguish TTE from genuine tumor progression. Whenever tumor enlargement was suspected on follow-up MRI at ≥ 2 years following GKRS, tumor volumes were measured using custom software. **RESULTS:** From 1994-2009, 235 patients underwent GKRS in Zurich for unilateral sporadic VS. Tumor progression with a volume increase of $\geq 20\%$ occurred in 21/235 (8.9%) patients at 3.4 \pm 0.9 years following GKRS. Seventeen out of 235 (7%) patients had a clinically relevant tumor progression requiring microsurgery or repeat radiosurgery. **CONCLUSIONS:** According to our data, time may be a good parameter distinguishing tumor progression due to tumor growth from TTE due to tumor swelling in VS following GKRS. Tumor growth seems to occur at about 3-4 years following GKRS for VS as opposed to TTE, which seems to be present at about 6-18 months following GKRS for VS.

[66] Significance of cochlear dose in the radiosurgical treatment of vestibular schwannoma: controversies and unanswered questions.

Neurosurgery. 2014;74(5):466-74; discussion 474

Jacob JT, Carlson ML, Schiefer TK, Pollock BE, Driscoll CL, Link MJ

PMID: 24476904 DOI: 10.1227/NEU.0000000000000299

BACKGROUND: Cochlear dose has been identified as a potentially modifiable contributor to hearing loss after stereotactic radiosurgery (SRS) for vestibular schwannoma (VS). **OBJECTIVE:** To evaluate the association between computed tomography-based volumetric cochlear dose and loss of serviceable hearing

after SRS, to assess intraobserver and interobserver reliability when determining modiolar point dose with the use of magnetic resonance imaging and computed tomography, and to discuss the clinical significance of the cochlear dose with regard to radiosurgical planning strategy. **METHODS:** Patients with serviceable pretreatment hearing who underwent SRS for sporadic VS between the use of Gamma Knife Perfexion were studied. Univariate and multivariate associations with the primary outcome of time to non-serviceable hearing were evaluated.

RESULTS: A total of 105 patients underwent SRS for VS during the study period, and 59 (56%) met study criteria and were analyzed. Twenty-one subjects (36%) developed non-serviceable hearing at a mean of 2.2 years after SRS (SD, 1.0 years; median, 2.1 years; range 0.6-3.8 years). On univariate analysis, pretreatment pure tone average, speech discrimination score, American Academy of Otolaryngology-Head and Neck Surgery hearing class, marginal dose, and mean dose to the cochlear volume were statistically significantly associated with time to non-serviceable hearing. However, after adjustment for baseline differences, only pretreatment pure tone average was statistically significantly associated with time to non-serviceable hearing in a multivariable model. **CONCLUSION:** Cochlear dose is one of many variables associated with hearing preservation after SRS for VS. Until further studies demonstrate durable tumor arrest with reduced dose protocols, routine tumor dose planning should not be modified to limit cochlear dose at the expense of tumor control.

[67] Long-term quality of life and tumour control following gamma knife radiosurgery for vestibular schwannoma.

Acta neurochirurgica. 2014;156(2):389-96

Wangerid T, Bartek J Jr, Svensson M, Forander P

PMID: 24193890 DOI: 10.1007/s00701-013-1924-5

INTRODUCTION: Gamma knife radiosurgery (GKRS) has for the last decades been an established treatment option for patients with small- or medium-sized vestibular schwannomas (VS), although little data is reported on long-term outcome regarding quality of life (QOL) and tumour control in this patient category. The objective of this study was to investigate long-term QOL and tumour control in GKRS-treated VS patients at our institution. **METHODS:** Data was reviewed from a consecutive cohort of 128 patients, 62 men and 66 women, diagnosed with VS and treated with GKRS at Karolinska University Hospital between 1997 and 2003. Patients previously treated for VS, patients from abroad, and patients with neurofibromatosis were excluded from the study. Median age at the time of treatment was 66 years (range 23-89), with a median follow-up time of 104 months (range 11-165) and radiological median follow-up of 86 months (range 5-170). Five patients were lost to follow-up. **RESULTS:** Data on QOL (EQ-5D score) was obtained in 90 % (98/109) of all cases at the end of follow-up, showing low morbidity and a high QOL with median index of 0.91 (max. score 1.0) in these patients. Tumour control was achieved in 92 % (118/128) of patients after a single GKRS treatment. Ten patients had loss of tumour control, either radiologically seen as growth progression, or due to the need for salvage treatment. Neither pre-treatment growth of the vestibular schwannoma, or a large tumour size (Koos grade 3 & 4) was correlated with a higher degree of treatment failure ($p = 0.695$ and $p = 0.647$, respectively). There was no difference in tumour control in young (<60 y/o) vs. elderly (≥ 60 y/o) patients ($p = 0.167$). **CONCLUSION:** We report a high QOL and low morbidity at long-term follow-up after GKRS treatment in VS patients. Furthermore, a high tumour control rate was achieved independent of tumour size, patient age or pre-treatment evidence of tumour growth.

[68] Change in tinnitus after treatment of vestibular schwannoma: microsurgery vs. gamma knife radiosurgery.

Yonsei medical journal. 2014;55(1):19-24

Park SH, Oh HS, Jeon JH, Lee YJ, Moon IS, Lee WS

PMID: 24339282 DOI: 10.3349/ymj.2014.55.1.19

PURPOSE: Tinnitus is a very common symptom of vestibular schwannoma, present in 45 to 80% of patients. We evaluated changes in tinnitus after translabyrinthine microsurgery (TLM) or gamma knife radiosurgery (GKS).

MATERIALS AND METHODS: Among 78 patients with vestibular schwannoma who underwent TLM or GKS at Severance Hospital from 2009-2012, 46 patients with pre- or postoperative tinnitus who agreed to participate were enrolled. Pure tone audiometry, tinnitus handicap inventory (THI), visual analogue scale (VAS) scores for loudness, awareness, and annoyance were measured before and after treatment. Changes of THI and VAS were analysed and compared according to treatment modality, tumour volume, and preoperative residual hearing.

