ORIGINAL ARTICLE

Radiosurgery for Vestibular Schwannomas

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Background: Radiosurgery has been established as an important alternative to microsurgery. We report our experience with radiosurgery for tumor control and the complications of unilateral vestibular schwannomas.

Methods: We reviewed our early experience regarding clinical presentation, management and outcomes in 45 patients with acoustic schwannomas who underwent gamma knife stereotactic radiosurgery. The median follow-up period was 25 months (range, 6–48 months). Thirteen patients had undergone 1 or more previous resections before radiosurgery; 32 underwent radiosurgery as the first procedure. Median tumor volume was 4.5 mL (range, 0.5–30.0), and median radiotherapy dose was 11.5 Gy (range, 10.5–14.0 Gy).

Results: Tumor control was achieved in 43 patients (95.6%). Loss of central contrast enhancement was a characteristic change and was noted in 29 patients (64.4%). Reduction in tumor size was shown in 15 patients (33.3%). Thirteen patients (28.9%) had good or serviceable hearing preoperatively, and in all of these, the preoperative status was retained immediately after radiosurgery. At follow-up, however, 10 patients (76.9%) had preserved hearing and 3 (23.1%) had reduced hearing on the treated side. Hearing in 1 patient that was not serviceable preoperatively later improved to a serviceable level. No patients had delayed facial palsy or lower cranial nerve dysfunction, but one had delayed trigeminal sensory loss.

Conclusion: Radiosurgery achieved a high tumor control rate and a relatively low post-radiosurgical complication rate for acoustic neuromas. [*J Chin Med Assoc* 2005;68(7):315–320]

Key Words: brain tumor, radiosurgery, schwannoma

Introduction

Surgical excision is generally considered the preferred treatment for unilateral acoustic neuromas in healthy, non-elderly patients who have useful hearing in the contralateral ear.[1] The location and relationship of such neuromas to neurovascular structures, and adherence to the brain stem or cranial base, pose challenges for preserving cranial nerve function, and render complete surgical resection difficult in some cases. Resection is frequently associated with the development of new neurologic deficits.[1–3]

The clinical application of stereotactic radiosurgery began in Sweden in 1967,[4] and the first patient with acoustic neuroma was treated in 1969.[5] Since then, major improvements in the accuracy and efficiency of stereotactic radiosurgery have resulted from combination of the procedure with advanced high-resolution imaging techniques such as magnetic resonance imaging (MRI).[6,7] In this report, we analyze the preliminary results from 45 patients who underwent radiosurgery as management for newly diagnosed or recurrent acoustic schwannoma.

Methods

Patient population

During a 4-year period, 45 patients with unilateral acoustic schwannomas underwent stereotactic radiosurgery with a 201-source, cobalt-60 gamma knife. Thirteen patients had undergone 1–3 (mean,

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l.4) previous surgical resections. Thirty-two patients underwent radiosurgery on the basis of clinical findings and imaging criteria. Tumors in these patients were found along the course of the acoustic nerve, and had the characteristics of vestibular schwannowa or acoustic neuroma (cerebello-pontine angle location, and tail extending into the internal acoustic meatus). In these patients, radiosurgery was performed for 1 of the following reasons: 1) the patient had little neurologic deficit; 2) the patient was elderly or declined to undergo microsurgical resection; or 3) the patient had residual or recurrent tumors after surgical excision. Patient age ranged from 24 to 82 years (mean, 55 years).

Preoperative assessment

All patients had a detailed history taken, underwent a physical examination, and preoperative high-resolution MRI. All patients were evaluated with pure-tone audiograms. Preoperative and postoperative hearing was classified according to the system of Gardner and Robertson,[8] a modification of the Silverstein and Norrell classification system, as shown in Table 1.

Radiosurgical technique

In all 45 patients, a Leksell Model G stereotactic coordinate frame (Elekta Instruments, Atlanta, GA, USA) was applied to the head, under local anesthesia supplemented with mild oral or intravenous sedation. A high-resolution, contrast-enhanced MRI scan was performed to localize the target tumor. Multiple isocenter computer dose planning was completed using the GammaPlan® dose-planning system (Elekta Instruments). Median tumor volume was 4.5 mL (range, 0.5–30.0 mL), and mean maximum tumor dose was 23 Gy (range, 22–28 Gy). Median tumor-margin dose was 11.5 Gy (range, 10.5–14.0 Gy) (Figure 1).

