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Stereotactic Radiation Techniques in the Treatment of Acoustic Schwannomas

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Medical decision-making is based on benefit-to-cost analysis. Optimally, treatment obtains a high degree of benefit while minimizing the physical, social, and financial costs. The goals of the treatment of acoustic schwannomas are prohibiting tumor growth and alleviation of symptoms caused by damage to local structures. These symptoms—tinnitus, ataxia, and hearing loss—secondary to eighth nerve dysfunction, as well as symptoms arising from damage to adjacent structures such as the facial nerve, trigeminal nerve, or pons, can be caused by tumor growth or treatment. Determination of optimal therapy must also take into account an understanding of the natural history of the disease, because acoustic schwannomas are slow-growing benign tumors that when left untreated, usually enlarge over time and cause problems.

Historical perspective

Archeological findings from 2500 BC provide evidence that acoustic nerve tumors have been present since antiquity. These tumors, called acoustic neuromas or, more properly, schwannomas, were diagnosed based on a recognized progression from deafness to death as early as 1810. The first documented successful removal of an acoustic schwannoma was performed by Thomas Annandale in 1896 in Edinburgh, Scotland. The patient, who was pregnant at the time of the operation, was able to go home and give birth to a healthy child [1].

During the twentieth century, different surgical approaches (suboccipital, translabrynthine, and middle fos) were developed for the resection of eighth-nerve tumors. Each sought to diminish the inherent anatomic issues associated with total removal. In addition to the obvious hearing loss associated with eighth nerve resection, there was also the risk of seventh nerve damage, cerebrospinal fluid leak, and hemorrhage. Because of difficulties with early diagnosis before modern imaging tests, the pattern of slow intermittent growth, and the morbidity of resection, observation instead of immediate intervention became a frequent consideration.

In 1951, Dr. Lars Leksell, a neurosurgeon, and Borje Larsonn, a physicist, using the Uppsala University cyclotron, ion Uppsala, Sweden, developed an approach to treating small brain lesions with multiple proton beams, using a fixed rigid Cartesian coordinate system to locate the target. Their idea was to develop a noninvasive therapy system to deliver ablative doses of radiation to a geometrically defined discrete volume of tissue, using multiple small beams of radiation. This concept evolved into the Gamma Knife (Elekta, Stockholm, Sweden) stereotactic radiosurgery. The Gamma Knife unit consists of 201 cobalt radiation sources placed in a helmet, within which lie shuttered channels directed toward the center of the helmet. The target lesion is placed at that center position of the helmet by using a stereotactic frame affixed to the patient's skull. Different dose patterns with sharp dose gradients can be obtained using multiple isocenters designed to match the shape of the tumor (Appendix).

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Dr. Leksell and his team working at the Karolinska Institute in Stockholm, Sweden were the first to treat acoustic neuromas with stereotactic radiosurgery (SRS). Their initial series (1969–1974) reported initial tumor control in eight of the nine cases; however, hearing loss was reported in the majority of patients treated [2]. In these early studies, high doses (25–35 Gray) were employed; targeting was crude compared with imaging studies available today. The first Gamma Knife unit in the United States was installed at the University of Pittsburgh in Pittsburgh, Pennsylvania under the direction of Dr. Dade Lunsford. Many of the early results involving radiosurgery for acoustic neuromas in North America were published by the University of Pittsburgh group.

An alternate stereotactic delivery platform was developed using linear accelerators (linacs). Linacs were already available in most modern radiation centers. Instead of multiple sources aimed at a central designated target, the linac systems rotated the treatment beam of the unit around the target in a varying number of rotational arcs. Betti and Colombo initially developed this technique in South America. Because the linac systems involve moving sources of radiation, special devices are needed to limit positional variation in beam delivery.

Both of these techniques require some method to limit patient and target movement. Fixation of target position in a geometric coordinate system can be achieved with metal frames screwed into the skull, which can obtain submillimetric accuracy, or with thermoplastic molded mask systems, which allow for more fractionated schedules, whereby treatment can be administered over several days without placing fixation screws into a patient's skull.

Treatment goals

The goal of treatment is to eradicate the effects of a tumor with the fewest side effects. In surgical series, the means of achieving this goal is the removal of the offending tumor. In most reports of radiation efficacy, the objective is to achieve tumor reduction; however, in slow-growing tumors such as acoustic schwannomas, the achievable goal in studies with shorter duration of follow-up is the prevention of both tumor growth and symptom progression. Tumor shrinkage assessed by radiographic size may take years before a complete response can be evaluated. Additionally, relapses might be late occurrences.

