The Changing Paradigm for the Surgical Treatment of Large Vestibular Schwannomas

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Abstract

Objective Planned subtotal resection followed by Gamma Knife surgery (GKS) in patients with large vestibular schwannoma (VS) has emerged during the past decade, with the aim of a better functional outcome for facial and cochlear function.

Methods We prospectively collected patient data, surgical, and dosimetric parameters of a consecutive series of patients treated by this method at Lausanne University Hospital during the past 8 years.

Results A consecutive series of 47 patients were treated between July 2010 and January 2018. The mean follow-up after surgery was 37.5 months (median: 36, range: 0.5–96). Mean presurgical tumor volume was 11.8 mL (1.47–34.9). Postoperative status showed normal facial nerve function (House–Brackmann I) in all patients. In a subgroup of 28 patients, with serviceable hearing before surgery and in which cochlear nerve preservation was attempted at surgery, 26 (92.8%) retained serviceable hearing. Nineteen had good or excellent hearing (Gardner–Robertson class 1) before surgery, and 16 (84.2%) retained it after surgery. Mean duration between surgery and GKS was 6 months (median: 5, range: 3–13.9). Mean residual volume as compared with the preoperative one at GKS was 31%. Mean marginal dose was 12 Gy (11–12). Mean follow-up after GKS was 34.4 months (6–84).

Conclusion Our data show excellent results in large VS management with a combined approach of microsurgical subtotal resection and GKS on the residual tumor, with regard to the functional outcome and tumor control. Longer term follow-up is necessary to fully evaluate this approach, especially regarding tumor control.

Keywords

- combined approach
- vestibular schwannoma
- surgery
- radiosurgery
- Gamma Knife

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Introduction

Large vestibular schwannomas (VSs) represent a significant challenge in the practice of skull base surgery. Due to the excellent results obtained by stereotactic radiosurgery (RS) in patients with small- and medium-sized VSs, the skull base neurosurgeon is often faced with the challenge of preserving facial and cochlear function even in large VS. Most patients with large VS, who present to a skull base clinic, are well informed regarding advances in the treatment of this disease and therefore expect similar results in the setting of large tumors. These factors stimulated us to develop a new concept of treatment for large VS that combines planned subtotal resection followed on by Gamma Knife RS. The idea is to minimize the risk for neurological deficits after surgery for large VS, thereby achieving good functional results, similar to those of patients with small tumors treated with upfront Gamma Knife. The surgical technique is aimed to achieve a subtotal microsurgical resection of the tumor, leaving a thin capsule, which protects the nerves against surgical damage. After a period of ~6 months, the pulsation of the brain allows the closing of the capsule on itself and the residual tumor to resemble a small sphere. This residual tumor then becomes a perfect target for subsequent Gamma Knife treatment.

In this article, we present our experience in the Lausanne University Hospital with this combined approach, focusing on the microsurgical technique guided by neurophysiology and the technical aspects of Gamma Knife RS. We present our case series, with the results on facial and cochlear nerve outcomes, in comparison with similar series published in the literature.

Materials and Methods

Patient Population

The study was designed as an open, nonrandomized, prospective series. A case report form was created since the first treated patient and prospectively filled in at baseline and during follow-up. Between July 2010 and January 2018, 47 patients with Koos grade IV VS were treated by a planned subtotal microsurgical resection, followed on by Gamma Knife surgery (GKS) of the residual tumor, in the framework of a combined approach. Inclusion criteria for not performing upfront GKS were size and/or significant brain stem compression. Neurofibromatosis type II was present in one (2%) case. Four (8.5%) patients, initially treated with upfront GKS, continued to present tumor growth and were considered as treatment failures after 3 years of follow-up; they were then treated by the same approach a second time and are also included in this study.

Outcome Measures

Patients and tumor characteristics were analyzed before surgery, at the time of GKS and during regular follow-up, at 6, 12, 24, 36, 48, 60, 72, and 84 months (unless clinical indication at another time point), respectively. Clinical examination and magnetic resonance (MR) imaging were

performed. The facial nerve function was assessed using the House–Brackmann (HB) grading scale.¹ The hearing assessment included pure tone audiometry and speech discrimination score and was graded according to the Gardner and Robertson (GR) classification scale.² Maximal diameter was defined as the largest one after measuring all the three axes (lateral, anteroposterior, and superoinferior). The volume was defined by automatic segmentation using the Leksell GammaPlan planning software (Elekta Instruments AB, Stockholm, Sweden) on all MR data, including the preoperative images. The tumor size (maximal diameter) and volume were measured on the serial MR imaging (MRI).³ Tumor control was considered achieved after combined approach if subsequent follow-up MRI showed stability or decrease in tumor size.

Surgical Technique

The surgical approach used in this series is the classical retrosigmoid approach in the park bench position. All patients had intraoperative neuromonitoring using a NIM-Eclipse (Medtronic, Minneapolis, United States) system. The main goals were to map the facial and cochlear nerves to guide the resection of the tumor, thereby minimizing the risk of nerve injury.

