

# Results of Linear Accelerator-Based Stereotactic Radiosurgery for Recurrent and Newly Diagnosed Acoustic Neuromas

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**SUMMARY** Stereotactic radiosurgery (SRS) is used to treat acoustic neuromas, but additional information is needed to firmly establish its safety and efficacy. We review our experience over 7 years treating 29 consecutive patients with a modified linear accelerator (linac) SRS system. Between August 1989 and October 1995, 29 patients with a median age of 67 years (range 26 to 83) underwent linac SRS treatment. Twenty-five patients had unilateral acoustic neuromas, and four patients with neurofibromatosis type II had bilateral vestibular schwannoma. Eligibility criteria for SRS were recurrent tumors ( $n = 9$ ), age  $>65$  ( $n = 16$ ), or patient preference ( $n = 6$ ). Follow-up magnetic resonance imaging scans were performed on all patients. The most common presenting symptoms were hearing impairment (18 patients) and gait difficulties (17 patients). Ten patients were deaf in the affected ear prior to treatment. Doses to the periphery of the tumor ranged from 800 to 2,400 cGy (median 1,600 cGy) prescribed to the 50% to 80% isodose line (median 80%). After a median radiographic follow-up of 49 months (range 4 to 110 months), 11 tumors were smaller, 17 were stable, and one had evidence of progression (at 41 months). The 5-year local disease control rate (Kaplan-Meier estimate) was 94%. Acute complications were minimal, with only two patients experiencing nausea and vomiting after the procedure. Long-term complications included new or progressive trigeminal and facial nerve deficits with estimated 5-year incidences of 15% and 32%, respectively. Subjective hearing reduction or loss occurred in 14 (74%) of the 19 patients who had useful hearing prior to treatment. Five patients died from unrelated causes. These results suggest that linac SRS provides excellent short-term tumor control rates. Since there was a high risk of cranial nerve neuropathy, we do not recommend using only computed tomography-based planning and high prescription doses. *Int. J. Cancer (Radiat. Oncol. Invest.)* 90, 145–151 (2000).

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## INTRODUCTION

Acoustic neuromas (vestibular schwannomas) are histologically benign, slow-growing tumors. Each year, an estimated 2,000 to 3,000 Americans are newly diagnosed with unilateral acoustic neuromas

[1]. These tumors have traditionally been treated with surgical resection or expectant observation. Surgical resection may be associated with considerable morbidity [2], and about 50% of acoustic neuromas that are not completely resected will recur [3,4]. Some authors have advocated expectant

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observation, but others have found that most untreated acoustic neuromas become larger within 1 to 2 years [5–7].

Some patients with acoustic neuromas are poor candidates for surgery because they are elderly or medically infirm, while others decline surgery. Minimally invasive techniques, such as stereotactic radiosurgery (SRS), provide an alternative to surgery for these patients. On the basis of the favorable results reported by several centers, SRS has become an attractive alternative to microsurgical resection for many patients. Most of the reports are from centers using the gamma knife, and a few are from centers using linear accelerator (linac) systems [1,8–10]. We report our experience of treating patients with acoustic neuromas with SRS using a modified linac system.

## MATERIALS AND METHODS

Our institution began a linac-based program in August 1989. This was a custom-built linac-based system as described by Winston and Lutz [11]. The linac (Varian 600c, Palo Alto, Calif.) was modified using a base plate and floor stand. To allow for adequate follow-up, patients treated after 1995 were not included in the analysis.

All patients with acoustic neuromas considered eligible for SRS were evaluated by a neurosurgeon and a radiation oncologist. The option of surgery was offered to all patients. Patients were eligible for SRS if they had a tumor that had recurred after surgery, were older than 65, or requested SRS. Patients arrived in the morning to have a Brown-Roberts-Wells (BRW) head frame (Radionics, Burlington, Mass.) placed. For the frame placement, local anesthesia with 2% lidocaine was administered. The entire cranium was scanned by computed tomography (CT) in 5 mm slices (Somatom Plus; Siemens, Erlangen, Germany). Non-ionic contrast solution (100–200 cc) was then administered intravenously, and the region of the tumor was scanned again in slices 2 to 3 mm apart. CT scans were transferred on magnetic tape to a treatment planning computer (Scandiplan, Ann Arbor, Mich.), which was used to determine the tumor's contours and to design a treatment plan that optimized tumor coverage and minimized the dose to normal surrounding tissues. The linac was not modified until after all regularly scheduled patients had completed treatment.

