Linear accelerator radiosurgery for vestibular schwannoma

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Object. The use of radiosurgery in the treatment of acoustic neuromas has increased substantially during the last decade. Most published experience relates to the use of the gamma knife. In this report, the authors review the methods and results of linear accelerator (LINAC) radiosurgery in 44 patients with acoustic neuromas who were treated between 1993 and 1997.

Methods. Computerized tomography scanning was selected as the stereotactic imaging modality for target definition. A single, conformally shaped isocenter was used in the treatment of 40 patients; two or three isocenters were used in four patients who harbored very irregular tumors. The radiation dose directed to the tumor border was the only parameter that changed during the study period: in the first 24 patients who were treated the dose was 15 to 20 Gy, whereas in the last 20 patients the dose was reduced to 11 to 14 Gy. After a mean follow-up period of 32 months (range 12–60 months), 98% of the tumors were controlled. The actuarial hearing preservation rate was 71%. New transient facial neuropathy developed in 24% of the patients and persisted to a mild degree in 8%. Radiation dose correlated significantly with the incidence of cranial neuropathy, particularly in large tumors (4 cm³).

Conclusions. Single-isocenter LINAC radiosurgery proved to be an effective treatment for acoustic neuromas in this series, with results that were comparable with those reported for gamma knife radiosurgery and multiple isocenters.

Key Words • acoustic neuroma • vestibular schwannoma • radiosurgery • linear accelerator • radiation dose

Vestibular schwannomas (also known as acoustic neuromas) are the most frequently occurring lesions arising in the cerebellopontine angle, with an annual incidence that has been estimated to be one per 100,000 persons. Ninety-five percent of these tumors present unilaterally. Since the beginning of the MR imaging era, there has been an increase in the diagnosis of small- and medium-sized tumors, with a corresponding decrease in the incidence of large-sized tumors.

Surgery has been the traditional treatment for vestibular schwannomas. Results have improved steadily since the introduction of the operative microscope and new imaging techniques that aid earlier diagnosis. Complete resection of a vestibular schwannoma with anatomical preservation of the facial nerve is standard therapy and is associated with a mortality rate of approximately 1%. Several radiation sources have been adapted to the delivery of radiosurgery, including charged and uncharged particle beams and naturally or electronically generated photon beams. For practical reasons, photon-beam radiosurgery has become the most widespread radiosurgical modality. The first photon-beam radiosurgery system, the gamma knife, was introduced by Leksell in 1968. Linear accelerator radiosurgery was developed during the early to mid-1980s and it led to a steep increase in the number of radiosurgery centers throughout the world. Despite its widespread use, there have been few reports including detailed results of LINAC radiosurgery for acoustic neuromas and these have lately been much surpassed in numbers by reports of fractionated stereotactic radiation treatment for this pathological entity.

In this paper, we review our experience at The Chaim Sheba Medical Center with LINAC radiosurgery of vestibular schwannomas.

Clinical Material and Methods

Patient and Tumor Characteristics

From February 1993 through December 1997, 48 patients in whom vestibular schwannomas had been diagnosed underwent LINAC radiosurgery in our unit. These patients represented 14% of our unit’s patient capacity.
Facial nerve function was assessed clinically before and after treatment according to the House–Brackmann classification system (Table 1). Ten patients exhibited facial neuropathy before radiosurgery. Two of them had not previously undergone surgery (one patient with Grade II paresis due to a 30-mm-diameter tumor and one patient with Grade VI paresis due to an 18-mm tumor). Eight patients displayed neuropathy after having undergone previous attempts (one–three procedures) at surgical removal (six patients with House–Brackmann Grade VI, one with Grade IV, and one with Grade V).

Trigeminal nerve function was assessed by examination of touch and pinprick sensation in the territories of the three nerve divisions. Sensation was assigned a score of 0 to 100% compared with sensation on the unaffected side and was registered by means of a graph on the patient’s chart. Sensory deficits were noted in seven patients before radiosurgery (in five patients after previous surgery).

Follow-Up Review

Patients attended follow up initially at intervals of 6 months. During the last 2 years of the study, our policy was changed to allow yearly intervals to elapse between follow-up examinations because few substantial changes are to be expected in shorter time spans. The mean follow-up period for this series was 32 months (range 12–60 months).

At each follow-up meeting all patients underwent physical examination that included clinical assessment of facial and trigeminal nerve function, contrast-enhanced MR imaging, and audiography (when warranted).

