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Hearing preservation in patients with vestibular schwannoma treated with Gamma Knife surgery

Clinical article

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Object. Hearing loss after Gamma Knife surgery (GKS) in patients with vestibular schwannoma has been associated with radiation dose to the cochlea. The purpose of this study was to evaluate serviceable hearing preservation in patients with VS who were treated with GKS and to determine if serviceable hearing loss can be correlated with the dose to the cochlea.

Methods. Forty patients with vestibular schwannoma with serviceable hearing were treated using GKS with a median marginal dose of 12.5 Gy (range 12.5–13 Gy) to the 50% isodose volume. Audiometry was performed prospectively before and after GKS at 1, 3, and 6 months, and then every 6 months thereafter. Hearing preservation was based on pure tone average (PTA) and speech discrimination (SD). Serviceable hearing was defined as PTA less than 50 dB and SD greater than 50%.

Results. The median cochlear maximum and mean doses were 6.9 Gy (range 1.6–16 Gy) and 2.7 Gy (range 0.7–5.0 Gy), respectively. With a median audiological follow-up of 35 months (range 6–58 months), the 1-, 2-, and 3-year actuarial rates of maintaining serviceable hearing were 93%, 77%, and 74%, respectively. No patient who received a mean cochlear dose less than 2 Gy experienced serviceable hearing loss ($p = 0.035$). Patients who received a mean cochlear dose less than 3 Gy had a 2-year hearing preservation rate of 91% compared with 59% in those who received a mean cochlear dose of 3 Gy or greater ($p = 0.029$). Those who had more than 25% of their cochlea receiving 3 Gy or greater had a higher rate of hearing loss ($p = 0.030$). There was no statistically significant correlation between serviceable hearing loss and age, tumor size, pre-GKS PTA, pre-GKS SD, pre-GKS Gardner-Robertson class, maximum cochlear dose, or the percentage of cochlear volume receiving 5 Gy. On multivariate analysis there was a trend toward significance for serviceable hearing loss with a mean cochlear dose of 3 Gy or greater ($p = 0.074$). Local control was 100% at 24 months. No patient developed facial or trigeminal nerve dysfunction.

Conclusions. With a median mean cochlear dose of 2.7 Gy, the majority of patients with serviceable hearing retained serviceable hearing 3 years after GKS. A mean cochlear dose less than 3 Gy was associated with higher serviceable hearing preservation.

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Key Words • **acoustic neuroma** • **Gamma Knife surgery** • **hearing loss** • **serviceable hearing** • **vestibular schwannoma** • **stereotactic radiosurgery**

Management options for VS, also known as acoustic neuroma, include observation, microsurgery, stereotactic radiosurgery, or fractionated radiation therapy. Gamma Knife surgery is a precise and common method of delivering intracranial stereotactic radiosurgery due to its frame-based nature and submillimeter accuracy. Gamma Knife surgery offers a less invasive approach than surgery and produces a 93%–98% long-term tumor control and less than 5% risk of facial or trigeminal neuropathy.[2,4] Some patients and treating physicians therefore prefer GKS over resection for small to moderate-sized tumors without brainstem compression, particularly in patients with serviceable hearing.

Given that GKS is well tolerated[11,12] and produces excellent tumor control, efforts are focused on decreasing morbidity, in particular preserving hearing. Preservation of serviceable or "useful" hearing (defined as PTA < 50 dB and SD > 50%) ranges from 74% at 3 years to 45% at 10 years.[2] Factors that have been associated with hearing loss include pretreatment PTA, SD, and Gardner-Robertson class,[3] tumor volume, age, and the dose to the central cochlea.[6] Previous studies have suggested that dose limits to the cochlea between 4.0 and 5.3 Gy have been associated with a greater chance of hearing preservation.[1,6–8,13] However, the dose–hearing response relationship is not fully known. In addition, there have only been 3 studies that have examined the relationship between dose and

Abbreviations used in this paper: GKS = Gamma Knife surgery; PTA = pure tone average; SD = speech discrimination; VS = vestibular schwannoma; V3 = volume of the cochlea receiving 3 Gy or greater.

hearing loss exclusively in patients with pretreatment serviceable hearing.[6,10,13]

At our institution, the policy has been to attempt to limit the mean dose delivered to the cochlea to less than 5 Gy in patients having serviceable hearing prior to undergoing GKS. In comparison with previous reported studies, we present a unique data set of patients with serviceable hearing who received a very low mean dose to the cochlea. The purpose of this study is to examine hearing preservation in these patients and to determine if the dose received by the cochlea or other factors predict for hearing loss.

