Preservation of functional hearing after gamma knife surgery for vestibular schwannoma

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Object. The goal of this retrospective study was to define the rates of preservation of functional hearing and growth control of vestibular schwannomas (VS) treated by gamma knife surgery (GKS) involving a consistent 12-Gy prescription dose.

Methods. One hundred thirty-four patients with unilateral VS underwent GKS between 1994 and 2000. The mean magnetic resonance (MR) imaging follow-up period was 31.7 months (maximum 72 months), and the mean audiometry follow-up interval was 26.3 months (maximum 60 months). The mean marginal dose was 12 ± 0.6 Gy. The mean maximum dose delivered to the tumor center was 25.4 Gy (range 17.4–34.3 Gy). The tumor control rate, defined as no change or a reduction in size at last follow up, was 96.7%. Of the patients studied, 97.7% remained free from the need to undergo tumor resection. Overall functional hearing preservation was 61.7%; the preservation rate for intracanalicular tumors was 63.6%, for those with an intracranial diameter less than 1.5 cm it was 54.5%, for those between 1.5 and 3 cm it was 68.2%, and for those larger than 3 cm it was 33.3%. Early in the series, three patients (2.2%) developed temporary facial weakness (House–Brackmann Grade II–III) in the posttreatment period, but this resolved within a few weeks. No case of facial weakness occurred after 1996.

Conclusions. The authors demonstrated the efficacy, safety, and in many ways, the advantage of GKS over microsurgery for VS. Patients harboring tumors 3 cm or smaller in intracranial diameter, regardless of their age and medical condition, should be given the option of undergoing GKS as primary treatment.

KEY WORDS • vestibular schwannoma • acoustic neuroma • gamma knife • radiosurgery • hearing preservation

In recent years, preservation of hearing has become an increasingly important issue in the management of VS. Because complete removal of the lesion and preservation of facial nerve function are routinely expected at centers of excellence, the next important achievement is preservation of functional hearing. In selected series in which small tumors have been resected by experienced surgeons, the authors have demonstrated that hearing, when functional preoperatively, can be preserved in 40 to 70% of the cases.^{12,35,36} Preservation of functional hearing after excision of medium-sized and large tumors, however, is technically demanding, and the preservation rate is less impressive than that for small lesions.^{4,6,11,12,15,19,22,23,28,29,35–37} In several studies of GKS for VS investigators have published more promising results.^{7,10,16–18,20,24–27,30}

This retrospective study was undertaken to study the potential of functional hearing preservation and growth control in VS when GKS is administered in a consistent manner with regard to dose level and dosimetry.

Abbreviations used in this paper: GKS = gamma knife surgery; LINAC = linear accelerator; MR = magnetic resonance; SRT = stereotactic radiotherapy; VS = vestibular schwannoma.

CLINICAL MATERIAL AND METHODS

All patients in whom the senior author (G.N.) performed GKS at the New England Gamma Knife Center between October 1994 and February 2000 were identified as the study cohort for analysis. Data were collected from all medical records. There were 134 patients with unilateral VS. Of these patients, 70 were female and 64 male, who ranged in an age from 13 to 86 years (mean age 55.3 years) at the time of treatment. Sixty-two tumors were right sided and 72 left sided. Because one patient required repeated GKS for further progression of his tumor, a total of 135 treatments were performed (Table 1).

Eighteen patients underwent subtotal tumor resection prior to GKS. In nine of these, GKS was the second part of a planned comprehensive treatment. In five patients, an intended complete excision was not achieved because of profuse hemorrhage, tumor tissue attached to the facial nerve, or other technical reasons. In four patients recurrences unexpectedly developed after seemingly complete resection. Four patients underwent GKS for a second time after it failed to effect a cure prior to this study period. A summary of the pretreatment characteristics is found in Table 1.