The margin dose was the dose selected to cover the contrast-enhanced tumor margin, using the conformal dose-planning technique. This dose served to cover 100% of the target volume. Using MRI, we found that irregularities in tumor shape could be readily identified, and greater numbers of isocenters were used to obtain conformal irradiation. In 41 patients, the 50% isodose line was targeted to the tumor margin, and in 4 patients, the 55% isodose line was targeted to the tumor margin. The mean number of isocenters per patient was 14 (range, 3–29). The dose selected was based on tumor volume, although as low a dose as possible was selected. Tumor location and the projected radiobiologic risk to the adjacent brain stem and cranial nerves were considered during dose planning. Immediately after radiosurgery, all patients were given a single intravenous dose of methylprednisolone 40 mg. All patients were discharged within 24 hours.

Postoperative evaluation

Follow-up ranged from 6 to 48 months (median, 25 months). Our protocol for post-radiosurgical assessment included serial clinical examinations and MRI scans at 3, 6 and 12 months during the first year, and every 6 months thereafter. In patients with grade IV or better hearing preoperatively, a pure-tone audiogram was requested at the same intervals.

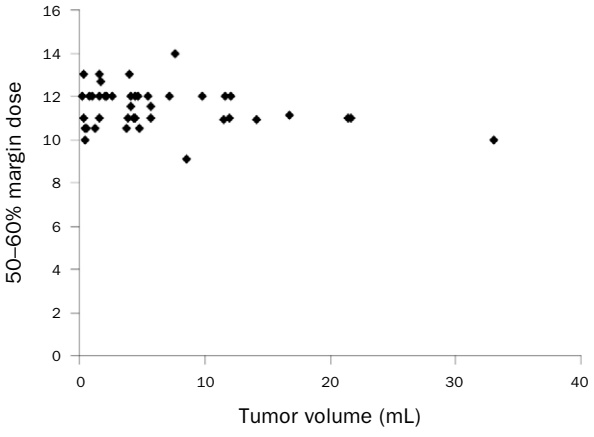

Figure 1. Scatter plot of tumor volume versus tumor-margin dose for radiosurgery in 45 patients with acoustic neuromas.

Table 1. Hearing classification in 45 patients with acoustic neuromas

Class description	Pure tone average (dB)	Speech discrimination score (%)	Number of tumors	
			Preoperative	Postoperative
I	0–30	70–100	4	3
II	31–50	50–69	9	8
III	51–90	5–49	10	12
IV	91–maximum	1–4	8	8
V	None detectable	0	14	14

Whenever possible, follow-up electrophysiologic studies, including evoked potential, and electromuscular electromyography, were performed, especially if delayed facial or trigeminal nerve dysfunction was reported.

Results

Eighty-five percent of patients were discharged from the hospital within 24 hours after radiosurgery, and all others within 48 hours. Fifteen percent of patients experienced transient headaches, and 27% had nausea and/or vomiting during the first 12 postoperative hours. These symptoms resolved after treatment with mild analgesics and antiemetics. In most cases, the single postoperative intravenous dose of methylprednisolone 40 mg prevented these symptoms.

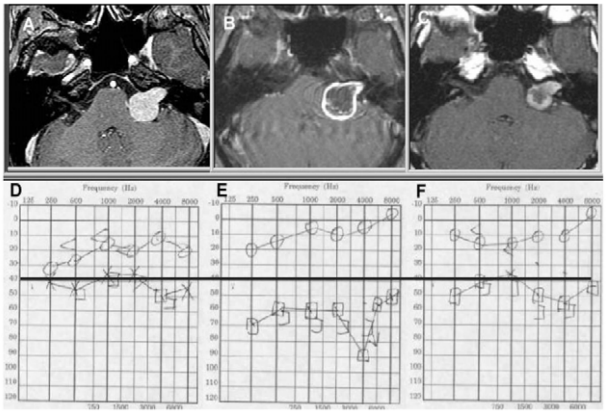

Figure 2. Axial plane, contrast-enhanced magnetic resonance images obtained in a 25-year-old man who underwent gamma knife radiosurgery (12 Gy at margin; 50% isocenter): (A) left-sided acoustic neuroma; (B) swollen tumor was seen 6 months after treatment; (C) tumor regression was noted 12 months later. (D, F) Preoperative hearing level was maintained after treatment, although (E) transient impairment was noted at the sixth month.

