Original Research Paper

Volume-9 | Issue-5 | May-2019 | PRINT ISSN No 2249 - 555X

Neurosurgery

AUDIOLOGICAL IMPLICATIONS IN VESTIBULAR SCHWANNOMA PATIENTS UNDERGOING GAMMA KNIFE SURGERY

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ABSTRACT **AIM:** The aim of the study was to evaluate the changes in hearing in vestibular schwannoma patients undergoing Gamma Knife Surgery (GKS) in the first six months following the procedure. **Material and Methods:** The study was a prospective clinical study done at Army Hospital (R&R), Delhi Cantt., done between March 2012 to March 2014. It had 26 patient included in the study who were evaluated with pre-GKS Contrast MRI (CEMRI), pure tone audiogram (PTA) and post-GKS evaluation with PTA at 3 months and 6 months and a CEMRI brain at the end of 6 months. Patient underwent GKS on Leksell Gamma Knife 4C unit installed at our institute. **Results:** Tumors with dimensions more than 2.4 cm had a definite deterioration in hearing levels. The critical tumor volume above which significant changes in hearing occurred came out to be 6.2 cc. Our study showed that a cochlear dose of 5.5 Gy was the critical dose above which significant changes in hearing occurred during the first six months. **Conclusions:** The radiation changes after GKS usually start to occur after 2 to 3 months of the procedure and about 3-5 year is required for the final changes to occur. Dose of irradiation to cochlea, size & volume of tumor affects audiological outcome in short term. Shielding of the cochlea by blocking the collimator with plugs, is a useful method of altering the dosimetry, thus affecting outcome.

KEYWORDS : Vestibular schwannoma, Gamma Knife Surgery, pure tone audiogram, cochlea, Lars Leksell

INTRODUCTION

The cerebellopontine angle (CP angle) is secluded area bounded by the union of cerebellum with the Pons. It is a furrow in which cranial nerves V & VII to XI traverse. The two most common neoplastic lesions of this region are the schwannomas and meningiomas. The schwannoma of the eighth nerve has various names viz, acoustic neuroma, neurinoma, schwannoma, neurilemmoma, and perineural fibroblastoma. Vestibular schwannoma (VS) is the most apt nomenclature, owing to the most common (85-90%) location of origin of this tumor from the Obersteiner-Redlich zone of the vestibular component of the eighth nerve. Rarely these tumors can arise from the Cochlear nerve as well (16).

The Auditory Brainstem Response (ABR) is the most sensitive audiometric test used in the diagnosis of vestibular schwannoma. ABR is able to detect more than 90 % cases of vestibular schwannoma(17). Pure tone audiogram is used to access the level of hearing losses, and when combined with speech discrimination score it further validates the sensorineural nature of hearing loss seen in VS. Contrast enhanced MRI is now the most useful method for assessment of lesions in the cerebellopontine angle and to ascertain intracanalicular extension. Lesions as small as 3 mm can be picked by this modality(19).

Discussing all the treatment with the patient is essential. Patient age, comorbid illnesses, hearing status, size of the tumor and location within the CP angle cistern, all play an important role in choosing the treatment modality. To observe a vestibular schwannoma rather than intervene (18) is a strategy for small, asymptomatic lesions and in patient with advanced age or who are medically unfit for surgery. Regular follow up is done and intervention planned if there is any evidence of growth.

Surgical intervention as a treatment option is mandatory for large tumor with mass effect over the brainstem or those causing hydrocephalus. Surgical approaches that warrant discussion are the retro mastoid, translabrynthine and middle fossa approaches, depending upon size, location and hearing status of the patient.

First use of GKS was done by Lars Leksell and Steiner in 1969 and since then there has been improvements in the delivery methods and reduction post procedure complications. There have been some reports published in literature which grade GKS to be superior to micro neurosurgical approach with regards to preservation of hearing (7). There is 93-98% tumor control with no reports of neoplastic transformations or development of new malignant lesions, with most patients retaining some hearing (16). Thus it is a safe modality of treatment.

Our study here tries to evaluate this claim with respect to the Indian circumstances. We would like to bring out the tumor size, tumor volume and dose to cochlea which affect hearing in the early post GKS period.