TABLE 1
Characteristics of patients with VS prior to GKS

Characteristic	No. of Cases (%)
no. of patients	134
age (yrs)	
mean	55.3
range	13–86
female	70 (52)
male	64 (48)
prior GKS	4 (3)
prior microsurgery	18 (13)
subjective hearing loss	123 (92)
tinnitus	72 (54)
dizziness	60 (45)
facial numbness	31 (23)
facial spasm	5 (4)

Facial nerve function was graded using the House–Brackmann grading system.¹⁴ Pre-GKS and post-GKS audiological evaluation included tone and speech audiometry from which a pure tone average-based on three frequencies (0.5, 1, 2 kHz)-and speech discrimination scores were obtained. The results were graded according to the Gardner–Robertson classification.¹¹

To enable an accurate and consistent comparison of findings on MR images, tumor size was defined by calculating the mean intracranial diameter according to measurements along three easily defined axes on Gd-enhanced T₁-weighted images. The maximum anteroposterior and mediolateral distances were measured on axial images, parallel and perpendicular to the sagittal plane. The maximum craniocaudal diameter was determined by assessing coronal images. The mean diameter as well as the greatest intracranial dimension were noted for each tumor. A decrease or increase of size was regarded as significant if the change of mean diameter was at least 2 mm. This cutoff was chosen based on limitations in spatial resolution of the standard 1.5-tesla MR imaging used for most follow-up studies. Intracranial tumors without intracranial extension were measured in all three dimensions, with change of size being defined as significant if the transverse diameter had decreased or increased 2 mm or more.

The GKS procedure included application of a Leksell stereotactic frame and evaluation with Gd-enhanced MR imaging. We acquired T₁- and T₂-weighted sequences as well as two- and three-dimensional volume sequences, the latter initially with a 1.5-mm slice thickness and later reduced to 1 mm. The images were transferred to the Leksell GammaPlan workstation for careful analysis. The margins of the tumor and the locations of the trigeminal, facial, and cochlear nerves were traced. Dose plans were created with a very tight fit between the tumor periphery and in general the 50% isodose line in the direction of the cranial nerves (mean prescription isodose line 47.2 ± 6%). A mean prescription dose of 12 Gy (± 0.6 Gy) was delivered to this isodose line. The mean maximum dose delivered to the tumor center was 25.4 Gy (range 17.4–34.3 Gy). The median number of isocenters (shots) per treatment was 15 (range 1–42). All treatments in this study were performed with a 201 ⁶⁰Co source gamma knife model U (Elekta Inc., Norcross, GA).

Follow-up study consisted of MR imaging and audiometry evaluations performed at 6 months, 1 year, annually for the first 5 years, and every 2 or 3 years thereafter.

RESULTS

Hearing Preservation

Hearing graded as Gardner–Robertson Class I or II frequently is defined as “useful” or “functional.” Of the 134 patients in whom pretreatment audiograms were acquired, 53 (39.5%) presented with Gardner–Robertson Class I or II hearing. Audiological follow-up studies were complete in 73.1% (98 patients) within a mean follow-up period of 26.3 months (range 12–60 months). Hearing was “functional” in 47 of these patients before radiosurgery and remained so post-GKS in 61.7% (29 patients) in a mean follow-up period of 26.3 months (range 12–50 months). In cases of intracranial tumors, functional hearing was preserved in seven (63.6%) of 11 patients. In cases involving tumors between 1.5 and 3 cm, hearing remained functional in 15 (68.2%) of 22 patients (Table 2). The MR images in Fig. 1 demonstrate a 2.3-cm tumor in a patient with Gardner–Robertson Class I hearing pre- and post-GKS. In addition, hearing improved from nonfunctional to functional in three (5.9%) of 51 patients after radiosurgery. Of these, two patients harbored tumors between 1.5 and 3 cm in maximum intracranial diameter, whereas the third tumor was smaller than 1.5 cm.

Tumor Control Rates

The goal of the treatment of VS with stereotactic radiosurgery is defined as “growth control” or “lack of growth;” tumors that decrease in size and those that remain stable in size following radiosurgery fall within this category. In approximately 90% of patients (121 of 134) complete MR imaging studies were collected during a mean follow-up period of 31.7 months (range 12–72 months). In this group, the tumors in 56 (46.3%) patients decreased in size, those in 61 (50.4%) remained unchanged, and those in four (3.3%) increased in size (Table 3). Of the tumors that grew after surgery, one was fewer than 1.5 cm and three were between 1.5 and 3 cm before treatment.

