Gamma Knife Radiosurgery for Vestibular Schwannomas

Tumor Control and Functional Preservation in 70 Patients

Benjamin J. Arthurs, BS,† Wayne T. Lamoreaux, MD,*‡ Alexander R. Mackay, MD,*§ John J. Demakas, MD,*¶ Neil A. Giddings, MD,*‖ Robert K. Fairbanks, MD,*‡ Barton S. Cooke,* Ameer L. Elaimy,*** Ben Peressini,†† and Christopher M. Lee, MD*‡*

Objective: We present the previously unreported outcomes of 70 patients treated with Gamma knife radiosurgery for vestibular schwannoma (VS), including comprehensive analysis of clinical outcomes and the effects of lower marginal doses.

Methods: We performed a retrospective study of patients treated for VS at Gamma knife of Spokane between 2003 and 2008. Endpoints measured include tumor control, hearing preservation, and facial nerve preservation, including the effect of tumor size and marginal dose. Statistical analysis was performed with Wilcoxon signed-rank test, paired Student *t* test, Mann-Whitney *U* test, Kendall's rank correlation, Fisher exact test, and Liddell's exact χ^2 test for matched pairs.

Results: With a mean follow-up of 26 months, 93.8% of tumors either shrank or remained static after receiving a mean marginal dose of 12.7 Gy. Tumor control was independent of marginal dose or tumor size. Hearing preservation was achieved in 64% of patients with serviceable function before the treatment. Hearing changes were independent of dose or tumor size. Preservation of good facial nerve function was achieved in 95% of patients. Post-treatment hydrocephalus occurred in 4.4% of patients, but no other significant morbidities were elucidated.

Conclusions: In the treatment of VS, contemporary radiosurgical techniques and the use of marginal doses below 13 Gy offer excellent tumor control, at high rates relative to surgical intervention. These findings are independent of marginal dose and tumor size. Patients should be informed about the benefits and risks of radiosurgery and microsurgery before choosing an intervention. Further analysis of post-treatment outcomes should be encouraged as follow-up times increase and the treatment protocols continue to evolve.

Key Words: vestibular schwannoma, acoustic neuroma, gamma knife, radiosurgery, radiation oncology

(*Am J Clin Oncol* 2010;XX: 000–000)

Vestibular schwannomas (VSs) are benign tumors arising within the internal acoustic meatus about the vestibulocochlear nerve (CN IX). Incidence is approximately 1 per 100,000 person-years and diagnosis occurs with a median age of 50 years.[1] Because of projecting into the cerebellopontine angle and mass effect, VS commonly cause symptoms of adjacent cranial nerves, brainstem nuclei, and the cerebellum. The most common ipsilateral symptoms are hearing loss, tinnitus, disequilibrium, vertigo, dizziness, facial numbness, and facial paresis.[2]

Patients diagnosed with VS have several management options. Ultimately, selection of a treatment modality may depend on tumor size, symptom profile, comorbidities, and patient preference. Choices include observation with serial magnetic resonance (MR) imaging, surgical resection, stereotactic radiosurgery (SRS), and fractionated radiotherapy (FRT). Conservative observation is non-invasive; however, up to 20% of patients will eventually require intervention, because of tumor growth or symptom progression.[3–7] Surgery offers the greatest rate of tumor control (>98%) but it is also the most invasive, offering the lowest preservation rates of cranial nerve function.[6,8] The use of external beam radiation, in the form of radiosurgery or radiotherapy, seeks to arrest tumor growth while minimizing morbidity rates. Reported rates of tumor control are more than 90% for both SRS and FRT, and side effect profiles appear better than microsurgery.[6,8–16]

The use of SRS in the treatment of VSs has been the subject of several meta-analyses. Reported rates of tumor control range from 91% to 95%.[3,6,8,16–18] The risk of morbidity associated with Gamma Knife (GK) treatment has also been assessed. Serviceable hearing, defined by the maintenance of a speech recognition threshold (SRT) less than 50 dB and speech discrimination score (SDS) more than 50%, has been maintained in 44% to 63% of patients following SRS.[6,8,15,17] Toxicity to the trigeminal and facial nerves has resulted in neuropathy rates reported between 9%–17% and 4%–19%, respectively.[6,8,16,17] Finally, post-treatment hydrocephalus occurs in rarely, affecting 2% to 3% of patients.[6,8,17] There is a small risk of radiation-induced malignancy, but definitive incidence rates have not been identified in patients treated for VS. The risk of mortality due to radiosurgery is essentially absent.