MATERIALS AND METHODS

This prospective study was conducted at the Army Hospital (Research & Referral), Delhi Cantt between May 2102 to May 2014. Approval of the ethical committee of the institute was taken prior to starting the study. It comprised 26 patient recruited from the patients attending the OPD of the hospital, and referred from network of service hospitals. The inclusion and exclusion criteria was as follows:

INCLUSION CRITERIA:

1. Patient presenting with fresh symptoms for the first time
2. Patient with lesion size less than 3 cm in maximum diameter
3. Patient having no symptoms of raised intra cranial pressure or hydrocephalus
4. Patients with no symptoms of brainstem compression

Exclusion criteria:

1. Tumor size more than 3 cm in maximum diameter
2. Failed Gamma knife surgery cases
3. Patient with Recurrent/Residual Schwannomas of the CP angle who have earlier undergone surgical excision
4. Patient with features of raised ICP or hydrocephalus
5. Patient with symptoms of brainstem compression

Formal written and informed consent was taken after discussing all the treatment options and risks and benefits of each option. Initial patient workup included, audiometric test viz, pure tone audiogram and a contrast enhanced MRI of the Brain. The audiogram is a plot of threshold intensity versus frequency. This was used for comparing pre and post GKS hearing changes. The hearing loss was classified as per standard chart (Table 1).

We had taken averages of 4 tones at 500, 1000, 2000 and 4000 Hz for pre and post GKS comparison of changes in hearing threshold. A

change of 15 dB was regarded as significant change in hearing for statistical analysis.

Our institute has the Electra Gamma Knife 4C unit installed and accompanying Gamma Plan software for treatment planning and volume calculation. All patients underwent GKS in the same unit.

Observations

Total 26 patients were included in the study comprising various age groups. 18 were males and 8 females. The study has greatest proportion of patient within 51-60-year age group, with the oldest patient being 60 year of age and the youngest patient being 21 year of age. The male to female ratio in the study is 2.25. (Table 2)

The maximum dimension of the tumor included in the study was 2.8 cm and the minimum was 0.5 cm. Maximum tumor volume as calculated during treatment planning included in the study was 7.6 cc and minimum 0.04 cc. Maximum dose to Cochlea was 9.5 Gy and minimum was 2 Gy. The coverage of the tumor ranged from 95 to 99% (Table 3).

For analysis we had divided the tumor as per their size in three groups. Group 1 comprised sizes between 0 to 1.5 cm, group 2 between 1.51 to 2.5 and group 3 2.51 to 3 cm (Table 4).

At the end of 3 months, when analyzing the maximum dimension of tumor with significant change in hearing only two patients showed significant changes, with the observation being insignificant with a p value of 0.066. Similarly, association with tumor volume, dose to cochlea and coverage showed insignificant observations at the end of 3 months (p values 0.20, 0.127 & 0.898 respectively) (Table 5).

Analysis at the end of 6 months showed 4 patients with significant hearing loss. There was a statistically significant relationship with maximum tumor dimension and tumor volume with p values of 0.006 and 0 respectively. The relationship with the dose to the cochlea and coverage correlated with increased dose to cochlea and increasing coverage but these observations were statistically insignificant with p-values of 0.80 and 0.261 respectively (Table 6).

With respect to location in our study we grouped then in 3 categories i.e. intracanalicular lesions, purely CP angle lesions and combined lesions. 7 cases were purely intracanalicular, 2 cases with tumors entirely within the CP angle cistern and 17 cases had combined lesions. (Tables 7 to 18). We could not deduce any statistically significant observations with respect to location.

We have analyzed the presenting symptom in our study and then correlated it with change in pure tone averages at 3 and 6 months. No significant correlation could be deduced with observations at the end of 3 months and 6 months (Tables 19,20,21,22).

With the above observation we found that maximum dimension, tumor volume and dose to cochlea were major determinants with significant observations. To find out the critical value above which significant changes occurred in our study at the end of 6 months with respect to these variables a ROC curve analysis was done. Dose to cochlea of more than 5.5Gy had the maximum specificity of 100 % and 2nd highest sensitivity value of 81.8% (Graph 1 & Table 23,24). Similarly, maximum dimension of 2.4 cm had specificity is 100% and sensitivity is 81.8% (Graph 2 & Table 25,26,27) and volume of 6.25 cc as the value with 100% specificity and 90.9% sensitivity (Graph 3 & Table 28,29,30). Tumor size and volume over this had a significant hearing change at the end of 6 months in this study.

DISCUSSION

Vestibular schwannoma (VS), accounts for about 5%–6% of all intracranial tumors (4). VS occur in a sporadic, mostly unilateral form and in a hereditary, mostly bilateral form, with the latter accounting for about 5%–10% of the VS cases.