Methods

Between January 2007 and March 2011, 114 patients with VS were treated with GKS at William Beaumont Hospital. Follow-up data were entered prospectively into a research database. Patients without serviceable hearing prior to GKS and patients without audiological follow-up were excluded from this study. Five patients with pretreatment serviceable hearing were excluded because they did not have follow-up data at the time of analysis. The study population included 40 patients. No patient with neurofibromatosis Type 2 was included in the analysis; in addition, no patient underwent previous microsurgical resection. The study was reviewed by and was granted approval by the William Beaumont Hospital Human Investigation Committee.

Radiosurgical Technique

Patients considered eligible for GKS included those presenting with neuroimaging evidence of a cerebellopontine angle tumor 3 cm or smaller in maximum dimension without significant brainstem compression, as well as those who were elderly or whose tumors were medically inoperable. If the patient's tumor was larger than 3 cm at presentation, surgery was recommended as the first line of treatment and GKS was reserved for residual disease or at recurrence. Patient preference was also taken into consideration.

All patients were treated using the Leksell Gamma Knife model 4C (Elekta), which became operational at Beaumont Hospital in December 2006. On the day of treatment and after the administration of local anesthesia and sedation to the patient, the Leksell stereotactic head frame was affixed to the patient's skull with 4 pins. All patients then underwent noncontrast-enhanced CT scanning and contrast-enhanced MRI. A T1-weighted postcontrast FLASH (fast low angle shot) sequence with 1-mm slice thickness was used to best delineate the index lesion. A T2-weighted high-resolution 3D gradient echo CISS (constructive interference in steady state) study was used to optimally visualize the cranial nerves and the inner ear structures (cochlea and semicircular canals). Once acquired, imaging data were sent via internal network to the GKS treatment planning workstation. Leksell GammaPlan, the 3D-based treatment planning system with MultiView (version 4C) was used by the treating neurosurgeon or neurootologist, medical physicist, and radiation oncologist to design an optimal treatment plan. Gross tumor volume was defined based on delineating the T1-weighted contrast-enhancing lesion, and the clinical target volume was equal to the gross tumor volume. The neurosurgeon or neurootologist and the radiation oncologist mutually contoured/outlined the target volume and critical structure volumes. Irradiation isocenters (shots) were used to formulate/construct isodose volumes to cover the clinical target volume, and the treatment plan was optimized to achieve maximum conformality to adequately deliver the prescribed dose to the tumor volume while limiting the dose to the cochlea and semicircular canals as much as possible. Collimator plugging was used at the discretion of the treating physicians to reduce dose to the cochlea. The radiation dose prescription was either 12.5 Gy or 13 Gy to the 50% isodose volume to cover the clinical target volume.

Dose Constraints

Critical structures were identified and contoured. The recommended dose constraint to the cochlea was a mean dose of less than 5 Gy in patients with serviceable hearing. The volume of the cochlea was determined based on the T1- and T2-weighted MR images as well as the bony windows of the planning CT images. The minimum, maximum, and mean doses to the cochlea as well as the percentage of cochlear volume receiving 3, 5, 8, and 10 Gy (V3, V5, V8, and V10) were calculated from dose-volume histograms produced by the Leksell GammaPlan planning software and were used to analyze outcomes with respect to hearing preservation.

Follow-Up Protocol

Our prospective follow-up protocol included conducting the following baseline tests: Gd-enhanced MRI, audiometry including PTA and SD, facial nerve function measured by the House-Brackmann scale,[5] and trigeminal nerve function.

Hearing preservation was assessed using formal audiological examinations performed by trained audiologists before and after GKS at 1, 3, and 6 months and then every 6 months thereafter. Pure tone audiometry was calculated using air conduction at 500, 1000, and 2000 Hz. Hearing acuity was classified according to the Gardner-Robertson Scale[3] (Table 1). Serviceable hearing was defined as a PTA less than 50 dB and SD greater than 50%, which includes Gardner-Robertson Classes I and II.

