

Gamma Knife Radiosurgery for Post-Operative Vestibulocochlear Schwannomas

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ABSTRACT

Background: The discovery of Schwann cells as the oncologic cells led to the recommendation by a consensus meeting in 1992 to use the term vestibular schwannoma. In the literature, the terms acoustic neurinoma, acoustic neuroma, and vestibular schwannoma are used interchangeably.

Objective: Evaluation of the outcome of the management of post-operative recurrent or residual vestibular schwannomas by using gamma knife radiosurgery (GKRS).

Patients and Methods: In this retrospective descriptive case series study during the year of 2018 on twenty (20) consecutive cases at the International Medical Center (IMC) with residual or recurrent post-operative vestibulocochlear schwannomas (VS) whom underwent gamma knife stereotactic radiosurgery (SRS). Clinical & radiological follow up done for a period of 6 months minimum up to 3 years.

Results: After GKRS, it was shown that the cerebellar ataxia improved in 7 cases (100%). 5th cranial nerve affection improved in 6 cases (100%). 7th cranial nerve affection improved in 5 cases (100%). Hearing affection deterioration occurred in 4 cases (20%), 16 cases had stationary course (80%), Local tumor control in 90% of patients & Regrowth of tumor in 10% of patients.

Conclusion: GKRS is the best choice in small size VSs less than 3 cm in maximum diameter X, Y, Z either prior surgery was done or not due to its advantageous preservation of all cranial nerves as they can withstand the prescribed SRS dose for VSs.

Keywords: Gamma Knife Radiosurgery, Vestibulocochlear Schwannomas.

INTRODUCTION

Vestibular schwannomas (VS) are benign tumors that arise from Schwann cells of the inferior division of the vestibular portion of the Vestibulocochlear nerve (VIII) inside the internal auditory canal. As they grow, they fill and extend beyond the internal auditory canal into the cerebellopontine angle (CPA) ⁽¹⁾. VSs account for approximately 8% of intracranial tumors and have an incidence approaches 20 per million per year ⁽²⁾.

Typical presentation of VSs occurs in the 5th or 6th decade of life. Its presentation is closely correlated with tumor size; progressive unilateral hearing decline is the most common. Early symptoms include triad: ipsilateral sensorineural hearing loss (insidious and progressive) (90%), tinnitus (high pitched) (>60%) and disequilibrium (true vertigo is uncommon). Imbalance, dizziness, vertigo and headache secondary to hydrocephalus can occur with larger VS due to brainstem and trigeminal nerve compression. Up to 12% of patients can present with facial paresthesia due to involvement of the trigeminal nerve, and up to 6% can present with facial nerve palsy. Rarely, intratumoral bleeding may lead to rapid enlargement of the mass ⁽³⁾.

Many patients prefer radiosurgery to surgical resection, rendering the gamma knife radiosurgery (GKRS) to be, currently, the most common primary treatment for small- to medium-sized VS. According to some studies, between 7 and 37% of the patients treated with GKRS for VS underwent previous surgery ⁽⁴⁾. Since the tumor control and patient-

oriented outcomes including preserving hearing and facial nerve function, therefore the impact of the treatment on quality of life over complete tumor resection will lead to the progressive validation and diffusion of combined strategies (such as a planned subtotal resection followed by radiosurgery) ⁽⁵⁾.

PATIENTS AND METHODS

Study Design

In this retrospective descriptive case series study during the year of 2018 on twenty (20) consecutive cases at the International Medical Center (IMC) with residual or recurrent post-operative vestibulocochlear schwannomas whom underwent gamma knife stereotactic radiosurgery (SRS). Clinical & radiological follow up was done for a period of minimum 6 months up to 3 years.

The study was approved by the Ethics Board of Al-Azhar University and an informed written consent was taken from each participant in the study.

Inclusion criteria

Post-operative recurrent or residual vestibular schwannomas.