Over the past decade, protocols for treating VSs using GK radiosurgery have evolved considerably. Changes come in the form of improved MR resolution and more powerful planning software for the GK, which ultimately allow greater precision in defining a conformal dose to the tumor volume.[19,20] In addition, doses prescribed to tumor margins have been lowered with the goal of minimizing morbidity rates.[19,21,22] Most recently, marginal doses of 12 to 13 Gy have been indicated for the treatment of VSs.[21] Yang et al reviewed the effect of such protocols finding a statistically significant difference between low dose (≤13 Gy) and high dose groups with respect to hearing preservation rates (59% vs. 53%, $P = 0.0285$) and facial neuropathy rates (1.5% vs. 5.3%, $P < 0.001$).[15,16] As additional data becomes available, we will be able to determine more definitively whether technique improvements and lower doses affect tumor control or morbidity rates.

Contributing to the available evidence evaluating contemporary radiosurgical techniques, we present the previously unreported results of 70 patients treated for VS at GK of Spokane. These patients were treated between 2003 and 2008, with a mean marginal dose of 12.7 Gy. We report retrospectively on tumor control, hearing preservation, facial neuropathy, and additional morbidity rates. In

From the *Gamma Knife of Spokane, Spokane, WA; †University of Washington School of Medicine, Seattle, WA; ‡Cancer Care Northwest, Spokane, WA; §Mackay & Meyer MDs, Spokane, WA; ¶Spokane Brain & Spine, Spokane, WA; ‖Spokane Ear Nose & Throat Clinic, Spokane, WA; **Carroll College, Helena, MT; and ††DataWorks Northwest, LLC, Coeur D'Alene, ID.

Supported by a Medical Student Research Training Program (MSRTP) grant from the University of Washington School of Medicine (to B.J.A.).

Reprints: Christopher M. Lee, MD, Cancer Care Northwest, 601 S. Sherman, Spokane, WA 99202. E-mail: lee@ccnw.net.

ISSN: 0277-3732/10/0000-0001
DOI: 10.1097/COC.0b013e3181dbc2ab

additional, we provide statistical analysis, shedding light on the effect of radiation dose, and tumor size on outcomes. These results will be valuable for guiding clinical decisions and for the purpose of future systematic review of VS treatments.

MATERIALS AND METHODS

We examined the pretreatment factors and clinical outcomes of 70 patients treated for VS at Cancer Care Northwest and Gamma Knife of Spokane (Deaconess Hospital, Spokane, WA) between 2003 and 2008. The following patient variables were captured from medical records: age at treatment, laterality of tumor, diagnosis of neurofibromatosis type 2, and previous intervention. Pretreatment records were examined for the presence of relevant symptoms or signs. These were also evaluated from post-treatment records, along with the incidence of morbidities. Follow-up length was determined as the difference between the date of treatment to the date of most recent clinical encounter (clinical follow-up), most recent imaging (imaging follow-up), and most recent audiogram (audiometric follow-up).

Efficacy of GK was determined based on the response of the tumor to treatment. Tumors were followed based on direct measurements, or values reported in radiology reports if images were not available for our review. Tumor size was defined as the largest linear dimension. Tumors growing in size by more than 1 mm in any direction were classified as growing. This accounts for the precision of tumor measurements, which are at best ±1 mm as a result of differences in contrast uptake and the resolution offered by the 2.5 to 5 mm slice thickness used in most imaging studies. Transient tumor enlargement during the first year following GK has been well documented, and so overall outcomes were based on comparison of the most recent study to the pretreatment magnetic resonance imaging.[23] Tumor control (GK success) was defined as the absence of growth.

The effect of radiation on hearing loss was quantitatively analyzed using audiometric records available for 41 patients. Pure tone hearing loss was evaluated at 250, 500, 1000, 2000, 4000, and 8000 Hz. Moreover, we recorded SRT, approximated from the average of pure tone hearing loss at 500, 1000, and 2000 Hz when appropriate, and SDS. Gardner-Robertson (GR) scores were used as an assessment of overall hearing function, assigned on the basis of SRT and SDS.[24] Serviceable hearing was defined as a GR score of 1 or 2, corresponding to a SRT ≤50 dB and SDS ≥50%, as has been the standard in the published data. Hearing preservation was defined as the maintenance of serviceable hearing following GK treatment.