Magnetic resonance images were obtained at 6 months in the 1st year and then yearly thereafter. Tumor control was assessed according to one of 2 definitions: 1) local control defined as absence of any 2 mm or larger temporary or sustained tumor growth visualized on serial MRI or 2) local control defined as freedom from any treatment intervention such as surgery or repeat GKS. Data regarding facial nerve or trigeminal nerve dysfunction were collected at 1, 3, and 6 months and every 6 months thereafter. Facial weakness was assessed according to the House-Brackmann grading system at each visit. For this analysis, facial nerve dysfunction was defined as a temporary or permanent decline in House-Brackmann grade. Trigeminal nerve dysfunction was assessed according to whether the patient had normal facial sensa-

TABLE 1: Gardner-Robertson scale*

Class	Description of Hearing	PTA (dB)	SD (%)
I	good to excellent	0–30	70–100
II	serviceable	31–50	50–69
III	nonserviceable	51–90	5–49
IV	poor	91–max	1–4
V	none	not testable	0

* If PTA and SD score do not qualify for the same class, the lower score is used.

tion, decreased sensation, no sensation, or any weakness of the muscles of mastication.

Statistical Analysis

Time intervals were calculated from the date of GKS. The actuarial rate of hearing loss was analyzed using the Kaplan-Meier method. For comparison of the mean cochlear dose between patients in whom serviceable hearing was maintained and those in whom it was not, a 2-tailed t-test was performed. Univariate analysis was performed using the Fisher exact test and the log-rank test. Multivariate analysis was performed using the Cox regression model. A p value of ≤ 0.05 was considered significant. Statistical analyses were performed using SPSS (version 20, IBM SPSS).

Results

Patient Characteristics

The study population included 40 patients with serviceable hearing prior to undergoing GKS (Table 2). The median age was 59 years (range 26–80 years). The median tumor volume was 0.23 cm^3 (range 0.05–4.3 cm^3), and the median maximum tumor dimension was 1.3 cm (range 0.15–2.46 cm). Prior to GKS, 28 patients (70%) had Gardner-Robertson Class I hearing and 12 (30%) had Gardner-Robertson Class II hearing. The median PTA was 28 dB (range 3–48 dB), and the median SD was 95% (55%–100%). Thirty-eight patients (95%) received a margin dose of 12.5 Gy prescribed to the 50% isodose volume. The other 2 patients (5%) received a marginal dose of 13 Gy prescribed to the 50% isodose volume. The median cochlear maximum and median cochlear mean doses were 6.9 Gy (range 1.6–16 Gy) and 2.7 Gy (range 0.7–5.0 Gy), respectively. The average of the cochlear mean doses was 2.7 Gy. Only 3 patients (7.5%) received a mean dose greater than 4 Gy. The median percentage of cochlear volumes receiving greater than 3, 5, 8, or 10 Gy were 24% (range 0%–100%), 3% (range 0%–44%), 0% (range 0%–10%), and 0% (range 0%–4%), respectively. Collimator plugging was used in 28 patients (70%).

TABLE 2: Patient characteristics*

Variable	Value†
no. of patients	40
age (yrs)	
median	59
range	26–80
GR class	
I	28 (70)
II	12 (30)
pretreatment PTA (dB)	
median	28
range	3–48
pretreatment SD (%)	
median	95
mean	55–100
max tumor dimension (cm)	
median	1.3
range	0.15–2.46
tumor vol (cm^3)	
median	0.23
range	0.05–4.30
isodose vol (cm^3)	
median	0.35
range	0.09–5.10
conformality index	
median	1.48
range	1.02–2.55
no. of shots	
median	6
range	2–16
marginal treatment dose 50% IDL	
12.5	38 (95)
13	2 (5)
plugging used	
yes	28 (70)
no	12 (30)
min dose to cochlea (Gy)	
median	1.0
range	0.2–3.0
max dose to cochlea (Gy)	
median	6.9
range	1.6–16
mean dose to cochlea (Gy)	
median	2.7
range	0.7–5.0

* GR = Gardner-Robertson; IDL = isodose line.
† Values are the number of patients (%) unless otherwise noted.