Vestibular schwannoma is a slow growing tumor which usually present in the 4 to 5 decade of life. . WY Chung et al reported median age of 51 years (with minimum age being 11 & maximum being 82 years) (20). Albertus TC and colleague had reported mean age of 58 in their study on hearing preservation in VS patients undergoing GKS (1). Our study had 42.3% i.e. 11 out of 26 patients in the age group of 51-60, with mean age of 41 years. The median age in our study was 50 years.
With respect to tumor dimension our data suggests that at the end of 3 months 2 cases out of 26 had significant changes in the PTA average, whereas 4 cases out of 26 had deterioration in hearing at the end of 6 months. The p value for observation at 6 months was significant (0.006). A ROC curve analysis revealed a value of 2.4 cm had the maximum specificity and sensitivity. The dimension of the lesion correlates with the length of VIII nerve exposed to the radiation and may correlate with the post GKS neuropathy.

The published data in world literature has conflicting opinion on effect of tumor dimension with post GKS changes. Ito K and colleagues commented that tumor diameter is one of the predictor for acoustic neuropathy (8). JC Flickinger et al, the Pittsburgh group which has the most experience and the largest series of VS patient undergoing GKS, had modified the dosimetry and used lower marginal dose and argued that tumor diameter and volume had small or no effect on the hearing after GKS. Albertus et al from Krefeld Germany also showed that size of tumor did not have long term effect on audiographic changes (1).

The minimum tumor volume in our study was 0.04 cc and maximum of 7.6 cc with a mean of 2.6 cc. Tumor volume showed inverse relation to change in PTA at 3 & 6 months. The p value was insignificant for observation at 3 months and significant for observation at 6 months (0.001). The ROC curve analysis showed that volumes above 6.2 cc had definite deterioration in PTA values at the end of 6 months.

ME Linskey et al showed clear inverse relation between the sizes of tumor and probability of worsening in hearing (10). They reported a threshold of 1 cc as the tumor volume under which hearing preservation occurred. D Prasad, M Steiner and L Steiner also reported similar observation with a threshold of 1 cc under which patient did better (2). Huai-Che Yang and colleagues stated that for larger tumor volumes less than 10 cc had a better chance of hearing preservation (6). Our study is a short term study and the deterioration in hearing in larger tumor can be explained by post radiation edema. Nagano O and colleagues in their study of 104 VS undergoing GKS reported peak tumor volume expansion at 8.6 months after GKS. The study concluded that most VS exhibit shrinkage 5 years after GKS (12). Thus early changes in the PTA values can be attributed to initial increase in the size of the lesion.

H Nakamura and colleagues in their follow-up MR studies of 10 and 63 months (mean, 34 months) duration after treatment showed temporary enlargement occurred within 2 years after radiosurgery. They concluded that an increase in tumor size up to 2 years after radiosurgery is likely to be followed by regression (5).

P Ashley Wackym and colleague in their study of dosimetry correlation to hearing loss concluded that longitudinal changes in hearing occur over time, with the largest changes seen in the first 12 months after treatment (15).

So the earliest the radiation change are expected to occur is 6 months, this coincides with the observation in our study that most of the patient with deterioration in hearing manifested that at 6 months. Further observation of the subjects would be needed to find out late deterioration.

Dose to the cochlea in our study ranged from 2 Gy to 9.5 Gy with a mean of 4.9 Gy. The cases with higher dose to the cochlea were larger tumors The Pearson correlation at 3 and 6 months both showed positive correlations suggestive of increase in the 4 tone average. The p value at 6 months was significant (0.002). Clinically significant change in hearing occurred in 2 patients at 3 months and 4 at 6 months. The p value for observation at 3 & 6 months were both not significant. We did a ROC curve analysis to find out a critical dose to cochlea above which there is definite deterioration in hearing. A dose of 5.5 Gy showed a sensitivity of 100 % and specificity of 81.8 %.

The optimal dose for the treatment of vestibular schwannoma & dose to cochlea is still debated. A review of literature revealed a trend to decrease the prescription dose of 25 to 100 Gy used in the early days to a current dose of 12-13 Gy (4,11). Noren et al, have prescribed doses of 25-30 Gy to the tumor periphery to ensure arrest of tumor growth (14); however, the high dose radiation had led to significant morbidity including compromised hearing. The Pittsburg group has over the years tried to reduce the radiation dose of 18-20 Gy (1987-1988) to 14-16 Gy (in 1992) (9). The lower dose was believed to reduce the chances of cranial nerve neuropathy, tumor swelling and worsening of hearing. Larson et al also suggested a single dose of 13.5 Gy given the

biological effect of late-responding tissue. Flickinger and associate questioned whether the tumor control rate would decrease with reduced radiation dose (9). Wen-Yuh et al reported a marginal dose 12-13 Gy, with 60% hearing preservation and that lower dose had not affected tumor control rates (20). Further Prasad and colleague have also stated that this inverse correlation is especially evident at dose of 12 Gy(2).