Facial nerve outcomes were defined using the House-Brackmann (HB) system for grading facial nerve function.[25] Scores were captured from pretreatment and post-treatment records, or estimated retrospectively based on the symptoms and signs described when necessary. Good facial nerve function was defined as normal or mild dysfunction, a HB score of I or II.

Statistical analysis was performed using StatsDirect (version 2.7.3) and Microsoft Excel. We used the following tests to identify dependent relationships among variables: Wilcoxon's signed-rank test, paired Student t test, Mann-Whitney U test, Kendall's rank correlation, Fisher exact test, and Liddell's exact χ^2 test for matched pairs. Statistical significance was arbitrarily set as a $P < 0.05$. Summary statistics are presented as a mean, with one standard deviation when appropriate, unless otherwise noted.

This study was performed in accordance with ethical standards guiding retrospective chart reviews. Our study and protocol were approved by Institutional Review Board Spokane (Institutional Review Board 1554) and the University of Washington Human Subjects Division (Human Subjects Application 36306).

TABLE 1. Summary of Study Population and Pretreatment Characteristics*

Study Population	
Patients (N)	70
Age (yr)	59 ± 14 (18–88)
Clinical follow-up (mo)	27 ± 18 (1–72)
Pretreatment tumor characteristics	
Tumor size (mm)	18 ± 7
Tumor volume (cm^3)	1.70 ± 2.17
Tumors growing (%)	61
Growth rate (mm/yr)	2.9 ± 4.7
Presenting symptoms and signs	
Subjective hearing loss (%)	94
Tinnitus (%)	71
Disequilibrium (%)	80
Vertigo (%)	39
Trigeminal neuropathy (%)	23
Facial neuropathy (%)	19
Headaches (%)	38

*Mean ± one standard deviation, range in parenthesis where appropriate.

TABLE 2. Summary of Gamma Knife Treatment Outcomes in 65 Patients*

Gamma Knife Treatment Outcome	Result
Marginal dose (Gy)	12.7 ± 1.1 (10–16)
Maximum dose (Gy)	26.2 ± 6.9
Tumor covered by marginal dose (%)	96.3 ± 4.7
Post-treatment tumor size (mm)	17 ± 7
Static tumors (%)	45
Shrinking tumors (%)	59
Growing tumors (%)	6

*Mean ± one standard deviation, range in parenthesis where appropriate.

RESULTS

We identified 70 patients treated for VS at our institution. A summary of the clinical data for these patients can be found in Table 1. Of our study population, 1 patient was diagnosed with neurofibromatosis type 2, and 12 patients had been subject to previous intervention for their tumors.

Pre- and post-treatment imaging records were available for 65 patients who were included in the analysis of tumor control. The mean imaging follow-up was 26 ± 18 months (range, 0.3–72). Treatment data and outcomes are summarized in Table 2. At most recent follow-up, 93.8% of tumors had been controlled by GK radiosurgery (Fig. 1). Tumor control rates were also calculated as a function of tumor size, as shown in Figure 1. Wilcoxon's signed ranks indicated a statistically significant difference between the tumor diameters pre- and post-treatment ($P < 0.0001$). The difference in tumor size, including an approximate 95% confidence interval (CI), was −1.65 mm (−2.05 to −0.85 mm). Mann-Whitney U tests failed to identify significant relationships between marginal dose, tumor size, and tumor volume with respect to tumor control.

Hearing outcomes were evaluated for 41 patients with pre- and post-treatment records, with a mean audiometric follow-up of 17 ± 16 months (range, 0.2–65). Pure tone hearing loss data are shown in Figure 2. Prior to GK, the mean SRT was 51.6 ± 25.5 dB, and SDS was 45.5% ± 36.0%. These were 68.8 ± 28.1 dB and