Imaging responses

During the median follow-up period of 25 months (range, 6–48 months), imaging studies showed a reduction in tumor volume in 15 patients (33.3%) and tumor-growth arrest in 28 patients (62.2%) (Table 2). Imaging revealed evidence of central tumor necrosis in 29 patients (64.4%). Thirteen of these patients eventually showed regression in tumor volume; the volume of central necrosis paralleled the reduction in tumor size (Figure 2). None of the patients developed local brain stem, high T2-signal MRI changes on long-repetition time images.

Clinical responses

The preoperative and postoperative hearing classification of 45 patients is presented in Table 1. Audiologic follow-up was performed 6–48 months (median, 18 months) after radiosurgery. Thirteen patients had either good (grade I) or serviceable (grade II) hearing preoperatively. Ten patients retained good or serviceable hearing postoperatively, but 3 developed hearing impairment. Improvement of preoperative hearing impairment was observed in 1 patient postoperatively. Preoperative examination had disclosed facial weakness in 15 patients, trigeminal sensory loss in 7, and reports of imbalance or ataxia in 6. These signs were usually relatively mild. In the follow-up period, no delayed facial nerve dysfunction occurred, and there was no exacerbation of preoperative complaints. Delayed trigeminal nerve dysfunction was observed in 1 patient. Another patient underwent microscopic removal of the tumor because of worsening ataxia 9 months after radiosurgery, although the tumor volume had not increased. One patient died from unrelated disease after 1.5 years of follow-up.

Discussion

Tumor control after radiosurgery

Although total tumor removal remains a reasonable goal of vestibular schwannoma surgery, alternative strategies must play a role in management because recurrence after subtotal resection is not rare. Therapeutic options for recurrent or residual tumors after surgery include re-operation, fractionated external-beam radiotherapy, and stereotactic radiosurgery.

Table 2. Postoperative magnetic resonance imaging results in 45 patients with acoustic neuromas

Change in tumor volume	Overall, *n* (%)	Loss of central enhancement, *n* (%)
Increased	2 (4.4)	0 (0)
Unchanged	28 (62.2)	16 (55.2)
Decreased	15 (33.3)	13 (44.8)

Table 3. Comparison of tumor control achieved by radiosurgery with the untreated natural history of acoustic neuroma (control group)

	Natural history (n = 242)	Stereotactic radiosurgery (n = 43)
Mean age, yr (range)	59 (11–81)	60 (24–74)
Mean duration of follow-up, yr (range)	2.3 (1.0–12.1)	2.5 (1.0–4.0)
Tumor condition, n (%)*		
Disease progression	107 (44.2)	2 (4.7)
Partial response	118 (48.8)	23 (53.5)
Stable disease	17 (7.0)	18 (41.9)

*Outcomes between the 2 groups were significantly different ($p < 0.001$, Chi-squared test).

The goal of radiosurgery is to achieve tumor control with a low risk of additional cranial nerve deficits. Further, the efficacy of radiosurgery in the treatment of vestibular schwannoma is reflected by the increasing number of patients managed at our center and others.[9,10] The radiobiologic mechanism of growth control achieved via radiosurgery is believed to be a combination of direct tumoricidal effects and delayed intratumoral vascular obliteration. *In vitro* studies suggest that Schwann cells are irreversibly damaged after a single-fraction radiation dose as low as 30 Gy.[11] It is thought that the tumor-cell response is both time-dependent and dose-dependent.

Our imaging studies showed that 1-third of patients had reduced tumor volume, and 62.2% had unchanged tumor size. However, Kondziolka et al[9] followed patients for a much longer time (5–10 years) after treatment at Pittsburgh University. These investigators noted a total tumor control rate of 98%, and reductions in tumor size of 25.5% in year 1, 46.9% in year 2, 58.8% in year 3, and 76.0% in year 5. Other reports revealed a tumor control rate ranging from 89% to 100%.[12,13]

To confirm the efficacy of radiosurgery, we compared the tumor control achieved by radiosurgery in our study with the natural history of untreated acoustic neuromas (Table 3). We reviewed all the published reports and included the 3 largest groups that provided definitive data about tumor growth (> 2 mm per year), no growth, and tumor regression.[14–16] Tumor size in the control group increased in 107 patients, was unchanged in 118, and decreased in 17, over an average follow-up period of 2.3 years. Based on our radiosurgical results for acoustic tumors, and on data from other investigators,[14–16] radiosurgery provides improved tumor control relative to untreated individuals ($p < 0.001$, Chi-squared test).