Radiosurgical Procedure

Patients were hospitalized for 24 hours. On admission, a Brown-Roberts-Wells stereotactic head ring was affixed to the patient’s head after a local anesthetic agent had been administered. Contrast-enhanced CT scanning was performed using a stereotactic localizer. The patient’s entire head was scanned using 5-mm contiguous slices. One- to 2-mm contiguous slices were made through the area of interest. The imaging data were transferred by tape to a computer workstation (Sun Sparc2; Sun Microsystems, Palo Alto, CA) with parallel processors and processed using software developed at the University of Florida (Gainesville, FL).

Forty cases were treated using a single isocenter (five–nine noncoplanar arcs). Different combinations of arc span, arc weighting, angle of arc incidence, and number of arcs were used to achieve maximum conformality of the treatment dose to the borders of the tumor, as well as the steepest radiation falloffs toward the brainstem and the anterior and superior aspects of the tumor, where the facial and the trigeminal nerves, respectively, were likely to course (Fig. 1). Four tumors with irregular shapes were treated using two (three cases) or three (one case) isocenters.

The mean radiation dose directed to the tumor margin was 1455 cGy (range 11–20 Gy). During the first 2 years of the study, treatment doses ranged between 15 Gy and 20 Gy. Thereafter, the maximum dose prescribed was reduced to 14 Gy for small tumors (# 16 mm in diameter). Larger tumors received lower doses (minimum 11

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**TABLE 1**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>normal facial function in all areas</td>
</tr>
<tr>
<td>II</td>
<td>mild dysfunction</td>
</tr>
<tr>
<td></td>
<td>1) gross: slight weakness noticeable on close inspection; may have very slight synkinesis</td>
</tr>
<tr>
<td></td>
<td>2) at rest: normal symmetry &amp; tone</td>
</tr>
<tr>
<td></td>
<td>3) motion: forehead, slight-moderate movement; eye, complete closure w/ effort; mouth, slight asymmetry</td>
</tr>
<tr>
<td>III</td>
<td>moderate dysfunction</td>
</tr>
<tr>
<td></td>
<td>1) gross: obvious but not disfiguring difference between 2 sides, noticeable but not severe synkinesis</td>
</tr>
<tr>
<td></td>
<td>2) motion: forehead, slight-moderate movement; eye, complete closure w/ effort; mouth, slightly weak w/ maximum effort</td>
</tr>
<tr>
<td>IV</td>
<td>moderate–severe dysfunction</td>
</tr>
<tr>
<td></td>
<td>1) gross: obvious weakness &amp;/or disfiguring asymmetry</td>
</tr>
<tr>
<td></td>
<td>2) motion: forehead, no movement; eye, incomplete closure; mouth, asymmetric w/ maximum effort</td>
</tr>
<tr>
<td>V</td>
<td>severe dysfunction</td>
</tr>
<tr>
<td></td>
<td>1) gross: only barely perceptible motion</td>
</tr>
<tr>
<td></td>
<td>2) at rest: asymmetry</td>
</tr>
<tr>
<td></td>
<td>3) motion: forehead, no movement; eye, incomplete closure</td>
</tr>
<tr>
<td>VI</td>
<td>total paralysis—no movement</td>
</tr>
</tbody>
</table>

* Based on House–Brackmann Scale.

Three of these patients were lost to follow-up review. Of the remaining 45, 44 completed 12 to 60 months of follow-up review (mean 32 months) at the time of writing; these constitute the population of this report. There were 18 men and 26 women, and the mean age was 57 years (range 29–78 years).

Tumors considered for radiosurgery had a maximum mediolateral diameter of 30 mm. Patients with larger tumors were offered conventional microsurgery. Three patients in these series underwent surgery after their initial referral, with the goal of achieving a reduction in tumor volume to a size considered compatible with radiosurgery. In those cases, radiosurgery was performed 6 to 12 months after suboccipital craniotomy. The delay between treatments was necessary to allow for resolution of early postoperative changes that might have precluded accurate assessment of the boundaries of the residual tumor. Seven other patients had undergone previous attempts at surgical removal (one–three procedures) and were referred for radiosurgery for residual or recurrent tumor. Tumor volumes ranged from 1 to 11 cm³ (mean 3.75 cm³). The maximum mediolateral tumor diameter ranged from 10 to 31 mm (mean 20 mm).

Volume changes after treatment were determined by examination of contrast-enhanced MR images. In each orthogonal view the maximum tumor diameter was measured under magnification and registered; it was then compared with the original volume assessment.

Assessment of Patients

Patients were assessed before treatment by clinical examination, gadolinium-enhanced MR imaging, and audiography. Hearing on the affected side was defined as serviceable when the patient’s speech-discrimination score was equal to or higher than 70%. Thirteen patients had serviceable hearing before radiosurgery. All patients harbored unilateral tumors.
Every effort was made to achieve homogeneity in dose distribution across the tumor by directing the treatment dose to the highest possible isodose area (68–90%, mean 79%).