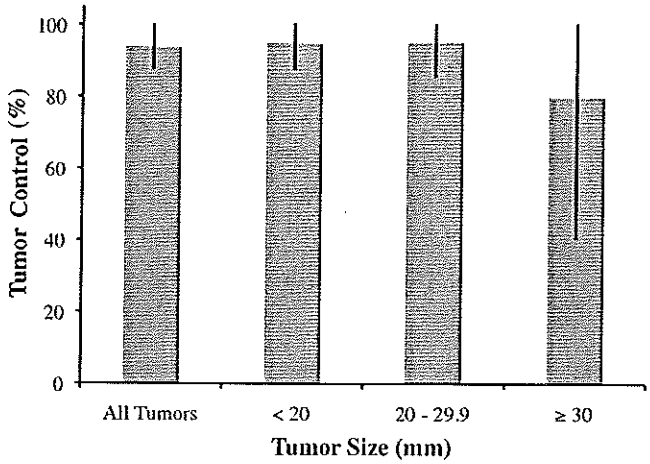

FIGURE 1. Tumor control rates grouped by tumor size. Error bars represent 95% confidence intervals.

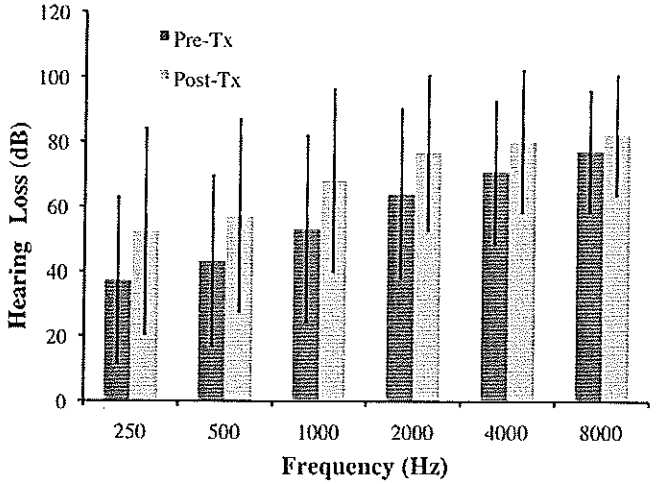

FIGURE 2. Pure tone hearing loss as a function of frequency, including pre- and post-treatment data. Error bars represent one standard deviation.

TABLE 3. Median Hearing Preservation Outcomes Following Gamma Knife Treatment

Hearing Outcome	Result (95% CI*)
Change in SRT† (dB)	17.2 (7.5–21)
Change in SDS‡ (%)	−11 (−20 to −2)
Hearing preservation (%)§	64.3 (38.2–90.3)

*Confidence interval.
†Speech recognition threshold.
‡Speech discrimination score.
§Based on outcomes in 14 patients with serviceable hearing prior to treatment.

34.4% ± 36.8% following GK radiosurgery, respectively. Wilcoxon's signed ranks test showed a significant change in SRT and SDS following GK ($P < 0.0001$ and $P = 0.0216$, respectively), shown in Table 3. Kendall's rank correlation tested the dependence of SRT and SDS changes with respect to marginal dose, tumor size, and tumor volume. Those relationships were found to be independent, and an approximate 2-side test adjusted for ties indicated that any correlation was not statistically significant. Hearing preservation rates in 14 patients with pre-GK serviceable hearing and audiometric follow-up are shown in Table 3.

The preservation of good facial nerve function (HB class I or II) was achieved in 95.3% of the 64 patients with good function before the treatment. A Liddell's exact χ^2 test for matched pairs yielded a 2-sided test statistic of 1.5 ($P = 0.5078$), indicating there was not a significant difference in facial nerve function following radiosurgical treatment. Identical tests performed for other symptoms and signs associated with VS suggest that any changes were statistically insignificant. These included trigeminal neuropathy ($P = 0.6875$), tinnitus ($P = 0.6250$), disequilibrium ($P = 0.9999$), vertigo ($P = 0.6072$), and headaches ($P = 0.7905$). The rate of post-GK hydrocephalus was 4.4%. There were no cases of secondary malignancy or mortality. At last follow-up, 2 patients had died of unrelated causes.

DISCUSSION

Several articles have identified the need for phase III clinical trials evaluating the efficacy of current radiosurgical or microsurgical techniques in the treatment of VSs.[3,8,21] There exists little prospective evidence on the topic, so for the moment, systematic meta-analysis of retrospective data remains the most powerful tool for basing clinical decisions. Contributing to the available evidence for such reviews, we present the previously unreported outcomes of 70 patients treated for VS with the GK at our center. Our comprehensive study evaluated tumor control, hearing preservation, facial nerve preservation, and other functional outcomes. Furthermore, we evaluate the dependence of such outcomes on tumor size and radiation dose.