During patient positioning (for brachial plexus protection), the contralateral median nerve is stimulated (200 μ s, 4.1 Hz, 20 mA) using bipolar electrodes and somatosensory evoked potentials are recorded between Fz–contralateral Erb point and Fz–ipsilateral C3 or C4. N9 latency increase or amplitude decrease recorded at Erb point could indicate brachial plexus compression. On the contrary, increased N20 latency or N20 amplitude reduction with constant N9 wave could reveal brain stem suffering during the tumor surgery.

Facial nerve branches were monitored using bipolar electrodes placed in the frontalis, orbicularis oculi, orbicularis oris, and mentalis muscles. Glossopharyngeal and vagus nerves were monitored using contact electrodes incorporated in the endotracheal tube (Xomed; Medtronic, Jacksonville, Florida, United States) and 11th nerve function was monitored by inserting electrodes into the trapezius muscle. Combination of free-running electromyography (EMG) and compound muscle action potential after direct monopolar 1 Hz, monophasic negative 200 μ s duration electrical stimulation were used to monitor cranial nerves of interest. Brain auditor evoked potential (BAEP) recorded between Cz–A1 and Cz–A2 derivations were used to monitor cochlear nerve function.

The retrosigmoid craniotomy allows exposure of the inferior border of the transverse sinus and the medial border of the sigmoid sinus. The opening of the lateral cerebello-medullary cistern allows the cerebrospinal fluid (CSF) to be aspirated and achieves relaxation of the cerebellum. The durotomy is then realized in a linear fashion, parallel to the sigmoid sinus on to the transverse sigmoid junction. Once the tumor is visualized, the posterior part of the tumor capsule is stimulated, to exclude the presence of a posteriorly placed facial nerve. The capsule is then opened and the

majority of the tumor is decompressed with an ultrasonic aspiration. During the decompression, the interior part of the tumor is stimulated often, to define the position of the facial nerve on the anterior part of the capsule. We usually start with a current of 4 to 5 mA and progressively decrease it until 1 to 2 mA. If we have a response on the facial nerve monitoring at 2 mA, we estimate that the thickness of the capsule covering the nerve in that region is more or less than 2 mm thickness. In fact, even if the relationship between the distance to the facial nerve and the stimulating electrode is not linear and depends on many factors (such as tissue impedance, presence of CSF, or the polarity/duration of the stimulus), the use of the standard monopolar stimulation protocol allows a rough correlation between the stimulation intensity and the thickness of the capsule to be ~1 mm for every increase of 1 mA.

When the internal decompression is deemed satisfactory, the tumor capsule is progressively mobilized from the arachnoid plane and excised leaving in place the portion of the capsule against the facial and cochlear nerves. During this phase, the capsule is inspected and stimulated from the external surface, to estimate the thickness of the capsule and identify the facial nerve from the external surface. Spontaneous EMG bursts lasting more than 30 seconds on the free-running EMG are considered alert signals. The uniformity of the thin capsule is the result of a combination of neuromonitoring and surgeon experience. The integrity of the facial nerve is tested at the end of the surgery by means of direct brain stem stimulation in the facial root entry zone with a small current of 1 mA. If there is a response in the facial nerve with a current of less than 1 mA and there is no persistent EMG-bursting activity, we assume that there is no lesion on the nerve (► Fig. 1).

To estimate the position of the cochlear nerve, because of the impossibility of monitoring this nerve directly, we map the course of the facial nerve from the internal auditory meatus to the root entry zone in the brain stem. We consider that the cochlear nerve is normally located inferiorly to the facial nerve and try to keep the thickness of the capsule over the presumed position of the cochlear nerve. We also use the BAEP and consider an alert sign as a reduction of peak III amplitude of more than 50%. The opening of the internal auditory meatus is not performed routinely because of the high risk of nerve injury in this region.

An early MRI is performed the day after surgery to estimate the volume of the residual tumor. Another MRI is usually performed 3 months later, to see if the new shape of the residual mass is suitable for the Gamma Knife treatment.

Gamma Knife Surgery Technique

The Leksell G stereotactic frame (Elekta Instruments AB) was fixed under local anesthesia, with specific attention to avoid the area of the previous retrosigmoid approach. All patients underwent stereotactic MRI (1.5 T, Siemens, Erlangen, Germany) and computed tomography (CT) with bone windows. The MR sequences used were T1 weighted with and without gadolinium contrast and T2 CISS/Fiesta without contrast (in small remnants) and/or with contrast (in larger remnants); T2 CISS with contrast is particularly useful to differentiate between the nerves and the tumor, while further being able to perform "microradiosurgery."⁴ Target definition, treatment dosimetry, and coregistration of follow-up MRI were performed with Leksell GammaPlan planning software versions 10 and 11. The modiolus of the cochlea was defined on bone CT images and the dose

Fig. 1 Compound muscle action potential (CMAP) recorded after facial nerve 1 mA stimulation. Monopolar stimulation (1 Hz, 1 mA, 200 µs) of the external side of the tumor's capsule induced a muscular depolarization of the four muscles innervated by the facial nerve (first four traces: frontalis, orb. oculi, orb. oris, and mentalis) with a time delay of 10 ms but no response of the muscle innervated by the cranial nerves IX to XI. This response denotes a very close proximity (around 1 mm) of the stimulating electrode to the facial nerve. Orb, orbicularis.

received was further calculated (as the dose received by the first 1% of the volume and as the maximum dose). If this dose was more than 4 Gy, in patients with serviceable hearing, additional sector blocking was used, aiming to preserve hearing on long-term basis.^{5,6} Special attention was also paid to the dose received by the vestibule,⁷ which is supposed to play a potential role in the development of acute vestibular effects after GKS. The stereotactic irradiation was delivered with Leksell Gamma Knife Perfexion (before June 2016) and further ICON (after June 2016; Elekta Instruments AB). The procedure was performed on an ambulatory basis.

