L’expérience radiochirurgicale
Résultats

ACOUSTIC NEUROMA RADIOSURGERY
Origins, contemporary use and future expectations

D. KONDZIOLKA MD, L. D. LUNSFORD MD, J. C. FLICKINGER MD

Departments of Neurological Surgery and Radiation Oncology,
The Center for Image-Guided Neurosurgery,
University of Pittsburgh, Pittsburgh, Pennsylvania, PA 15213, USA.

SUMMARY: Acoustic neuroma radiosurgery. Origins, contemporary use and future expectations


Patients who have an acoustic neuroma (vestibular schwannoma) can be managed with observation, open surgical resection, stereotactic radiosurgery, or fractionated radiotherapy. Increasing numbers of patients are choosing radiosurgery over resection for their tumor. In this report we discuss the history of stereotactic radiosurgery, and the evolution in technique that has led to current results with this approach. We discuss the indications for and expectations with the different treatments. The literature on radiosurgery and radiotherapy is reviewed. It is expected that clinical and basic studies will further improve results.

Key-words: acoustic neuroma, vestibular schwannoma, radiosurgery, gamma knife.

RÉSUMÉ : Radiochirurgie des neurinomes de l’acoustique : origines, utilisation courante et attentes pour l’avenir

Les options thérapeutiques pour les patients ayant un neurinome de l’acoustique (schwannome vestibulaire) sont l’observation, l’excision ouverte, la radiochirurgie stéréotaxique, ou la radiothérapie fractionnée. Un nombre croissant de patients choisissent la radiochirurgie au lieu d’une excision ouverte. Dans cet article, nous présentons l’histoire de la radiochirurgie stéréotaxique et l’évolution des techniques permettant cette nouvelle approche. Nous discutons des indications des différentes techniques et des résultats attendus et présentons une revue de la littérature. Nous attendons des études cliniques et fondamentales une contribution à l’amélioration progressive des résultats.

“This paper is important in that it calls attention to the possibility of using a highly collimated radiation treatment to treat acoustic neuroma. I would not suggest that this become standard therapy”.

Albert L. RHOTON, Jr., MD.

In 1971, Lars Leksell described the indications and technique of acoustic tumor radiosurgery, as first performed in a patient in 1969 [30]. Since the initial radiosurgical concept (1951), many basic studies were performed to determine the effects of different radiosurgery doses in normal brain, particularly as they applied to functional radiosurgery. After the first radiosurgical patient was treated with the gamma knife in 1967 (a patient with craniopharyngioma), the era of tumor radiosurgery had begun. The management of selected patients with pituitary tumors and pineal region tumors, lesions that could be identified using plain x-rays or studies such as cisternography or ventriculography, ushered in a new era. Leksell was challenged by disorders that were associated with high rates of...
management morbidity. Surgery for acoustic neuromas certainly met that criteria. Hearing loss was the norm. Facial weakness was extremely common and hemiparesis, significant ataxia and death were relatively common occurrences. In a large resection series reported by Olivecrona in 1967, the overall mortality was 22%, but in the smaller tumors, only 9%. Facial nerve function was preserved in only 21% of patients [44]. In a series reported by House in 200 patients (1969) there were 56 partial removals and a mortality rate of 7%. In 1957, Pool stated that acoustic neuroma resection was, "not only one of the most exacting and laborious, but also one of the most dangerous and unpredictable operations in the entire neurosurgical repertoire". Leksell believed that stereotactic radiosurgery offered a new approach to this problem. Using his first generation gamma unit with 179 cobalt-60 radiation beams, the tumor was targeted with air or contrast encephalography. He stated that doses of 5-7 krad were administered to the center of the tumors in the first three patients. Results were reported in his initial 1971 publication.

A comprehensive evaluation of the initial Swedish patient series was reported by Norén in 1983 [41]. He and his colleagues described 14 patients who were managed over a six month period in 1975, who had at least four years follow up. Two of these patients had prior partial resections. Radiosurgical planning was aided by pre-operative CT scanning, metrizamide cisternography and in some cases, pneumoencephalography. These patients received a radiosurgical dose at the tumor margin that varied between 7 and 45 Gy. Interestingly, six of fourteen patients had tumor margin doses in excess of 30 Gy. Such doses may have followed work from a 1981 laboratory study that evaluated human vestibular schwannoma cells in culture treated to 30 Gy. Such doses may have followed work from a 1981 laboratory study that evaluated human vestibular schwannoma cells in culture treated to 30 Gy. On imaging after radiosurgery, 8 tumors decreased in size, 2 were unchanged and 3 had increased. Later, questions were raised regarding the accuracy of early radiosurgery targeting with such crude imaging and calculations performed without computers.