Characteristics of our patients before treatment (Table 1) are similar to existing studies.[6,8,15,18] Patients presented with a spectrum of symptoms and signs related to dysfunction of the vestibulocochlear nerve and anatomically adjacent structures. The incidence rates identified for hearing loss, tinnitus, vertigo, trigeminal neuropathy, and facial neuropathy (Table 1) were similar to those reported by Matthies and Samii.[2] These facts suggest that our study population does not consist of a unique demographic of patients with VS.

Patients in this study were treated according to standard American Society of Therapeutic Radiation Oncology guidelines, using a mean marginal dose of 12.7 Gy. The majority of patients (55, 79%) were prescribed a marginal dose of 13 Gy or less. Flickinger et al reported that 12 to 13 Gy offer tumor control and greater hearing preservation, and this has remained an arbitrary cutoff point for low-dose classification in the field.[21] Therefore, our study results are relevant for evaluating the efficacy of lower doses in the radiosurgical treatment of VSs.

Patients in our study were followed-up clinically, with MR imaging, and with audiometry. Results are based on a mean clinical follow-up of 27.6 months, imaging follow-up of 26.2 months, and audiometric follow-up of 17.1 months. This magnitude of follow-up is appropriate for determining the efficacy of GK radiosurgery for treating patients with VS. However, longer-term endpoints are required to fully evaluate the benefits and risks of SRS, especially risks of tumor recurrence and secondary malignancy. These outcomes should be the objective of future studies at our center.

GK radiosurgery provided tumor control for 94% of patients, with a 95% CI of 88% to 100%. This fits well with control rates published in existing systematic reviews (91%–95%).[3,6,8,15–18] We identified a statistically significant decrease in tumor size following GK intervention and determined that tumor control was determined independent of marginal dose. These results indicate that treating patients with lower doses of 12 to 13 Gy continue to offer significant control of VSs, as reported elsewhere.[21]

When grouped by tumor size, similar control rates were achieved in tumors smaller than 30 mm in diameter (Fig. 1). Only 5 patients with tumors more than 30 mm existed in our patient population, and so the significance of results for that group is limited. However, it is noteworthy that radiosurgical treatment of tumors more than this size is rare, and it has been suggested that surgery should be the sole option for such patients.[26] Statistical tests identified an independent relationship between tumor control and either tumor size or volume, suggesting that the efficacy of GK radiosurgery not dependent on such factors. Future studies may seek to elucidate whether this trend is equally relevant to patients treated with tumors greater than 30 mm in size.

Hearing function decreased on average following radiosurgery. Mean pure tone hearing loss was worse at all frequencies tested when compared with pretreatment levels (Fig. 2). It has been previously postulated that dose margins overlapping the cochlear nuclei in the brainstem would preferentially cause low-frequency hearing deficits, whereas exposure to the cochlea would cause high-frequency deficits.[20] We see a similar magnitude of loss at all frequencies, which may be attributed to the exposure to both the brainstem and cochlea. Dose-dependent toxicity beyond the tumor margin has been reported previously.[27] To determine what doses are toxic, future studies should seek to examine relationships between pure tone hearing loss and dose to the brainstem or cochlea.

As a summary of overall hearing function, we also evaluated changes in SRT and SDS (Table 3). SRT increased by a mean value of 17 dB (95% CI: 8–21), corresponding to a decrease in function. SDS also exhibited a statistically significant trend toward worse function, changing by −11% (95% CI: −20 to −2). Marginal dose, tumor size, and tumor volume had no effect on the changes in SRT or SDS upon statistical analysis.

In the treatment of VS, preservable hearing function is typically defined using the GR scoring system, where SRT <50 dB and SDS >50% correspond to good function. Before the treatment we had 17 patients who fit this criteria, with GR scores of 1 or 2. Audiometric outcomes were available for 14 patients, and hearing was preserved in 64% of that population (95% CI: 38–90). In assuming that patients without follow-up lost function, the preservation rate drops to 53%. These values fit well with the preservation rates elucidated in large meta-analyses published since 2003 (54%–63%).[6,15,17] In an older meta-analysis by Kaylie et al, hearing was preserved in only 44% of patients using a significantly higher mean dose (17.3 Gy). Furthermore, a 2009 review by Yang et al identified a statistically significant difference in preservation rates in those patients treated with 12.5 Gy or less ($P = 0.0285$).[15] Our study contained too few candidates for hearing preservation to perform meaningful analysis on the effect of dose. However, we achieve a preservation rate comparable to other studies using a mean marginal dose of 12.7 Gy, supporting the conclusion that low-dose therapy offers lower risk of hearing loss.