After the secondary collimator was set to a  $4 \times 4$  cm field, a tertiary radiosurgery collimator holder was attached to the gantry. A floor stand was mounted onto the floor to accommodate the BRW

head frame on the patient [11]. Circular collimators with sizes ranging from 1.0 to 3.5 cm at 0.5 cm increments were inserted into the holder. The error due to mechanical misalignment of the collimator was kept within 0.5 cm. To minimize the collimator mechanical misalignment and the gantry sag, offset coordinates were obtained at each treatment couch angle to keep the isocenter drift within 0.5 mm throughout the gantry arc span. To verify the accuracy, films were taken with a metal target ball before treatment. The offset coordinates were added to the treatment coordinates.

The prescribed dose was delivered using multiple non-coplanar arcs. The total gantry arc span was a minimum of 400 degrees. General anesthesia was used for the first five patients as part of the start-up management of the radiosurgery program but discontinued after we were comfortable with the reproducibility of the system. Treatment time varied from 20 to 40 min. After treatment, the head frame was removed, and the patient was admitted overnight because treatment generally was completed after 8 PM. All patients, except for one, were discharged the following day. One patient remained in the hospital several days after the procedure for a planned percutaneous endoscopic gastrostomy tube placement. All patients were placed on a schedule of tapering dexamethasone over 1 to 2 weeks.

Follow-up examinations and magnetic resonance imaging (MRI) studies were performed. Since pretreatment audiograms were not routinely performed, patients did not undergo post-SRS audiograms. All patients were seen 6 to 8 weeks after the procedure and then at 6-month intervals. All patients were available for the first follow-up visit. Post-SRS MRI studies were available for all 29 patients (median 49 months, range 4–110 months).

Any new or worsening cranial nerve complication was scored as a complication. Acute complications were defined as those occurring within 3 months after the procedure. Complications were considered long-term if they occurred after 3 months. Hearing loss or worsening was not coded as a long-term complication since most patients presented with poor hearing. All patients with useful hearing were asked if they had noted any subjective decrease in hearing or had become deaf. Local control was defined as no increase in tumor size on subsequent scans.

## Statistical Methods

The reference time points for the study were the date of the radiosurgery, date of neuropathy, and

**Table 1. Pretreatment Tumor Characteristics of the 29 Patients Undergoing Linear Accelerator-Based Stereotactic Radiosurgery**

Maximum tumor diameter (mm)	Tumor volume (cm <sup>3</sup> )			Total
	<1	1–4	>4	
<10	3	0	0	3
11–20	3	10	0	13
21–30	0	1	7	8
>30	0	0	5	5
Total	6	11	12	29

date of last follow-up. The Kaplan-Meier method was used to estimate the incidence of new or progressive facial or trigeminal neuropathy and treatment failure. The log-rank test was used to analyze possible factors leading to neuropathy.

## RESULTS

From August 1989 to October 1995, 29 patients with acoustic neuromas (18 women, 11 men) underwent linac SRS at our institution. Ages at treatment ranged from 26 to 83 years (median 67 years). The most common presenting symptoms were decreased or lost hearing (18 patients) and gait difficulties (17 patients). Ten patients were deaf in the affected ear before undergoing SRS. Indications for treatment included recurrent disease (nine patients), age above 65 years (16 patients), or patient preference (six patients). Twelve patients had undergone previous surgical procedures (nine resections, two shunt placements, and one aspiration). Of the nine patients who had undergone resections, eight had subtotal resection and one had gross total resection. Seven patients underwent more than one operation. One patient had a ventricular peritoneal shunt placed after SRS treatment. Four patients had neurofibromatosis type II. No patient had previously received external beam radiation treatment.