Increased tumor volumes and irregularly shaped tumor volumes are associated with increased integral dose (energy deposition) within the tumor for Gamma Knife and cone-based linac SRS systems. Gamma Knife doses are prescribed to the tumor periphery. These peripheral doses are frequently 50% of the peak dose delivered within the central volume treated. This dose profile with areas of very high dose within the target volume (hot spots) is less a problem with single isocenter treatment plans using a multileaf collimator, where dose is more uniform. Shaped-beam peripheral doses are usually prescribed to the 90% to 95% isodose line. Central hot spots are 10% to 20% higher than the dose prescribed to the tumor periphery; however, the multileaf collimated treatment plans do not produce dose patterns that are as conformal or tightly fitting as the multiple isocenter systems or Gamma Knife systems. Single isocenter treatment techniques typically treat a small rim of normal tissue surrounding an irregularly shaped tumor.

Stereotactic radiosurgery

The initial studies from Pittsburgh demonstrated the ability of stereotactic radiosurgery to achieve control rates of 95% or more with doses of 16 to 20 Gray; however, these doses were associated with an increased risk of trigeminal nerve injury, seventh nerve injury, and decreased hearing. Before 1992, when using these higher doses, reports of treatment results in patients who were in the Pittsburgh patient cohort receiving stereotactic radiation demonstrate that 34% developed facial nerve weakness, although one half of these were transient. Thirty-two percent developed new trigeminal neuropathy. Useful hearing could be preserved in 38% at 1 year [3]. Foote and colleagues [4] reported similar side-effect profiles from the University of Florida in Gainesville, Florida when higher doses were used, with fewer side effects when doses lower than 13 Gray were prescribed to the tumor margin.

Reduced toxicity to the trigeminal and facial nerves was accomplished by decreasing the marginal SRS dose given to the tumor. Rates of morbidity decreased from 29% to 5% for facial neuropathy, and similarly, to 2% or less for trigeminal neuropathy. Tumor control rates did not appear to be compromised until the marginal dose was decreased to 10 Gray or less [4]. Doses to the tumor margin of 12 to 13 Gray were

associated with 5-year tumor control rates of 92% to 98% [4–6]. Maximum doses were 20 to 26 Gray. Useful hearing was noted in 56% to 78% after treatment.

Optimal dose prescription balances tumor kill and normal tissue survival. Radiation oncologists have long recognized the limited tolerance of cranial nerves to radiation. The best-delineated toxicity data for stereotactic radiation relate to the optic nerves and chiasm. Limits of 8 Gray in one fraction and 50 Gray using standard fractionation (1.8 to 2 Gray per day), serve as dose restraints for this nerve. Radiation toxicity must also take into consideration the length of nerve radiated as well as the dose absorbed. The idea of volume at risk may be a function of vascular damage or of repopulation limits. The dose given to the tumor margin and more plausibly, the maximal dose within the volume treated reflect the degree of tissue damage.

A group from Seoul, Korea related hearing loss in relationship to the cochlear dose received during radiosurgery [7]. The mean dose to the cochlea in those maintaining useful hearing was 6.9 Gray. When the mean dose was greater than 11 Gray, hearing declined. Massager and colleagues [8] also found cochlear dose to be lower in patients retaining useful hearing. They found a significant relationship regarding intracanalicular tumor volume (<100 mm^3 versus 100 mm^3) as well as intracanalicular integrated dose as determinants of hearing loss. Their paper postulates that ''hearing worsening after the gamma knife radiosurgery (GKR) procedure can be attributed to cochlear injury inside the internal acoustic canal caused by the enlargement of the intracanalicular part of the vestibular schwannomas during the inflammatory edema phase after radiosurgery through an increase of the intracanalicular pressure.''

Fractionated stereotactic radiation therapy

Whereas some centers were investigating lowering the marginal peripheral dose with single dose treatment regimens, others investigated using fractionated radiation therapy. The theory behind fractionated or multiple treatment radiation therapy is that multiple smaller doses of radiation can achieve a similar tumor effect (cell death) while allowing normal tissue time to repair between each dose, and thereby limit toxicity. This approach involves a greater total dose of radiation than a single-dose treatment to overcome whatever repairs the tumor has been able to achieve. Standard fractionation involves doses of 1.8 to 2.0 Gray per day given daily for 25 to 30 treatments. A total dose to tumors as measured at their periphery is 45 to 60 Gray. Central portions of the tumor volume receive 5% to 10% more than the periphery. This regimen has been used for decades in the treatment of malignant tumors to maximize soft tissue repair from radiation damage.

Several institutions have reported their results for fractionated radiotherapy using radiosurgical techniques in the treatment of acoustic schwannomas, with excellent tumor control rates and with minimal toxicity. Relocatable, molded face masks have been used for skull immobilization. These treatments have been delivered using linac-based therapy, with tumor doses prescribed to a peripheral dose encompassing the tumor, plus a small margin (2 mm) to account for the small amount of movement that occurs between daily fractions and any movement within the face mask during treatment.