The radiation source was a standard LINAC (model 600 C; Varian Medical Systems, Palo Alto, CA) modified by using removable precision parts for dose delivery. A floor-mounted stereotactic positioning device was placed at the machine isocenter before treatment, and a metallic holder for small-aperture collimators (diameters 10–35 mm at isocenter, in 2.5-mm increments) was affixed to the LINAC radiation gantry. The mechanical precision of the setup was verified before each treatment session by using the method developed by Lutz and Winston. The maximum isocenter deviation was 0.5 mm in all cases. The patient was brought to the LINAC suite and placed supine on the couch while the stereotactic ring surrounding his or her head was firmly attached to the isocentric positioner. Radiation was delivered through multiple noncoplanar radiation arcs. Treatment time varied from 20 to 45 minutes, depending on the radiation dose, radiation volume, and number of isocenters. The stereotactic ring was removed from the patient’s head immediately after irradiation. Patients usually stayed overnight in the hospital and were discharged on the morning after treatment. They were allowed to return immediately to their normal activities. No specific medication was prescribed apart from nonnarcotic analgesic agents.

Results

Acute Side Effects

In one patient with a recurrent tumor, facial neuropathy developed 3 days after treatment. Several other patients complained of headaches lasting 2 to 3 days. No other acute side effects were noted.

Tumor Changes

Early Imaging-Confirmed Changes. In patients assessed 3 and 6 months after radiosurgery, two different early imaging changes were seen. 1) Loss of the tumor’s central contrast enhancement was frequently observed on MR images. This change was usually transient, with several tumors recovering homogeneous contrast enhancement later during the follow-up period. Loss of central contrast enhancement was not correlated with the occurrence of untoward volume changes. 2) Early tumor enlargement was observed in 11 patients during the 1st year of the follow-up period. Concomitant facial neuropathy developed in eight of these patients. Two other patients already suffered full facial palsy before they underwent LINAC ra-
In one case, the early tumor enlargement was clearly not associated with neuropathy. Early tumor enlargement was always associated with a loss of contrast enhancement on MR imaging. This enlargement may have been the result of hyperacute tumor ischemia with edema. Imaging studies demonstrated volume reductions in all these tumors later during the follow-up period, compared with the sizes of these tumors at the time of radiosurgery (Fig. 2).

Late Volume Changes. In this series, MR imaging revealed volume reductions ranging from 15 to 90% in 33 (75%) of 44 tumors beginning at least 12 months after treatment. In these 33 tumors, the peak incidence of shrinkage was observed between 24 months and 36 months after radiosurgery (80% at 24 months and 84% at 36 months). No volume changes were apparent in nine of these tumors during the first 3 years of follow-up; however, shrinkage was identified in five of those tumors later (37–60 months posttreatment). At the end of the follow-up period, 10 tumors (23%) were shown to have preserved their original volumes. In one patient, a tumor that initially enlarged and later shrank proceeded to display a 15% asymptomatic volume enlargement on MR images obtained 48 months after treatment. This patient has not undergone surgery and is stable at the time of this writing (60 months postradiosurgery). In summary, 98% of tumors in this series are currently controlled.

Hearing Preservation

Hearing was preserved in 13 patients before treatment. Nine of these patients retained serviceable hearing at the end of the follow-up period. In another patient with a 50% speech discrimination rate before radiosurgery, that rate improved to 80% 24 months after treatment. The hearing preservation rate was therefore 71%.

Trigeminal Nerve

New trigeminal neuropathy developed in 18% of patients and was always accompanied by facial neuropathy. One patient experienced deafferentation pain in the hypesthetic facial area.

Facial Nerve

New facial neuropathy developed in nine (24%) of the 37 patients who had normal or partial facial nerve function before radiosurgery. This includes one patient who exhibited postoperative House–Brackmann Grade II paresis that worsened transiently to Grade III before returning to baseline. The neuropathy appeared in all cases within 1 year after radiosurgery. All facial neuropathies improved or resolved over time. At the time of this writing, three of the nine patients still have facial weakness (Grades IV, III, and II, respectively). This represents an actuarial facial neuropathy rate of 8%.

Aside from the concomitant imaging changes we described earlier (early tumor enlargement), the occurrence of neuropathy correlated closely in this series with two variables: treatment dose and tumor volume.

Facial neuropathy developed in one (5.5%) of 18 patients who received a dose to tumor of up to 14 Gy, whereas it developed in eight (42%) of 19 patients who received a dose of 15 to 20 Gy.