Nicolas Massager and colleagues published their study evaluating the effect of irradiation on cochlear structure and associated hearing outcomes (13). Their study evaluated this relationship using a fixed marginal dose of 12 Gy. They used the Leksel Gamma Knife 4 C unit and included 82 patients with a 2-year follow-up. Tumor control was attained in 81 of the patient. 52 (63.4%) had no hearing deterioration, 50 (61%) remained at same level and 2 showed improvement. 30 patients (36.6%) showed worsening after the procedure. The summary of the dosimetric parameters of the cochlea related to hearing outcome showed that 52 patients, who had preserved hearing, received 3.7 Gy as the median dose with a range of 1.3 to 7.10 Gy. The 30 cases who had worsening of hearing had a median dose of 5.33 Gy irradiated to the cochlea with a range of 1.90 to 10.0 Gy. H Kano et al, published that a radiation dose < 4.2 Gy to the central cochlea was significantly associated with better odds of preserving hearing (3). P Ashley Wackym and colleague commented that limiting the dose of radiation to the cochlea to no more than 4 Gy would likely reduce vascular injury to the stria vascularis and improve hearing outcomes (15). Shielding the cochlea during the treatment planning process would be one mechanism to accomplish this goal.

The pathophysiology for hearing deterioration following GKS could be direct radiation injury to nerve fibers or compression of nerve fibers by radiation induced tumor edema, compression or thrombosis of internal auditory artery, leading to ischemic injury of the cochlea or direct radiation injury to the inner ear In our study we have found that patients with doses less than 5.5 Gy had not shown any significant worsening in PTA levels at 6 months. H Nakamura and colleagues in their follow-up MR studies of 10 and 63 months (mean, 34 months) duration after treatment showed temporary enlargement occurred within 2 years after radiosurgery. They concluded that an increase in tumor size up to 2 years after radiosurgery is likely to be followed by regression (5). P Ashley Wackym and colleague in their study of dosimetry correlation to hearing loss concluded that longitudinal changes in hearing occur over time, with the largest changes seen in the first 12 months after treatment (15). Nagano O and colleagues in their study of 104 VS undergoing GKS reported peak tumor volume expansion at 8.6 months after GKS. The study concluded that most VS exhibit shrinkage 5 years after GKS (12). Thus early changes in the PTA values can be attributed to initial increase in the size of the lesion.
Our study had 7 patients with purely intracanalicular tumors, and none of these cases showed any significant change in PTA levels after 6 months. N Massager and colleagues have published an analysis of relationship between the dosimetric parameters of intracanalicular part of VS treated using GKS and hearing outcome (13).

They found that a high volume of VS inside the auditory canal and highly integrated radiation doses delivered to this volume are significantly correlated with a worse hearing outcome. A large volume of tumor that extends deep into the canal results in dosimetry planning with a marginal dose that deeply fills the IAC, and subsequently gives a higher dose of radiation to the cochlea. Thus 2 separate dosimeter parameters are linked to worsening in hearing viz, radiation delivered to cochlea and radiation dose inside the IAC. Massager and colleague suggested that to improve the audiological outcome reduction in the dose delivered to the cochlea could be done by using plugs which block the beam channel. This procedure will consequently modify the dosimetry and increase the integrated dose delivered to the intracanalicular portion of the lesion.

At our center we have used the plug device to modify the dosimetry in cases with intracanalicular lesions. The results obtained in this study after 6 months have been favorable but further observation is required as the changes after GKS usually start to occur after about 6 months to 1 year of the procedure. P Ashley Wackym and colleagues have showed that keeping the cochlear dose to below 4 Gy by shielding is a good ploy to preserve hearing albeit leaving some tumor behind(15).

In our study we had 2 cases with tumor purely in CP angle cistern and 20 cases with lesion extending out from the internal auditory canal into the CP angle cistern. All cases with significant change in PTA were tumors within the internal auditory canal with extension with in the CP angle cistern. No significant relation could be deduced for changes in hearing with respect to location of the lesion.

