Evaluation of hearing function after Gamma Knife surgery of vestibular schwannomas

ALBERTO FRANZIN, M.D., GIORGIO SPATOLA, M.D., CARLO SERRA, M.D., PIERO PICCOZZI, M.D., MARZIA MEDONE, M.D., DAVIDE MILANI, M.D., PAOLA CASTELLAZZI, M.D., AND PIETRO MORTINI, M.D.

Department of Neurosurgery and Radiosurgery, Division of Neuroscience, IRCCS San Raffaele, Milan, Italy

Object. Due to technological advances in neuroradiology in recent years, incidental diagnoses of vestibular schwannomas (VSs) have increased. The aim of this study was to evaluate the hearing function after treatment with Gamma Knife surgery (GKS) for VSs in patients adequately selected with “good” or “useful” hearing before treatment and to assess the possible predictive factors for hearing function preservation.

Methods. Of all patients treated in the authors’ hospital between 2001 and 2007, they retrospectively studied 50 patients with a unilateral VS in whom there was serviceable hearing (Gardner-Robertson [GR] Class I or II). Additional inclusion criteria were: no Type 2 neurofibromatosis, no previous treatment, and at least 6 months’ follow-up of neuroradiological and audiological data. The median patient age was 54 years (range 24–78 years). The median tumor volume was 0.73 ml (range 0.03–6.6 ml), and the median radiation dose to the tumor margin was 13 Gy (range 12–16 Gy) with an isodose of 50%.

Results. Patient age, tumor volume, and presenting symptoms were found to correlate with hearing function. At a median of 36 months after radiosurgery, tumor growth control was 96% and no patient required any other additional treatment. Serviceable hearing was preserved in 34 patients (68%): 21 (62%) with GR Class I hearing and 13 (38%) with GR Class II hearing. The remaining 16 patients had poor hearing function: 15 with GR Class III and 1 with GR Class IV hearing function. In 19 (58%) of 33 patients with GR Class I function before GKS the same class was maintained posttreatment; 29 (88%) maintained functional hearing (GR Class I or II). In all patients with an intracanalicular lesion, functional hearing was maintained. Significant prognostic factors for maintaining serviceable hearing were GR Class I function before treatment, symptoms at presentation, patient age younger than 54 years, and Koos Stage T1 disease.

Conclusions. The results of the study show that the probability of preserving functional hearing in patients undergoing GKS treatment for unilateral VSs is very high. Patients with GR Class I, age younger than 54 years, with presenting symptoms other than hearing loss, and a Koos Stage T1 tumor have better prognosis. The prescribed dose of 13 Gy appears to represent an excellent compromise between controlling the disease and preserving auditory function. (DOI: 10.3171/2009.9.FOCUS09196)

KEY WORDS • vestibular schwannoma • Gamma Knife • hearing function

Vestibular schwannomas are benign, extraxial, slow-growing tumors that arise from the vestibulocochlear nerve. Unilateral VSs account for approximately 8–10% of all intracranial tumors and for > 90% of all tumors of the cerebellopontine angle. The mean age of patients at diagnosis is approximately 50 years. More than 95% of diagnosed VSs appear in a sporadic and unilateral form, with an incidence of about 1/100,000 per year, without any sex prevalence.43,52

Several scientific studies have shown how radiosurgery is currently considered the best treatment for small-sized tumors.9,14,21,22,26,41,44

According to the guidelines for the treatment of VSs approved by the International RadioSurgery Association15 published in May 2006, patients with intracanalicular tumors in whom growth has been documented on imaging, patients with tumors of maximum diameter < 3 cm and no brainstem distortion, and patients with a postsurgical residual lesion, even if > 3 cm, are candidates for GKS.

Indeed, recent studies have shown a tumor growth control rate of 93–100% after GKS.4,6–14,16,22–25,30,32 Complications (deficit of CNs V and VII) are extremely rare.
Given the efficacy and low morbidity rate associated with GKS of VS, the aims of the present study were to analyze to what extent this treatment allows hearing preservation and to investigate the existence of predictive factors of hearing preservation.