Our early experience with acoustic neuromas has shown that tumors with central necrosis after radiosurgery often have delayed volume reduction. Loss of central contrast enhancement may result from radiation-induced vascular injury and occlusion. Indeed, obliteration of blood supply to the tumor may be 1 of the most significant mechanisms controlling tumor growth after surgery. Although Noren et al[17] reported that the absence of a post-radiosurgical decrease in tumor size was unrelated to a loss of contrast enhancement, we found the latter factor to be a good prognostic indicator of delayed tumor shrinkage.

Hearing preservation

Hearing preservation is a pertinent surgical goal in relatively few patients with acoustic neuromas. The initial rate of hearing preservation after surgery for acoustic neuroma was 33%, as reported by Gardner and Robertson.[8] Samii and Matthies[18] also reported a 39% rate of hearing preservation, and other groups documented a tumor control rate of 15–48%.[19,20]

Seventy-eight percent of our patients remained at the preoperative hearing level at follow-up, but further follow-up is needed to verify this finding. In patients with less than 90 dB pure tone average preoperative hearing loss, Noren et al[17] reported preserved hearing in 56% of patients 1 year after radiosurgery, 54% at 2 years, and 28% at 6 years. Hirsh and Noren[21] reported 9 patients with preoperative pure tone average values of 55 dB or less who were treated with radiosurgery and followed for 4–9 years. Two patients completely lost their hearing, 3 had their hearing preserved, and the remaining 4 experienced varying degrees of hearing loss.[21] Linskey et al[22] reported 7 patients with serviceable hearing preoperatively: 3 became deaf within the first year of treatment; but in 4, hearing stayed within 1 level above or below their initial grade. Kondziolka et al[9] reported hearing preservation in 51% of patients with a median dose of 15.5 Gy, and recently, hearing preservation after radiosurgery for acoustic neuroma

appeared promising when patients were treated with a dose lower than 15 Gy.[23] Flickinger et al[23] reported a 71% rate of hearing preservation when patients were treated with a median dose of 13 Gy, and Petit et al[24] reported that 87% of patients had hearing preserved during audiogramic follow-up. A trend in our series, and other reports, was that low-dose treatment had a good hearing preservation effect without sacrificing tumor control. Delayed hearing loss after radiosurgery may be related to a direct radiation effect on the cochlear division if it lies within the tumor, or to injury of vascular supply to the cochlear nerve, or potentially, to the cochlea itself, if it is inadvertently included in the treated volume.

Other cranial nerve preservation

In our study, 1 patient showed trigeminal dysfunction with sensory loss on 1 side of the face; other patients had no further worsening of other cranial nerve function. Further, in our patients, temporary or permanent postoperative facial paresis and trigeminal neuropathy were less common than in the studies conducted by Noren et al[17] and Linskey et al.[22] This is not surprising because we selected 11–12 Gy as the usual marginal tumor dose; in most patients, the minimum effective dose is now generally accepted. Based on the observations of Noren et al,[17] most patients with delayed trigeminal neuropathy will recover. However, the mechanism of delayed cranial nerve dysfunction remains unclear. Dysfunction occurring several weeks to 6 months after radiation is temporary, and appears to be related to demyelination. Dysfunction occurring several months to years after treatment may be associated with compromised vascular supply.

Patients undergoing surgery for acoustic neuromas consider adjustment to postoperative facial palsy to be the most difficult problem. About 80% of patients have temporary or permanent facial nerve dysfunction after open surgery, although the facial nerve has been preserved anatomically in 82–99% of patients in some series.[25–27] Facial nerve dysfunction in the immediate postoperative period has been noted in 8–44% of patients, and long-term follow-up studies found restoration of normal facial nerve function in 46–100% of patients.[25–27]

Low morbidity and a high rate of tumor control were achieved in our series. There was no mortality or major preoperative morbidity; hospitalization time and costs were reduced compared with microsurgery; and rates of hearing preservation, and trigeminal and facial neuropathy were also more favorable than in most of the best published reports of microsurgery.[25–27]

In conclusion, gamma knife radiosurgery is an important alternative treatment for selected patients with acoustic neuromas, especially in the elderly and in patients with small- to moderate-sized tumors. However, because of the low-dose treatment used in most of our patients, a longer follow-up period is needed to substantiate our findings.

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