Exclusion criteria

- De novo vestibular schwannomas.
- Vestibular schwannomas size > 3 cm.
- Disturbed level of consciousness.
- Bilateral vestibulocochlear schwannoma (NFL).

Data collection was extracted from hospital records (Admission ICU books, patient sheets, GKRS planning and treatment protocols and progressive notes).

All patients involved in this study will be subjected to:

Clinical assessment

- 1) Neurosurgical sheet:
 - Personal history
Name, age, residence, occupation, handedness, marital status and special habits of medical significance.
 - Complaint
In patients own words
 - Present history
This included the mode of onset, the duration and the course of illness. The patient was asked about the following symptoms if he did not mention them; headache, tinnitus, unsteadiness, facial numbness, facial asymmetry, vomiting and blurring of vision.
 - Past history
History of trauma, previous surgery, irradiation.
 - Family history
Diabetes mellitus, hypertension similar conditions and positive consanguinity between the parents.
- 2) Clinical Examination
 - General examination
 - Including general body build, pulse, blood pressure, respiratory rate, temperature, chest, heart and abdomen, urogenital and skeletal systems.
 - Special consideration for neurocutaneous syndromes.
 - Neurological examination
 - A. General intellectual performance.
 - B. Speech and articulation.
 - C. Cranial nerves:
 - ❖ Olfactory nerve (I) affection: anosmia (unilateral or bilateral)
 - ❖ Optic nerve (II) affection: visual acuity, field of vision and fundus examination (papilledema or optic atrophy)
 - ❖ Ocular nerves (III, IV, VI) affection: ocular movements, pupillary reaction, gaze, ptosis and nystagmus.
 - ❖ Trigeminal nerve (V) affection: sensations in the face, corneal reflex and muscles of mastication.
 - ❖ Facial nerve (VII) affection: facial muscle weakness (U.M.N.L. or L.M.N.L.).
 - ❖ Cochleo-vestibular (VIII) Nerve affection: (hearing acuity) deafness, tinnitus and vertigo.
 - ❖ Glossopharyngeal, vagus and accessory nerves (IX, X, XI.) affection: bulbar affection with dysphagia, hoarseness of voice and loss of pharyngeal and palatal reflexes.
 - ❖ Hypoglossal nerve (XII) affection: tongue movements and power.

- D. Motor system:
Tone, power, reflexes and state of muscles.
- E. Sensations: superficial, deep and cortical.
- F. Coordination, balance and gait.
- Audiological examination and evaluation: consists of testing the patients hearing acuity using audiogram to assess sensory neural hearing loss.

Investigations

1. **Routine lab investigations.**
2. **Radiological investigations:**
 - a. Temporal bone CT for detailed bony anatomy, high resolution CT scans (axial and coronal images).
 - b. MRI brain with and without contrast:
 - Both T1 and T2 weighted MRI imaging was performed in three planes: MRI was the diagnostic modality of choice in this study. Site and size of the tumor, presence or absence of hyperostosis are among the information that were obtained and reported from both imaging procedures.
 - c. Audiometric evaluation:
 - Pure tone audiometry.
 - Speech discrimination.

Procedure

After each patient had received local anesthesia with adequate sedation, GKS started with placement of the patient's head in a rigid- fixation Leksell stereotactic frame. Treatment was performed using the Elekta Leksell model C4 Gamma plan by neurosurgeon in all cases.

Stereotactic MRI brain T₁WI with contrast axial and coronal cuts and T₂WI for dose planning, (TR 45 msec, TE 3.5 msec, angle 0°-degree, slice thickness 1mm, interslice gap 0 mm) using gamma plan. Prescription dose and doses to surrounding structures were determined by LGP workstation.

After irradiation is initiated, the shielding door to the central body of the unit opens and the couch advances the patient so that the collimator helmet docks with the central body containing all 201 sources. As soon as the helmet docks with the central body, target irradiation commences. Once the treatment time has elapsed, the couch moves out and the shielding door closes.

Twenty patients were treated by the Gamma Knife using the multiple isocenter technique and sat the optimal peripheral dose at 12 Gy directed to the 35%-50% isodose line, changing this value according to individual situations such as tumor size.