Another definition of success often used when reviewing radiosurgical results is freedom from the need for resection. Because of the lesion’s continued growth, three patients required post-GKS resection, representing 2.2% of the study population. These resections were performed at 13, 26, and 40 months after radiosurgery. In three pa-

TABLE 2
Results for preservation of hearing stratified by tumor size

Tumor Size (cm)	Patients W/ Functional Hearing		
	Preop	Postop	% Preservation
intracranial	11	7	63.6
1–1.5	11	6	54.5
1.5–3	22	15	68.2
>3	3	1	33.3

Functional hearing after GKS for VS

Fig. 1. Gadolinium-enhanced axial MR images obtained at treatment (A) and four years after GKS (B) demonstrating excellent growth control of a 2.3-cm tumor in a patient in whom Gardner–Robertson Class I hearing was retained.

tients a shunt had been placed prior to GKS. A ventricular shunt for hydrocephalus was required in four patients after treatment. In these patients the mean intracranial tumor diameter was 1.6 to 3.3 cm prior to and 1.3 to 3.2 cm after treatment.

Rates of Facial Nerve Dysfunction

Facial weakness was present in 10 patients prior to GKS; five after subtotal and four after complete tumor resection. The tenth, an 81-year-old patient, developed weakness (House–Brackmann Grade III) after failure of a 3.5 cm partially cystic VS to respond to GKS and was retreated. Five of the 10 patients suffered complete facial paralysis (House–Brackmann Grade VI). Consequently, of the population studied, 129 (96.3%) of 134 patients were at risk of developing new or increased facial weakness. Of those at risk, impairment of facial nerve function occurred in three (2.3%) after radiosurgery. Facial nerve function in these patients was House–Brackmann Grade I prior to radiosurgery, which declined transiently for a few weeks' duration to Grades II to III and resolved completely thereafter. No case of facial weakness of any degree after GKS has occurred since 1996.

Prior to GKS, five (3.7%) of 134 patients presented with hemifacial spasm. In one of these five GKS had been conducted prior to inclusion into this study. None of these five had previously undergone microsurgery. The spasm resolved in four patients during the posttreatment period. Eight (6.2%) of 129 patients at risk developed new temporary hemifacial spasm in the post-GKS period.

Rates of Trigeminal Nerve Dysfunction

Twenty-three percent (31) of the patients suffered some degree of facial numbness before GKS. Of the 31 patients with preexisting numbness, nine (29%) experienced complete resolution after GKS. In none of these patients did the facial hypesthesias worsen after treatment. Of the 103 patients with normal facial sensation prior to treatment, de novo transient hypesthesias developed in six patients (5.8%) following the treatment.

DISCUSSION

Many clinical studies have shown that preservation of

TABLE 3

Results for growth control, stratified by pretreatment tumor size

Tumor Size (cm)	Posttreatment Growth, No. of Cases (%)		
	Decreased	No Change	Increased
intracanalicular	3	20	0
1.5	10	20	1
1.5–3	36	19	3
>3	7	2	0
total	56 (46.3)	61 (50.4)	4 (3.3)

useful hearing is more difficult to achieve than complete resection or growth control and preserved facial nerve function in the treatment of VS, regardless of treatment modality. This is especially true in the microsurgical series, in which the cochlear system is often sacrificed to undertake a complete resection (Table 4). Norén, et al.,²⁷ reviewed 254 GKS-treated tumors at the Karolinska Institute between 1969 and 1991, of which 132 tumors were associated with a pure tone acuity of better than 90 dB; they reported hearing preservation in 77% of patients. In a review of 71 patients treated at the same institution between 1989 and 1990, Norén²⁵ showed a hearing preservation rate of 75% (12 of 16 cases) in patients with Gardner–Robertson Grade I/II at 1 year and 60% at 2 years. It was concluded that any impairment of hearing in general occurs within 1 year from GKS and usually remains stable thereafter.¹³ Investigators at the University of Pittsburgh reported preservation of functional hearing, as defined previously, to be between 35.1 and 71% in different series treated at their institution.^{7–9,18,20,30} Functional hearing preservation of 50% was achieved in cases of small tumors with a pons–petrous diameter of less than 10 mm.²⁹ Foote, et al.,¹⁰ reported a functional hearing preservation rate of 41.7%.