Time Frame between Surgery and GKS

GKS was generally planned to take place around 3 to 6 months after microsurgical resection. However, the exact scheduling depended on the appropriateness of the target for RS, mainly the shape and the volume of the residual tumor capsule on follow-up MRI. One supposes that the open residual capsule at the end of surgery gradually closes on itself due to brain pulsations and reduction of the mass effect; ideally, a complete closure therefore converts a large debulked VS into a small more globular tumor with a shape and size that becomes more suitable for GKS (► Fig. 2). A vast majority of patients had early (within 48 hours) postoperative MRI, and all patients had MRI 3 to 4 months after surgery (► Fig. 3). Depending on the size and shape of the residual tumor at that time, GKS was scheduled, or patients were further followed up with MRI. Five patients needed staged surgery (i.e., they were operated twice) before GKS because the residual volume after the first surgery was still considered too large for safe GKS.

Data Analysis

All collected data were analyzed for the whole group (47 patients). Moreover, data were examined separately in the subgroup of patients with residual hearing before surgery and in which preservation of cochlear nerve function was attempted (Group A, GR 1–3, $n = 28$) and in patients with poor or no residual preoperative hearing (Group B, GR 4 and 5, $n = 19$).

Statistical Analysis

Statistical analysis were conducted using Stata (STATA version 11, STATA Corp., Texas, United States). For the two-sample t -test (continuous variables), a p -value of <0.05 was considered statistically significant. For categorical variables, chi-square test was performed.

Results

Basic Demographic and Preoperative Data

Combined approach was performed in 47 cases (male:female ratio 22:25). Mean age at the time of microsurgical resection was 51.2 years (range: 22–85). Clinical presentation was progressive hearing loss (30 patients, 63.8%), sudden hearing loss (2 patients, 4.25%), gait problems (4 patients, 8.5%), trigeminal nerve symptoms (2 patients, 4.25%), tinnitus (2 patient, 4.25%), vertigo (4 patients, 8.5%), and was an incidental finding in 3 patients (6.4%). The VS was solid in 44 patients (93.6%) and mixed (solid and cystic) in 3 patients (6.4%). All patients had normal facial nerve function (HB I) before surgery, except for one with HB IV. All patients had preoperative hearing evaluation consisting of tonal and vocal audiometry (► Table 1).

The overall ($n = 47$) mean presurgical tumor volume was 11.8 mL (1.47–34.9) and mean presurgical maximal diameter was 33 mm (median: 31.5, range: 20–45). The mean tumor volume was 9.5 mL (range: 1.47–25) in Group A and 15.2 mL (range: 3.6–34.9) in Group B ($p = 0.01$, two sample t -test). The mean maximal diameter in Groups A and B were 30.7 (median: 30, range: 20–42) and 36.3 (median: 37.7, range: 26.1–45), respectively ($p = 0.003$, two sample t -test).

Postoperative Data and Functional Outcome

The mean follow-up after surgery was 37.5 months (median: 36, range: 0.5–96). Immediate postoperative clinical examination showed normal facial nerve function (HB I) in all patients (including the recovery from HB IV to HB I for one case with preoperative facial palsy). Cochlear nerve preservation surgery was attempted for 28 patients in Group A, who presented with GR class 1 ($n = 19$), 2 ($n = 3$), or GR 3 ($n = 6$) before surgery. In 19 patients in GR class 1, postoperative audiogram showed

Fig. 2 Schematic diagram in the coronal plane showing the treatment paradigm for large vestibular schwannoma. From left to right, the images show the tumor at presentation, residual tumor immediately after surgery, and on serial follow at 3 and 6 months. When the shape of the tumor resembles a small sphere, Gamma Knife (GK) surgery is performed.

Fig. 3 Axial images of T1-weighted contrast-enhanced MRI, showing preoperative size of the tumor (A), the residual capsule the day after surgery (B), the folding of the capsule 6 months after surgery on the day of GKS (C), and the follow-up MRI, 3 years after GKS (D). GKS, Gamma Knife surgery; MRI, magnetic resonance imaging.

that 16 (84.2%) retained normal hearing after surgery, 2 passed in GR class 3 (10.5%), and 1 (5.3%) lost hearing (GR class 5). All patients with preoperative GR 2 remained in GR 2 after surgery. In six patients with GR class 3, two improved and passed in GR2, three remained stable, and one lost hearing (GR 5).

In group B ($n = 19$), in 17 patients presenting with preoperative GR 5, one improved to GR 1 and two improved to GR 3 after microsurgical resection. For two patients in GR 4 preoperatively, one remained in the same hearing class and one passed to GR 5 after surgery.