After Procedure ended, removal of the Leksell stereotactic frame with tight compression. Patients were given mild analgesia and corticosteroid.

Follow up

- ❖ Follow up of all patients by the following methods:
 - ❖ Clinically focusing on:

- Clinical examination and comparison between symptoms and signs pre- and post-GKRS including:
 - Hearing loss
 - Cerebellar ataxia
 - V Cr N affection
 - VII Cr N affection
 - VIII Cr N affection
 - Tinnitus
 - Vertigo
 - Hydrocephalus
- Post-procedure occurrence of neurological deficits e.g. CSF leak.
- ❖ Serial contrast-enhanced MRI brain
 - every 6 months for a year to compare between the size of the tumors for local tumor control and regrowth pre- and post GKRS.
 - then annually and audiogram if needed.

Management

The use of SRS as an adjuvant to surgical resection is known to result in a high rate of facial nerve function preservation (> 95%)⁽⁶⁾.

RADIOSURGERY OF VESTIBULAR SCHWANNOMAS

Due to the uniform localization of the VSs, it is easy to evaluate and compare surgical results and the most important variable is the size of the tumor. Functional evaluation of the treatment is performed by audiometric testing of hearing using the Gardner - Robertson classification or speech discrimination

tests. Facial nerve function is assessed according to the House-Brackmann classification. More detailed examinations include brainstem evoked response audiometry (BERA), videonystagmography (VNG) and caloric reflex tests⁽⁷⁾.

Current gamma knife radiosurgery (GKS) for VSs involves the use of magnetic resonance imaging (MRI) for targeting, the application of low marginal doses (usually between 12 and 13 Gy) and highly conformal treatment planning using multiple small isocenters. This is a highly successful treatment with a low risk of complications while providing the patient with the convenience of a short treatment time without the necessity for convalescence. The level of conformal treatment planning and the precision of the treatment is enhanced using the Leksell gamma knife model C with APS (automatic positioning system) or with the Perfexion - fully robotic version, allowing the use of dynamic shaping and hybrid shots. This technique achieves an average tumor control rate of 95%, facial nerve function preservation in up to 99% of cases and usually between a 70-80% chance of preserving serviceable hearing⁽⁷⁾.

CONSERVATIVE APPROACH - NATURAL COURSE OF THE DISEASE

The growth of vestibular schwannoma can be variable. In cases where the “watch and scan” policy is chosen for individual patients, magnetic resonance should be repeated at least once a year in order not to miss the progression of the tumor⁽⁸⁾.

Microsurgery [SURGICAL APPROACHES]

Retro-sigmoid Approach

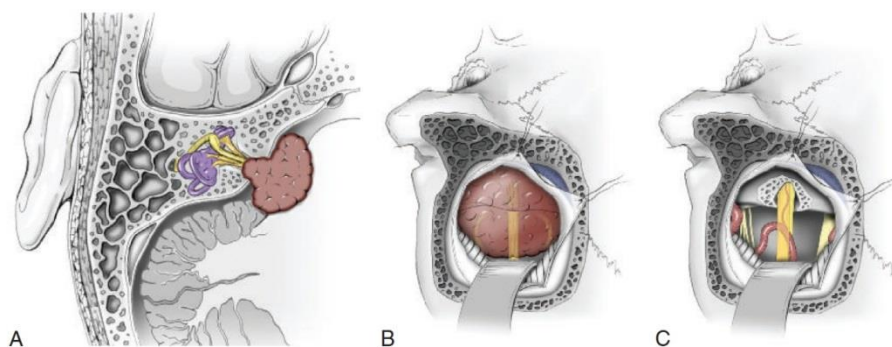


Figure 1. A, The RS approach was used primarily for medium to large tumors with a predominantly cisternal component. Often the most familiar approach to neurosurgeons, the RS approach affords an excellent view of the posterior cranial fossa contents, including the interface between the tumor and cerebellum/brainstem. B, A suboccipital craniotomy is performed medial to the sigmoid sinus, including exposure of the sigmoid and transverse sinuses and their junction. C, the posterior wall of the porus could be drilled to expose the internal auditory canal⁽⁹⁾.