H Kano and colleagues in their clinical article "Predictors of hearing preservation after stereotactic radiosurgery for acoustic neuroma" stated that among several factors younger age is also associated with improved outcome (3). They had evaluated a total of 77 cases for 20 months. Isaac Yang et al, in their review article, studies 45 articles representing 4234 patients and concluded that older patient had a trend towards improved hearing preservation rates. Patients with age more than 65 years had 71% rate of hearing preservation and those less than 65 years had 56 % hearing preservation. They concluded that advanced age was not a significant prognostic factor for increased risk of hearing loss after GKS(7).

Most of the patient in our study presented with hearing loss that is 15, with tinnitus being the second highest presenting complaints. 3 patients were incidentally detected to have a CP angle SOL, for evaluation done for some other reason. One patient had presented with c/o facial pain. She had decreased sensation over the V1 and V2 distribution and had a large tumor volume of 7.5 cc. We had tried to find out any correlation between tumor size and initial level of hearing deficits and post GKS changes in hearing. The observations both at 3 and 6 months were insignificant with p-value of 0.258 and 0.634 respectively.

Tumor coverage in our study was over 95 % in all the cases and no positive correlation could be deduced from it. Isaac Yang and colleagues reported increased coverage of tumor results in greater chances of hearing deterioration (7). They also commented that tumor size and age have no relation to post procedure hearing deficits.

CONCLUSION

This study evaluated the changes in the audiological profile in the patients of vestibular schwannoma undergoing GKS. Our study showed that smaller size and volume of tumor had a favorable outcome with respect to the changes in the hearing. Tumors with dimensions more than 2.4 cm had a definite deterioration in hearing levels. The critical tumor volume at which significant changes in hearing occurred came out to be 6.2 cc.

We had studied the dose irradiated to the cochlea and hearing loss. Patient with higher cochlear dose had more chances of significant changes. Out study showed that a cochlear dose of 5.5 Gy was the critical dose above which significant changes in hearing occurred. Marginal dose of 12 Gy is the standard now, only modification we apply in the dosimetry during planning is applying plugs to the collimators to shield the cochlea in intracanalicular tumors. The standard dose and plugging has already been mentioned by the Pittsburg group (9).

The radiation changes after GKS usually start to occur after 6 months of the procedure and about 3-5 year is required for the final changes to occur. Thus a longer period of observation is needed to validate the findings in our study.

Table 1

Hearing Loss Degree	Decibel
Normal hearing	0-25 dB
Mild hearing loss	26-40 dB
Moderate hearing loss	41-55 dB
Moderately severe hearing loss	56-70 dB
Severe hearing loss	71-90 dB
Profound hearing loss	> 90 dB

Table 2: Demographic data

Age (in years)	Frequency	Percent
21 - 30	7	26.9
31 - 40	4	15.4
41 - 50	4	15.4
51 - 60	11	42.3
Total	26	100.0

Table 3: Observations

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age (in years)	26	21.00	60.00	43.0385	13.03988
Max. Dimension (cm)	26	.50	2.80	1.7308	.74015
Tumor Volume (cc)	26	.04	7.60	2.6998	2.89750
Dose to Cochlea (Gy)	26	2.00	9.50	4.9346	1.88381
Coverage	26	95	99	96.65	1.719

Table 4: Classification as per size

Max. Dimension (cm)	Frequency	Percent
0 - 1.5	10	38.5
1.51 - 2.5	12	46.2
2.51 - 3	4	15.4
Total	26	100.0

Table 5: Observations at 3 months

Descriptives

	Change in AC at 3mths	N	Mean	Std. Deviation	p-value
Max. Dimension (cm)	< 15	24	1.6542	.71686	
	>= 15	2	2.6500	.21213	.066
	Total	26	1.7308	.74015	
Tumor Volume (cc)	< 15	24	2.3290	2.69245	
	>= 15	2	7.1500	.49497	.020
	Total	26	2.6998	2.89750	
Dose to Cochlea (Gy)	< 15	24	4.7708	1.84072	
	>= 15	2	6.9000	1.55563	.127
	Total	26	4.9346	1.88381	
Coverage	< 15	24	96.67	1.736	
	>= 15	2	96.50	2.121	.898
	Total	26	96.65	1.719	