Median tumor volume was 2.1 cm<sup>3</sup> (range 0.18–28.7 cm<sup>3</sup>). The maximum pretreatment tumor dimensions are summarized in Table 1. Dose to the periphery ranged from 800 to 2,400 cGy (median 1,600 cGy). In general, the dose was selected based on the volume and diameter of the tumor, with smaller tumors receiving higher doses. For the initial cases, lower doses were chosen (800 to 1,200 cGy) out of concern for potential brain stem toxicity. The distribution of doses is listed in Table 2. A single isocenter was used in 24 cases, and two isocenters were used in five cases. The number of non-coplanar arcs ranged from two to six per isocenter. Dose was prescribed to the 50% to 80% isodose line (median 80%), with attempts to en-

compass the entire target. Collimator sizes ranged from 10 to 35 mm (median 17.5 mm).

## Survival

After a median follow-up of 57 months (range 9–110 months), 24 patients were alive and five had died from other causes (three from ovarian, renal cell, or colon cancer; one from neurofibromatosis; and one from heart problems). One patient with renal cell carcinoma metastatic to the brain was subsequently treated with whole-brain radiation (3,000 cGy in 10 fractions).

## Local Control

Radiographic follow-up studies were available on all 29 patients with a median follow-up of 49 months (range 4–110 months). Local control was achieved in 28 of 29 patients, for an actuarial 5-year control rate of 94%. In one patient, the tumor progressed 41 months after SRS. Overall, tumor size decreased in 11 patients and was stable in 17.

## Acute Complications

The treatments were well tolerated by most patients. Acute complications occurred in only two of 29 patients and consisted of nausea and vomiting soon after the procedure. Neither delivered tumor dose, tumor diameter, nor tumor volume could predict acute complications.

## Long-Term Complications

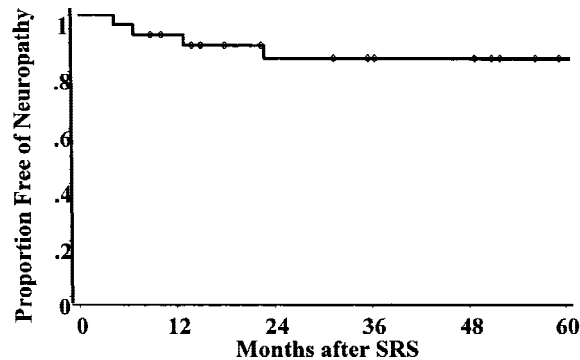
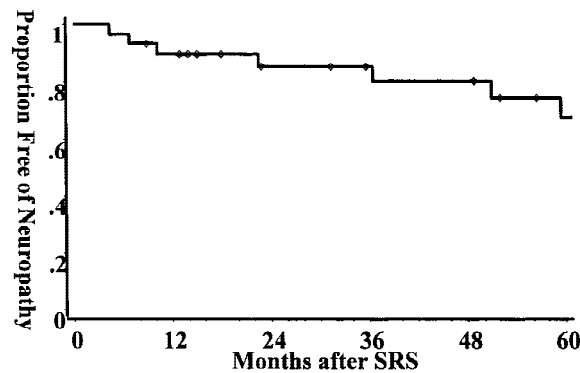
Five patients had new or worsening facial numbness, which was permanent in four. Three patients (10%) had ataxia, which resolved. Eight (28%) patients had new or worsening seventh cranial nerve deficits, which were permanent in seven. One patient required surgery to correct difficulty in closing the eye. The 5-year actuarial incidence rates of trigeminal and facial neuropathy were estimated at 15% and 32%, respectively (Figs. 1, 2).

Two patients underwent shunt insertion for hydrocephalus. In one patient, a follow-up MRI scan showed marked brain stem edema on T2 images. This patient had balance difficulties and was started on dexamethasone. Radiographs showed gradual improvement after shunt insertion. Of the 19 patients with functional hearing, seven reported becoming deaf (37%) and another 7 reporting diminished hearing, for a total incidence of 74%. We did not test hearing as part of this study; however, seven of the patients who were not deaf at the time of radiosurgery reported becoming deaf after SRS, and an additional seven reported some hearing loss.