RESULTS: In the TLM group ($n=27$), vestibulocochlear nerves were definitely cut. There was a higher rate of tinnitus improvement in TLM group (52%) than GKS group (16%, $p=0.016$). The GKS group had a significantly higher rate of tinnitus worsening (74%) than TLM group (11%, $p<0.001$). Mean scores of THI and VAS scores significantly decreased in the TLM group in contrast to significant increases in the GKS group. Tumor volume and preoperative hearing did not affect the changes in THI or VAS. **CONCLUSION:** GKS can save vestibulocochlear nerve continuity but may damage the cochlea, cochlear nerve and can cause worsening tinnitus. In cases where hearing preservation is not intended, microsurgery with vestibulocochlear neurectomy during tumor removal can sometimes relieve or prevent tinnitus.

2013

[69] Working disability in Norwegian patients with vestibular schwannoma: vertigo predicts future dependence.

World neurosurgery. 2013;80(6):e301-5

Breivik CN, Nilsen RM, Myrseth E, Finnkirk MK, Lund-Johansen M

PMID: 23548845 DOI: 10.1016/j.wneu.2013.03.069

OBJECTIVE: We examined whether reduced hearing, tinnitus, dizziness, and unsteadiness affected the patients' ability to maintain work within a time frame of 2-10 years after diagnosis. **METHODS:** A total of 434 consecutive patients were followed at regular intervals. Data on symptoms were scored prospectively and dichotomized by visual analog scales for tinnitus and vertigo. Study design is retrospective. Hearing acuity was scored according to the Gardner-Robertson scale, and unsteadiness was measured on a balance platform. Patients were asked about working status, and scored as receiving governmental compensation for disability. **RESULTS:** Two hundred six patients were eligible for study. Of these, one died and nine were lost to follow-up. Ninety-seven patients received conservative management, 49 patients received gamma knife radiosurgery, and 50 patients were treated by microsurgery. Mean follow-up time was 58.7 months (range, 20-132 months). There was a significant increase in the number of individuals receiving compensation during the study period ($P < 0.0001$). At baseline, the proportion of pension receivers was within same range as that of the age- and sex-matched Norwegian population (5.61% vs. 6.91%; case-control odds ratio, 0.82; 95% confidence interval 0.45-1.49; $P = 0.51$, not significant). At the final time point, the increase in the number of receivers deviated significantly from the reference population (case-control odds ratio, 3.80; 95% confidence interval 2.71-5.33; $P < 0.001$). Examining symptoms at first presentation as predictors of future dependence revealed that vertigo and higher mean age were associated with a higher risk ($P < 0.001$ and $P = 0.015$, respectively). No other symptoms were predictive of dependence. **CONCLUSIONS:** In a prospectively followed cohort of Norwegian patients with vestibular schwannoma, vestibular complaints were significant predictors for becoming dependant of disability pension.

[70] Conservative management or gamma knife radiosurgery for vestibular schwannoma: tumor growth, symptoms, and quality of life.

Neurosurgery. 2013;73(1):48-56; discussion 56-7

Breivik CN, Nilsen RM, Myrseth E, Pedersen PH, Varughese JK, Chaudhry AA, Lund-Johansen M

PMID: 23615094 DOI: 10.1227/01.neu.0000429862.50018.b9

BACKGROUND: There are few reports about the course of vestibular schwannoma (VS) patients following gamma knife radiosurgery (GKRS) compared with the course following conservative management (CM). In this study, we present prospectively collected data of 237 patients with unilateral VS extending outside the internal acoustic canal who received either GKRS (113) or CM (124).

OBJECTIVE: The aim was to measure the effect of GKRS compared with the natural course on tumor growth rate and hearing loss. Secondary end points were postinclusion additional treatment, quality of life (QoL), and symptom development. **METHODS:** The patients underwent magnetic resonance imaging scans, clinical examination, and QoL assessment by SF-36 questionnaire. Statistics were performed by using Spearman correlation coefficient, Kaplan-Meier plot, Poisson regression model, mixed linear regression models, and mixed logistic regression models. **RESULTS:** Mean follow-up time was 55.0 months (26.1 standard deviation, range 10-132). Thirteen patients were lost to follow-up. Serviceable hearing was lost in 54 of 71 (76%) (CM) and 34 of 53 (64%) (GKRS) patients during the study period (not significant, log-rank test). There was a significant reduction in tumor volume over time in the GKRS group. The need for treatment following initial GKRS or CM differed at highly significant levels (log-rank test, $P < .001$). Symptom and QoL development did not differ significantly between the groups. **CONCLUSION:** In VS patients, GKRS reduces the tumor growth rate and thereby the incidence rate of new treatment about tenfold. Hearing is lost at similar rates in both groups. Symptoms and QoL seem not to be significantly affected by GKRS.

[71] Do we really still need an open surgery for treatment of patients with vestibular schwannomas?

Acta neurochirurgica. Supplement. 2013;116:25-36

Hayashi M, Chernov MF, Lipski SM, Tamura N, Yomo S, Horiba A, Tsuzuki S, Izawa M, Okada Y, Muragaki Y, Iseki H, Ivanov P, Regis J, Takakura K
PMID: 23417455 DOI: 10.1007/978-3-7091-1376-9_5

BACKGROUND: Gamma Knife surgery (GKS) should be considered a standard treatment option for small and medium-sized vestibular schwannomas (VSs). It results in a tumor control rate similar to that seen with microsurgery and provides better preservation of facial nerve function and hearing. **METHODS:** From December 2002 to April 2011, a total of 260 patients with VS underwent GKS using Leksell Gamma Knife model 4C with an automatic positioning system. There were 30 Koos stage I tumors, 112 stage II, 100 stage III, and 18 stage IV. All patients were treated with the use of high-resolution magnetic resonance imaging; creation of the highly precise conformal and selective multi-isocenter dose planning with small collimators, carefully sparing adjacent cranial nerves of any excessive irradiation; and creation of a wide 80 % isodose area within the tumor while applying a low marginal dose (mean 11.9 Gy) at the 50 % isodose line. **RESULTS:** Among 182 patients who were followed for more than 3 years after treatment, the tumor control and shrinkage rates were 98.4 % and 76.4 %, respectively. Volume reduction of >50 % was marked in 54.9 % of VSs. Preservation of facial nerve function and hearing at the pretreatment level was noted in 97.8 % and 87.9 %, respectively. There was marked improvement of facial nerve function and hearing after GKS in 2.2 % and 3.8 %, respectively. There was no major morbidity. **CONCLUSION:** Due to contemporary technological and methodological achievements GKS can be focused not only on growth control but on shrinking the VS, with possible reversal of the neurological deficit.

[72] Whether gamma knife radiosurgery is really necessary for treatment of patients with vestibular schwannomas.