At the present time, radiosurgery is associated with minimal risk for facial neuropathy. This was not always the case. In the 1983 report by Norén, 5 of the 6 patients without facial nerve deficits had received an estimated radiation dose to the facial nerve of 32 Gy or less [41]. The patients with facial nerve dysfunction all had received a higher radiation dose that varied between 42 and 70 Gy. This is remarkable given the close attention now paid to ensuring that the tumor margin receives a dose held within facial nerve tolerance (<15 Gy). At a time when radiosurgery was planned with early generation and relatively poor quality CT scans or with air or contrast studies, developing a radiosurgical plan that fit the tumor margin precisely was difficult to achieve. Nevertheless, it was such early data that suggested that the facial nerve could tolerate a dose in the range of "32 Gy or less", setting up treatment plans for the late 1980's where the nerve would commonly receive between 18 and 20 Gy.

The modern era of acoustic tumor radiosurgery was ushered in at the University of Pittsburgh under Dr. L. Dade Lunsford. As the fifth center in the world to use the gamma knife, and the first in the United States to install a 201 source unit, radiosurgery was performed using higher resolution imaging techniques. Lunsford began a commitment to rigid outcomes evaluations, publication and presentation of results, and education. Together with Donald Kamerer of the Department of Otolaryngology in Pittsburgh, they reported their early experience in 9 patients using this technique [25]. A more comprehensive evaluation of 20 patients was reported by Lunsford and Goodman in the 1988 Surgical Forum [35]. In that report, results from 20 patients were presented, 8 of whom had had residual tumor after prior surgery. Four of the patients had neurofibromatosis. In early follow up no tumor enlarged, and in six reduced tumor contrast enhancement was found. No patient developed a new facial neuropathy. The average dose to the tumor margin was 20 Gy significantly higher than that currently used. Lunsford was also the first to report the economic benefits of radiosurgery, noting an average 65% reduction in hospital charges compared to the cost of microsurgical removal. Within two years, both Linskey et al. (n=26 patients) and Kondziolka et al. (n=85 patients) reported the expanding Pittsburgh experience [27, 31]. In the latter paper, Kondziolka noted a 3% onset for new trigeminal deficits and a 20% onset of facial weakness, although these usually were mild and transient [27]. In that report, 11 patients had excellent pre-radiosurgery hearing and at follow up six were unchanged. This report was the first to emphasize the role of radiosurgery as primary management to achieve preservation of cranial nerve function. Prior to that time, radiosurgery had been seen as a therapeutic tool to reduce overall treatment risks particularly for elderly patients, those with concomitant medical problems, or those that had already failed surgery. The concept that radiosurgery could be used in younger patients in order to provide effective treatment with lower risks than those associated with resection was novel. Reports on acoustic neuroma radiosurgery then spread outside the neurosurgical or otolaryngology literature when Flickinger et al. published their comprehensive review of the Pittsburgh experience in Cancer [12].
Norén continued his comprehensive review of the Stockholm experience with a report on 254 patients managed from 1969 through 1991 with a minimum follow up of 12 months [21]. Some degree of facial weakness was seen in 17% of patients and the incidence of trigeminal neuropathy was 19%. These symptoms were usually transient. They had some preservation of hearing in 77%. Given the higher doses that were used, one would not expect to see a high rate of useful hearing preservation in that early Stockholm series.

EVOLUTION OF RADIOSURGERY TECHNIQUES

In the early 1990’s, radiosurgical techniques evolved considerably. These changes included improvements in stereotactic imaging, dose planning, and refinements in dose prescription. Tumor imaging (beginning with pneumoencephalography and angiography, and even early-generation computed tomography (CT)), was inadequate for fully defining the tumor by today’s standards. The intracanalicular portion of the tumor was usually not covered in the plan. The early radiosurgery dose plans were not created with the assistance of computers.

By 1987, double isocenter radiosurgery plans could take more than forty minutes to calculate [14]. Because of difficulties in treatment planning, all institutions limited the number of isocenters used as much as possible. Treatment volumes were less conformal than today. Presently, multiple isocenters are used frequently and each isocenter calculation takes less than two seconds. Gamma knife vestibular schwannoma treatment plans usually consisted of one isocenter for the smaller intracanalicular tumor portion in the porus acousticus (usually treated with 4-mm diameter collimators) and if possible, one isocenter for the extracanalicular (intracranial) portion (see figure 1 for the anatomy). More than one isocenter was used for the extracanalicular portion only when the 18-mm diameter collimator couldn’t cover the diameter of that portion, or if the tumor was highly irregular in shape. Early linear accelerator (Linac) treatment plans usually consisted of one isocenter centered in the extracanalicular portion of the tumor [40].