In patients with good facial nerve function, defined as a HB score of I or II, we achieved a preservation rate of 95%. Contemporary meta-analyses quote control rates of 93% to 96%.[6,16,17] Notably, a study published in 2000 identified a facial nerve preservation rate of 81% in patients treated with an mean of 17 Gy.[8] We did not analyze the consequence of dose on facial nerve preservation, but doses less than 13 Gy have been indicated to offer lower risk ($P < 0.0001$).[16] Current radiosurgical techniques appear to offer the greatest benefits with respect to facial nerve preservation as compared with alternative interventions, as meta-analyses of surgical outcomes have identified facial preservation rates much lower (81%–86%).[6,8]

Treating VSs with radiation also poses potential risks of toxicity to other intracranial structures. However, we found no statistically significant difference between pre- and post-treatment status for the following symptoms and signs: facial neuropathy, trigeminal neuropathy, tinnitus, disequilibrium, vertigo, and headaches. Risk of hydrocephalus was 4.4%, which is slightly higher than the 3% identified elsewhere.[6] Treatment posed no risk of mortality or secondary malignancy; however, definitive risks of radiation-induced neoplasm will require longer follow-up in future studies.

CONCLUSIONS

We retrospectively evaluated the outcomes of 70 patients treated for VS with GK radiosurgery. Our study population represents a cohort of patients treated since 2003 using low marginal doses (mean, 12.7 Gy) and modern radiosurgical techniques. Radiosurgery offered excellent tumor control, with 94% of tumors shrinking or remaining static after a mean follow-up of 26 months. Control was independent of dose or tumor size. A statistically significant decrease in hearing function was observed; however, in those patients with serviceable hearing before treatment, 64% preserved function at last follow-up. Changes in audiometric parameters were also independent of dose and tumor size. Facial nerve function was preserved in 95% of patients following treatment. These results support the conclusion that lower marginal doses, adopted over the past decade, offer excellent tumor control and functional preservation. In the future, prospective studies and meta-analysis of contemporary data, such as that published here, will offer more robust evidence for guiding clinical decisions. For now, our results reveal that GK radiosurgery is a viable option for all patients with VSs less than 30 mm in diameter, and we believe that further study is needed to quantify the efficacy of treatment for patients with larger tumors. Practitioners should inform their patients of the benefits and risks associated with radiosurgery, as well as those of alternatives like observation, microsurgery, and FRT.

ACKNOWLEDGMENTS

The authors thank Rachel Garman and Michelle Osso as well as the entire Cancer Care Northwest research staff for their contributions to this manuscript.

REFERENCES

1. Propp JM, McCarthy BJ, Davis FG, et al. Descriptive epidemiology of vestibular schwannomas. *Neuro Oncol.* 2006;8:1–11.
2. Matthies C, Samii M. Management of 1000 vestibular schwannomas (acoustic neuromas): clinical presentation. *Neurosurgery.* 1997;40:1–9; discussion 9–10.
3. Battaglia A, Mastrodimos B, Cueva R. Comparison of growth patterns of acoustic neuromas with and without radiosurgery. *Otol Neurotol.* 2006;27:705–712.
4. Smouha EE, Yoo M, Mohr K, et al. Conservative management of acoustic neuroma: a meta-analysis and proposed treatment algorithm. *Laryngoscope.* 2005;115:450–454.
5. Sughrue ME, Yang I, Aranda D, et al. The natural history of untreated sporadic vestibular schwannomas: a comprehensive review of hearing outcomes. *J Neurosurg.* 2010;112.
6. Yamakami I, Uchino Y, Kobayashi E, et al. Conservative management, gamma-knife radiosurgery, and microsurgery for acoustic neurinomas: a systematic review of outcome and risk of three therapeutic options. *Neurol Res.* 2003;25:682–690.
7. Yoshimoto Y. Systematic review of the natural history of vestibular schwannoma. *J Neurosurg.* 2005;103:59–63.
8. Kaylie DM, Horgan MJ, Delashaw JB, et al. A meta-analysis comparing outcomes of microsurgery and gamma knife radiosurgery. *Laryngoscope.* 2000;110:1850–1856.
9. Andrews DW, Werner-Wasik M, Den RB, et al. Toward dose optimization for fractionated stereotactic radiotherapy for acoustic neuromas: comparison of two dose cohorts. *Int J Radiat Oncol Biol Phys.* 2009;74:419–426.