Chan and colleagues [9], from Massachusetts General Hospital-Harvard in Boston, Massachusetts, report a 5-year tumor control rate of 98% using a regimen of 54 Gray given in 1.8 Gray fractions as prescribed to the 95% isodose line. They note a distinct relationship between tumor sizes and tumor control. Surgical resection was required for three patients with larger tumors and increasing symptoms at a median of 37 months. At 5-year follow-up, freedom from any surgical intervention was 97% for tumors smaller than 8 cm^3, and 47% for tumors greater than 8 mm^3.

Selch and colleagues [10] from the University of California, Los Angeles (UCLA), using a similar radiation regimen—54 Gray in 30 treatments as prescribed to the 90% isodose line—reported a local control rate of 100% at 36-month median follow-up in 50 patients. Useful hearing was preserved in 93%, with a median follow-up of 36 months. Facial numbness occurred in 1 patient (2.2%) and 1 patient experienced the new onset of facial palsy. Twelve of their patients experienced tumor growth. In 6 of the 12, the growth was transient, and was felt to represent a treatment effect. The transient type of enlargement shows subsequent shrinkage within 2 years, and is frequently associated with loss of central enhancement on MRI. The phenomenon of transient enlargement has also been a common finding in other institutions for both SRS and fractionated stereotactic radiation therapy (FSRT) [11,12].

A Heidelberg, Germany group treated 106 patients who had acoustic neuromas using standard fractionation, given to a total dose of

57.6 Gray. Local control at 5 years was 93%. Trigeminal and facial toxicity were 3.4% and 2.3%, respectively. Useful hearing was preserved in 94% [13]. In a more recent publication by that same group, Combs and colleagues [14] report that hearing preservation in patients who had useful or serviceable hearing before radiation therapy was 55% at 9 years after SRS, compared with 94% showing serviceable hearing 5 years after FSRT.

Attempts to decrease toxicity by decreasing total tumor dose for ractionated stereotactic radiotherapy have also been described. Thomas Jefferson University in Philadelphia, Pennsylvania presented a retrospective analysis showing no tumor control difference in two cohorts of patients treated with either 50.4 Gray or 46.8 Gray. Although tumor control rates were equivalent (98% versus 100%) with a median follow-up of 3 years, hearing preservation was better in the lower dose group. Hearing preservation was measured by pure tone averages and speech discrimination. Corrected for follow-up and initial hearing, the rate of preservation was 93% for the low-dose group versus 67% for the higher-dose cohort. The median follow-up time for the low-dose group was 29 months [15]. A group at Hokkaido, Japan used 40 to 50 Gray in 20 to 25 fractions. Their actuarial tumor control rate at 5 years was 91%, with no new permanent facial weakness. The rate of useful hearing preservation (Gardner-Robertson Class I or II) was 71%. Complications were mild—transient facial nerve palsy was 4%, trigeminal neuropathy was 14%, and balance disturbance occurred in 17% of patients [16].

In another low-dose FSRT study, Shirato and colleagues [17] matched a group of patients who had vestibular schwannoma who underwent observation only against a cohort of patients treated with fractionated radiotherapy delivering 36 to 44 Gray in 20 to 22 treatments. The conclusion of the study was that there were no differences in the actuarial Gardner/Robertson hearing class preservation curves after the initial presentation. The rate of hearing deterioration in the treated arm was comparable to that of untreated patients. The mean growth of the tumor in the observation arm was 3.87 mm per year, whereas there was tumor reduction in the radiated cohort.

Hypofractionation

In an attempt to maximize hearing preservation rates without the need for several weeks of daily radiation treatments, a third alternative—hypofractionation—has also been studied. Using biological modeling to provide theoretically equivalent results as standard fractionation, hypofractionation gives higher doses per treatment for fewer treatments than standard fractionation schemes, but less dosage per day than single-dose prescriptions. Hypofractionation regimens use doses in the range of 3 to 7 Gray per day for 3 to 10 days, for total doses in the range of 21 to 30 Gray.

Meijer and colleagues [18] from Vrije Universiteit University Medical Center in Amsterdam used a hypofractionation schedule of 4 to 5 Gray for 5 days as measured at the 80% isodose line. The 20 to 25 Gray was delivered in 1 week. Five-year local control in 80 patients was 94%. Facial nerve function was preserved in 97%. The study authors compared these patients to a group of 49 patients treated at the same institution with a single fraction of 10 to 12.5 Gray, and found no significant differences in outcome in regard to tumor control or facial nerve damage. Five-year hearing preservation favored the fractionated group (75% versus 61%). At Johns Hopkins in Baltimore, Maryland, a similar rate (70%) of hearing preservation was also achieved using 5 Gray for 5 days for smaller tumors or 3 Gray for 10 treatments for larger tumors [19].