Middle Cranial Fossa Approach

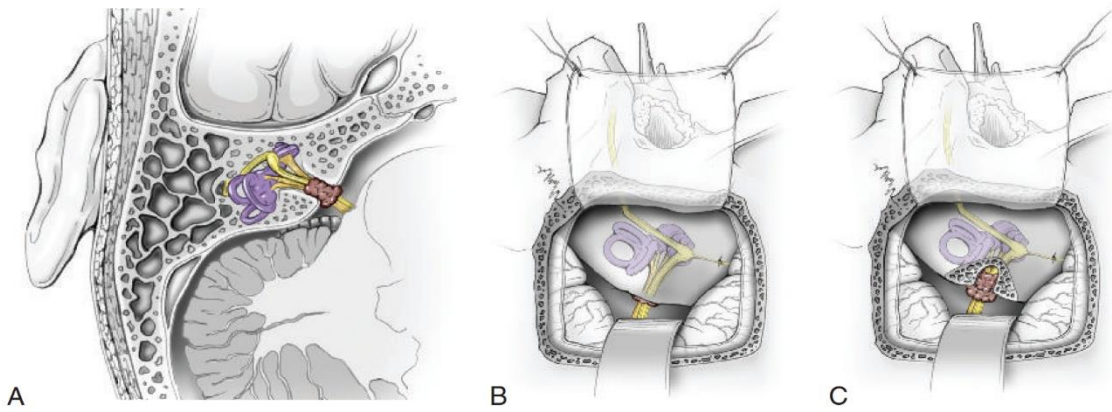


Figure 2. A, The MCF approach was typically employed for small tumors with a primarily canalicular component in the setting of preserved hearing. Because the MCF approach limits the exposure of the posterior cranial fossa and requires temporal lobe retraction, it is not well suited for tumors with a large cysternal component. After the temporal craniotomy has been performed (B), the MCF approach allowed for exposure of the internal auditory canal from the porus to the fundus through the superior aspect of the petrous temporal bone (C) ⁽¹⁰⁾.

Translabyrinthine Approach

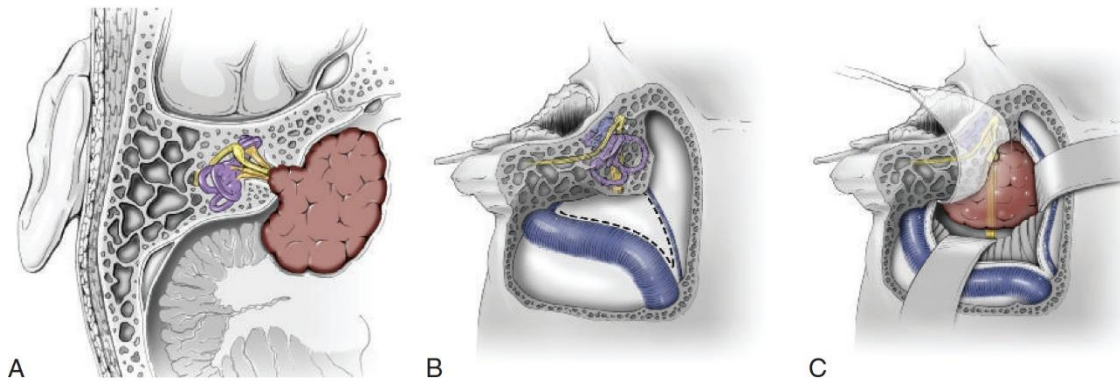


Figure 3. A, The TL approach was best suited for large tumors with significant cysternal and canalicular components in the setting of absent hearing. The TL approach allows access to the internal auditory canal and the cerebellopontine angle without cerebellar retraction, at the expense of sacrificing the labyrinth and hearing. B, The TL approach was performed by exposing Trautmann's triangle (between the bony labyrinth laterally, the sigmoid sinus medially, and the dura covering the superior petrosal sinus superiorly). C, the exposure is further expanded by drilling the bony labyrinth and gently retracting the sigmoid sinus medially ⁽¹¹⁾.