Hearing Preservation

The median audiological follow-up time was 34.5 months (range 6.1–57.8 months). The 1-, 2-, and 3-year actuarial rates of maintaining serviceable hearing were 93%, 77%, and 74%, respectively (Fig. 1). Ten of 40 patients (6 with Gardner-Robertson Class I and 4 with Gardner-Robertson Class II hearing) had loss of serviceable hearing, yielding a crude hearing preservation rate

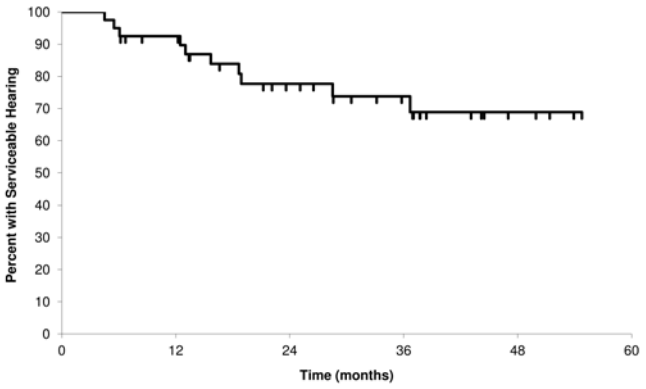

Fig. 1. Preservation of serviceable hearing. Kaplan-Meier actuarial curve of serviceable hearing preservation in patients with Gardner-Robertson Class I and II hearing.

of 75%. The median time to hearing loss for these 10 patients was 14.4 months (range 4.5–36.7 months). Sixteen patients (40%) remained in the same Gardner-Robertson class. Twenty-four patients (60%) had a decrease in their Gardner-Robertson class. Seventeen patients had their hearing reduced by 1 class: 14 from Gardner-Robertson Class I to II and 3 from Gardner-Robertson Class II to III. Seven patients had their hearing reduced by 2 Gardner-Robertson classes: 6 from Gardner-Robertson Class I to III and 1 from Gardner-Robertson Class II to IV.

Univariate analysis using the Fisher exact test and the log-rank method was performed in an attempt to identify predictors of serviceable hearing loss or a decrease in Gardner-Robertson class. Age, pre-GKS Gardner-Robertson class, pre-GKS PTA, pre-GKS SD, tumor volume, collimator plugging, mean and maximum dose levels to the cochlea, and the percentage of cochlear volume receiving 3 Gy or more and 5 Gy were all analyzed (Table 3). More patients with Gardner-Robertson Class I hearing had a decline in their hearing class than patients with Gardner-Robertson Class II hearing (71% vs 33%, respectively; $p = 0.037$, Fisher exact test). This was not statistically significant with log-rank testing (Table 3). The average mean dose to the cochlea was 2.2 Gy in the patients who maintained serviceable hearing compared with 3.1 Gy in patients who did not maintain serviceable hearing ($p = 0.049$, 2-tailed t-test). Various mean cochlear dose levels were thoroughly analyzed. No patient who received a mean cochlear dose less than 2.0 Gy experienced serviceable hearing loss ($p = 0.035$; Fig. 2). The 3-Gy mean dose level was found to be the most significant predictor of hearing loss. Patients who received a mean cochlear dose less than 3 Gy had a 2-year serviceable hearing preservation rate of 91% compared with 59% in those who had a mean dose of 3 Gy or greater ($p = 0.029$, log-rank test; Fig. 3). Patients with more than 25% of their cochlear volume receiving 3 Gy or greater (V3) had worse hearing preservation than those with a cochlear V3 of 25% or less ($p = 0.030$, log-rank test; Fig. 4). The percentage of cochlear volume receiving 5 Gy (V5) was not found to be significant. There was a trend for improvement in preservation of serviceable hearing with the use of collimator plugging ($p = 0.11$, log-rank test; Fig. 5). The average mean cochlear dose with collimator plugging was 2.5 Gy compared with 3.0 Gy when plugging was not used ($p = 0.095$, 2-tailed t-test).