By 1992, high resolution-stereotactic MR imaging was being used for targeting by many Gamma knife centers [16, 26, 33]. Because treatment-planning programs were faster and fully integrated with imaging, elaborate, highly conformal, multi-isocenter treatment plans could be developed in minutes. Gamma knife centers began using 6-13 isocenters in more than half the cases to achieve a high degree of conformality [10]. Thus, the use of multiple isocenters to achieve conformality represents the ultimate form of intensity-modulated irradiation. By 1994, some linac centers were adopting multiple isocenter techniques, switching to multiple static conformal fields to improve conformality, or switching to fractionated techniques with lower radiation doses [57]. Later years saw the introduction of inverse treatment planning wherein the computer itself was programmed to indentify a treatment volume based on three dimensional tracing of the tumor volume. For the most part, inverse planning has not yet proven to be of significant benefit.

Prescription doses for radiosurgery declined until the early 1990’s. Initially minimum tumor doses of 16-20 Gy were prescribed at Pittsburgh according to tumor volume. Prescription doses were lowered slowly, because of the fear of compromising long-term tumor control for lower morbidity. So far that has not occurred. Since 1992 the most commonly used prescription doses (marginal doses) today are in the range of 12-13 Gy, with no compromise in tumor control seen so far in prospective analysis [9, 11, 13, 42, 43]. How much radiosurgery doses for vestibular schwannoma may be safely lowered is unclear [24, 45]. Fractionated stereotactic radiotherapy has been used with some early success with doses as low as 20 Gy in five fractions. The single-fraction equivalent for a dose of 20 Gy in five fractions predicted by the linear quadratic formula with alpha/beta ratios of 0, 2.5, or 5 would be 8.9, 9.2, or 11.1 Gy respectively. Arguing against using doses this low, is the observation by Foote of a trend (p=0.207) for poorer tumor control with radiosurgery doses less than 10 Gy in the University of Florida series [15].

THE INITIAL RADIOSURGERY EXPERIENCE IN PITTSBURGH

The early radiosurgical experience in treating vestibular schwannomas is well documented in the Kondziolka et al. analysis of the University of Pittsburgh experience from 1987-1992 [28]. We recently reanalyzed this experience with further follow-up [29].

From 1987-1992, 157 patients with underwent Gamma knife radiosurgery for unilateral vestibular schwannoma at the University of Pittsburgh. During the initial years, only patients who were poor surgical candidates or refused recommended surgical resection were accepted for treatment. Work from our laboratory confirmed the histological effects of radiosurgery on vestibular schwannoma tissue [32]. After the first two years when preliminary results confirmed the safety and efficacy seen...
in Sweden, more patients who were reasonable surgical candidates were accepted for treatment. The median age for this series was 60 years (range: 28-83). The number of prior surgical resections was zero in 117 patients, one in 26 patients, two in 12 patients, and three or four resections in 2 patients. Of the last operations performed before radiosurgery, 7 tumors recurred after “total” resections, 29 were irradiated after subtotal resection, and in 4 cases records were unclear whether the procedure was a complete or partial resection. The most common presenting symptom was hearing loss (60 patients) followed by tinnitus (35 patients). Facial weakness was present in 33 patients prior to radiosurgery and decreased facial sensation also in 33 patients.

Follow-up physical exams with CT or MR images were requested every six months for the first two years and then yearly afterwards. Tumor sizes were carefully measured on follow-up films with calipers. Tumor enlargement or regression was defined as a 2-mm change in tumor diameter from treatment baseline. For patients with preserved hearing, audiograms were requested at similar intervals for the first three years but follow-up audiograms were performed more selectively after three years.

The median follow-up was 9.1 years (10.2 years for patients alive at the time of last follow-up after excluding intercurrent unrelated deaths). Three patients had a surgical procedure after radiosurgery (at 19, 33 and 40 months). The first patient had a prior subtotal resection of a vestibular schwannoma that may have been related to a prior mantle radiotherapy field extending up to the mastoids. In the second patient, follow-up imaging documented growth of the extra-canicular portion of their tumor. The other patient had a cystic recurrence initially drained and then partially resected. An additional patient had surgery for an adjacent arachnoid cyst even though the tumor had not enlarged. Serial imaging studies after radiosurgery (n=157) showed a decrease in tumor size in 114 patients (73%), no change in 40 (25.5%), and an increase in three patients who had later resection (1.9%). Counting the arachnoid cyst progression as a failure of radiosurgical management, the long-term actuarial tumor control rate was 97.0±1.3%.