Large tumors

Tumor size can affect control. Foster and colleagues [20] showed that tumors larger than 3 cm had a control rate of 33%, whereas tumors of 2 to 3 cm had a control rate of 86%, and tumors of 2 cm or less could be controlled in 89% of their SRS series. Chan [9] also showed a relationship between increasing tumor volume and the need for surgical intervention (shunt or resection) following FSRT.

Park and colleagues [21] reviewed 50 cases of acoustic neuromas measuring over 3 cm on MRI. Microsurgery was performed on all patients. Among eight patients who underwent subtotal resection followed by radiosurgery, all had tumor control with a median follow-up of 113 months (9.4 years). Gross total resection alone resulted in failure in one patient, and subtotal resection without radiation resulted in a 32% recurrence rate. The facial nerve preservation rate was inversely proportional to the extent of tumor removal.

Neurofibromatosis-2

Approximately 5% of patients who have acoustic neuromas have neurofibromatosis type 2 (NF-2). These patients present a special management problem, because their tumors are often bilateral, placing them at risk for total hearing loss. Both microsurgical techniques and stereotactic radiosurgery have been associated with poorer rates of hearing preservation in NF-2 patients. Tumor control rates following single-dose stereotactic radiosurgery are reported as 50% to 98%, with preservation of functional hearing being achieved in 40% to 50% [22–25]. This decrease in functional hearing following therapy is also noted in some fractionated stereotactic radiotherapy series. Combs and colleagues [14] saw hearing preservation rates fall from 98% in sporadic vestibular schwannoma cases treated with 57.6 Gray given in 1.8 Gray fractions to 64% in NF-2 patients treated with the same regimen. Chan and colleagues [9] saw no differences in results between their NF-2 and sporadic cases in regard to tumor control or hearing preservation rates, using a fractionated schedule. The Stanford, California CyberKnife (Accuray, Sunnyvale, California) group obtained hearing preservation rates of 67% at 2 years, using a hypofractionated technique of 21 Gray delivered in three fractions of 7 Gray, with 90% tumor control at a mean follow-up of 26 months. Nine percent developed trigeminal nerve injury [24].

Radiographic follow-up

MRI scans should be obtained at regular intervals following therapy. Loss of central enhancement is a common finding, usually associated with enlargement and capsular thickening. A group at UCLA reported the loss of central tumor enhancement in two thirds of their patients at a median of 6 months following stereotactic radiotherapy [9]. The increase in tumor size was less than 2 mm. Radiographic enlargement occurring after 2 years, or growth 3 mm or greater, is indicative of tumor regrowth. Resection can be performed after radiation therapy; however, some authors feel it is more difficult than resection as initial treatment. Conversely, radiation therapy following resection has a higher complication rate as well.

Clinical follow-up

Most patients undergoing treatment for acoustic neuromas tolerate their treatments well, and tumor growth is controlled. At the doses currently used, the majority of patients do not develop new symptoms. A minority of patients experience an improvement in symptoms, and a minority experience worsening symptoms.

Hydrocephalus

Hydrocephalus in the absence of progressive tumor growth has been described as occurring in 3% to 11% of patients in both SRS and FSRT series [26,27]. The hydrocephalus occurs at a median of 1 year. Hydrocephalus is believed to be the result of tumor necrosis, with proteinaceous debris blocking cerebrospinal fluid (CSF) flow. The development of hydrocephalus is more common following treatment of larger (>25 mm) tumors. The hydrocephalus sometimes resolves spontaneously [10]. Shunting may be required if hydrocephalus becomes symptomatic.

Tinnitus

Pittsburgh radiosurgery experience describes symptoms of tinnitus resolving in approximately one half of patients, whereas the UCLA FSRT experience with stereotactic fractionated radiotherapy provided improvement in 6 of 50 patients, whereas two patients experienced worsening [9]. Karpinos and colleagues [27], in comparing microsurgery and radiosurgery, found more tinnitus at long-term follow-up in patients undergoing radiosurgery. In their radiosurgery group, 26% reported increase in tinnitus, whereas 10% reported decreased tinnitus.

Vertigo

Karpinos and colleagues [27] noted no significant difference in experiencing postprocedural imbalance between microsurgery and Gamma Knife radiosurgery: 22% worsened, whereas 14% improved. Niranjan and colleagues [28] describe episodic vertigo continuing following radiosurgery in 3 of 11 patients presenting with this symptom. Balance disturbances worsened in 17% of patients treated in Hokkaido using a low-dose, fractionated stereotactic radiation scheme [16].

Malignant transformation

Malignant transformation can occur, but the risk is estimated to be very rare. Bari and colleagues [29], in a literature review of malignancy in vestibular schwannomas, describe malignant degeneration in both radiated and unirradiated eighth-nerve tumors. In their literature review,

they describe the incidence of malignant transformation as being very low [29]. Most series are not sufficiently mature to have along-term follow-up in this regard. In the 20-year experience published by Maire [30], one case of malignant transformation is described in the cohort of 45 patients. Isolated case reports have been cited by others as well.