One of the two patients, who presented with secondary trigeminal neuralgia before surgery, had transient facial hypoesthesia following surgery. Trigeminal neuralgia disappeared in both cases. One patient had a partial vagus nerve deficit. No other neurological deficits were encountered after surgery.

Gamma Knife Radiosurgery Data and Outcome

Forty-three patients have undergone GKS after surgery by January 2018. Mean duration between surgery and GKS was 6 months (median: 5, range: 3–13.9). The mean tumor volume at the time of GKS was 3.3 mL (range: 0.5–12.8),

which corresponded to a mean residual volume of 31% compared with the presurgical volume.

The volume at the time of GKS, when compared with the presurgical one, was higher when cochlear nerve preservation was attempted (group A, 36.8% of presurgical volume; group B, 26.1% of presurgical volume) ($p = 0.03$, two sample t -test). This is essentially related to the fact that a larger tumor capsule needs to be left behind to preserve cochlear nerve function.

The mean prescription isodose volume was 3.8 mL (range: 0.6–13.4). The mean number of isocenters was 19.6 (median: 20, range: 7–33) and the mean marginal prescription dose was 12 Gy (median: 12, range: 11–12 Gy); there was no dose reduction for patients with prior GKS or other forms of radiation.

Following GKS, one patient presented with HB II 3 years later (see below). Hearing remained stable in all patients with postsurgery preserved hearing.

Tumor Control after Combined Approach

Four patients (8.5%) had continuous growth of the VS after the combined approach, with clinical worsening (see later),

Table 1 Demographic data

Patient characteristics (n = 47)	
Male:female ratio	22:25
Age: mean (range)	51.2 (22–85)
Clinical presentation	
• Hearing loss	30 (63.8%)
• Sudden hearing loss	2 (4.25%)
• Gait problems	4 (8.5%)
• Vertigo	4 (8.5%)
• Trigeminal nerve symptoms	2 (4.25%)
• Tinnitus	2 (4.25%)
• Incidental	3 (6.4%)
Presurgical tumor volume: mean (range)	11.8 mL (1.47–34.9)
Presurgical maximal diameter: mean (range)	33 mm (20–45)
GKS tumor volume: mean (range)	3.3 mL (range 0.5–12.8)
Residual volume treated at GKS as compared with presurgical	Mean 31%, median 31.7%

Abbreviation: GKS, Gamma Knife surgery.

and have been considered as failure at 2.6, 2, 1.25, and 3 years after GKS, respectively.

From the four patients who were considered as failures, three already underwent a new combined approach and one is under current analysis. The first patient (patient 3 in the series) was considered a failure 2 years after the first GKS. She presented with recurrent secondary trigeminal neuralgia and a new MRI showed a continuous increase in tumor volume. She has been further reoperated 2 years after the first GKS. She kept hearing (GR class 1) and facial nerve function (HB I) at 3 years after the second GKS. The second patient (patient 9 in the series) was considered as a failure 2.6 years after GKS. He presented with recurrent gait instability, and the new MRI displayed a significant increase in tumor volume. He has been further reoperated 2.6 years after the first GKS. He had already no residual hearing before the first combined approach. Facial nerve function was normal (HB I) after the second surgery. The third patient (patient 11 in the series) was considered as a failure 1.25 years after GKS. She presented with intractable headaches and serial MRI controls that displayed a continuous major increase in tumor volume. She was further reoperated 1.25 years after GKS. She had already lost hearing after the first combined approach, and facial nerve function remained normal (HB I) after the new surgery. The fourth patient (patient 14 in the series) was initially a failure of an upfront GKS, who underwent a combined approach. Two-year follow-up MRI showed decrease in size of the treated tumor. However, 3 years after the second GKS (e.g., in the frame of the combined approach), she presented in our emergency department with new HB III. She underwent CT and further

MRI evaluation, showing a major increase in tumor volume, with compression of the fourth ventricle and perilesional edema. In patients who had two surgeries, review of the pathology did not show any change in the histopathological grade, and there were no signs of malignant transformation. The distinction between transient tumor expansion and tumor growth is not always easy. However, in our cases, due to the clinical examination and symptoms, as well as the continuous growth on MR was in favor of treatment failure, we decided to perform on a new combined approach on these patients. As illustrated in the literature, the decision whether to continue to wait-and-scan or to act by a new therapeutic mean is always a clinical decision and “never just a matter of volume measurements.”^{8–10}

Four patients in this series needed a ventriculoperitoneal shunt for persistent hydrocephalus.