The risk for long-term complications was not associated with history of previous surgery, age,

**Table 2. Distribution of Peripheral Tumor Dose and Isodose Prescription for Patients Undergoing Linear Accelerator-Based Stereotactic Radiosurgery to Treat Acoustic Neuromas**

Isodose line (%)	Peripheral tumor dose (cGy)				Total
	<1000	1000–1500	1501–1999	>2000	
50	1	3	0	4	8
60	0	1	0	0	1
70	0	1	1	0	2
80	1	2	7	8	18
Total	2	7	8	12	29

**Fig. 1.** Actuarial incidence of cranial V deficits for 29 patients after linear accelerator-based stereotactic radiosurgery for acoustic neuroma.**Fig. 2.** Actuarial incidence of cranial VII deficits for 29 patients after linear accelerator-based stereotactic radiosurgery for acoustic neuroma.

sex, history of neuropathy, history of neurofibromatosis type II, maximal tumor diameter, or tumor volume. Patients who received high doses (>1,500 cGy) were more likely to experience facial neuropathy than those receiving low doses, with 5-year actuarial incidence rates being 38% and 9%, respectively. However, the difference did not reach statistical significance ( $P = 0.35$ ). The degree of conformality (prescription isodose volume/tumor volume) could not be calculated for all patients given the limitations of the software.

## DISCUSSION

Treatment options for acoustic neuromas include observation, surgical resection, SRS, and fractionated stereotactic radiotherapy. For healthy patients with symptomatic unilateral tumors, surgical resection has been considered the standard treatment [12]. The goals of surgical resection are complete removal of the tumor and preservation of function in the seventh and eighth cranial nerves. Each of the surgical approaches (translabyrinthine, suboccipital, middle fossa, or retrosigmoid transmeatal) has advantages and disadvantages in a trade-off between tumor removal and cranial nerve preservation. Samii and Matthies [13] reported a 98% rate of tumor removal and a 93% rate of anatomic preservation of the facial nerve in a surgical series of 1,000 patients. Gormley and colleagues [14] reported a 99% rate of complete tumor removal.

Both microsurgical resection and SRS provide acceptable disease control. To compare surgery and gamma knife radiosurgery, Pollock and colleagues [1] retrospectively evaluated 87 patients with acoustic neuromas <3 cm in diameter. SRS was significantly more effective at preserving hearing and facial function and resulted in an earlier return to pretreatment status, with lower costs and shorter hospital stays. Another study from the Netherlands also demonstrated that the direct and indirect costs of radiosurgery were less than those of microsurgery [15].

Other researchers believe that surgery should be the treatment of choice for patients <70 years old with no medical contraindications to surgery and that SRS is not an alternative for this subset of patients [16]. Patients with small tumors (<1.5 cm), good hearing, and facial function are expected to have the best results. Still other researchers believe that for tumors >2 cm in diameter, hearing cannot be preserved [17,18]. For patients who are older, are medically infirm, or have recurrent tumors after surgery, SRS may be a more appropriate alternative.

In our series, acute complications were mini-



mal and manageable. No pretreatment or tumor characteristics appeared to predict for acute complications. In contrast, some surgical series have reported serious perioperative complications associated with microsurgical resection. Harner et al. [19] reported postoperative complications in 332 patients, including otorrhea (12%), meningitis (5%), aspiration pneumonia (2%), intracranial hemorrhage (2%), and postoperative death (0.6%). A survey conducted by the Acoustic Neuroma Association of 541 postsurgical patients revealed potentially serious perioperative complications, including meningitis (6%), cerebrospinal fluid leakage (7%), and stroke (1%) [2]. A more recent survey of nearly 1,600 patients found a 44% incidence of facial numbness, an 11% incidence of cerebrospinal fluid leakage, and a 9% incidence of balance problems [20].