Discussion

In patients presenting with large tumors or tumors causing pontine compression, surgery is necessary. Otherwise, patients who have acoustic schwannomas should be given the option of having either SRS or FSRT. The major advantage of stereotactic radiation over surgery is the ability to achieve tumor control while minimizing morbidity and cost. In an outcomes analysis of treatment of small (<3 cm) acoustic neuromas, Pollack, and colleagues [31] concluded that SRS was more effective in preserving hearing compared with microsurgery. Microsurgery is associated with a greater rate of facial and trigeminal neuropathy in the immediate postoperative period, as well as with long-term follow-up. Both surgery and radiosurgery had similar effects on other preoperative symptoms such as tinnitus or imbalance. Patient satisfaction was higher in the radiosurgery group. Quality of life studies favor the use of radiation over microsurgery.

The initial hearing preservation data favor fractionation for those patients who have functional hearing and larger tumors, but there has been no randomized trail between the two techniques. Comparative studies [18,26] in Philadelphia and Amsterdam describe early advantages with FSRT for hearing preservation, but favor SRS for NF-2. Many studies show equivalency in effect. Longer follow-up is necessary, because further hearing decline with time might occur in both groups. Doses to critical structures need to be further studied in an attempt to steer high-dose deposition away. The advantage of SRS or the hypofractionated techniques is convenience, because tumor control for smaller tumors is equivalent.

St. Thomas brain and spinal cord tumor center experience

The same radiosurgical team, comprising a neurosurgeon, a radiation oncologist, and a medical physicist, accounts for over 30 patients treated for acoustic neuroma who have at least 6 months follow-up in the authors' linac-based program. Patients admitted to our radiosurgical program follow the scrutiny of our interdisciplinary brain tumor board for enrolment. We have developed a treatment algorithm that places patients indicated for treatment into one of three categories:

- Surgery: occipital, translabrynthine, or middle fossa approach
- Stereotactic radiosurgery/radiotherapy (SRS/SRT): radiosurgery is here defined as single treatment, whereas radiotherapy refers to our capability to fractionate stereotactic doses (Novalis Shaped Beam Surgery TM, BrainLAB, Feldkirchen, Germany).
- Fourth pathway: intra-operative recognition that aggressive dissection might be mitigated with SRS as back-up after tumor debulking and mass effect reduction goals have been attained

The basis of which treatment is offered often depends upon patient predilection. Because our center has vast experience, with surgical extirpation as well as SRS/SRT, our patients are afforded the opportunity to extensively discuss all treatment modalities.

Surgery is recommended when patient's age, health, and tumor mass effects and size predispose. Brainstem and cerebellar mass effect correlated to tumor size greater than 3.0 cm, and resulted in placement in the surgical extirpation treatment arm of our algorithm. Medical contraindications—age and strong patient predilection—mitigate the surgical algorithm. When tumor size is less than 3.0 cm and there is a paucity of mass effect, either radiographically or symptomatically, our algorithm favors SRS/SRT.

Discussion of SRS/SRT includes the procedure and expected outcomes based on our experience, as well as, the existing literature. We cite SRS/SRT greater than 80% tumor control rates documented in existing literature with less than 5% complication rates of facial, trigeminal, or cranial nerve palsy. Hearing preservation is an ongoing concern, and we are currently audiometrically surveying our patients beginning at 1-year intervals, comparing to pretreatment baseline. Current hearing preservation rates reported range 85% to 95%. No hearing loss has been documented to date in our patient cohort.

Materials and methods

Between June 2003 and September 2006, 30 patients were treated by one of the radiosurgical

teams at our institution, composed, as noted, of one neurosurgeon, one of two radiation oncologists, and one medical physicist. Patients are pre-evaluated for SRS/SRT treatment by neurosurgical examination as well as neuro-otologic assessments. Patients are clinically evaluated per cranial nerve involvement, specifically facial nerve function and vestibular and trigeminal nerve function, and audiometrically tested at baseline. Follow-up neurosurgical evaluation of cranial nerve function at 6 weeks post-SRT and at 3-month intervals for the first year. Six-month clinical follow-up ensues thereafter. MRI surveillance is obtained at the 6-week post-SRT appointment, and at 6-month intervals thereafter up to 2 years. There is 1-year MRI follow-up thereafter until 5-year post-treatment. MRIs are evaluated according to tumor volume, axial anterior-posterior dimensions at the porous, medial-lateral dimensions at porous, and coronal rostral-caudal dimension at porous. Signal characteristics of MRI are also noted—contrast degradation and necrotic or cystic breakdown of tumor consistency on MRI.