Table 6: Observations at the end of 6 months

Descriptives

	Change in AC at 6mths	N	Mean	Std. Deviation	p-value
Max. Dimension (cm)	< 15	22	1.5682	.68479	
	>= 15	4	2.6250	.15000	.006
	Total	26	1.7308	.74015	
Tumor Volume (cc)	< 15	22	1.8816	2.32638	
	>= 15	4	7.2000	.40825	.000
	Total	26	2.6998	2.89750	
Dose to Cochlea (Gy)	< 15	22	4.6591	1.88115	
	>= 15	4	6.4500	1.08781	.080
	Total	26	4.9346	1.88381	
Coverage	< 15	22	96.82	1.736	
	>= 15	4	95.75	1.500	.261
	Total	26	96.65	1.719	

Table 7: Hearing changes in purely intracanalicular tumors at 3 months

Intracanalicular only	Change in AC at 3mths		Total
	< 15	>= 15	
No	17	2	19
	89.5%	10.5%	100.0%
Yes	7	0	7
	100.0%	.0%	100.0%
Total	24	2	26
	92.3%	7.7%	100.0%

Table 8: Chi square test for intracanalicular tumors at 3 months

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.798[b]	1	.372		
Continuity Correction[a]	.004	1	.949		
Likelihood Ratio	1.315	1	.251		
Fisher's Exact Test				1.000	.526
Linear-by-Linear Association	.768	1	.381		
N of Valid Cases	26				

a. Computed only for a 2x2 table

b. 2 cells (50.0%) have expected count less than 5. The minimum expected count is . 54.

Table 9: Hearing changes in purely intracanalicular tumors at 6 months

Intracanalicular only	Change in AC at 6mths		Total
	< 15	>= 15	
No	15	4	19
	78.9%	21.1%	100.0%
Yes	7	0	7
	100.0%	.0%	100.0%
Total	22	4	26
	84.6%	15.4%	100.0%

Table 10: Chi square test for intracanalicular tumors at 3 months

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.742[b]	1	.187		
Continuity Correction[a]	.500	1	.480		
Likelihood Ratio	2.768	1	.096		
Fisher's Exact Test				.546	.259
Linear-by-Linear Association	1.675	1	.196		
N of Valid Cases	26				

a. Computed only for a 2x2 table

b. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1. 08.

Table 11: Changes in hearing in purely CP angle lesions at 3 months

Purely in CPA cistern	Change in AC at 3mths		Total
	< 15	>= 15	
No	22	2	24
	91.7%	8.3%	100.0%
Yes	2	0	2
	100.0%	.0%	100.0%
Total	24	2	26
	92.3%	7.7%	100.0%

Table 12: Chi square test for purely CP angle lesions at 3 months

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.181[b]	1	.671		
Continuity Correction[a]	.000	1	1.000		
Likelihood Ratio	.334	1	.563		
Fisher's Exact Test				1.000	.849
Linear-by-Linear Association	.174	1	.677		
N of Valid Cases	26				

a. Computed only for a 2x2 table

b. 3 cells (75.0%) have expected count less than 5. The minimum expected count is . 15.

Table 13: Changes in hearing in purely CP angle lesions at 6 months

Purely in CPA cistern	Change in AC at 6mths		Total
	< 15	>= 15	
No	20	4	24
	83.3%	16.7%	100.0%
Yes	2	0	2
	100.0%	.0%	100.0%
Total	22	4	26
	84.6%	15.4%	100.0%

Table 14: Chi square test for purely CP angle lesions at 3 months

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.394[b]	1	.530		
Continuity Correction[a]	.000	1	1.000		
Likelihood Ratio	.698	1	.404		
Fisher's Exact Test				1.000	.711
Linear-by-Linear Association	.379	1	.538		
N of Valid Cases	26				

a. Computed only for a 2x2 table

b. 3 cells (75.0%) have expected count less than 5. The minimum expected count is . 31.

Table 15: Changes in hearing in intracanalicular + CP angle lesions at 3 months

Intracanalicular+ CPA Cistern	Change in AC at 3mths		Total
	< 15	>= 15	
No	9	0	9
	100.0%	.0%	100.0%
Yes	15	2	17
	88.2%	11.8%	100.0%
Total	24	2	26
	92.3%	7.7%	100.0%

Table 16: Chi square test for combined lesions at 3 months

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.147[b]	1	.284		
Continuity Correction[a]	.089	1	.766		
Likelihood Ratio	1.787	1	.181		
Fisher's Exact Test				.529	.418
Linear-by-Linear Association	1.103	1	.294		
N of Valid Cases	26				

a. Computed only for a 2x2 table

b. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .69.