Acta neurochirurgica. Supplement. 2013;116:19-23

Hori T, Maruyama T

PMID: 23417454 DOI: 10.1007/978-3-7091-1376-9_4

The present study was directed at establishing the role of Gamma Knife radiosurgery (GKS) in the management of vestibular schwannomas (VSs), particularly those that are large. We analyzed a consecutive series of 222 tumors operated on by a single neurosurgeon (T. Hori) at Tottori University (1981-1998)

and Tokyo Women's Medical University (1998-2011). The surgical strategy for sporadic unilateral VSs was typically total or nearly total tumor removal with facial nerve preservation, whereas in some cases of neurofibromatosis type 2 intentional subtotal resection was performed. In all, 15 patients (8.6 %) in the series underwent GKS before (4 cases), after (9 cases), or before and after (2 cases) tumor removal. Overall, 211 patients (95 %) were cured by microsurgery alone. Of note, six patients underwent primary radiosurgery but were operated later on for regrowth of the neoplasm, and in four of them near-total resection led to good long-term tumor control. GKS was required in only 5 % of cases for management of residual VS or, more frequently, its regrowth. Radiosurgery resulted in volume reduction in one-third of these tumors. In other cases it stabilized the lesion, preventing further progression. Thus, GKS is considered a reasonable management option for residual or regrowing small VSs to obtain maximum tumor growth control after initially attempting complete surgical removal.

[73] Long-term safety and efficacy of stereotactic radiosurgery for vestibular schwannomas: evaluation of 440 patients more than 10 years after treatment with Gamma Knife surgery.

Journal of neurosurgery. 2013;118(3):557-65

Hasegawa T, Kida Y, Kato T, Iizuka H, Kuramitsu S, Yamamoto T

PMID: 23140152 DOI: 10.3171/2012.10.JNS12523

OBJECTIVE: Little is known about long-term outcomes, including tumor control and adverse radiation effects, in patients harboring vestibular schwannomas (VSs) treated with stereotactic radiosurgery > 10 years previously. The aim of this study was to confirm whether Gamma Knife surgery (GKS) for VSs continues to be safe and effective > 10 years after treatment. **METHODS:** A total of 440 patients with VS (including neurofibromatosis Type 2) treated with GKS between May 1991 and December 2000 were evaluable. Of these, 347 patients (79%) underwent GKS as an initial treatment and 93 (21%) had undergone prior resection. Three hundred fifty-eight patients (81%) had a solid tumor and 82 (19%) had a cystic tumor. The median tumor volume was 2.8 cm³ and the median marginal dose was 12.8 Gy. **RESULTS:** The median follow-up period was 12.5 years. The actuarial 5- and >= 10-year progression-free survival was 93% and 92%, respectively. No patient developed treatment failure > 10 years after treatment. According to multivariate analysis, significant factors related to worse progression-free survival included brainstem compression with a deviation of the fourth ventricle ($p < 0.0001$), marginal dose ≤ 13 Gy ($p = 0.01$), prior treatment ($p = 0.02$), and female sex ($p = 0.02$). Of 287 patients treated at a recent optimum dose of ≤ 13 Gy, 3 (1%) developed facial palsy, including 2 with transient palsy and 1 with persistent palsy after a second GKS, and 3 (1%) developed facial numbness, including 2 with transient and 1 with persistent facial numbness. The actuarial 10-year facial nerve preservation rate was 97% in the high marginal dose group (> 13 Gy) and 100% in the low marginal dose group (≤ 13 Gy). Ten patients (2.3%) developed delayed cyst formation. One patient alone developed malignant transformation, indicating an incidence of 0.3%. **CONCLUSIONS:** In this study GKS was a safe and effective treatment for the majority of patients followed > 10 years after treatment. Special attention should be paid to cyst formation and malignant transformation as late adverse radiation effects, although they appeared to be rare. However, it is necessary to collect further long-term follow-up data before making conclusions about the long-term safety and efficacy of GKS, especially for young patients with VSs.

[74] Hearing preservation in patients with vestibular schwannoma treated with Gamma Knife surgery.

Journal of neurosurgery. 2013;118(3):571-8

Baschnagel AM, Chen PY, Bojrab D, Pieper D, Kartush J, Didyuk O, Naumann IC, Maitz A, Grills IS

PMID: 23216466 DOI: 10.3171/2012.10.JNS12880

OBJECTIVE: Hearing loss after Gamma Knife surgery (GKS) in patients with vestibular schwannoma has been associated with radiation dose to the cochlea. The purpose of this study was to evaluate serviceable hearing preservation in

patients with VS who were treated with GKS and to determine if serviceable hearing loss can be correlated with the dose to the cochlea. **METHODS:** Forty patients with vestibular schwannoma with serviceable hearing were treated using GKS with a median marginal dose of 12.5 Gy (range 12.5-13 Gy) to the 50% isodose volume. Audiometry was performed prospectively before and after GKS at 1, 3, and 6 months, and then every 6 months thereafter. Hearing preservation was based on pure tone average (PTA) and speech discrimination (SD). Serviceable hearing was defined as PTA less than 50 dB and SD greater than 50%. **RESULTS:** The median cochlear maximum and mean doses were 6.9 Gy (range 1.6-16 Gy) and 2.7 Gy (range 0.7-5.0 Gy), respectively. With a median audiological follow-up of 35 months (range 6-58 months), the 1-, 2-, and 3-year actuarial rates of maintaining serviceable hearing were 93%, 77%, and 74%, respectively. No patient who received a mean cochlear dose less than 2 Gy experienced serviceable hearing loss ($p = 0.035$). Patients who received a mean cochlear dose less than 3 Gy had a 2-year hearing preservation rate of 91% compared with 59% in those who received a mean cochlear dose of 3 Gy or greater ($p = 0.029$). Those who had more than 25% of their cochlea receiving 3 Gy or greater had a higher rate of hearing loss ($p = 0.030$). There was no statistically significant correlation between serviceable hearing loss and age, tumor size, pre-GKS PTA, pre-GKS SD, pre-GKS Gardner-Robertson class, maximum cochlear dose, or the percentage of cochlear volume receiving 5 Gy. On multivariate analysis there was a trend toward significance for serviceable hearing loss with a mean cochlear dose of 3 Gy or greater ($p = 0.074$). Local control was 100% at 24 months. No patient developed facial or trigeminal nerve dysfunction. **CONCLUSIONS:** With a median mean cochlear dose of 2.7 Gy, the majority of patients with serviceable hearing retained serviceable hearing 3 years after GKS. A mean cochlear dose less than 3 Gy was associated with higher serviceable hearing preservation.