SRS/SRT was performed using Novalis Shaped Beam Surgery TM. SRS refers to a single-dose treatment plan, whereas treatment planning using Novalis affords fractionation capability. We term this modality treatment as SRT to distinguish this capability. We are currently evaluating our cranial nerve data to corroborate previous experience that fractionation affords greater cranial nerve preservation rates, or to determine that it does not. We are also determining evaluation of specific cochlear dosing as it pertains to fractionation, in order to consider its impact on hearing preservation in SRS/SRT.

All patients were treated at a single institution using the Novalis Shaped Beam Surgery TM 6-Mev linac. Initial imaging consisted of 1-mm thick slice MRI scans, with T1-weighted images with gadolinium contrast enhancement. The BrainLAB-compatible MRI is obtained and entered into the Novalis work station. Meticulous contouring shaping is performed by the neurosurgeon. Consideration of the cerebello-pontine angle, brainstem, skull base, cranial nerve, and surrounding neuroanatomy was incorporated into the treatment planning to ensure high conformality and selectivity. CT scans were then performed while the patient was immobilized in a BrainLAB mask. These image sets were fused for treatment planning. All target volumes were defined jointly by the attending neurosurgeon and radiation oncologist. The plan was then exported to the radiation oncologist and medical physicist for dosimetry.

Target doses were prescribed to the 905 isodose volume using a single isocenter with multileaf collimation. Doses range from 30 Gray given in 10 fractions to 45 to 54 Gray delivered in 20 to 35 fractions, depending on brainstem limitations (45 Gray) and the preference of the radiation oncologist. Patients treated with shorter fractionation schemes usually lived a longer distance from our institution, or already had some decrease in hearing. No patients were treated in a single fraction in our institution. Maintenance dose steroid is administered through treatment; typified by medrol dose pack, or three-times-a-day dosing if fractionation lasts longer than five sessions.

Results

As noted, patients have undergone surveillance MRI and clinical evaluation by the treating neurosurgeon.

Magnetic resonance imaging response

Of the 30 patients treated, all but one had either tumor control or signal degradation. Tumor control is typified by tumor volume dimensions as outlined above under Materials and methods. As previously anecdotally reported, we too have appreciated small millimetric variability at the initial 6-week post-SRT MRI. The millimetric expansion at this MRI interval is thought to reflect early SRT effects, and subsides on subsequent MRI surveillance. Tumor volumes either maintained control or demonstrated signal degradation in ongoing MRI surveillance. Degradation is typified by contrast diminishment or fading, or actual necrotic cavitations on MRI. (Fig. 1A, B) has two MRIs showing a typical sequence. One patient went on to millimetric expansion of tumor beyond the 6-week post-SRT tolerance. This patient will be considered for retreatment after ongoing MRI surveillance, because no clinical sequelae have ensued.

Cranial nerve preservation

We are currently evaluating hearing audiometric data of our patients at 1-year follow-up versus baseline pre-SRT testing. As previously reported, we expect very high hearing preservation rates, at least through the current follow-up time frame. We have not as yet documented hearing degradation in our experience through close clinical follow-up. We have no reported facial nerve or

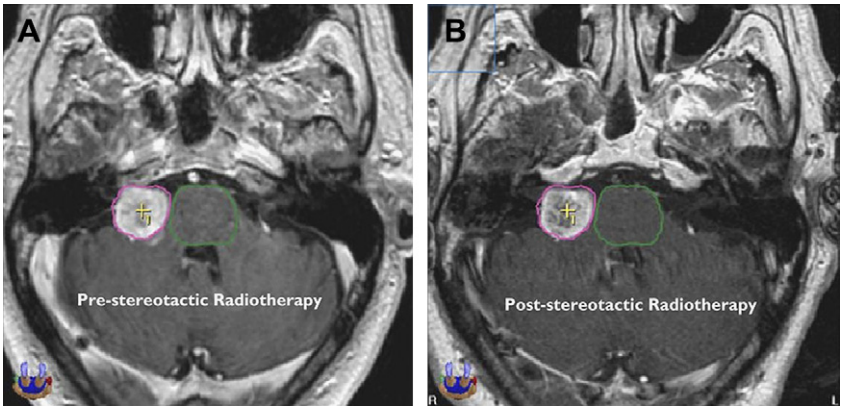

Fig. 1. Demonstrating degradation of contrast signal and contraction of size of acoustic neuroma. (*A*) Pre-stereotactic radiotherapy. (*B*) Post-stereotactic radiotherapy.

trigeminal nerve clinical sequelae following SRT. We have no incidence of brainstem symptomotology following SRT. We have not experienced exacerbations of ataxia, dysphagia, paresthesia, or vertigo in our patients post-SRT. In our clinical review of our SRT experience, we have appreciated cases of chronic symptom abatement in respect to ataxia, paresthesia, and vertigo. We have not documented abatement of symptomatic tinnitus post-SRT.