**Methods**

**Patient Population**

At the Neurosurgery Clinic of San Raffaele Hospital in Milan, 430 patients underwent GKS between January 2001 and December 2007. Patients were candidates for radiosurgery based on International RadioSurgery Association guidelines. Documented tumor growth was considered a strong indication for radiosurgery, particularly for young patients, even if the initial tumor volume was small or if the patient exhibited no symptoms. Prior to the GKS, all patients underwent complete otorhinolaryngological evaluation, including tonal and vocal audiometric testing, and neurosurgical evaluation with Gd-enhanced MR imaging.

The admission criteria of this study included the following: 1) Good hearing or hearing that passed the audiometric test prior to the treatment (GR Class I or II); 2) unilateral tumor; 3) absence of Type 2 neurofibromatosis; 4) no history of surgical treatments of the targeted tumor; and 5) follow-up of at least 6 months, including both audiometric and neuroradiological data.

Fifty patients treated at our institution who had pre-treatment functional hearing met the study admission criteria (Table 1). There were 18 men (36%) and 32 women (64%) whose mean age was 52.2 years (median 54 years, range 24–78 years). The tumor was right sided in 27 patients (54%) and left sided in 23 (46%).

The mean tumor volume was 1.34 ml. According to the Koos classification, 8 patients (16%) harbored a Stage T1, 16 (32%) a Stage T2, 21 (42%) a Stage T3a, 3 (6%) a Stage T3b, and 2 (4%) a stage T4a tumor. No patient had a Koos Stage T4b lesion.

The initial symptom was decreased hearing function in 34 patients (68%), tinnitus in 14 (28%), dizziness in 14 (28%), facial numbness in 2 (4%), slight facial muscle weakness (House-Brackman Grade II) in 2 (4%), and headaches in 1 patient (2%). Six patients (12%) were asymptomatic. A decrease in hearing was also considered the first/initial symptom when the patient was reporting a sensation of transitory weakening of the hearing or a slight subjective difference compared with normal function. In some patients (19 cases) there was a combination of some of the aforementioned symptoms (more often a combination of hearing decrease and dizziness or hearing decrease and tinnitus).

In all patients selected for the study, hearing function was GR Class I or II prior to the treatment. Thirty-three patients (66%) had GR Class I function with an average hearing loss at the tonal audiometry from 0 to 30 dB, or with a vocal discriminative ability equal to 70–100%. Seventeen patients (34%) had GR Class II function with an average loss at the audiometry of 31–50 dB, or with a vocal discriminative ability equal to 51–69%.

**Radiosurgical Technique**

All patients underwent stereotactic radiosurgery in which the Leksell Gamma Knife model C (Elekta Instrument AB) was used. A Leksell stereotactic head frame (model G) was positioned after mild sedation and local anesthetic administration. Magnetic resonance images (1.5-T Magnetom Vision model, Siemens) were acquired for tumor visualization. The MR images were Gd-enhanced axial and coronal T1-weighted (2-mm thickness without gap, TR = 650 msec, TE = 14 msec, matrix 512 × 512, and double acquisition), 3D CISS (reconstructed to 1.2-mm thickness without gap, TR = 4000, TE = 250, matrix 512 × 512), and axial T2-weighted (2-mm thickness without gap, TR = 3000 msec, TE = 120 msec, matrix 512 × 512) sequences. The GammaPlan system (Elekta Instruments) was used for treatment planning and dose calculation.

Patients were monitored during the day of treatment and discharged the following day, without any additional medical indications other than those given during hospitalization. The tumor volume varied between 0.03 and 6.6 ml (mean 1.34 ± 0.22 ml, median 0.73 ml). To obtain more conformal planning, multiple isocenters were used (mean 11, median 11, range 1–25 isocenters). The mean peripheral prescribed dose was 13.0 Gy (range 12–16 Gy). The 50% isodose line was used in the majority of patients.
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Follow-Up

After the radiosurgical treatment, patients underwent periodic evaluated clinical and audiological assessment (contrast-enhanced MR imaging and total and vocal audiometry every 6 months for the 1st year and then yearly thereafter). Follow-up MR images were analyzed using OsiriX (imaging software DICOM viewer) for the calculation of the volume in milliliters. Tumor growth control was defined as evidence of no further tumoral growth or tumor reduction as evidenced by volumetric calculation on follow-up images. This technique appeared to be the gold standard for the evaluation since it introduced fewer biases linked to the operator.

Statistical Analysis

All statistical calculations were performed using the standard statistical processing software (SPSS, Inc., version 13.0).