[75] Long-term hearing outcomes following stereotactic radiosurgery for vestibular schwannoma: patterns of hearing loss and variables influencing audiometric decline.

Journal of neurosurgery. 2013;118(3):579-87
Carlson ML, Jacob JT, Pollock BE, Neff BA, Tombers NM, Driscoll CL, Link MJ
PMID: 23101446 DOI: 10.3171/2012.9.JNS12919

OBJECTIVE: The goals of this retrospective cohort study were as follows: 1) to describe the long-term prevalence and timing of hearing deterioration following low-dose (12- to 13-Gy marginal dose) stereotactic radiosurgery (SRS) for vestibular schwannoma (VS); and 2) to identify clinical variables associated with long-term preservation of useful hearing following treatment. **METHODS:** Patients with serviceable hearing who underwent SRS for VS between 1997 and 2002 were studied. Data including radiosurgery treatment plans, tumor characteristics, pre- and posttreatment pure tone average, speech discrimination scores, and American Academy of Otolaryngology-Head and Neck Surgery hearing class were collected. Time to non-serviceable hearing was estimated using the Kaplan-Meier method. Univariate and multivariate associations with time to non-serviceable hearing were evaluated using Cox proportional hazards regression models. **RESULTS:** Forty-four patients met the study criteria and were included. The median duration of audiometric follow-up was 9.3 years. Thirty-six patients developed non-serviceable hearing at a mean of 4.2 years following SRS. The Kaplan-Meier estimated rates of serviceable hearing at 1, 3, 5, 7, and 10 years following SRS were 80%, 55%, 48%, 38%, and 23%, respectively. Multivariate analysis revealed that pretreatment ipsilateral pure tone average ($p < 0.001$) and tumor size ($p = 0.009$) were statistically significantly associated with time to non-serviceable hearing. **CONCLUSIONS:** Durable hearing preservation a decade after low-dose SRS for VS occurs in less than one-fourth of patients. Variables including preoperative hearing capacity and tumor size may be used to predict hearing outcomes following treatment. These findings may assist in pretreatment risk disclosure. Furthermore, these data demonstrate the importance of long-term follow-up when reporting audiometric outcomes following SRS for VS.

[76] Nervus intermedius dysfunction following Gamma Knife surgery for vestibular schwannoma.

Journal of neurosurgery. 2013;118(3):566-70
Park SH, Lee KY, Hwang SK
PMID: 23101447 DOI: 10.3171/2012.10.JNS12747

OBJECTIVE: The purpose of this study was to evaluate the function of the nervus intermedius, the nonmotor component of the facial nerve, following modern Gamma Knife surgery (GKS) for the treatment of vestibular schwannoma. **METHODS:** Sixty-five consecutive patients at our center underwent GKS as a primary treatment option for vestibular schwannoma between 2005 and 2010. The authors interviewed patients with a functional questionnaire to evaluate the function of the nervus intermedius before and after radiosurgery from their subjective point of view. Data from 50 patients treated using GKS for a unilateral vestibular schwannoma were obtained. **RESULTS:** Nine (18%) of 50 patients presented with at least one preradiosurgical disturbance of the nervus intermedius caused by the vestibular schwannoma itself, with dysfunctions of lacrimation, salivation, nasal secretion, and taste. Of the 41 patients without preradiosurgical disturbances, 9 (22%) experienced the onset of at least one new disturbance after GKS. Specifically for each dysfunction, of the 45 patients without a lacrimal disturbance before GKS, 5 (11.1%) had a new lacrimal disturbance after GKS. New onset of a salivary disturbance after GKS was reported in 3 (6.2%) of 48 patients. In 1 patient (2%), increased nasal secretion was noted 1 year after GKS. Five (10.6%) of 47 patients without a preradiosurgical taste disturbance experienced the symptom after GKS. No facial palsy developed in any patient before or after GKS. There was no significant correlation between postradiosurgical nervus intermedius dysfunction and tumor size, margin dose, or patient age. **CONCLUSIONS:** The authors demonstrated that 22% of patients undergoing modern GKS for vestibular schwannoma experience various disturbances of nonmotor components of the facial nerve as a result of the radiosurgery. Through this study, we can provide useful information about the likelihood of certain postradiosurgical symptoms for vestibular schwannoma.

[77] Grading of vestibular schwannomas and corresponding tumor volumes: ramifications for radiosurgery.

Acta neurochirurgica. 2013;155(1):71-4; discussion 74
Mindermann T, Schlegel I
PMID: 23160632 DOI: 10.1007/s00701-012-1553-4

BACKGROUND: Patients with vestibular schwannomas (VS) are either assigned to watchful waiting, microsurgical resection, or radiosurgery. Decision making on how to proceed is based on parameters such as age, tumor growth, loss of hearing, and the tumor's Koos grading. **METHODS:** In order to correlate Koos grading with tumor volume, patient records of 235 patients with VS who underwent Gamma Knife radiosurgery (GKRS) were retrospectively reviewed. **RESULTS:** From 1994 to 2009, 235 consecutive patients underwent GKRS for sporadic VS at the Zurich Gamma Knife Center. Median follow up was 62.8 +/- 33.0 months. Of the 235 tumors, 32 (13.6 %) were graded Koos I with a volume of 0.25 +/- 0.3 cc; 71 (30.2 %) were graded Koos II with a volume of 0.57 +/- 0.54 cc; 70 (29.8 %) were graded Koos III with a volume of 1.82 +/- 1.88 cc; and 62 (26.4 %) were graded Koos IV with a volume of 4.17 +/- 2.75 cc. Tumor progression was defined as a volume increase > 20 % at 2 years or later following GKRS. Overall tumor progression occurred in 21/235 (8.9 %) patients at 3.4 +/- 0.9 years. Tumor progression did not differ statistically significantly in the various Koos grades: 1/32 (3.1 %) patients with VS Koos Grade I, 7/71 (9.8 %) patients with VS Koos Grade II, 6/70 (8.6 %) patients with VS Koos Grade III, and 7/62 (11.3 %) patients with VS Koos Grade IV. **CONCLUSION:** To our knowledge, this is the first work correlating the various Koos grades of VS to their respective tumor volumes. In our patients, tumor volumes of VS Koos Grade IV were limited because all of our patients were eligible for radiosurgery. In our series, the outcome following GKRS for patients with VS Koos Grade IV tumors did not differ from patients with VS Koos Grades I-III. We therefore suggest to limit Koos Grade IV VS to tumor volumes < 6 cc that may be eligible for radiosurgery, and introduce an additional VS Grade V for large VS with tumor volumes of > 6 cc that may not be eligible for radiosurgery.