Of recent reports that have been focused on preservation of hearing by administering reduced radiation doses, Prasad, et al.,³³ reported a useful hearing preservation rate of 40% when using a marginal dose of 13.3 Gy in a series of 153 patients. Flickinger, et al.,⁷ reported a preservation

TABLE 4

Summary of hearing preservation rates after microsurgery for VS*

Authors & Year	Overall Hearing Preservation % [†]
Nadol, et al., 1987	73 (IC only)/22
Baldwin, et al., 1990	31.8
Ebersold, et al., 1992	23.5
Fischer, et al., 1992	29.3
House & Shelton, 1992	31–59
Nedzelski, et al., 1994	38
Koos, et al., 1995	78
Post, et al., 1995	39
Samii & Matthies, 1995	38
Gormley, et al., 1997	38
Rowed & Nedzelski, 1997	50 (IC only)/29
Samii & Matthies, 1997	47

* IC = intracanalicular.

[†] Authors vary in their definition of functional or useful hearing.

rate of 71% when using a 13-Gy dose in 190 patients. Petit, et al.,³¹ demonstrated a preservation rate of 87% when administering 12 Gy in 45 cases. Collective findings in this sequence of reports suggests a direct relationship between hearing preservation and the marginal radiation dose. Furthermore, Petit, et al., interpreted this data to indicate that a steep portion of the dose-response curve relating to complications with cochlear nerve function as a function of marginal dose had been reached and that further slight dose reduction may improve the function of that nerve. Andrews, et al.,² however, reported a 33% preservation rate when applying a 12-Gy dose in 69 patients. With our functional hearing preservation rate of 61.7% when using 12 Gy in 98 patients—a rate that falls between those of the two previous studies^{2,31}—the exact slope of this portion of the dose-response curve has yet to be determined.

There are limited published data available regarding hearing preservation after single-dose LINAC-based radiosurgery for VS. The series from the University of Florida at Gainesville contained a majority of patients without useful hearing and thus pre- and posttreatment audiometry studies were not routinely obtained.²¹ Spiegelmann, et al.,³⁸ reported on 44 patients who underwent single-dose LINAC radiosurgery with an actuarial preservation rate of 71% but a 24% rate of facial weakness. These results are tempered by those of Suh, et al.,³⁹ who reported a hearing preservation rate of 29% after single-dose LINAC radiosurgery (prescription dose 8–24 Gy) for VS.

There is currently more interest in fractionated LINAC-based SRT, resulting in an increase in published data for this modality. Andrews, et al.,¹ originally published results after fractionated SRT in seven patients with serviceable hearing. Immediately posttreatment, five (71.4%) of seven patients still had serviceable hearing. In a more recent review by the same group the authors reported an 81% actuarial preservation rate at a median follow up of 38 weeks in a larger cohort of 56 patients.² The results for fractionated SRT are promising but suffer from a lack of long term follow-up outcome data compared with GKS.

CONCLUSIONS

As microsurgical techniques for VS treatment have advanced over the decades, supported by better facial and cochlear nerve monitoring techniques, so has radiosurgery progressed with improved imaging and dose-planning techniques. With equivalent rates of tumor control across all modalities discussed, minimizing cranial nerve comorbidities has become the goal in establishing the primary treatment modality. This is now especially important with regard to hearing preservation.

Our overall hearing preservation rate of 61.7% in tumors up to 3.8 cm in size is comparable with or better than those reported in recent radiosurgical series. Gamma knife surgery is clearly superior to single-dose LINAC-based radiosurgery. Fractionated SRT remains promising but has yet to prove itself in the long term. Although microsurgery has yielded better results for intracanalicular and small tumors, the rate of functional hearing preservation demonstrated in the present study is superior to those reported in any microsurgical series for tumors greater than 1.5 cm in size. Given the high level of functional hearing preser-

vation and growth control, we believe that GKS should be considered to be a primary treatment modality in any patient harboring a VS of up to 3 cm in intracranial diameter.

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