There was no difference in hearing loss when an age of 60 years was used as a cutoff. More patients younger than 50 years old had loss of serviceable hearing ($p = 0.054$, log-rank test). It is important to note that there were only 10 patients who were younger than 50 years. There was no association between hearing loss, tumor size, pretreatment hearing status, and maximum cochlear dose (Table 3).

A multivariate analysis using the Cox proportional hazards model was performed using the following 4 factors: age, pre-GKS PTA, pre-GKS SD, and mean cochlear dose less than 3 Gy or 3 Gy or more. When controlling for these factors, there was a trend toward significance for a mean cochlear dose of 3 Gy or greater to be associated with hearing loss ($p = 0.074$; Table 4). A mean cochlear dose less than 2 Gy or 2 Gy or more was not significant on multivariate analysis when using the same parameters ($p = 0.96$).

Tumor Control and Cranial Nerve Toxicity

With a median imaging follow-up of 24.7 months (range 3.4–49.1 months), local control defined as the absence of any growth of 2 mm or more or defined as no treatment intervention was 100%. No patient developed facial neuropathy after GKS, which was defined as a temporary or permanent decline in House-Brackmann facial nerve grade. No patient developed trigeminal nerve dysfunction after GKS.

Discussion

In our cohort of patients with VS and serviceable hearing treated with GKS, the actuarial rate of maintaining serviceable hearing at 1 and 3 years was 93% and 74%, respectively. This rate compares favorably with other studies that have reported a rate of serviceable hearing preservation ranging from 32% to 78% (Table 5).[1,2,4,8–10,13,14] Only 10 patients (25%) lost serviceable hearing. The median cochlear mean dose was 2.7 Gy. All patients received a mean cochlear dose less than 5 Gy, and only 3 patients had a mean dose greater than 4 Gy. No hearing loss was observed in patients who received a mean cochlear dose less than 2 Gy. There was statistically significant better hearing preservation at 2 years in patients who received a mean cochlear dose less than 3 Gy (90% vs 59%, $p = 0.029$; Fig. 2). The rate of hearing preservation was also better in those with a V3 less than 25% ($p = 0.030$). No other factors were found to be significant for hearing loss. Excellent tumor control was obtained, and no cranial nerve toxicities were observed.

Hearing loss has been defined and reported in various ways. The most common method is to classify patients as having serviceable or nonserviceable hearing. Serviceable hearing is typically defined as a PTA ≤ 50 dB or SD ≥ 50%, which corresponds to a Gardner-Robertson class of I or II.[3] Other studies have reported hearing loss as any decline in Gardner-Robertson class or a specified decrease in PTA or SD. Many studies have also included

TABLE 3: Univariate analysis for predictors of hearing preservation*

Variable	Serviceable Hearing Preservation		Maintaining the Same GR Class	
	Fisher Exact Test	Log-Rank Test	Fisher Exact Test	Log-Rank Test
age (yrs)				
≥50 vs <50	0.085	0.054	0.71	0.82
≥60 vs <60	0.47	0.48	1.0	0.20
pre-GKS GR Class				
I vs II	0.51	0.29	0.037	0.32
pre-GKS PTA (dB)				
>20 vs ≤20	1.0	0.92	0.73	0.27
>30 vs ≤30	0.41	0.22	0.08	0.49
pre-GKS SD (%)				
<80 vs ≥80	1.0	0.88	0.67	0.84
<90 vs ≥90	0.71	0.54	0.50	0.59
<100 vs ≥100	1.0	0.90	0.75	0.94
tumor vol (cm^3)				
<0.3 vs ≥0.3	0.26	0.26	0.10	0.40
conformity index				
<1.5 vs ≥1.5	0.72	0.42	0.75	0.66
no. of isocenters				
<6 vs ≥6	0.27	0.15	1.0	0.16
plugging used				
yes vs no	0.13	0.11	0.30	0.20
max dose to cochlea (Gy)				
<7 vs ≥7	0.72	0.63	1.0	0.56
mean dose to cochlea (Gy)				
<2.0 vs ≥2.0	0.019	0.035	0.83	0.49
<3.0 vs ≥3.0	0.059	0.029	0.47	0.24
% cochlea vol receiving ≥3 Gy				
≤25% vs >25%	0.065	0.030	0.75	0.28
% cochlea vol receiving ≥5 Gy				
≤3% vs >3%	0.30	0.36	0.75	0.44

* All Fisher exact test and log-rank test values are p values. Shaded values are statistically significant.

patients with nonserviceable hearing in their analyses, making the results difficult to interpret for patients with serviceable hearing. It is critical to recognize how hearing preservation is defined and reported when comparing these studies.