Discussion

Optimal decision making in newly diagnosed VS remains a matter of debate. For small- to medium-sized lesions (Koos grades I–III), the options are RS, microsurgery, or a “wait-and-scan” approach.¹¹ This is mainly based on the hospital setting, as well as surgeon's preference. It is worth noting that comparative studies advocate that GKS compares favorably with microsurgery, with high local tumor control, much lower rate of facial nerve palsy, and much higher rate of serviceable hearing preservation.^{12–16} Modern clinical research protocols have suggested proactive radiosurgical management, even in small Koos grade I intracanalicular tumors.¹⁷ The outcomes, in terms of facial and cochlear nerve preservation after GKS in patients with small- to medium-sized lesions have considerably increased expectations also for those cases with large tumors.^{13,18}

Large symptomatic VS are generally considered to be an indication for microsurgical excision because of the need of immediate surgical decompression and symptom alleviation. The sole exceptions are patients with major comorbidities, in which GKS can be used.¹⁹ However, it must be kept in mind that there is a risk of transient tumor expansion during the following 6 to 18 months after GKS, with subsequent risk of additional clinical deterioration.^{10,20} A combined approach with planned subtotal removal followed by GKS has been increasingly adopted as the main strategy for preserving cranial nerve functions along with long-term tumor control, as a paradigm shift in the past decade.^{20–26} The mechanical stress related with direct dissection can be reduced or avoided in case of subtotal resection and represents the “nerve-centered” tumor surgery approach inherent in this treatment philosophy.²⁶ This surgical perspective reintegrates the preservation of auditory function as an essential part of the treatment strategy, often neglected because of the need of total resection.²⁶

Two different strategies have been reported for this paradigm of a combined approach. One involves a planned subtotal resection focusing on mass effect decompression and on rendering the tumor volume compatible with RS, in a second step of a unified treatment strategy. The goal of a

proper intracapsular resection is to obtain the same degree of thickness of the residual capsule over the cochlear and the facial nerve and to avoid performing the dissection between the nerves and the tumor.²⁶ The second implicates an intraoperative decision on whether to perform a subtotal or near-total extirpation (e.g., leaving only a small tumor remnant) in case where tumor capsule dissection may impede the functional preservation. Compared with this last approach, the first one seems to be associated with better functional outcomes.^{24,26} This can be explained by the fact that no nerve dissection is intended, yielding to a more restrictive surgical intention. Thus, subtotal resection achieves better facial nerve preservation rates, between 82 and 88%^{27,28} (HB I and II), and even almost 100% in some reports.²⁰ When using a combination of microsurgery and RS for large VS, the authors reported facial nerve function preservation (HB I and II) ranging between 85.7 and 95%.^{20,22,23,28,29}

Overall outcomes for total microsurgical excision in large VS are also related to the tumor size, which seems to be the main predictor for preservation of the facial nerve, both anatomically and functionally.^{30,31} The risk of facial nerve dysfunction in patients with VS more than 3 cm is approximately sixfold bigger than in patients with smaller tumors.³² In Samii et al's series of large VS,³¹ even though a facial nerve function considered as excellent/good was achieved in 75%, subgroup analysis shows that the patients retaining HB I facial nerve function after surgery were only 25%. Following total microsurgical resection of large VS (larger than 3 cm in size), facial nerve function preservation (HB I or II) has been achieved in 27 to 58%^{30,33–37} in the main reported series. Usually, most of the series reporting facial nerve function after microsurgical resection use the terminology of “excellent” or “good” results, and classically include patients in HB I or II (or sometimes reaching HB I to III), which from the functional point of view and quality of life of the patients is not similar to “normal” facial nerve function (i.e., HB I).

In terms of serviceable hearing at the time of presentation, VSs do not necessarily correlate.³⁸ Large tumors can also present with good hearing levels. Hearing preservation rates following microsurgical resection in large VS varies between 0 and 29%.^{31,32,35,39–42} In a surgical series of 54 patients (75.9% total removal) with preserved hearing at the time of surgery and VS $\geq$ 20 mm of extrameatal diameter (16 patients with $\geq$ 30 mm), hearing preservation was achieved in 53.7%, but only 31% had maintenance (or improvement) of hearing at the same level as before surgery.⁴³ In Samii et al,³¹ probability of hearing preservation after total excision was estimated to be 11%. In a recent systematic review on VS surgery, Ansari et al⁴⁴ reported on 127 patients with tumors larger than 3 cm in maximal diameter, in which hearing preservation was found to be possible in only 28.3%.⁴⁴ By comparison, for small- to medium-sized tumors, RS data show a hearing preservation rate ranging between 38 and 94%.^{6,45–52} Recent literature reveals better hearing outcomes with subtotal excision of large VS, with or without additional RS. van de Langenberg et al²² reported hearing preservation in only one of four patients with presurgical serviceable

hearing. In another series of 11 patients who underwent intracapsular decompression of VS followed by GKS, Pan et al²³ reported hearing to be preserved in all patients, even though surprisingly, they reported only 89% of facial nerve preservation in the same series. Cochlear nerve preservation is more difficult to achieve due to the lack of a specific direct monitoring; brain stem auditory evoked responses are used to monitor intraoperatively the cochlear function in a continuous manner with defined alert criteria such as reduction of peak III amplitude of more than 50%.²⁶