Long-term complications were common in this series. This result is not surprising because all patients were treated with CT-based planning and higher radiation doses than most would advocate today. Flickinger et al. [9] reported results for 273 patients with unilateral acoustic neuromas who underwent gamma knife radiosurgery. The mean actuarial 7-year tumor control rate was  $96.4\% \pm 2.3\%$  for clinical end points and  $91\% \pm 3.4\%$  for radiographic end points. Patients undergoing MRI-based planning had significantly lower rates of facial, trigeminal, and auditory neuropathy than those who underwent CT-based planning. Smaller transverse tumor diameters and lower minimum tumor doses were associated with lower rates of facial and trigeminal neuropathy. A series from the Mayo Clinic also reported lower rates of facial nerve complication when the tumor margin dose was  $<1,800$  cGy [21]. Mendenhall et al. [10] reported that complications were related to the dose and treatment volume. Overall, 23% of patients experienced complications. When the treatment volumes exceeded  $5.5 \text{ cm}^3$  and the dose was between 15 and 17.5 Gy, 71% of patients experienced complications. Three of three patients experienced complications when the entire volume received 20 to 22.5 Gy.

In our series, patients receiving lower doses were less likely to experience long-term facial neuropathy, although our sample was too small for the difference to reach statistical significance. We currently treat all patients with MRI-based planning, using multiple isocenters to achieve conformity and lower radiation doses (median 1,300 cGy).

Although audiograms were not performed in all patients, our results suggest that patients are at risk for hearing loss following the procedure as 14

of the 19 patients who were not deaf at the time they received SRS reported partial or total hearing loss afterward. Because this occurred in patients without evidence of tumor progression, it must be assumed to be a result of SRS. Foote et al. [8] reported that patients can retain useful hearing after SRS, and the 1- and 2-year actuarial rates of preservation of useful hearing (Gardner-Robertson class I or II) were 100% and 47%, respectively. For patients with useful hearing, an alternative strategy may be stereotactic radiotherapy [22]. Fractionated stereotactic radiotherapy combines the focal dose distribution of SRS with the radiobiological advantages of fractionation. This approach appears to preserve useful hearing and to decrease the likelihood of injury to nerves V and VII [23]. In this preliminary report from the Joint Center for Radiation Therapy [23], nine of nine patients treated with stereotactic radiotherapy maintained useful hearing after a median follow-up of 26.5 months.

Five of our 29 patients experienced new or worsening trigeminal numbness. No pretreatment characteristics or treatment factors appeared to predict for this risk. Linskey et al. [24] reported that the estimated length of the irradiated nerve predicted the risk of delayed facial and trigeminal neuropathy. Dysfunction of the fifth and seventh cranial nerves is also related to tumor diameter [25]. The use of MRI-based planning has resulted in lower rates of trigeminal neuropathy [9].

Although we found a high rate of cranial neuropathies, we can corroborate the results of others, who have documented the usefulness of SRS in managing acoustic neuromas. Our actuarial local control rate at 5 years was excellent at 94%. This confirms the results of Mendenhall et al. [10], who treated acoustic neuromas with linac SRS and achieved a 5-year actuarial local control rate of 95%.

Despite this and other reports of the efficacy of SRS in treating acoustic neuromas, some have argued that SRS does little to alter the natural history of these slow-growing tumors. For this reason, they have argued for observing patients who are medically infirm and who have small, slow-growing, and relatively asymptomatic tumors [26,27]. In these series, the growth rate was 0.11 to 0.16 cm/year, with 20% to 26% of patients requiring intervention. Some authors have also argued that follow-up has been too short to adequately assess SRS results. Others have found that SRS does affect tumor growth after up to 17 years of follow-up [28]. Kondziolka et al. [29] reported on 162 consecutive patients treated with the gamma knife from 1987 to 1992. These patients achieved

98% local control, with 62% of tumors becoming smaller on follow-up scans.

In conclusion, our data suggest that SRS can achieve local control rates for acoustic neuroma that are comparable to the results of surgery and better than those of expectant observation. They also suggest that SRS has fewer short-term complications than surgery but that SRS, at least when planned with CT and using relatively high peripheral doses, may be followed by long-term complications, including facial and trigeminal neuropathy and hearing loss. We believe that MRI-based planning and lower peripheral doses should be used to minimize side effects. Longer follow-up will determine if lower peripheral doses will provide local control rates as high as those achieved by surgical resection. Results from other centers suggest that SRS may be less appropriate for patients with useful hearing or larger tumors, who may be better treated with fractionated stereotactic radiotherapy. On the basis of our results and of other published results, we believe that patients should be told of the potential advantages and disadvantages of SRS and allowed to make a judicious decision regarding treatment.

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