[78] Hearing outcomes after stereotactic radiosurgery for unilateral intracanalicular vestibular schwannomas: implication of transient volume expansion.

International journal of radiation oncology, biology, physics. 2013;85(1):61-7
Kim YH, Kim DG, Han JH, Chung HT, Kim IK, Song SW, Park JH, Kim JW, Kim YH, Park CK, Kim CY, Paek SH, Jung HW
PMID: 22580122 DOI: 10.1016/j.ijrobp.2012.03.036

PURPOSE: We evaluated the prognostic factors for hearing outcomes after stereotactic radiosurgery (SRS) for unilateral sporadic intracanalicular vestibular schwannomas (IC-VSs) as a clinical homogeneous group of VSs. **METHODS AND MATERIALS:** Sixty consecutive patients with unilateral sporadic IC-VSs, defined as tumors in the internal acoustic canal, and serviceable hearing (Gardner-Roberson grade 1 or 2) were treated with SRS as an initial treatment. The mean tumor volume was 0.34 +/- 0.03 cm³ (range, 0.03-1.00 cm³), and the mean marginal dose was 12.2 +/- 0.1 Gy (range, 11.5-13.0 Gy). The median follow-up duration was 62 months (range, 36-141 months). **RESULTS:** The actuarial rates of serviceable hearing preservation were 70%, 63%, and 55% at 1, 2, and 5 years after SRS, respectively. In multivariate analysis, transient volume expansion of >=20% from initial tumor size was a statistically significant risk factor for loss of serviceable hearing and hearing deterioration (increase of pure tone average >=20 dB) (odds ratio=7.638; 95% confidence interval, 2.317-25.181; P=.001 and odds ratio=3.507; 95% confidence interval, 1.228-10.018; P=.019, respectively). The cochlear radiation dose did not reach statistical significance. **CONCLUSIONS:** Transient volume expansion after SRS for VSs seems to be correlated with hearing deterioration when defined properly in a clinically homogeneous group of patients.

2012

[79] Use of apparent diffusion coefficients in evaluating the response of vestibular schwannomas to Gamma Knife surgery.

Journal of neurosurgery. 2012;117 Suppl:63-8
Chuang CC, Chang CS, Tyan YS, Chuang KS, Tu HT, Huang CF
PMID: 23205791 DOI: 10.3171/2012.7.GKS121003

OBJECTIVE: Cellular density is a major factor responsible for changes in apparent diffusion coefficients (ADCs). The authors hypothesized that loss of tumor cells after Gamma Knife surgery (GKS) might alter ADC values. Magnetic resonance imaging, including diffusion-weighted (DW) imaging, was performed to detect cellular changes in brain tumors so that the authors could evaluate the tumor response to GKS as well as the efficacy of the procedure. **METHODS:** The authors conducted a prospective trial involving 31 patients harboring solid or cystic vestibular schwannomas (VSs) that were treated with GKS. The patients underwent serial MR imaging, including DW imaging, before GKS and at multiple intervals following the procedure. The authors observed the patients over time, evaluating MR imaging findings and clinical outcomes at 6-month intervals. The ADCs were calculated from echo-planar DW images, and mean ADC values were compared at each follow-up. **RESULTS:** The mean follow-up period was 36.5 months (range 18-60 months). Imaging studies showed a reduction in tumor volume in 19 patients (61.3%) and tumor growth arrest in 9 patients (29%). In the remaining 3 patients (9.7%), tumor enlargement was documented at 18, 36, and 42 months. The mean ADC value before GKS for all solid VSs was 1.06 +/- 0.17 x 10(-3) mm²/second, which significantly increased 6 months after GKS and continued to increase with time (p = 0.0086). The mean ADC value for treated solid tumors as of the last mean follow-up of 36 months (range 18-60 months) was 1.72 +/- 0.26 x 10(-3) mm²/second (range 1.50-2.09 x 10(-3) mm²/second), which was significantly higher than that before GKS (p = 0.0001). Tumor volumes were positively related to ADC values (p = 0.03). The mean ADC value before GKS for all cystic VSs was 2.09 +/- 0.24 x 10(-3) mm²/second (range 1.80-2.58 x 10(-3) mm²/second).

The mean ADC value for treated cystic tumors as of the last mean follow-up of 38 months (range 18-48 months) was 1.89 +/- 0.22 x 10(-3) mm²/second. In 3 patients harboring solid VSs, the tumor enlarged after GKS but the ADC values were higher than those before GKS. The authors considered these tumors to be controlled and continued follow-up in the patients. **CONCLUSIONS:** Apparent diffusion coefficient values may be useful for evaluating treatment results before any definite volume change is detected on imaging studies and for distinguishing radiation-induced necrosis from tumor recurrence in cases in which other imaging results are not definitive, as in cases of increased tumor volume or no volume change. The authors suggest that ADC measurements be included during routine MR imaging examinations for the evaluation of GKS results.

[80] Intracapsular decompression or radical resection followed by Gamma Knife surgery for patients harboring a large vestibular schwannoma.