Approach Selection

The main factors influencing surgical approach selection are tumor size, extent of cysternal versus intra-canalicular growth, and baseline hearing function. Other important factors, include patient preference and the surgeon's preference and comfort level⁽¹²⁾.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean \pm standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (χ^2) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following:
 - P-value <0.05 was considered significant.
 - P-value <0.001 was considered as highly significant.
 - P-value >0.05 was considered insignificant.

RESULTS

Age

Most of the patients were in 5th and 6th decade representing 60 %.

Table (1): Showing age distribution of the studied patients.

Age (years)	No. of patients	Percentage
< 40	6	30%
40-60	12	60%
> 60	2	10%

Symptoms

Progressive hearing loss in the 20 cases (100%), tinnitus in 20 cases (100%), unsteadiness 10 cases (50%), facial affection in 5 cases (25%), headache in 4 cases (20%), facial numbness in 6 cases (30%).

Table (2): Represent the mean symptoms of the studied patients

Symptoms	No. of patients	Percentage
Hearing Affection	20	100%
Tinnitus	14	70%
Unsteadiness	9	45%
Facial weakenss	5	25%
Facial numbness	6	30%
Headache	4	20%

Signs

The clinically detected signs in these studied cases of VSs as follow:

Hearing affection in 20 cases (100%), cerebellar affection in 7 cases (35%), facial affection in 5 cases (25%) trigeminal affection 6 cases (30%).

Table (3): Represent the mean signs of the studied patients.

Signs	No. of patients	Percentage
Hearing Affection	20	100%
Cerebellar ataxia	7	35%
5 th cr. Affection	6	30%
7 th cr. Affection	5	25%

Imaging procedure

1. CT brain (post contrast axial and coronal cuts) revealed the following:

- **Tumor site:** Intra & Extra canalicular 18 case

(90%) Intracanalicular 2 cases (10%).

- **Tumor size:** < 3 cm in maximum diameters 17 cases (85%).

3 cm in maximum diameters 3 cases (15%).

- **Enhancement pattern:** Heterogeneous enhancement in 20 cases (100%). Cystic component in 6 cases (30%).

2. MRI brain T₁WI (Postcontrast), T₂WI coronal and axial cuts:

- **Tumor site:** Intra & Extra canalicular 18 case (90%).

Intracanalicular 2 cases (10%).

Tumor size: < 3 cm in maximum diameters 17 cases (85%).

3 cm in maximum diameters 3 cases (15%).

- **Enhancement pattern:** Heterogeneous enhancement in 20 cases (100%). Cystic component in 6 cases (30%)

- **T₁WI (Postcontrast):** Anatomic Image, showing the cochlea, semicircular apparatus.

- **T₂WI coronal and axial cuts:** Pathological image, showing the site of tumor and its extension. The actual size of tumor. The surrounding edema, post-operative changes like gliosis.

Table (4): Represent the location of tumor of the studied patients.

Location	No. of	Percentage
Intra Canalicular & Extra	18	90%
Intra Canalicular	2	10%

Audiogram

Sensory neural hearing affection in 20 cases (100%)

- 11 cases (55%) severe sensory neural hearing loss.
- 2 case (10%) moderate sensory neural hearing loss.
- 7 cases (35%) has mild sensory neural hearing loss.

Table (5): Show the audiographic affection of the studied patients pre-gamma knife.

Hearing acuity	No. of patients	Percentage
Mild affection	7	35%
Moderate affection	2	10%
Severe affection	11	55%

Table (6): The follow up symptoms after GKRS of the studied patients.