The earliest studies that examined hearing loss included patients with nonserviceable hearing. Lasak et al.[7] examined 33 patients with Gardner-Robertson classes ranging from I to IV (only 10 had serviceable hearing) and reported that a median cochlear dose greater than 4.75 Gy correlated with a detrimental change in PTA and SD score at 12 months compared with baseline. This correlation, however, was not significant when analyzed with stepwise linear regression. Massanger et al.[8] reported on 82 patients with Gardner-Robertson Classes I–IV and found that the median mean cochlear dose in patients with a preserved Gardner-Robertson class was 3.70 Gy compared with 5.33 Gy in patients with a decrease in Gardner-Robertson class. They did not report whether this as-

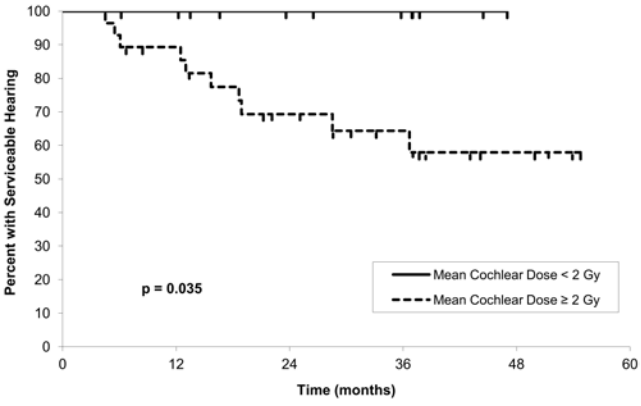

Fig. 2. Serviceable hearing preservation according to a mean cochlear dose of 2 Gy. Kaplan-Meier actuarial curves of serviceable hearing preservation in patients with Gardner-Robertson Class I and II hearing who received a mean cochlear dose of less than 2 Gy versus 2 Gy or more (p = 0.035).

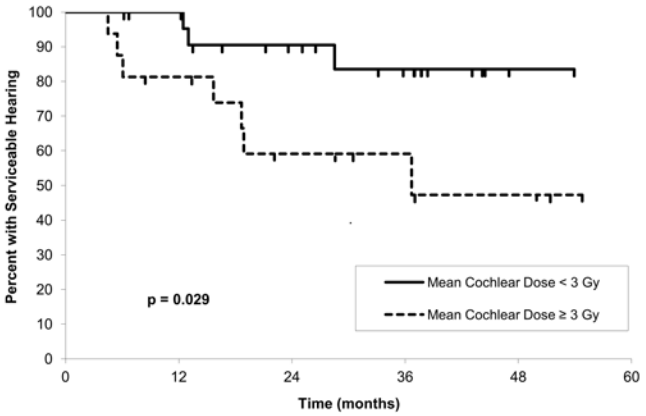

Fig. 3. Serviceable hearing preservation according to a mean cochlear dose of 3 Gy. Kaplan-Meier actuarial curves of serviceable hearing preservation in patients with Gardner-Robertson Class I and II hearing who received a mean cochlear dose of less than 3 Gy versus 3 Gy or more (p = 0.029).

sociation held up in patients with serviceable hearing. A retrospective study from the University of Pennsylvania, which included patients with Gardner-Robertson Classes I–IV, found that age and mean cochlear dose greater than 5.3 Gy were significant predictors of a greater than 20 dB decline in PTA.[1] However, results were not stratified by serviceable hearing.