Table 17: Changes in hearing in intracanalicular + CP angle lesions at 6 months

Intracanalicular+ CPA Cistern		Change in AC at 6mths < 15	Change in AC at 6mths >= 15	Total
No		9	0	9
		100.0%	.0%	100.0%
Yes		13	4	17
		76.5%	23.5%	100.0%
Total		22	4	26
		84.6%	15.4%	100.0%

Table 18: Chi square test for combined lesions at 6 months

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2.503[b]	1	.114		
Continuity Correction[a]	1.022	1	.312		
Likelihood Ratio	3.775	1	.052		
Fisher's Exact Test				.263	.159
Linear-by-Linear Association	2.406	1	.121		
N of Valid Cases	26				

a. Computed only for a 2x2 table

b. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1. 38.

Table 19: Presenting symptoms & changes in hearing at 3 months

1st Symptom		Change in AC at 3mths < 15	Change in AC at 3mths >= 15	Total
Hearing Loss		14	1	15
		93.3%	6.7%	100.0%
Tinnitus		7	1	8
		87.5%	12.5%	100.0%
Others		3	0	3
		100.0%	.0%	100.0%
Total		24	2	26
		92.3%	7.7%	100.0%

Table 20: Chi square test for presenting symptoms and changes in hearing at 3 months

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.533[a]	2	.766
Likelihood Ratio	.726	2	.696
Linear-by-Linear Association	.006	1	.936
N of Valid Cases	26		

a. 4 cells (66.7%) have expected count less than 5. The minimum expected count is .23.

Table 21: Presenting symptoms & changes in hearing at 6 months

1st Symptom		Change in AC at 6mths < 15	Change in AC at 6mths >= 15	Total
Hearing Loss		12	3	15
		80.0%	20.0%	100.0%
Tinnitus		7	1	8
		87.5%	12.5%	100.0%
Others		3	0	3
		100.0%	.0%	100.0%
Total		22	4	26
		84.6%	15.4%	100.0%

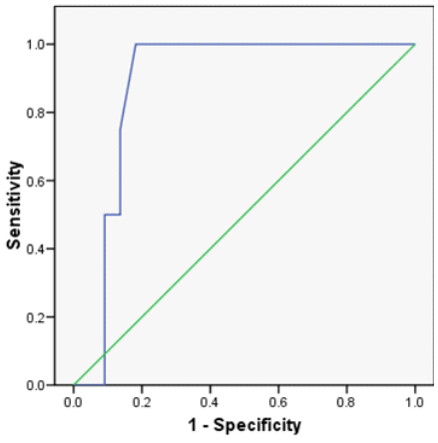
Table 22: Chi square test for presenting symptoms and changes in hearing at 6 months

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.842[a]	2	.656
Likelihood Ratio	1.284	2	.526
Linear-by-Linear Association	.789	1	.374
N of Valid Cases	26		

a. 4 cells (66.7%) have expected count less than 5. The minimum expected count is .46.

ROC Curve



Diagonal segments are produced by ties.

Graph 1: ROC Dose to Cochlea

Table 23: ROC analysis dose to cochlea

Area Under the Curve

Test Result Variable(s): Dose to Cochlea (Gy)

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval Lower Bound	Asymptotic 95% Confidence Interval Upper Bound
.881	.067	.017	.750	1.011

The test result variable(s): Dose to Cochlea (Gy) has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Graph 24: ROC dose to chochlea

Coordinates of the Curve

Test Result Variable(s): Dose to Cochlea (Gy)

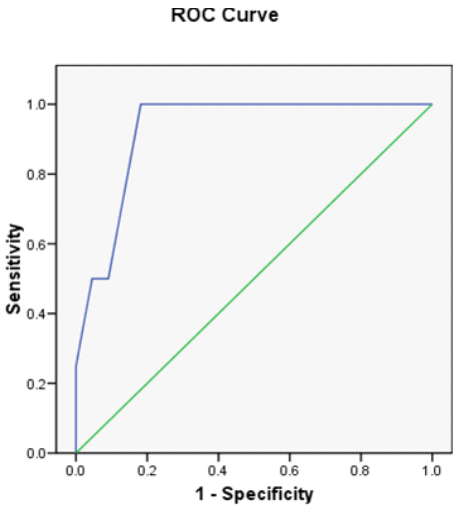
Positive if Greater Than or Equal To[a]	Sensitivity	Specificity
1.0000	1.000	.000
2.1000	1.000	.045
2.3500	1.000	.091
2.7500	1.000	.136
3.1000	1.000	.182
3.3000	1.000	.227
3.4500	1.000	.273
3.6500	1.000	.318
4.0000	1.000	.364
4.2500	1.000	.409
4.3500	1.000	.500
4.7000	1.000	.545
5.1000	1.000	.636