Symptoms	Improved		Stationary		Deteriorated	
	No.	Percent	No.	Percent	No.	Percent
Hearing loss	0	0%	6	80%	4	20%
Tinnitus	5	35%	7	50%	2	15%
Unsteadiness	9	100%	0	0%	0	0%
Facial affection	5	100%	0	0%	0	0%
Headache	4	100%	0	0%	0	0%
Facial numbness	6	100%	0	0%	0	0%

Table (7): The follow up signs after GKRS of the studied patients.

Signs	Improved		Stationary		Deteriorated	
	No. of patients	Percentage	No. of patients	Percentage	No. of patients	Percentage
Hearing affection	0	0%	16	80%	4	20%
Cerebellar ataxia	7	100%	0	0%	0	0%
5 th cr. Affection	6	100%	0	0%	0	0%
7 th cr. Affection	5	100%	0	0%	0	0%

MRI Brain with contrast follow up shows:

- 2 cases (10%) with regrowth of C.P.A schowanoma after 3 years follow up.
- 18 cases (90%) show local tumor control along the period of follow up.

Table (8): Follow up MRI Brain contrast after GKRS of the studied patients.

MRI Brain contrast	No. of patients	Percent
Local tumor control	18	90%
Regrowth of tumor	2	10%

Final Outcome according to Hearing Acuity**Table (9): The follow up of hearing acuity after GKRS of the studied patients according to audiographic study.**

Hearing acuity	N. Pre	N. Post	% Pre	% Post
Mild	7	3	35%	15%
Moderate	2	6	10%	30%
Severe	11	11	55%	55%

Final outcome of the studied patients over the follow up period:

- Cerebellar ataxia improved in 7 cases (100%).
- 5th cranial nerve affection improved in 6 cases (100%).
- 7th cranial nerve affection improved in 5 cases (100%).
- Hearing affection deterioration occurred in 4 cases (20%), 16 cases had stationary course (80%).
- No cases developed hydrocephalus or the need for

VP shunt.

- MRI brain with contrast along the period of follow up show:
 - I. 18 cases (90%) show local tumor control.
 - II. 2 cases (10%) with regrowth after 3 years follow up whom underwent a second treatment with SRS.

Final outcome in this study.**Table (10): final outcome after GKRS of the studied patients.**

	No. of patients	Percentage
Good (L.T.C)	18	90%
Fair	2	10%
Total	20	100%

DISCUSSION

SRS is an accepted alternative to microsurgery for recurrent or residual smaller VSs offering similar tumor control rates. A recent review identified a range of control rates, from 89-100% that were reported in various studies. Many of these studies reported that Gamma Knife technology and treatment planning continues to undergo significant evolution. Improvements in imaging resolution and computer planning software, have allowed physicians to better spare adjacent brainstem and nerve structures⁽¹³⁾.

In our study, the most frequent symptoms were progressive hearing loss in the 20 cases (100%), tinnitus in 14 cases (70%), unsteadiness 9 cases (45%), facial affection in 5 cases (25%), headache in 4 cases (20%) and facial numbness in 6 cases (30%). On examination, the most frequent signs were hearing affection in 20 cases (100%),

cerebellar affection in 7 cases (35%), facial affection in 5 cases (25%) and trigeminal affection 6 cases (35%). CT brain showed that the tumor site was intra-canalicular in 2 cases (10%) and intra and extra-canalicular in 18 (90%) cases. The tumor size was < 3 cm in 17 cases (85%) and 3 cm in 3 cases (15%). The enhancement pattern was heterogenous in 20 cases (100%). Audiogram showed that 11 cases (55%) had severe hearing acuity affection, only 2 (10%) had moderate affection and 7 (35%) had mild affection. Follow up after gamma knife showed that the cerebellar ataxia improved in 7 cases (100%), 5th cranial nerve affection improved in 6 cases (100%) and 7th cranial nerve affection improved in 5 cases (100%). Hearing deterioration occurred in 4 cases (20%) and 16 cases had stationary course (80%).