VSs are known to have a small annual rate of growth.⁵³ Despite this, recurrences may occur between 7 and 11% when surgical resection is considered to be total^{34,36} and between 7 and 53% in subtotal resection.^{54–57} There is a clear relationship between the residual tumor volume and further recurrence. GKS tumor control rates is considered as high as 97.5%, with a median decrease in size of 40% at 7 years follow-up.⁵⁸ The recent meta-analysis and guidelines for radiosurgical treatment of VS have also evaluated tumor growth after RS.⁵⁹ Five-year tumor control rates for these studies were 89 to 98% for the Gamma Knife series and 90 to 100% for the single fraction Linac RS series. Some of these publications included treatments given during the pioneering period of single fraction RS, where very high doses were given for benign disease. For the contemporary series, which included marginal doses of 12 to 14 Gy, the 5-year tumor control rates were 91 to 98% for the Gamma Knife series and 90 to 100% for the single fraction Linac RS series.⁵⁹

We had recently published a systematic review and meta-analysis of reported series of 240 patients treated by planned subtotal resection and followed on by RS.⁶⁰ This analysis showed that the tumor control rate after a mean follow-up of 46 months (range: 28–68.8) was 93.9%. Treatment failure was seen in 18 patients (7.26%), of which 13 patients required salvage treatment. Facial nerve preservation rate (HB grades I and II) was reported to be 96.1%. No new case of permanent functional deterioration was described after GKS, but rather a progressive facial nerve recovery to a serviceable state after GKS in 17 patients^{20,22,23,25} at the time of last follow-up compared with the early postoperative status. Cochlear nerve preservation was 73.4% at early postoperative follow-up and decreased to 59.9% following RS after a mean follow-up of 46 months (range: 28–68.8) (all published series included).

Conclusion

The treatment paradigm for large VS, which has traditionally focused on total excision of the tumor, but with a consequent important risk of facial and cochlear nerve damage, has recently changed with an increased emphasis on preservation of facial function and hearing. Our data in a consecutive series of patients treated with planned subtotal microsurgical subtotal resection and follow on Gamma Knife RS have achieved excellent results with respect to facial and cochlear nerve function and also for tumor control. This nerve-centered approach offers better results in terms of functional outcome when compared with the tumor-centered approach

that has been the norm till recently. However, longer term follow-up and larger case series are essential to validate this new treatment paradigm for large VS.

Conflict of Interest

None.