Journal of neurosurgery. 2012;117 Suppl:69-77
Pan HC, Sheehan J, Sheu ML, Chiu WT, Yang DY
PMID: 23205792 DOI: 10.3171/2012.6.GKS12697

OBJECTIVE: Microsurgery is the primary treatment used for patients harboring a large vestibular schwannoma (VS). However, its outcome may lead to hearing impairment and facial nerve dysfunction particularly when resection is extended outside the tumor capsule. When surgery for a large VS consists of intracapsular resection and decompression, better preservation of facial and hearing function are obtained. In this study, the authors compared outcomes of intracapsular decompression followed by Gamma Knife surgery (GKS) with outcomes of standard microsurgery followed by radiosurgery. **METHODS:** Between August 2003 and October 2008, 35 patients harboring large VSs (> 3 cm in diameter) were enrolled in this study. Eighteen patients underwent intracapsular decompression followed by GKS (Group I), and 17 patients underwent radical extracapsular resection followed by GKS (Group II). In all cases GKS was performed with a margin dose of 12 Gy. All patients were followed up for at least 3 years. All patients also underwent periodic audiography, electroneurography (ENoG), MR imaging, and testing with the SF-36 form. The Student t-test and repeated ANOVA were used for statistical analysis. **RESULTS:** The mean ages of the patients (+/- SEM) in Groups I and II were 50 +/- 3.0 and 49 +/- 2.3 years, respectively. The female/male ratios were 8:10 in Group I and 7:10 in Group II. All patients had excellent facial function as measured according to the House-Brackmann Facial Grading System (Grade I or II) preoperatively. After the operation, 16 patients (89%) in Group I retained excellent facial function, whereas only 6 patients (35%) in Group II had excellent facial function (p < 0.01). In Group I, 11 patients had serviceable hearing, and all 11 (100%) retained hearing function after the operation. In Group II, 11 patients had serviceable hearing, but none retained hearing function postoperatively (p < 0.001). In Group I, the mean tumor volume (+/- SEM) was 17.5 +/- 1.1 cm³, and the postoperative volume was 9.35 +/- 1.02 cm³. In Group II, the mean tumor volume was 16.4 +/- 0.95 cm³, whereas the postoperative volume was 1.1 +/- 0.14 cm³ (p < 0.001). After GKS, the tumor volume was reduced to 5.12 +/- 1.1 cm³ and 0.9 +/- 0.1 cm³ in Groups I and II, respectively. No patients experienced adverse effects after GKS. The mean return-to-work times were 2.4 +/- 0.16 and 33.4 +/- 4.3 weeks in Groups I and II, respectively (p < 0.001). According to the results obtained using the 36-Item Short Form Health Survey (SF-36), patients in Group I enjoyed more significant improvements in quality of life than patients in Group II (p < 0.001). **CONCLUSIONS:** Intracapsular decompression followed by GKS afforded a better neurological outcome and quality of life than radical extracapsular resection followed by GKS. Further application of this approach in patients harboring large VSs seems warranted.

[81] Long-term follow-up studies of Gamma Knife surgery with a low margin dose for vestibular schwannoma.

Journal of neurosurgery. 2012;117 Suppl:57-62
Sun S, Liu A
PMID: 23205790 DOI: 10.3171/2012.7.GKS12783

OBJECTIVE: The aim of this study was to assess long-term clinical outcomes in patients who underwent Gamma Knife surgery (GKS) with a low margin dose-14 Gy or less to treat vestibular schwannoma (VS) unrelated to neurofibromatosis Type II. **METHODS:** Between December 1994 and December 2001, 200 patients with VSs underwent GKS, which was performed using the Leksell Gamma Knife model B. More than 10 years of follow-up is available in these patients. One hundred ninety patients (88 male and 102 female patients) were followed up using MRI (follow-up rate 95%). The mean age of these patients was 50.6 years (range 10-77 years). Gamma Knife surgery was the primary treatment for VS in 134 cases (70.5%) and was an adjunctive management approach in 56 cases (29.5%). The median tumor margin dose was 13.0 Gy (range 6.0-14.4 Gy), and the median maximum tumor dose was 28.0 Gy (range 15.0-60.0 Gy). The median tumor volume was 3.6 cm³ (range 0.3-27.3 cm³). The median duration of follow-up in these patients was 109 months (range 8-195 months). **RESULTS:** In the 190 patients, the latest follow-up MRI studies demonstrated tumor regression in 122 patients (64.2%), stable tumor in 48 patients (25.3%), and tumor enlargement in 20 patients (10.5%). The total rate of tumor control was 89.5%. Using the Kaplan-Meier method, the authors found the estimated 3-, 5-, 10-, and 15-year tumor control rates to be 95%, 93%, 86%, and 79%, respectively; and the estimated 3-, 5-, and 10-year hearing preservation rates to be 96%, 92%, and 70%, respectively. Twenty-six patients (13.7%) exhibited transient mild facial palsy or facial spasm, and 2 patients (1.1%) suffered persistent mild facial palsy. Thirty-nine patients (20.5%) had transient trigeminal neuropathy, and 5 patients (2.6%) suffered from persistent mild facial numbness. The incidence of persistent severe facial and trigeminal neuropathy was 0.0%. **CONCLUSIONS:** With a low prescribed margin dose of 14 Gy or less, GKS was confirmed to provide long-term tumor control for small to medium-sized VSs and largely to prevent cranial nerves from iatrogenic injury. Based on the findings of this study, GKS is also a reasonable option for the treatment of large, heterogeneously enhancing tumors without symptomatic brainstem compression. Gamma Knife surgery can preserve a high quality of life for most patients with VS who do not have symptomatic brainstem compression. Long-term follow-up is required because of the risk of delayed recurrence of VS.

[82] Are frequent dental x-ray examinations associated with increased risk of vestibular schwannoma?

Journal of neurosurgery. 2012;117 Suppl:78-83

Han YY, Berkowitz O, Talbott E, Kondziolka D, Donovan M, Lunsford LD
PMID: 23211211 DOI: 10.3171/2012.5.GKS12615

OBJECTIVE: The authors evaluated the potential role of environmental risk factors, including exposure to diagnostic or therapeutic radiation and to wireless phones that emit nonionizing radiation, in the etiology of vestibular schwannoma (VS). **METHODS:** A total of 343 patients with VSs who underwent Gamma Knife surgery performed between 1997 and 2007 were age and sex matched to 343 control patients from the outpatient degenerative spinal disorders service at the University of Pittsburgh Medical Center. The authors obtained information on previous exposure to medical radiation, use of wireless phone technologies, and other environmental factors thought to be associated with the development of a VS. Conditional multivariate logistic regression was used to estimate adjusted odds ratios (aORs) and 95% confidence intervals (CIs). **RESULTS:** After adjusting for race, education, cigarette smoking, alcohol consumption, occupational exposure to noise, use of cell phones, and family history of cancer, the authors identified only a single factor that was associated with a higher risk of VS: individuals exposed to dental x-rays once a year (aOR = 2.27, 95% CI = 1.01-5.09) or once every 2-5 years (aOR = 2.65, 95% CI = 1.20-5.85), compared with those exposed less than once every 5 years. Of interest, a history of exposure to radiation related to head or head-and-neck computed tomography was associated with a reduced risk of VS (aOR = 0.52, 95% CI = 0.30-0.90). No relationship was found between the use of cell phones or cordless phones and VS. **CONCLUSIONS:** Patients with acoustic neuromas reported significantly more exposure to dental x-rays than a matched cohort control group. Reducing the frequency of dental x-ray examinations may decrease the potential risk of VS.