It is important to know whether patients with serviceable hearing before GKS can preserve their hearing after treatment. Currently, there are 3 studies that have examined hearing loss only in patients with serviceable hearing. The first, reported by Paek et al.,[10] found that a maximum cochlear nucleus dose greater than 10 Gy was a significant predictor of serviceable hearing loss. Kano et al.[6] from the University of Pittsburgh School of Medicine reported that pretreatment Gardner-Robertson Class I hearing, SD 80% or greater, PTA less than 20 dB, age younger than 60 years, and intracanalicular tumor location or a tumor volume less than 0.75 cm^3 were significant independent predictors of preserving serviceable hearing. In their series, patients who received a dose of less than

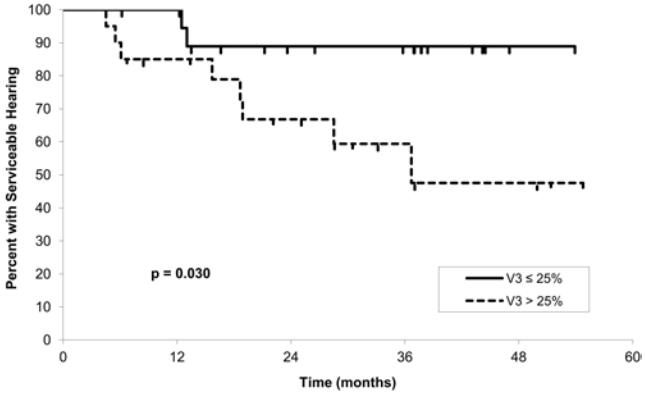

Fig. 4. Serviceable hearing preservation according to a V3 less than or equal to 25% or greater than 25%. Kaplan-Meier actuarial curves of serviceable hearing preservation in patients with Gardner-Robertson Class I and II hearing who had a V3 of less than or equal to 25% versus greater than 25% (p = 0.030).

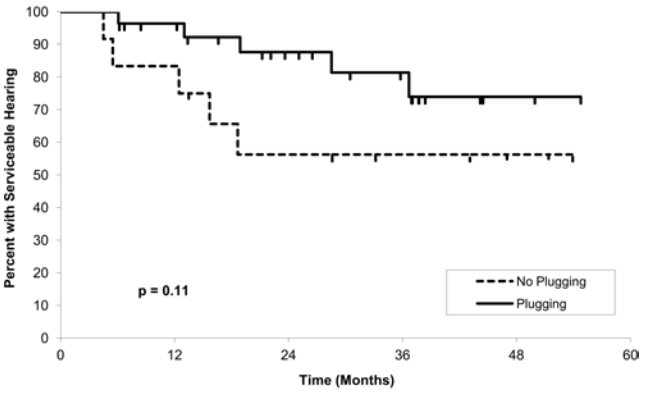

Fig. 5. Serviceable hearing preservation according to the use of plugging. Kaplan-Meier actuarial curves of serviceable hearing preservation in patients with Gardner-Robertson Class I and II hearing who received collimator plugging versus no plugging (p = 0.11).

4.2 Gy to the central cochlea had a significantly better chance of maintaining their Gardner-Robertson class. A study by Tamura et al.[13] examined hearing preservation only in patients with Gardner-Robertson Class I hearing. With a median follow-up of 3 years in 74 patients, the authors found that patients who received a mean cochlear dose less than 4 Gy or were younger than 50 years old had a significantly better chance of preserving serviceable hearing.

Based on the above studies and our own data, we would recommend keeping the mean cochlear dose as low as possible and would advocate for a mean cochlear dose less than 3 Gy or, if not achievable, then less than 4 Gy in patients with serviceable hearing. Our series differs from the previously published series in that our mean cochlear dose is much lower (93% received < 4 Gy). For example, in the study by Kano et al.[6] the median cochlear mean dose in their cohort was 4.5 Gy compared with a median cochlear mean dose of 2.7 Gy in our series. Our study shows that even in patients who received a low mean cochlear dose there is a still a dose–hearing loss relationship. Our data support the concept that a very low mean cochlear dose may be essential in achieving high hearing preservation in patients with serviceable hearing who undergo treatment for VS with GKS; however, this will need to be confirmed with long-term follow-up and a larger cohort of patients. The use of plugging or blocking of collimator channels to shape the dose distribution is one way to minimize the dose to the cochlea and may be necessary to reach a low mean dose less than 3 Gy. Plugging was used in 70% of our patients with all of the collimator plugging being selected manually. The GammaPlan software has automated plugging options, and