References

- House JW, Brackmann DE. Facial nerve grading system. *Otolaryngol Head Neck Surg* 1985;93(02):146–147
- Gardner G, Robertson JH. Hearing preservation in unilateral acoustic neuroma surgery. *Ann Otol Rhinol Laryngol* 1988 97(01):55–66
- Koos WT, Spetzler RF, Pendl G, Perneczky A, Lang J. *Color Atlas of Microsurgery*. Stuttgart, Germany: Georg Thieme Verlag; 1985
- Hayashi M, Ochiai T, Nakaya K, et al. Current treatment strategy for vestibular schwannoma: image-guided robotic microradiosurgery. *J Neurosurg* 2006;105(Suppl):5–11
- Massager N, Nissim O, Delbrouck C, et al. Irradiation of cochlear structures during vestibular schwannoma radiosurgery and associated hearing outcome. *J Neurosurg* 2007;107(04):733–739
- Régis J, Tamura M, Delsanti C, Roche PH, Pellet W, Thomassin JM. Hearing preservation in patients with unilateral vestibular schwannoma after Gamma Knife surgery. *Prog Neurol Surg* 2008;21:142–151
- Tuleasca C, George M, Faouzi M, et al. Acute clinical adverse radiation effects after Gamma Knife surgery for vestibular schwannomas. *J Neurosurg* 2016;125(Suppl 1):73–82
- Mindermann T, Schlegel I. How to distinguish tumor growth from transient expansion of vestibular schwannomas following Gamma Knife radiosurgery. *Acta Neurochir (Wien)* 2014;156(06):1121–1123
- Régis J, Delsanti C, Roche PH. Editorial: vestibular schwannoma radiosurgery: progression or pseudoprogession? *J Neurosurg* 2017;127(02):374–379
- Nagano O, Higuchi Y, Serizawa T, et al. Transient expansion of vestibular schwannoma following stereotactic radiosurgery. *J Neurosurg* 2008;109(05):811–816
- Kondziolka D, Mousavi SH, Kano H, Flickinger JC, Lunsford LD. The newly diagnosed vestibular schwannoma: radiosurgery, resection, or observation? *Neurosurg Focus* 2012;33(03):E8
- Pollock BE, Lunsford LD, Kondziolka D, et al. Outcome analysis of acoustic neuroma management: a comparison of microsurgery and stereotactic radiosurgery. *Neurosurgery* 1995;36(01):215–224, discussion 224–229
- Régis J, Pellet W, Delsanti C, et al. Functional outcome after Gamma Knife surgery or microsurgery for vestibular schwannomas. *J Neurosurg* 2002;97(05):1091–1100
- Myrseth E, Møller P, Pedersen PH, Vassbotn FS, Wentzel-Larsen T, Lund-Johansen M. Vestibular schwannomas: clinical results and quality of life after microsurgery or Gamma Knife radiosurgery. *Neurosurgery* 2005;56(05):927–935, discussion 927–935
- Myrseth E, Møller P, Pedersen PH, Lund-Johansen M. Vestibular schwannoma: surgery or Gamma Knife radiosurgery? A prospective, nonrandomized study. *Neurosurgery* 2009;64(04):654–661, discussion 661–663
- Pollock BE, Driscoll CL, Foote RL, et al. Patient outcomes after vestibular schwannoma management: a prospective comparison of microsurgical resection and stereotactic radiosurgery. *Neurosurgery* 2006;59(01):77–85, discussion 77–85
- Régis J, Carron R, Park MC, et al. Wait-and-see strategy compared with proactive Gamma Knife surgery in patients with intracranial vestibular schwannomas. *J Neurosurg* 2010;113(Suppl):105–111
- Golfinos JG, Hill TC, Rokosh R, et al. A matched cohort comparison of clinical outcomes following microsurgical resection or stereotactic radiosurgery for patients with small- and medium-sized vestibular schwannomas. *J Neurosurg* 2016;125(06):1472–1482
- Yang HC, Kano H, Awan NR, et al. Gamma Knife radiosurgery for larger-volume vestibular schwannomas: clinical article. *J Neurosurg* 2013;119(Suppl):801–807
- Iwai Y, Yamanaka K, Ishiguro T. Surgery combined with radiosurgery of large acoustic neuromas. *Surg Neurol* 2003;59(04):283–289, discussion 289–291
- Yang SY, Kim DG, Chung HT, Park SH, Paek SH, Jung HW. Evaluation of tumour response after Gamma Knife radiosurgery for residual vestibular schwannomas based on MRI morphological features. *J Neurol Neurosurg Psychiatry* 2008;79(04):431–436
- van de Langenberg R, Hanssens PE, van Overbeeke JJ, et al. Management of large vestibular schwannoma. Part I. Planned subtotal resection followed by Gamma Knife surgery: radiological and clinical aspects. *J Neurosurg* 2011;115(05):875–884
- Pan HC, Sheehan J, Sheu ML, Chiu WT, Yang DY. Intracapsular decompression or radical resection followed by Gamma Knife surgery for patients harboring a large vestibular schwannoma. *J Neurosurg* 2012;117(Suppl):69–77
- Iwai Y, Ishibashi K, Watanabe Y, Uemura G, Yamanaka K. Functional preservation after planned partial resection followed by Gamma Knife radiosurgery for large vestibular schwannomas. *World Neurosurg* 2015;84(02):292–300
- Radwan H, Eisenberg MB, Sandberg Knisely JP, Ghaly MM, Schuller M. Outcomes in patients with vestibular schwannoma after subtotal resection and adjuvant radiosurgery. *Stereotact Funct Neurosurg* 2016;94(04):216–224
- Daniel RT, Tuleasca C, George M, et al. 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 Neurochir (Wien)* 2017;159(07):1197–1211
- Lownie SP, Drake CG. Radical intracapsular removal of acoustic neurinomas. Long-term follow-up review of 11 patients. *J Neurosurg* 1991;74(03):422–425
- Park CK, Jung HW, Kim JE, Son YJ, Paek SH, Kim DG. Therapeutic strategy for large vestibular schwannomas. *J Neurooncol* 2006;77(02):167–171
- Fuentes S, Arkha Y, Pech-Gourg G, Grisoli F, Dufour H, Régis J. Management of large vestibular schwannomas by combined surgical resection and Gamma Knife radiosurgery. *Prog Neurol Surg* 2008;21:79–82
- Jung S, Kang SS, Kim TS, et al. Current surgical results of retrosigmoid approach in extralarge vestibular schwannomas. *Surg Neurol* 2000;53(04):370–377, discussion 377–378
- Samii M, Gerganov VM, Samii A. Functional outcome after complete surgical removal of giant vestibular schwannomas. *J Neurosurg* 2010;112(04):860–867
- Wiet RJ, Mamikoglu B, Odom L, Hoistad DL. Long-term results of the first 500 cases of acoustic neuroma surgery. *Otolaryngol Head Neck Surg* 2001;124(06):645–651
- Briggs RJ, Luxford WM, Atkins JS Jr, Hitselberger WE. Translabrynthine removal of large acoustic neuromas. *Neurosurgery* 1994;34(05):785–790, discussion 790–791
- Mamikoglu B, Wiet RJ, Esquivel CR. Translabrynthine approach for the management of large and giant vestibular schwannomas. *Otol Neurotol* 2002;23(02):224–227
- Samii M, Gerganov V, Samii A. Improved preservation of hearing and facial nerve function in vestibular schwannoma surgery via the retrosigmoid approach in a series of 200 patients. *J Neurosurg* 2006;105(04):527–535
- Samii M, Matthies C. Management of 1000 vestibular schwannomas (acoustic neuromas): surgical management and results with an emphasis on complications and how to avoid them. *Neurosurgery* 1997;40(01):11–21, discussion 21–23