Tumors were grouped according to their volumes into two categories: small (0.8–3.7 cm³) and large (4–11 cm³). In 21 patients with small-volume tumors there were two neuropathies (9.5%); seven neuropathies (54%) were observed in 13 patients with large-volume tumors.

Because radiation dose in this series was not preselected according to tumor size but was instead adjusted for all tumors at a given time point, we were able to assess in an unbiased way the relative contributions of both radiation dose and tumor volume.
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dose and tumor volume to the incidence of neuropathy. As may be seen in Fig. 3, tumor volume was the most significant risk factor for facial neuropathy, with prevalence peaking in patients in whom radiation doses were 15 Gy or greater.

Two patients with preoperative facial nerve dysfunction displayed improvement in facial nerve function after treatment.

Other Complications

No patient experienced hydrocephalus, vagal or glosso-pharyngeal nerve dysfunction, or cerebellar or long-tract signs.

Discussion

Acoustic neuromas have been the target of surgical removal procedures since the early days of modern neurosurgery. Refinements in technique have resulted in increased rates of facial nerve preservation and have also improved the chance of hearing preservation. Nonetheless, a recent survey of 1579 patients who underwent resection of acoustic neuromas between 1989 and 1994 found a 44% rate of facial weakness, an 11% rate of postoperative cerebrospinal fluid leakage, and a 9% rate of persistent balance disturbance after 1 year. Recurrent or persistent tumor was found in 7.8% of patients.

In a recent study by Matthies and Samii's 979 of 1000 tumors were totally removed. The recurrence rate was 0.7%. Complications included a mortality rate of 1.1%, an acute facial paresis rate of 45% (13% House–Brackmann Grade II, 15% Grade III, 6% Grade IV, 11% Grade V, and 4% Grade VI), and other major neurological complications in approximately 6% of the patients. The rate of hearing preservation was 39.5%.2

The Swedish experience in treating these tumors by using gamma knife radiosurgery began in 1968. In 1988 Norén and colleagues reviewed their results for the first 180 patients and reported a 15% facial neuropathy rate with doses to the periphery of the tumor that ranged between 18 Gy and 25 Gy. When radiosurgery at these doses was introduced in the United States during the second half of the 1980s, it rapidly became obvious that the incidence of facial neuropathy was much higher than previously reported.3 Flickinger and associates reported facial neuropathy in 33% and trigeminal neuropathy in 37% of patients treated with the gamma knife in Pittsburgh. All facial and trigeminal neuropathies improved during the follow-up period. The rate of useful hearing preservation was 46% in that study. Mendenhall, et al.4 reported similar results in their experience with LINAC radiosurgery.

A gradual lowering of the prescribed radiation dose to these tumors was initiated at the end of the 1980s to reduce neuropathic complications. No data were available to define how much to reduce the radiation dose and, no less important, how this dose reduction would affect the tumor growth–control rate.

The mean dose used initially in our series of acoustic neuromas (15.86 Gy) was part of this trend and was empirically determined. Our subsequent experience showed that radiosurgery was still associated with a relatively high rate of neuropathy (close to 30% transient facial and/or trigeminal nerve complications). Although this acute neuropathy rate was already lower than that reported for the “best microsurgical series” (40% acute facial neuropathy in the series of Samii and Matthies4,20,21), it was still considered excessive for a noninvasive therapy.

In 1995 we further reduced the therapeutic radiation dose for acoustic neuromas to 11 to 14 Gy, varying the dose according to tumor size (in particular, the mediolateral extent of the tumor). Use of this dose range virtually eliminated the incidence of neuropathies in the last 20 patients whose tumors were irradiated in this series. A similar experience has recently been reported by other centers.10

The indications for radiosurgery in acoustic neuromas have changed during the past few years, paralleling the experience gained using the technique.

During our first few years of using LINAC radiosurgery, we recommended radiosurgery for acoustic tumors in the elderly population, for tumors located on the only hearing side, or in patients with a medical infirmity that posed a significant risk for surgery. Radiosurgery was also offered to patients with recurrent tumors, because these lesions are intrinsically more difficult to remove surgically.

Currently and based on the comparative results presented herein for tumor control, facial nerve function, and hearing preservation, we believe that radiosurgery can be offered as the primary treatment modality for acoustic neuromas of suitable size, regardless of the patient’s medical status.