Wowra *et al.* ⁽⁷⁾ reported that facial nerve palsy varies between 0-5%, usually less than 1%. The deterioration of useful hearing can be expected up to 2 years, but usually not later. After radiosurgery in 21-32% of cases for intracanalicular tumors, this risk was lower: 0-10% ⁽¹³⁾.

Yang *et al.* ⁽¹⁵⁾ in an analysis of 45 articles, which represented 4,234 patients, found an overall hearing preservation rate of 51%. Hearing preservation is correlated to the maximal radiation dose at the cochlea ⁽¹⁶⁾.

Post-irradiation trigeminal nerve neuropathy (paresthesia or hypoesthesia) was observed in between 3-8 % of cases. Complete anesthesia or neuropathic pain is not observed ⁽¹⁷⁾.

In our study, MRI follow up of the brain showed that local tumor control was found in 18 (90%) case, while 2 (10%) cases showed re-growth of tumor.

Litvack *et al.* ⁽¹⁸⁾ reported termination of tumor growth after radiosurgery in 95% of cases. He observed shrinkage of the tumor in 32% of cases one year after gamma knife treatment, 40% after 2 years, 60% after 4 years and 91% after 10 years. If recurrence was not observed within 5 years after radiosurgery, later regrowth was unlikely.

Favorable results can also be achieved with cystic VSs, although the risk of complications might be slightly higher than in tumors without cystic components.

Delsanti *et al.* ⁽¹⁹⁾ describes 54 patients with cystic VSs in a group of 1,000 patients treated by radiosurgery. He observed the preservation of hearing in 53% of cases with cystic tumors. While in tumors without cystic component, continued tumor growth was observed in 2% of patients and with cystic tumors, this was 6.4%. On the other hand, the most pronounced shrinkage after treatment was in

cystic tumors, which agrees with our own observations.

In our study, follow up after gamma knife showed that hearing was deteriorated in 4 cases (20%) and stationary in 16 cases (80%). Follow up audiogram showed that 7 cases (35%) mildly affected that decreased to be only 3 cases (15%) after gamma knife radio-surgery and the moderately affected cases increased to become 6 cases (30%) instead of 2 (10%) after gamma knife surgery.

Paek *et al.* ⁽²⁰⁾ found that during the follow-up period, 13 (52%) of the 25 patients had preserved serviceable hearing and 9 (36%) retained their pre-GK grades.

The answer to the question as whether prior radio-surgical treatment complicates any subsequent open surgery is often subjective and affected by whether the surgeon has participated in gamma knife treatment. Surgeons, who perform gamma knife radiosurgery and, if necessary, later perform microsurgical removal, do not see any significant difference. Difficulties can usually be observed when partial resection preceded radiosurgery, so the open surgery was the second in the row.

A steep fall in the dose, which is inherent to single session gamma knife radiosurgery as opposed to fractionated radiotherapy, does not induce adhesion around the tumor ⁽²¹⁾.

CONCLUSION

GKRS is the best choice in small size VSs less than 3 cm in maximum diameter X, Y, Z either prior surgery was done or not due to its advantageous preservation of all cranial nerves as they can withstand the prescribed SRS dose for VSs.

RECOMMENDATION

Any patients with unilateral SNHL or tinnitus must be evaluated for possible VS. Although the differential diagnosis of C.P.A tumors is quite large the vast majority are VSs. GKRS doesn't solve surgical problems (hydrocephalous, brain stem compression), so surgical removal of VSs still the first choice of treatment.

If VS is large size to begin with (Unfit for GKRS) and the patient can tolerate the surgical intervention that is given, go for it with keen prospective that if total excision could not be achieved unless sacrificing any of the cranial nerves, we would recommend partial or subtotal excision then assess the possibility of GKRS.

Follow up after GKRS better extend to become once / year, for examination and assessment of the patient for developing any neurological symptoms and signs. M.R.I brain with contrast must be done for discovering any regrowth of the tumor to

solve the problem as early as possible (second gamma knife set if needed).

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