- 37 Zhang X, Fei Z, Chen YJ, et al. Facial nerve function after excision of large acoustic neuromas via the suboccipital retrosigmoid approach. *J Clin Neurosci* 2005;12(04):405–408
- 38 van de Langenberg R, de Bondt BJ, Nelemans PJ, Dohmen AJ, Baumert BG, Stokroos RJ. Predictors of volumetric growth and auditory deterioration in vestibular schwannomas followed in a wait and scan policy. *Otol Neurotol* 2011;32(02):338–344
- 39 Fischer G, Fischer C. [Preservation of hearing in acoustic surgery]. *Bull Mem Acad R Med Belg* 1995;150(10-11):420–427, discussion 427–429
- 40 Fischer G, Fischer C, Rémond J. Hearing preservation in acoustic neurinoma surgery. *J Neurosurg* 1992;76(06):910–917
- 41 Fischer G, Morgon A, Fischer C, et al. [Complete excision of acoustic neurinoma. Preservation of the facial nerve and hearing]. *Neurochirurgie* 1987;33(03):169–183
- 42 Hecht CS, Honrubia VF, Wiet RJ, Sims HS. Hearing preservation after acoustic neuroma resection with tumor size used as a clinical prognosticator. *Laryngoscope* 1997;107(08):1122–1126
- 43 Wanibuchi M, Fukushima T, McElveen JT Jr, Friedman AH. Hearing preservation in surgery for large vestibular schwannomas. *J Neurosurg* 2009;111(04):845–854
- 44 Ansari SF, Terry C, Cohen-Gadol AA. Surgery for vestibular schwannomas: a systematic review of complications by approach. *Neurosurg Focus* 2012;33(03):E14
- 45 Chung WY, Liu KD, Shiau CY, et al. Gamma Knife surgery for vestibular schwannoma: 10-year experience of 195 cases. *J Neurosurg* 2005;102(Suppl):87–96
- 46 Hasegawa T, Fujitani S, Katsumata S, Kida Y, Yoshimoto M, Koike J. Stereotactic radiosurgery for vestibular schwannomas: analysis of 317 patients followed more than 5 years. *Neurosurgery* 2005;57(02):257–265, discussion 257–265
- 47 Kano H, Kondziolka D, Khan A, Flickinger JC, Lunsford LD. Predictors of hearing preservation after stereotactic radiosurgery for acoustic neuroma. *J Neurosurg* 2009;111(04):863–873
- 48 Liu D, Xu D, Zhang Z, Zhang Y, Zheng L. Long-term outcomes after Gamma Knife surgery for vestibular schwannomas: a 10-year experience. *J Neurosurg* 2006;105(Suppl):149–153
- 49 Lunsford LD, Niranjan A, Flickinger JC, Maitz A, Kondziolka D. Radiosurgery of vestibular schwannomas: summary of experience in 829 cases. *J Neurosurg* 2005;102(Suppl):195–199
- 50 Niranjan A, Mathieu D, Flickinger JC, Kondziolka D, Lunsford LD. Hearing preservation after intracanalicular vestibular schwannoma radiosurgery. *Neurosurgery* 2008;63(06):1054–1062, discussion 1062–1063
- 51 van Eck AT, Horstmann GA. Increased preservation of functional hearing after Gamma Knife surgery for vestibular schwannoma. *J Neurosurg* 2005;102(Suppl):204–206
- 52 Wowra B, Muacevic A, Jess-Hempfen A, Hempel JM, Müller-Schunk S, Tonn JC. Outpatient Gamma Knife surgery for vestibular schwannoma: definition of the therapeutic profile based on a 10-year experience. *J Neurosurg* 2005;102(Suppl):114–118
- 53 Stangerup SE, Caye-Thomasen P, Tos M, Thomsen J. The natural history of vestibular schwannoma. *Otol Neurotol* 2006;27(04):547–552
- 54 Ramina R, Coelho Neto M, Bordignon KC, Mattei T, Clemente R, Pires Aguiar PH. Treatment of large and giant residual and recurrent vestibular schwannomas. *Skull Base* 2007;17(02):109–117
- 55 Kameyama S, Tanaka R, Honda Y, Hasegawa A, Yamazaki H, Kawaguchi T. The long-term growth rate of residual acoustic neurinomas. *Acta Neurochir (Wien)* 1994;129(3-4):127–130
- 56 Kameyama S, Tanaka R, Kawaguchi T, Honda Y, Yamazaki H, Hasegawa A. Long-term follow-up of the residual intracanalicular tumours after subtotal removal of acoustic neurinomas. *Acta Neurochir (Wien)* 1996;138(02):206–209
- 57 Godefroy WP, van der Mey AG, de Bruine FT, Hoekstra ER, Malessy MJ. Surgery for large vestibular schwannoma: residual tumor and outcome. *Otol Neurotol* 2009;30(05):629–634
- 58 Régis J, Carron R, Delsanti C, et al. Radiosurgery for vestibular schwannomas. *Neurosurg Clin N Am* 2013;24(04):521–530
- 59 Tsao MN, Sahgal A, Xu W, et al. Stereotactic radiosurgery for vestibular schwannoma: International Stereotactic Radiosurgery Society (ISRS) Practice Guideline. *J Radiosurg SBRT* 2017;5(01):5–24
- 60 Starnoni D, Daniel RT, Tuleasca C, George M, Levivier M, Messerer M. Systematic review and meta-analysis of the technique of subtotal resection and stereotactic radiosurgery for large vestibular schwannomas: a “nerve-centered” approach. *Neurosurg Focus* 2018;44(03):E4