It is frequently argued that radiosurgery does not actually cure acoustic neuromas because the tumor shadow continues to be observable on control imaging studies years after treatment; by physically removing the tumor

Fig. 3. Bar graph demonstrating the incidence of facial neuropathy, expressed as percentages (y axis), as a function of dose and volume. The significant contribution of volume to the appearance of neuropathy is evidenced by the high complication rate observed in large tumors irradiated with doses higher than 15 Gy (p = 0.02, Fisher’s exact probability test).
from the skull, surgery achieves a more definitive outcome. Certainly, complete surgical resection of a benign tumor offers a straightforward measure of outcome: the tumor is no longer there. Nonetheless, even the absence of a tumor shadow is no proof of cure, as attested by recurrence rates of 1 to 10% after seemingly complete removals.

In a long-term follow-up review of patient outcomes after gamma knife radiosurgery, Norén, et al., found a tumor growth–control rate (shrinkage or unchanged tumor size) of 95%.

Radiosurgery of a benign tumor does not result in and is not even designed to achieve physical elimination of the lesion. Rather, its goal is the biological elimination of the tumor. Because radiosurgery deals with tumors that, if unchanged in volume, will not jeopardize the patient’s life or neurological function, the physical persistence of the tumor shadow is irrelevant to outcome.

The reported recurrence rate of acoustic neuroma after surgery varies from less than to 8% for totally resected tumors to 16% for subtotally resected tumors. Most recurrences become apparent during the first 4 years after surgery. Consequently, in the absence of findings on imaging studies 5 to 6 years after surgery, follow-up examination is usually discontinued.

Verification of tumor control after radiosurgery requires a more extended follow-up period because there is currently no imaging modality with which clinicians can assess the tumor’s biological viability. Nonetheless, in tumors that shrink, we perform control imaging studies at 2-year intervals.

Linear accelerator radiosurgery was developed almost 20 years after the introduction of the gamma knife, and gained momentum at the end of the 1980s. Radiation delivery in LINAC radiosurgery is most commonly accomplished using the multiple noncoplanar arc method. The LINAC gantry rotates around the patient’s head while the radiation dose is delivered. The rotation span usually varies between 80° and 120°, and five to nine arcs of radiation are commonly used. After an arc has been completed, the patient’s head is rotated so that a different area of the vault is exposed to the rotating gantry. For dosimetric purposes, each arc is the summation of multiple beams that are calculated individually every 5° of rotation in most systems. The LINAC can distribute radiation beams in a manner similar to that of the gamma knife.

The main disadvantage attributed to LINAC systems is their potentially reduced mechanical accuracy because both the radiation source and the patient’s couch move continuously during dose delivery. This disadvantage can easily be overcome by adding mechanical gadgets and by continuously verifying the system’s isocentricity. The system in use at our center has a maximum isocenter deviation of 0.5 mm, which is roughly similar to the best reported gamma knife accuracy (0.3 mm).

Because most acoustic neuromas are roughly elliptical, we have treated most of them with a single, conformal isocenter, including the tumor within a high isodose area (mean 79%) to preserve a steep radiation falloff outside the target area. In four very irregular tumors, we had to resort to two (three cases) or three (one case) isocenters. As described previously, we took great care to conform the treatment dose to the boundary of the tumor in its anteri-
After treatment, the patient returns immediately to his or her normal activities. Radiosurgery significantly decreases the social and financial impact of these tumors on the patient, family, and community.

In an era of growing concern about cost efficiency in healthcare management, the role of radiosurgery in acoustic neuromas is bound to grow. Currently, administration of radiosurgery as a primary treatment tool in newly diagnosed patients appears justified in the older population.

In young patients, on the other hand, concern remains about the theoretical long-term complications of radiation therapy for benign tumors. Radiosurgery has been used to treat acoustic neuromas for 30 years, with several thousand patients participating in follow-up review. To date there is only one report suggesting the possible malignant transformation of an acoustic neuroma following radiosurgery. Unlike the secondary radiation-induced malignancies reported after conventional radiation therapy, malignancies following radiosurgery appear to be extremely rare events. Nonetheless, until more long-term data are accumulated, this possibility should be taken into consideration when counseling young patients.

In making practical choices between microsurgery and radiosurgery, neurosurgeons should take into account the quality of the microsurgical methods at their disposal. If a neurosurgeon with extensive experience and a track record of good results with vestibular schwannoma surgery is available, young patients should be offered microsurgical removal as the treatment of choice.

Tumors compressing the brainstem and those with an intracranial diameter larger than 3 cm are, in our opinion, contraindicated for radiosurgical treatment. Fractionated stereotactic radiation treatment should be considered in these cases when microsurgery is refused or contraindicated for medical reasons.

For intracanalicular tumors in elderly patients, no treatment may be the best choice—especially in those whose hearing is preserved on the affected side.

References


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