[83] Longitudinal analysis of hearing before and after radiosurgery for vestibular schwannoma.

Journal of neurosurgery. 2012;117(5):877-85

Yomo S, Carron R, Thomassin JM, Roche PH, Regis J
PMID: 22937934 DOI: 10.3171/2012.7.JNS10672

OBJECTIVE: The aim of this study was to perform an accurate analysis of changes in hearing in patients with vestibular schwannoma (VS) who have undergone Gamma Knife surgery (GKS) and distinguish the impact of radiosurgery from the natural course of hearing deterioration due to the tumor itself. **METHODS:** This study was a retrospective review of prospectively collected patient data. A group of 154 patients with unilateral nonsurgically treated VS was conservatively monitored for more than 6 months and then treated with GKS between July 1997 and September 2005. They were followed up with serial clinical examination, MRI, and audiometry. The annual hearing decrease rate (AHDR) was measured before and after radiosurgery, and the possible prognostic factors for hearing preservation were investigated. **RESULTS:** The mean dose prescribed to the tumor margins was 12.1 Gy. The mean radiological follow-up period after GKS was 60 months (range 7-123 months). The tumor control rate was 94.8%, and 8 patients underwent subsequent intervention due to tumor progression. The mean audiological follow-up times before and after GKS were 22 and 52 months, respectively. The mean AHDRs before and after GKS were 5.39 dB/year (95% CI 3.31-7.47 dB/year) and 3.77 dB/year (95% CI 3.13-4.40 dB/year), respectively (p > 0.05). The mean pre- and post-GKS AHDRs in patients who initially had Gardner-Robertson (GR) Class I hearing were -0.57 dB/year (95% CI -2.95 to 1.81 dB/year) and 3.59 dB/year (95% CI 2.52-4.65 dB/year), respectively (p = 0.007). The mean pre- and post-GKS AHDRs in patients who initially had GR Class II hearing were 5.09 dB/year (95% CI 1.36-8.82 dB/year) and 4.98 dB/year (95% CI 3.86-6.10 dB/year), respectively (p > 0.05). A subgroup of 80 patients had both early and late post-intervention AHDR assessment (with early referring to the period from GKS to the assessment closest to the 2-year follow-up point and late referring to the period from that assessment to the most recent one); in these patients, the mean early post-GKS AHDR was 5.86 dB/year (95% CI 4.25-7.50 dB/year) and the mean late post-GKS AHDR was 1.86 dB/year (95% CI 0.77-2.96 dB/year) (p < 0.001). A maximum cochlear dose of less than 4 Gy was found to be the sole prognostic factor for hearing preservation. **CONCLUSIONS:** The present study demonstrated the absence of an increase in AHDR after radiosurgery as compared with the preoperative AHDR. There was even a trend indicating a reduction in the annual hearing loss after radiosurgery over the long term. To fully elucidate a possible protective effect of radiosurgery, longer-term follow-up with a larger group of patients will be required.

[84] Gamma knife treatment of growing vestibular schwannoma in Norway: a prospective study.

International journal of radiation oncology, biology, physics. 2012;84(2):e161-6

Varughese JK, Wentzel-Larsen T, Pedersen PH, Mahesparan R, Lund-Johansen M
PMID: 22682805 DOI: 10.1016/j.ijrobp.2012.03.047

PURPOSE: Gamma Knife radiosurgery (GKRS) has been increasingly used in the treatment of vestibular schwannoma (VS). Very few studies relate tumor control and post-treatment growth rates to pretreatment growth rates. **METHODS AND MATERIALS:** We prospectively included 45 consecutive VS patients who were initially treated conservatively and then received GKRS between 2000 and 2007 because of demonstrated tumor growth. Pretreatment and post-treatment tumor volumes were estimated. Patients underwent audiograms, reported their symptoms, and responded to the Short Form General Health Survey (SF-36) questionnaire on each visit. **RESULTS:** Volume doubling times before and after treatment were 1.36 years (95% confidence intervals, 1.14-1.68) and -13.1 years (95% confidence intervals, -111.0 to -6.94), respectively. Tumor control, defined as a post-GKRS growth rate \leq 0, was achieved in 71.1% of patients, with highest odds for tumor control among older patients and those with larger tumors. The 5-year retreatment-free survival rate was 93.9% (95% confidence intervals, 76.5-98.5). None of the clinical endpoints investigated showed statistically significant

changes after GKRS, but improvement was seen in a few SF-36 parameters.

CONCLUSIONS: GKRS alters the natural course of the tumor by reducing growth. Mathematic models yield poorer tumor control rates than those found by clinical assessment. Symptoms were unaffected by treatment, but quality of life was improved.

[85] Risk factors and tumor response associated with hydrocephalus after gamma knife radiosurgery for vestibular schwannoma.

Acta neurochirurgica. 2012;154(9):1679-84

Lee SH, Seol HJ, Kong DS, Nam DH, Park K, Kim JH, Lee JI
PMID: 22535199 DOI: 10.1007/s00701-012-1350-0

BACKGROUND: This study was designed to investigate the clinical characteristics and risk factors of hydrocephalus after gamma knife radiosurgery (GKRS) for vestibular schwannoma. **METHODS:** The authors retrospectively reviewed clinical and neuroimaging findings of 221 patients who underwent GKRS for newly diagnosed vestibular schwannoma. Mean patient age was 54.1 years (range 7-83 years), mean tumor volume was 3,010.4 mm³ (range 34.7 to 14,300 mm³), mean marginal dose was 12.5 Gy (range 11 to 15 Gy), and mean follow-up duration was 31.9 months (range 1 to 107.6 months). **RESULTS:** Surgical intervention for cerebrospinal fluid (CSF) diversion after GKRS was necessary in 11 (5%) of the patients. Median time between GKRS and ventriculoperitoneal (VP) shunt placement was 15.5 months (range 1.8-37.8 months). These 11 patients showed female predominance (11 females) and mean tumor volume was significantly larger than in the other without hydrocephalus (6,509 vs. 2,726 mm³; $p < 0.01$). Decreases in tumor enhancement and swelling were observed in all 221 patients, and CSF protein was found to be elevated in five of nine patients with available data at the time of the shunt procedure. Hydrocephalic symptoms improved after VP shunt and tumor sizes further decreased at last follow-up in all patients. **CONCLUSIONS:** Hydrocephalus after radiosurgery may co-occur with a temporary change of tumor volume after radiation treatment. Therefore, hydrocephalus should be kept in mind during the time of tumor volume transition. Furthermore, the authors suggest that frequent patient monitoring for hydrocephalus be maintained for up to 3-4 years after GKRS.