Conclusions

The management options of acoustic neuroma include observation, microsurgery, and SRS/SRT. We also include consideration of what has been termed "the fourth pathway" of SRS/SRT after microsurgical debulking, to acknowledge tumors that are otherwise too large or mass effectively symptomatic for SRS/SRT alone. Surgical risks are minimized by the planned postoperative use of SRS/SRT. We have developed a treatment algorithm to guide our patients through these treatment options (Figs. 2 and 3).

The goal of SRS/SRT is permanent control of tumor growth, while preserving neurologic function. Tumors greater than 3.0 cm, exhibiting mass effect, and harboring acute symptomatic evolution are not thought to be appropriate for SRT. The dose distribution required for larger tumors as well as the abatement of mass effects is not appropriate for the time frame of SRT to address. For tumor sizes less than 3.0 cm and a paucity of radiographic mass effects, SRT affords high rates of tumor control and neurologic preservation. MRI surveillance demonstrates the realization of

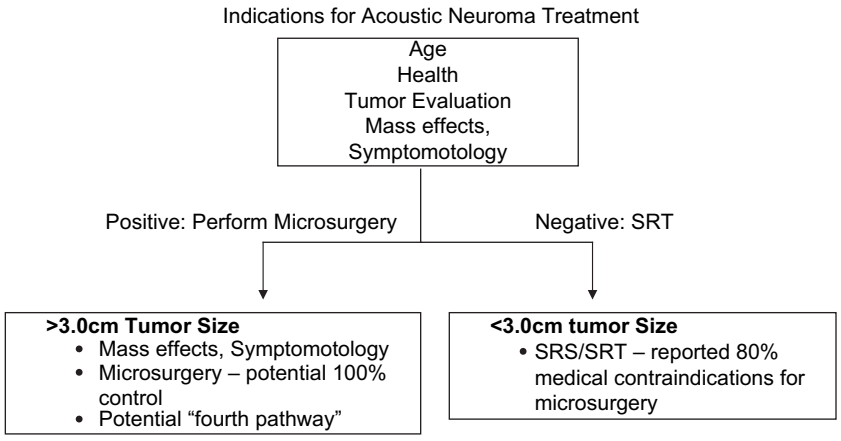

Fig. 2. Indications for acoustic neuroma treatment.

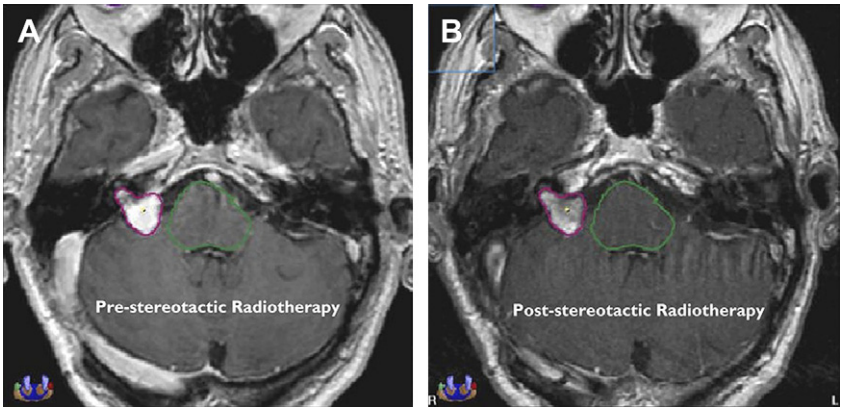

Fig. 3. Demonstrating degradation of contrast signal and contraction of size of acoustic neuroma. (*A*) Pre-stereotactic radiotherapy. (*B*) Post-stereotactic radiotherapy.

the goal of tumor control as its growth has been inactivated by SRT. Close clinical follow-up has not demonstrated neurologic deterioration. We have appreciated symptom abatement in the post-SRT clinical assessments. Symptoms of vertigo, ataxia, and paresthesia have abated in a number of our cases. We differentiate acutely progressive mass effect symptoms as microsurgical indicators, but appreciate chronic symptomotology as appropriate to consider SRT indicators. SRT is not only confined to asymptomatic lesions.

Our experience has evolved an algorithm considering tumor size (less than 3.0 cm), location, or paucity of mass effect (eg, intra- versus extracanalicular) and symptom chronicity to favor SRS/SRT in treating acoustic neuromas. The dramatic achievement in tumor control, preservation of neurologic function, and even abatement of chronic symptoms are countered to advances in microsurgery. Microsurgery is relegated to larger tumors (greater than 3.0 cm), significant radiographic extracanalicular mass effect, and acute symptoms the natural history of which SRS/SRT would not address.

Summary

SRT is appealing as a modality to obviate surgery related morbidity, which remains an issue despite microsurgical advances. In the authors' experience, SRT prevents acoustic neuroma growth, preserves neural function, and is not associated with treatment-related complications. We offer SRT as a first-line treatment choice in patients harboring small to medium sized tumors, even when chronically symptomatic. SRT will be offered more frequently as a primary option as tumors are more frequently identified at smaller sizes.