Continuous data were examined according to homogeneity of variance and are expressed as mean ± SEM. The predictive pre- and peritreatment factors, assumed as able to affect the hearing function of the patients, were calculated with uni- and multivariate analyses. The Kaplan-Meier method was used to calculate the disease-free survival curve. The comparison among continuous variables was performed with the Mann-Whitney 2-sample t-test, whereas categorical variables were calculated using the Fisher exact probability test. The multivariate analyses were performed with multiple logistic regression analyses, using the Newton-Raphson method.

In case of numeric, not regularly distributed variables, the logarithm was calculated with base number 10; nonetheless, to improve the interpretation, the data will be indicated with their natural value. Some correlations with continuous numeric variables were made by subdividing the sample into 2 groups according to the mean value.

The results were considered statistically significant for p values < 0.05.

Results

Monitoring the Disease

All patients underwent neuroradiological follow-up for a minimum of 6 months (median 36 months, mean 38.4 months, range 6–96 months); 27 patients (54%) had a follow-up ≥ 36 months. The mean tumor volume at treatment was 1.34 ± 0.22 ml, whereas at the last neuroradiological follow-up it was 0.93 ± 0.17 ml (p < 0.001).

At the last neuroradiological follow-up evaluation, 34 patients (68%) exhibited a reduction in the size of their tumor, and no significant changes were identified in 14 patients (28%). In the remaining 2 patients (4%), the size of the tumor increased after 12 months in one and 24 months in the other. Overall, the tumor growth control rate was 96% (Fig. 1).

Analysis of Pretreatment Hearing Function

Prior to the GKS, 7 (21%) of 33 patients with GR Class I hearing had Koos Stage T1 disease, while only 1 (6%) of 17 patients with GR Class II hearing harbored a tumor that was exclusively intracanalicular (not significant, p = 0.237, Fisher exact test).

The mean and median ages of patients with GR Class I hearing were 49.8 and 50.0 years, respectively; those in patients with GR Class II hearing were 56.9 and 58, respectively (p = 0.047, Mann-Whitney U-test). The mean and median tumor volumes in patients with GR Class I hearing were 0.92 and 0.58 ml, respectively; those in patients with GR Class II function were 2.16 and 1.3 ml, respectively (p = 0.013 Mann-Whitney U-test).

Thirty-four patients (68%) presented with hearing decrease as an initial symptom, whereas the remaining 16 patients (32%) presented with other symptoms or were asymptomatic during the diagnosis. Of the 16 patients without subjective hearing decrease at presentation, function was GR Class I in 15 and Class II in 1 (p = 0.04, Fisher exact test).

General Results of Hearing Function

Prior to the GKS, hearing function was GR Class I in 33 patients (66%) and GR Class II in 17 (34%). The mean audiometric follow-up period was 41 ± 3.5 months (median 36.5 months, range 6–90 months). At the last follow-up session, all patients retained some testable hearing. In 24 patients (48%), the same GR class was maintained. The deterioration of hearing function from one GR class to a lower one occurred at a mean of 17 months (median 12 months, range 3–59 months). Five patients, for whom follow-up exceeded 59 months, did not experience GR class deterioration. At the last follow-up, 34 patients (68% of the total) possessed functional hearing; 21 (61.8%) of these had GR Class I hearing and 13 (38.2%) had GR Class II hearing. The remaining 16 patients (32% of the overall population) instead had impaired hearing; 15 (93.8%) had GR Class III function and 1 (6.2%) had class IV function. The mean time to functional hearing loss was 18.7 months (median 12.5 months, range 3–59 months).

Nineteen (58%) of 33 patients with GR Class I hear-
Analysis of Predictive Parameters of Hearing Function

The probability of maintaining functional hearing after GKS was partially linked to the initial symptoms and partially linked to the tumor characteristics.

Patients with pretreatment GR Class I hearing function exhibited a better preservation of hearing after the treatment than those with more impaired hearing at presentation (p < 0.001, Fisher exact test).

Patients with initial symptoms other than hearing decrease (for example, tinnitus and dizziness) had also a statistically significant probability of retaining functional hearing after treatment compared with those who had experienced even a sensation of transitory weakening of the hearing or a slight subjective difference (p = 0.001, Fisher exact test). Patients with an exclusively intracanalicular tumor (Koos Stage T1) had a greater probability of retaining good or functional hearing after treatment (p = 0.043, Fisher exact test). All patients with Koos Stage T1 disease maintained functional hearing after GKS.