TABLE 4: Cox multivariate regression analysis

Parameter	Variable	p Value
age	continuous	0.15
pre-GKS PTA (dB)	>30 vs ≤30	0.54
pre-GKS SD (%)	<70 or ≥70	0.99
mean dose (Gy)	<3 vs ≥3	0.074

TABLE 5: Serviceable hearing preservation results after GKS from selected studies

Authors & Year	Institution	No. of Patients	Follow-Up Time	Hearing Preservation Rate (%)
Unger et al., 2002	Karl-Franzens University	29	crude rate (range 1–8 yrs)	55
Paek et al., 2005	Seoul National University Hospital	25	5-yr actuarial	46
Myrseth et al., 2005	Haukeland University Hospital	31	crude rate	32
Hasegawa et al., 2005	Komaki City Hospital	74	crude rate (median 7.8 yrs)	68 (<13 Gy)
		16		18 (>13 Gy)
Pollock et al., 2006	Mayo Clinic	30	1-yr actuarial	63
Kano et al., 2009	University of Pittsburgh	77	1-yr actuarial	89
			2-yr actuarial	67
Chopra et al., 2007	University of Pittsburgh	106	3-yr actuarial	77
			10-yr actuarial	44.5
Massager et al., 2007	Université Libre de Bruxelles	60	crude rate (median 2 yrs)	65
Tamura et al., 2009	Hôpital de la Timone	74	4-yr actuarial	78*
Brown et al., 2011	University of Pennsylvania	50	crude rate (mean 15.5 mos)	61
current study	William Beaumont	40	1-yr actuarial	93
			3-yr actuarial	74 (entire cohort)
			3-yr actuarial	100 (cochlear mean dose <2 Gy)
			3-yr actuarial	91 (cochlear mean dose <3 Gy)

* Includes only patients with Gardner-Robertson Class I hearing.

there are proposed dose optimization algorithms that may help determine the best shape of the plug pattern of each individual isocenter.[15]

Older age has been reported in other series as a predictor for hearing loss. In our series the median age was 59 years, and when using 60 years as a cutoff, there was no difference in hearing preservation between patients 60 years or older and those younger than 60 years. However, when analyzing patients 50 years or older versus those younger than 50 years, there was a trend for worse hearing preservation in the younger patients. Note that there were only 10 patients in the age group younger than 50 years, and these younger patients had a higher mean cochlear dose (3 Gy vs 2.4 Gy) as well as longer follow-up, which could explain the results.

Hearing can continue to deteriorate over time. Chopra et al.[2] reported a 10-year actuarial serviceable hearing preservation rate of 44% and reported that loss of useful hearing is seen up to 100 months after GKS. The median audiological follow-up of our cohort is 35 months. We plan to continue to observe these patients along with new patients for long-term results.

Conclusions

By keeping the mean cochlear dose less than 5 Gy, with the majority of patients receiving less than 4 Gy, our patients with VS had a high preservation rate of serviceable hearing 3 years after GKS treatment. Even in patients who received a low mean cochlear dose there appears to be a dose response to hearing loss. No patient who received a dose less than 2 Gy had loss of serviceable hearing. There was statistically significant better hearing preservation at 2 years in those who received a mean dose to the cochlea of less than 3 Gy. Our high hearing preservation rate supports limiting the dose to the cochlea to less than 3 Gy. Since the dose to the cochlea is a factor that can be controlled, attention must be given to minimize the dose to that structure. Future studies will be important to further define and refine the appropriate dose constraint for the cochlea that maximizes hearing preservation.

Disclosure

The following individuals have direct stock ownership in the Greater Michigan Gamma Knife Facility: Inga Grills, Dennis Bojrab, Daniel Pieper, Jack Kartush, and Peter Chen.

Author contributions to the study and manuscript preparation include the following. Conception and design: Grills, Baschnagel, Chen, Bojrab, Pieper, Kartush. Acquisition of data: Baschnagel, Didyuk, Naumann, Maitz. Analysis and interpretation of data: Grills, Baschnagel, Chen. Drafting the article: Baschnagel. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Grills. Statistical analysis: Baschnagel. Administrative/technical/material support: Grills, Chen, Bojrab, Pieper, Kartush, Maitz. Study supervision: Grills, Chen, Bojrab.

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