Appendix

A physicist's perspective: comparisons of Gamma Knife circular collimated stereotactic radiotherapy and accelerator-based, micro-multileaf, collimated stereotactic radiotherapy

The treatment of acoustic neuromas has been performed with stereotactic radiotherapy for quite some time. The benefits of a noninvasive procedure reduce the risks inherent with surgery, and also limit damage to normal tissues that might be injured with a surgical approach. Initially, such therapy was limited to SRS. This denoted a single fraction of radiation delivered to the patient, whose head was fixated with a frame capable of three-dimensional target placement. A frame was necessary so that a consistent coordinate system could be mapped to the patient's skull. For the Gamma Knife patient, this frame was applied by the neurosurgeon the morning of the procedure. After framing, the patient would then be sent to MRI for imaging; the Leksell frame used by the Gamma Knife being compatible with MRI. After imaging with a spoiled gradient (SPGR)-type sequence such that the voxel sizes of the scan were equivalent in all dimensions, the patient would then wait in a holding area while the physicist transferred the images into the planning computer.

Although all planning was performed on the MRI, the actual dose calculations were performed

by taking an approximation of the shape of the patient's skull and entering those data into the computer. The physicist would then review a wire-frame model of the interpolated skull radii measurements, and then the neurosurgeon would commence the planning process. This was performed by placing several isocenters of discrete sizes to cover the acoustic neuroma with the 50% isoshell. The collimators available were 18 mm, 14 mm, 8 mm, and 4 mm. A three-dimensional plan could be easily performed on a regularly shaped spherical acoustic neuroma that had a diameter similar to that of the collimators described. When the acoustic neuroma was irregularly shaped and large, however, treatment planning became a challenge because of sphere packing. The normalization of the plan was constantly updated to reflect the maximum dose location and magnitude as more isocenters were placed. Locating isocenters too close to one another would significantly renormalize the plan. This could cause a complex plan to fall apart, and then time would need to be taken to space out the corresponding isocenters and regain a reasonable dose distribution.

Another issue with large lesions related to the number of isocenters needed to cover the target was penumbra enlargement. A single isocenter has a very sharp penumbra, and therefore is exceptionally good at tumor conformality; however, because more and more isocenters are required to cover a large or irregularly shaped lesion, the penumbra of the lesser isoshell values broadens considerably. Also, dose heterogeneity is a commonplace side effect of dose sphere-generated plans. Some say this heterogeneity is of value for malignant tumors, but might be questionable for benign lesions.

Finally, it is difficult to calculate a verification of the treatment times of a Gamma Knife plan independently of the treatment planning computer. Linac-based stereotactic therapy has its own benefits and liabilities. The commissioning of such a system is very difficult because of the increased number of degrees of freedom of the unit. Once completed, the treatment delivery can be every bit as accurate as a Gamma Knife. Treatments can be mimicked with frame fixation and stereotactic cones to replicate a Gamma Knife dose distribution, with the same liabilities denoted above. The true benefit lies in being able to mask the patient in a way such that the documented maximum deviation should not exceed 1.5 mm and, in practice, is approximately 1 mm, this leads to the delivery of stereotactic radiotherapy or SRT.

The ability to fractionate the treatment gives the advantage of dose escalation for increased control, without increased probability of normal tissue damage. The masking system also allows several steps of the treatment planning process to be completed without the presence of the patient.

All of the steps of therapy are not required to be completed in a single day, meaning the patient does not need to spend considerable time at the center awaiting treatment. An additional advantage can be the inclusion of a miniature multileaf collimator (MMLC). With this apparatus, 3-mm leaves can shape to any desired target, and have penumbra that averages 2.5 mm, from 2-cm to 10-cm field sizes. The main advantage is the ability to treat the lesion with a single isocenter of 9 to 12 static beams, conforming to the target shape, and spaced out in a Gamma Knife-like fashion to equally distribute the radiation entry areas. The patient benefits from a much shorter treatment time with such an accelerator-based system, and a decreased margin for positional error because of a single isocenter placement rather than multiple placements. A typical isoshell that covers the tumor nicely is approximately 90% rather than 50%, and lends itself to a more homogeneous distribution. The ability to perform hand-calculation second checks of the accelerator beams also gives more confidence in the treatment delivery. The treatment planning systems use the CT scan of the patient for dose calculation, thus giving the ability to use heterogeneous dose calculations to account for bone and air density differences as well.

For truly difficult lesions, intensity modulated radiotherapy (IMRT) is also an option. Benefits of a linac-based system are fractionated therapy, improved dose calculation, decreased planning time for difficult lesions, and, in most instances, decreased treatment times for the patient.

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