With univariate analysis we also found a correlation between the tumor being right sided and the hearing function after the treatment (p = 0.014, Fisher exact test). Age also seemed to be related to the hearing outcome (p = 0.036, Fisher exact test); patients who were younger than the mean age (54 years) of the group maintained functional hearing in 85.5% of the cases, whereas the remaining patients kept a functional hearing in 52.2% of the cases.

In the multivariate analysis, all of the parameters lost their statistical relevance except for the pretreatment GR class. The initial symptoms and Koos classification can be deemed fairly significant (Table 3).

Other correlations have not been found between the posttreatment result and other patient characteristics such as sex, deficit of CN VII, and tumor volume. Significant correlations were not found in the number of isocenters used during the treatment.

To exclude a possible influence of the audiometric follow-up period on the result, a univariate analysis was carried out, based on the mean value, which resulted in no statistically significant differences (p = 0.762, Fisher exact test).

**Analysis of Predictive Parameters of Hearing Function**

<table>
<thead>
<tr>
<th>Before GKS</th>
<th>GR Class</th>
<th>After GKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>II</td>
<td>III</td>
</tr>
<tr>
<td>I</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>II</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>total</td>
<td>21</td>
<td>13</td>
</tr>
</tbody>
</table>

**TABLE 2: Analysis of hearing function**

The hearing function improved after treatment in 2 patients (4%) from Class II to I.

**TABLE 3: Summary of statistical findings**

<table>
<thead>
<tr>
<th>Tendency</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>M &gt; F</td>
<td>0.351</td>
<td>0.960</td>
</tr>
<tr>
<td>lrt &gt; lt</td>
<td>0.014†</td>
<td>0.304</td>
</tr>
<tr>
<td>other sign &gt; hearing decrease</td>
<td>0.001†</td>
<td>0.108</td>
</tr>
<tr>
<td>HB I &gt; HB III</td>
<td>1.000</td>
<td>0.995</td>
</tr>
<tr>
<td>T1 &gt; other stage</td>
<td>0.043†</td>
<td>0.193</td>
</tr>
<tr>
<td>&lt;54 yrs</td>
<td>0.036†</td>
<td>0.596</td>
</tr>
<tr>
<td>large &gt; small‡</td>
<td>1.000</td>
<td>0.995</td>
</tr>
<tr>
<td>I &gt; II</td>
<td>&lt;0.001†</td>
<td>0.022†</td>
</tr>
<tr>
<td>low &gt; high‡</td>
<td>0.271</td>
<td>0.242</td>
</tr>
</tbody>
</table>

* HB = House-Brackman grade.
† Significant parameter on hearing outcome.
‡ Tendency refers to the median value.

**Conservation of the Function of CNs V and VII**

The function of the trigeminal nerve was preserved in all the patients except for those 2 patients with hypesthesia and trigeminal neuralgia as initial symptoms. In these patients the preexisting symptoms persisted even after the treatment.

- None of the patients developed a facial nerve deficit. The 2 patients with facial weakness (House-Brackman Grade II) as an initial symptom experienced a regression of the deficit even though the tumor volume remained unchanged.

**Discussion**

- The therapeutic options for patients with VS and functional hearing at diagnosis include clinical observation, resection, fractionated radiotherapy, and stereotactic radiosurgery. Surgery has been the only therapeutic option available for a long time, and the costs are high mortality and morbidity rates. In the past the preservation of hearing function was a difficult goal to achieve. With the evolution of diagnostic techniques, an early diagnosis of small schwannomas in patients with functional hearing is common. The preservation of functional hearing is therefore a relevant topic. The introduction of radiosurgery has added a powerful management tool for VS as it allows good tumor growth control with minimal risks of collateral effects.