5.1000	1.000	.636
5.3000	1.000	.682
5.4500	1.000	.727
5.5500	1.000	.818
5.7000	.750	.864
5.9000	.500	.864
6.2000	.500	.909
7.2000	.250	.909
8.5000	.000	.909
9.2500	.000	.955
10.5000	.000	1.000

The test result variable(s): Dose to Cochlea (Gy) has at least one tie between the positive actual state group and the negative actual state group.

a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

Table 25: ROC Maximum dimension



Diagonal segments are produced by ties.

Graph 2: ROC maximum dimension

Table 26: ROC maximum dimension

Area Under the Curve

Test Result Variable(s): Max. Dimension (cm)

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.926	.054	.008	.821	1.032

The test result variable(s): Max. Dimension (cm) has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Table 27: ROC maximum dimension

Coordinates of the Curve

Test Result Variable(s): Max. Dimension (cm

Positive if Greater Than or Equal To[a]	Sensitivity	Specificity
-.5000	1.000	.000
.6500	1.000	.091
.8500	1.000	.136
1.0000	1.000	.273
1.2500	1.000	.364
1.4500	1.000	.409
1.5500	1.000	.455
1.6500	1.000	.591
1.8000	1.000	.682
2.0500	1.000	.727
2.2500	1.000	.773
2.4000	1.000	.818
2.5500	.500	.909
2.6500	.500	.955
2.7500	.250	1.000
3.8000	.000	1.000

The test result variable(s): Max. Dimension (cm) has at least one tie between the positive actual state group and the negative actual state group.

a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

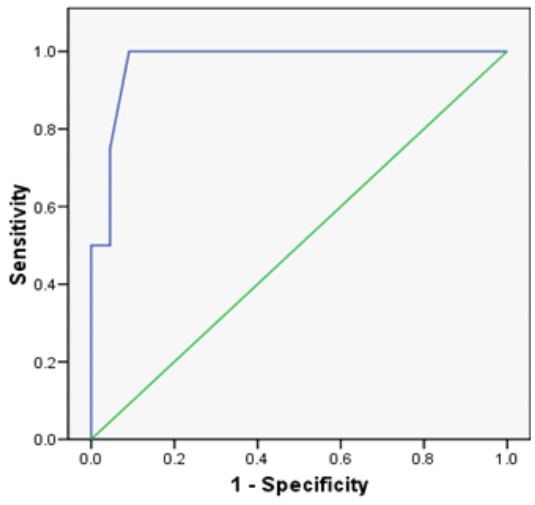
Table 28: ROC Tumor Volume

Case Processing Summary

Change in AC at 6mths	Valid N (listwise)
Positive[a]	4
Negative	22

Larger values of the test result variable(s) indicate stronger evidence for a positive actual state.

a. The positive actual state is >= 15.



Diagonal segments are produced by ties.

Graph 3: ROC tumor volume

Table 29: ROC tumor volume

Area Under the Curve

Test Result Variable(s): Tumor Volume (cc)

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.972	.030	.003	.912	1.031

The test result variable(s): Tumor Volume (cc) has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Table 30: ROC tumor volume

Coordinates of the Curve

Test Result Variable(s): Tumor Volume (cc)

Positive if Greater Than or Equal To[a]	Sensitivity	Specificity
-.9600	1.000	.000
.0425	1.000	.045
.0475	1.000	.091
.0650	1.000	.136
.0950	1.000	.182
.1250	1.000	.227
.2200	1.000	.273
.3550	1.000	.318
.4550	1.000	.364
.5950	1.000	.409
.7450	1.000	.455
.9750	1.000	.545
1.2750	1.000	.591
1.4400	1.000	.636
1.6900	1.000	.682
2.4000	1.000	.727
3.4000	1.000	.773
4.3500	1.000	.818
5.2500	1.000	.864
6.2500	1.000	.909
6.8500	.750	.955
7.1500	.500	.955
7.4500	.500	1.000
7.5500	.250	1.000
8.6000	.000	1.000

The test result variable(s): Tumor Volume (cc) has at least one tie between the positive actual state group and the negative actual state group.

a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

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