[86] Stage II vestibular schwannoma: predictive factors for postoperative hearing loss and facial palsy.

European annals of otorhinolaryngology, head and neck diseases. 2012;129(2):87-92

Milhe de Saint Victor S, Bonnard D, Darrouzet V, Bellec O, Franco-Vidal V
PMID: 22226671 DOI: 10.1016/j.anorl.2011.09.001

OBJECTIVES: To assess predictive factors for deafness and facial palsy after vestibular schwannoma surgery on a translabyrinthine or retrolabyrinthine approach, and to compare sequela results to those for gamma knife radiosurgery. **PATIENTS AND METHODS:** A retrospective study included 70 patients operated on for stage II vestibular schwannoma (Kos classification). Postoperative hearing was assessed on pure-tone average and speech discrimination score, and facial palsy on the House and Brackmann classification, preoperatively and at 1 year postoperatively. Various predictive factors were assessed for both. Statistical analysis used the Fischer exact test, with a significance threshold of $P < 0.05$. **RESULTS:** Hearing was conserved in 18.9% of patients operated on with a retrolabyrinthine approach, with 8.1% conserving useful hearing. Facial function was conserved in 91.4%. Predictive factors for hearing conservation did not achieve statistical significance, but showed trends for: preoperative pure-tone average threshold ≤ 30 dB and speech discrimination score $\geq 70\%$, age less than 55 years, tinnitus, nearly normal auditory brainstem response (ABR) latency, and homogeneous tumor on MRI. Predictive factors for conserved facial function likewise did not achieve statistical significance, but showed trends for: age less than 55 years, deafness of progressive onset, absence of cardiovascular risk factors, nearly normal ABR latency and tumor size < 13.5 mm on MRI. **CONCLUSION:** Facial nerve risk is largely the same with surgery or gamma knife radiosurgery. Concerning hearing, gamma knife radiosurgery seems to provide better hearing conservation, but only over the short term.

[87] Predicting nonauditory adverse radiation effects following radiosurgery for vestibular schwannoma: a volume and dosimetric analysis.

International journal of radiation oncology, biology, physics. 2012;82(5):2041-6
Hayhurst C, Monsalves E, Bernstein M, Gentili F, Heydarian M, Tsao M, Schwartz M, van Prooijen M, Millar BA, Menard C, Kulkarni AV, Laperriere N, Zadeh G
PMID: 21531086 DOI: 10.1016/j.ijrobp.2011.02.017

PURPOSE: To define clinical and dosimetric predictors of nonauditory adverse radiation effects after radiosurgery for vestibular schwannoma treated with a 12 Gy prescription dose. **METHODS:** We retrospectively reviewed our experience of vestibular schwannoma patients treated between September 2005 and December 2009. Two hundred patients were treated at a 12 Gy prescription dose; 80 had complete clinical and radiological follow-up for at least 24 months (median, 28.5 months). All treatment plans were reviewed for target volume and dosimetry characteristics; gradient index; homogeneity index, defined as the maximum dose in the treatment volume divided by the prescription dose; conformity index; brainstem; and trigeminal nerve dose. All adverse radiation effects (ARE) were recorded. Because the intent of our study was to focus on the nonauditory adverse effects, hearing outcome was not evaluated in this study. **RESULTS:** Twenty-seven (33.8%) patients developed ARE, 5 (6%) developed hydrocephalus, 10 (12.5%) reported new ataxia, 17 (21%) developed trigeminal dysfunction, 3 (3.75%) had facial weakness, and 1 patient developed hemifacial spasm. The development of edema within the pons was significantly associated with ARE ($p = 0.001$). On multivariate analysis, only target volume is a significant predictor of ARE ($p = 0.001$). There is a target volume threshold of 5 cm³, above which ARE are more likely. The treatment plan dosimetric characteristics are not associated with ARE, although the maximum dose to the 5th nerve is a significant predictor of trigeminal dysfunction, with a threshold of 9 Gy. The overall 2-year tumor control rate was 96%. **CONCLUSIONS:** Target volume is the most important predictor of adverse radiation effects, and we identified the significant treatment volume threshold to be 5 cm³. We also established through our series that the maximum tolerable dose to the 5th nerve is 9 Gy.

[88] Tumor pseudoprogression following radiosurgery for vestibular schwannoma.

Neuro-oncology. 2012;14(1):87-92

Hayhurst C, Zadeh G

PMID: 22028389 DOI: 10.1093/neuonc/nor171

We sought to characterize vestibular schwannoma (VS) pseudoprogression after radiosurgery to assess its incidence, causative factors, and association with radiation-induced adverse effects. We performed a retrospective study of VS treated with Gamma Knife radiosurgery during 2005-2009. Seventy-five patients had at least 24 months of clinical and radiographic follow-up (median, 29 months) and were included. Tumor response was calculated volumetrically using Gamma plan software on consecutive MRIs. All treatment plans were reviewed for dosimetry characteristics. Forty-nine VS (65%) were stable or regressed after treatment. Seventeen (23%) underwent pseudoprogression, with onset of enlargement at 6 months. Seven (9%) remained larger than initial treatment volume at last follow-up. Nine (12%) had persistent growth. Three patients underwent subsequent microsurgery. One patient required intervention at 3 months for cystic enlargement; otherwise, all patients with progressive enlargement had stable VS until at least 24 months. Twenty-six patients (34.7%) developed nonauditory adverse radiation effects after treatment, including cranial neuropathy, ataxia, and hydrocephalus. There was no statistical association between onset of clinical deterioration and tumor response. Volume changes in the first 24 months after radiosurgery rarely herald treatment failure. Any volume change after 24 months is indicative of treatment failure. Pseudoprogression does not appear to be independently linked to radiation-induced morbidity, and there are no patient-related or radiosurgical parameters that predict tumor response.