- The optimal management of VS, however, is still debated because of the unclear natural history of the disease. Tumor growth, incidence and rate, and hearing outcome of the wait-and-see policy are not precisely known at present. These tumors are commonly considered to be slow-growing lesions. Several studies analyzing the natural history of VS with a wait-and-see policy have been performed but conflicting results have been shown. In conservatively managed patients with VS, tumor growth is reported to vary from 15% to 85%, with hearing pres-
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... studies published between 1987 and 1992. For the specific purpose of hearing outcome, the yearly growth rate seems also to be an important factor as outlined by Sughrue and colleagues in a recent meta-analysis. Different patterns of growth have in fact been shown; some tumors exhibit no growth, whereas others tend to grow very quickly. In an interesting prospective and consecutive single-center registration study of all patients diagnosed with a VS in Denmark between 1989 and 2004 and not allocated to treatment (552 patients, mean follow-up 3.6 years, range 1–15 years; extrameatal maximum diameter ≤ 20 mm), Stangerup et al. found that tumors with an extrameatal extension were more likely to grow than purely intrameatal tumors (28.9 vs 17%, respectively). Tumor volume was not assessed but maximum tumor diameter was. However, as correctly pointed out by Yoshimoto, studies conducted with a wait-and-see strategy are often biased by the inclusion criteria, which vary among the different studies, and especially by short follow-up. Moreover the choice of conservative management is often offered to subsets of patients with specific characteristics—namely, old age, poor general health status, and small tumor size. Therefore, the results obtained in these studies are not easily adaptable to the whole population and in particular to healthy young patients with medium-sized tumors and with reasonably a long life expectancy. Studies with longer median follow-up are therefore necessary to establish the real natural history of VS, particularly to ascertain which tumors are more likely to grow and become symptomatic, and thereby to know the best candidates for treatment.

Several studies have strongly influenced decision-making in the management of VSs. Yamakami et al. reported the results of a wait-and-see strategy in a group of patients with VS and a follow-up duration of 3 years; half of the patients had tumor growth, one-third had a serious hearing impairment, and one-fifth eventually needed surgery. In a prospective study comparing surgery and GKS, Pollock and colleagues demonstrated how radiosurgery offers better functional results and a better quality of life for the patient.

The Pittsburgh group, in contrast, has pointed out, based on the same follow-up of the disease in the longer term, that modern treatment plans involving the Gamma Knife offer a lower morbidity rate than that seen in previous studies published between 1987 and 1992.

Today, an increasing number of studies are focusing on the possibilities of preserving hearing in patients undergoing GKS for VS. Our study is an effort to help to better clarify this topic.

Tumor Growth Control

The most recent reports point out a range of tumor growth control after GKS of 93–100%, also in the long term.

In our study, with a mean neuroradiological follow-up of 38.4 months (median of 36 months in all patients; ≥ 36 months in 54% of patients), growth control was 96%. At the last neuroradiological follow-up, 34 (68%) of 50 patients exhibited a reduction in tumor size, whereas no significant changes were identified in 14 patients (28%). In the remaining 2 patients (4%), the size of the tumor increased after 12 months in one individual and 24 months in the other. In the first of these 2 patients, a 56-year-old woman with a Koos Stage T4a VS, there was an increase in size of few millimeters due to cell swelling; in the second patient, a 61-year-old woman with a Koos Stage T3b tumor, the size increased by 22.5% (from 4.0 to 4.9 ml), and this was also reconfirmed in the subsequent neuroradiological follow-up evaluation.

None of the patients with dimensional growth of the tumor needed a second treatment for the purpose of tumor control. The patient in whom the tumor grew 24 months after GKS (reconfirmed after 36 months) underwent a ventriculoperitoneal shunt implantation for obstructive hydrocephalus.

Kondziolka et al. and Litvack et al. have reported a tumor growth control of 98% in their studies. In both studies, only patients with a tumor growth confirmed on serial follow-up imaging were considered to reflect dimensional growth. Considering these criteria, the disease control percentage seems to be identical to that of our study. Kondziolka et al. also reported an increase of 1–2 mm for some tumors during the first 12 posttreatment months, with loss of contrast in the central area (probably due to cell swelling) of the tumor. By extending the observation period, a size reduction was experienced compared with that seen before treatment. Tumor growth control was judged based on 2 methods: evidence of no further growth on neuroimages or calculation of the volume reduction.

Hearing Function After GKS

In the management of VS the functional prognosis of hearing function is different from that of other CNs. The onset of a facial nerve deficit in the natural history of this disease is rare and occurs only in cases of fairly large tumors; thus, the rare appearance of a deficit of this nerve in the months following radiosurgery must be interpreted as a collateral effect of the treatment.

Due to the high frequency of hearing loss (acute or progressive) in untreated patients, however, it is difficult to determine whether hearing loss is due to the treatment or not.