10. Chan AW, Black P, Ojemann RG, et al. Stereotactic radiotherapy for vestibular schwannomas: favorable outcome with minimal toxicity. *Neurosurgery*. 2005;57:60–70; discussion 60–70.
11. Combs SE, Volk S, Schulz-Ertner D, et al. Management of acoustic neuromas with fractionated stereotactic radiotherapy (FSRT): long-term results in 106 patients treated in a single institution. *Int J Radiat Oncol Biol Phys*. 2005; 63:75–81.
12. Koh ES, Millar BA, Menard C, et al. Fractionated stereotactic radiotherapy for acoustic neuroma: single-institution experience at The Princess Margaret Hospital. *Cancer*. 2007;109:1203–1210.
13. Maire JP, Huchet A, Milbeo Y, et al. Twenty years' experience in the treatment of acoustic neuromas with fractionated radiotherapy: a review of 45 cases. *Int J Radiat Oncol Biol Phys*. 2006;66:170–178.
14. Thomas C, Di Maio S, Ma R, et al. Hearing preservation following fractionated stereotactic radiotherapy for vestibular schwannomas: prognostic implications of cochlear dose. *J Neurosurg*. 2007;107:917–926.
15. Yang I, Aranda D, Han SJ, et al. Hearing preservation after stereotactic radiosurgery for vestibular schwannoma: a systematic review. *J Clin Neurosci*. 2009;16:742–747.
16. Yang I, Sughrue ME, Han SJ, et al. Facial nerve preservation after vestibular schwannoma Gamma knife radiosurgery. *J Neurooncol*. 2009;93:41–48.
17. Shin YJ, Lapeyre-Mestre M, Gafsi I, et al. Neurotological complications after radiosurgery versus conservative management in acoustic neuromas: a systematic review-based study. *Acta Otolaryngol*. 2003;123:59–64.
18. Weil RS, Cohen JM, Portarena I, et al. Optimal dose of stereotactic radiosurgery for acoustic neuromas: a systematic review. *Br J Neurosurg*. 2006; 20:195–202.
19. Flickinger JC, Kondziolka D, Pollock BE, et al. Evolution in technique for vestibular schwannoma radiosurgery and effect on outcome. *Int J Radiat Oncol Biol Phys*. 1996;36:275–280.
20. Linskey ME. Hearing preservation in vestibular schwannoma stereotactic radiosurgery: what really matters? *J Neurosurg*. 2008;109(suppl):129–136.
21. Flickinger JC, Kondziolka D, Niranjan A, et al. Acoustic neuroma radiosurgery with marginal tumor doses of 12 to 13 Gy. *Int J Radiat Oncol Biol Phys*. 2004;60:225–230.
22. Miller RC, Foote RL, Coffey RJ, et al. Decrease in cranial nerve complications after radiosurgery for acoustic neuromas: a prospective study of dose and volume. *Int J Radiat Oncol Biol Phys*. 1999;43:305–311.
23. Nagano O, Higuchi Y, Serizawa T, et al. Transient expansion of vestibular schwannoma following stereotactic radiosurgery. *J Neurosurg*. 2008;109: 811–816.
24. Gardner G, Robertson JH. Hearing preservation in unilateral acoustic neuroma surgery. *Ann Otol Rhinol Laryngol*. 1988;97:55–66.
25. House JW, Brackmann DE. Facial nerve grading system. *Otolaryngol Head Neck Surg*. 1985;93:146–147.
26. Nikolopoulos TP, O'Donoghue GM. Acoustic neuroma management: an evidence-based medicine approach. *Otol Neurotol*. 2002;23:534–541.
27. Paek SH, Chung HT, Jeong SS, et al. Hearing preservation after gamma knife stereotactic radiosurgery of vestibular schwannoma. *Cancer*. 2005;104:580–590.