The exact mechanism of delayed hearing loss after radiosurgery is still unclear. Perhaps direct damage to primary sensory cells, radiation damage to the cochlear nerve, or direct damage to the nerve or internal auditory artery caused by the lesion result in compression or thrombosis with consequent ischemic damage to the cochlea.

There are only a few studies in the literature that analyze hearing preservation exclusively in patients with normal or subnormal hearing (GR Class I). Studies regarding the possibility of retaining functional hearing are increasing in number. In these studies the probability of retaining functional hearing in patients with GR Class I or II function varies from 33 to 74%.

In our study, patients were treated with a mean marginal radiation dose of 13 Gy. With a mean audiometric follow-up of 41 ± 3.5 months (range 6–90 months), 34 patients (68%) of 50 retained functional hearing.
In a recent publication, Lunsford et al.,33 using a mean marginal dose of 13 Gy, reported posttreatment functional hearing in 50–77% of their patients, with a peak of 90% in the subgroup with exclusively intracanalicular tumors (Koos Stage T1). With a long-term follow-up of <3 years, Chopra and colleagues3 reported functional hearing in 77% of their patients.

In a recent study by Kano and colleagues,20 the hearing preservation rate was 71% in 77 patients for whom the mean follow-up period was 20 months. Iwai and coworkers3 demonstrated that, with marginal radiation doses \( \leq 12 \) Gy, it is possible to obtain 92% growth control after 5 years and a hearing function preservation rate of 56%. Our data also appear to be in line with the literature.50

Crude rates of hearing preservation must be weighted with the time course of hearing in the long term. Hearing impairment usually occurs gradually over 6–24 months. However, as indicated by Chopra and colleagues,7 hearing can deteriorate even up to 100 months after radiosurgery. Of the 26 patients in our series in whom hearing deteriorated, only 4 experienced hearing impairment after 2 years and 1 before 6 months.

All our patients retained some testable hearing. In a study of 74 patients with GR Class I hearing function at treatment, Tamura et al.50 reported that 5 patients (8.1%) in a subgroup of 58 individuals experienced total hearing loss. Their larger sample size (74 vs 50 patients) and their longer median follow-up (48 vs 36 months) than in ours does not allow us to exclude the possibility that some events may also occur in our patients as follow-up continues.

In 52% of patients in our series there was a deterioration of one or more GR class. This finding is in line with the literature where the GR class remains stable in 37–84% of the patients. However, there are a few radiosurgical series with a median follow-up exceeding 36 months. In a study on 73 patients with a median follow-up of 135 months, Hasegawa et al.12 reported GR class preservation in 37% of 19 patients with GR I or II at treatment. Chopra et al.1 however, reported GR class preservation of 56.6% in 106 patients with GR Class I or II at treatment. In our series the mean time to deterioration was 17 months (median 12 months, range 3–59 months). Iwai et al.18 reported that 41% of their patients experienced hearing loss with a similar mean onset time of 19.8 months (range 6–36 months).

In the present study the mean time to functional hearing loss was 18.7 months (median 12.5, range 3–59). Retention of functional hearing (that is, either GR Class I or II function at treatment and at least GR Class II after treatment) occurred in 68% of our patients. Still in 110 patients with follow-up exceeding 3 years, Chopra et al.1 reported a rate of serviceable hearing preservation in 77%. In our series 59% of patients (16 of 27) with follow-up exceeding 3 years retained functional hearing. Iwai and coworkers,18 on the other hand, reported results more similar to ours, with 56% of patients retaining serviceable hearing.

Nineteen (58%) of 33 patients with GR Class I before GKS maintained the same functional class in a mean follow-up period of 33.5 months (median 36 months, range 6–84 months), whereas 29 (88%) of 33 (Table 2) main-
tained functional hearing (GR Class I or II) with a median onset of deterioration of 18 months (range 6–39 months). In our series follow-up periods exceeding 3 years (average 57.2 months, median 53 months, range 36–90 months) were present in 19 cases in which function was GR Class I at presentation. Of these, 16 retained serviceable hearing (84.2%), and 10 of the 16 (62.5%) retained GR Class I function. Tamura et al.,50 however, who reported on a larger sample size with a longer follow-up duration, noted that 50% of their patients retained GR Class I three years after radiosurgery and 78.4% retained serviceable hearing. As stated above, we cannot exclude the possibility that further hearing impairment will not occur during the ongoing follow-up. In our study, however, we performed GKS at a marginal mean dose of 12 Gy in an attempt to try to preserve functional hearing in a larger percentage of patients. During the last follow-up of 74 patients, 78.4% retained functional hearing and the disease was controlled in 93% of the cases.

If we consider the subgroup of patients in our study with exclusively intracanalicular tumors (8 of 50 patients), then hearing function was preserved in 100% of the cases at a mean follow-up of 50 months.

In the literature, there are 2 studies that focus on the preservation of hearing function in exclusively intracanalicular tumors. In a prospective study, Iwai and colleagues37 analyzed data in 29 patients undergoing GKS in which the marginal dose was 12 Gy; hearing function was preserved in 64% during a mean follow-up period of 89 months. The second is a study conducted by Niranjana and colleagues.36 They analyzed a sample of 96 patients in whom the marginal dose was 13 Gy and found that hearing function was preserved in 64.5% during a mean follow-up period of 42 months.36

Based on these data, it appears that there is no difference in the hearing outcome between tumors receiving marginal doses of 13 or those receiving 12 Gy for intracanalicular tumors; however, as pointed out by Pollock and colleagues40 in a retrospective study, there was a reduction of tumor growth control in patients treated with marginal doses \( \leq 13 \) Gy (\( p = 0.03 \)). Because of the encouraging hearing preservation rate in our study and because of the good tumor growth control rate, it would be interesting to expand the sample to obtain more statistically significant results.

**Predictive Factors of Hearing Function**

The results reported in the literature are often difficult to compare from study to study due to the high heterogeneity of patient populations and variables considered to be possible predictive factors. In our study, the factors that appeared to be significantly associated with retention of hearing function after the treatment are as follows: GR Class I hearing (\( p < 0.001 \)); age younger than 54 years (\( p = 0.036 \)); initial symptoms other than hearing decrease (\( p = 0.001 \)); and Koos Stage T1 disease (\( p = 0.043 \)).

In the multivariate analysis, only GR class prior to the GKS appeared to be significantly associated with the preservation of functional hearing. Nonetheless, it must be pointed out that the latter is significantly influenced by age, pretreatment symptoms, and tumor volume.
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These same factors also appeared to be statistically significant in other studies. In one of the published studies, Régis and colleagues reported a hearing preservation rate of 60% in 183 patients and a statistically significant association with tinnitus as the initial symptom, in addition to the factors already discussed.

Kano and colleagues also found GR Class I, the age of the patient at treatment, and the location of the lesion to be predictive factors; the association of the initial symptoms and outcome was not analyzed, but the authors found an association between tumor size and the hearing outcome (p = 0.014, log-rank test).

Based on the results of published articles and our study, we believe that identification of the aforementioned factors prior to GKS may provide a better index by which to estimate the hearing outcome. The comparison of the data in the present study and previous publications confirms the repeatability of our results.

Functional Preservation of CNs V and VII

It is now well known that most of the posttreatment damage to CNs V and VII appears 1–24 months after radiosurgery, with an average onset after 6 months. During the follow-up period, none of our patients has developed new facial and trigeminal nerve deficits. This finding is also in line with previously published studies. In our series, a later onset of CN damage cannot be excluded as follow-up continues. Some authors in fact have reported facial and trigeminal nerve disfunction even up to 36 and 48 months after radiosurgery. The 2 patients (4%) who, at treatment, were suffering from a slight facial nerve deficit (House-Brackman Grade II) ipsilateral to the tumor recovered during the follow-up period. This finding has also been reported in the literature and is often used as comparison between the radiosurgical treatment and microsurgery.

Conclusions

Stereotactic radiosurgery involving the Gamma Knife is a very effective option for treating VS. It is a safe, effective, and minimally invasive technique associated with better tumor growth control rates and preservation of hearing and facial nerve function than surgical treatment. The prescribed dose of 13 Gy appears to represent an excellent compromise between monitoring of the disease and hearing preservation.

The identification of prognostic factors can also further improve the already good results and allow us to understand if the immediate treatment of properly selected patients, even with small tumors, could offer greater changes to retain functional hearing after the treatment. Gardner-Robertson class prior to the GKS seems to be a predictive factor for hearing functional outcome.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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A. Franzin et al.