Some degree of facial weakness in this early series developed after radiosurgery in 26/157 (16.6%) patients (none worse than House-Brackman grade 3 at last follow-up) [22]. In five patients, facial weakness improved after radiosurgery. Reduced facial sensation developed in 25/157 (15.9%) patients after radiosurgery while facial sensation improved in six patients. The Gardner-Robertson hearing grade remained unchanged in 43/85 (51%) patients with testable hearing pre-radiosurgery. Serviceable hearing (grade 1-2) remained in 15/32 (47%) patients with Gardner-Robertson grade 1-2 hearing prior to radiosurgery.

This series clearly documented the long-term safety and efficacy of radiosurgery for vestibular schwannomas. Despite the higher rates of cranial nerve side effects seen after radiosurgery in this early experience compared to that seen with present techniques, these results represented a substantial improvement over tumor resection with equal or better long-term tumor control.

THE RECENT RADIOSURGERY EXPERIENCE

Results for modern Gamma knife radiosurgery techniques are found in recently published series from Pittsburgh, Baltimore, Marseille, and Osaka [13, 24, 45, 51]. Regis recently published a carefully documented comparison of 110 surgery and 97 radiosurgery (12 or 14 Gy) vestibular schwannoma patients with close follow-up (4 year minimum) [51]. Facial nerve preservation was 100% in the radiosurgery group compared to 63% in the microsurgery group. Functional hearing preservation was 70% in the radiosurgery group. A larger study from their group on 211 patients undergoing radiosurgery for unilateral vestibular schwannoma found a hearing preservation rate of 73%. They found that hearing preservation was related to pre-operative Gardner Robertson stage 1 (versus 2), planning with multiple isocenters, and marginal tumor doses <13 Gy. A stage 1 intracanalicular tumor with Gardner and Robertson Class 1 hearing treated at a marginal dose <13 Gy had a >95% chance of functional conservation at 2 years.

We recently reviewed 313 patients with previously untreated unilateral vestibular schwannomas who underwent Gamma knife radiosurgery at the University of Pittsburgh between Feb 1991 and Feb 2001 with marginal tumor doses of 12-13 Gy (median=13 Gy) [13]. Maximum doses were 20-26 Gy (median, 26 Gy). Treatment volumes were 0.04-21.4 cc (median=1.1 cc). Median follow-up was 24 months (maximum=115 months, 56 patients <60 months). The actuarial six-year resection-free clinical tumor control rate (defined as no requirement for surgical intervention) was 98.6±1.1%. Two patients required surgical resection. One had a complete resection for continued solid tumor growth and the other required partial resection for an enlarging adjacent subarachnoid cyst (despite control of the irradiated tumor). The six-year actuarial rates for preserved cranial nerve function, normal trigeminal nerve function, unchanged hearing level, and useful hearing were 100%, 95.6±1.8%, 70.3±5.8%, and 78.6±5.1% respectively. Among the
eight patients developing new trigeminal neuropathy (5-48 months post-radiosurgery), six developed numbness (six-year actuarial rate: 2.5±1.5%) and the other two developed new typical trigeminal neuralgia (six-year actuarial rate: 1.9±1.5%). The risk of developing any trigeminal neuropathy correlated with increasing tumor volume (p=0.038).

Iwai et al. analyzed the outcome of Gamma knife radiosurgery (8-12 Gy, median=12 Gy) in 51 consecutive vestibular schwannoma patients treated from 1992-1996, with median follow-up of 60 months (range: 19-96 months) [24]. Resection-free tumor control was 96%. Freedom from any new facial weakness or new facial numbness was 100% and 100%, although 4% of patients with pre-existing facial neuropathy experienced worsening of facial numbness post-radiosurgery. Preservation of Class 1-2 (serviceable) hearing was achieved in 56% of patients.

CURRENT MANAGEMENT OPTIONS

Patients with acoustic neuromas have several treatment options including observation, surgical resection, stereotactic radiosurgery, and fractionated radiotherapy [3]. Many patients choose between radiosurgery and resection based on their own specific goals and their understanding of possible results. The expected results after modern microsurgical resection are well reported [4, 6, 18, 19, 38, 50, 53]. The decision can be difficult for some patients and easier for others, depending on the sources of information given to the patient. These include discussions with surgeons and other physicians, written material from peer-reviewed medical journals, handouts from support groups, internet based reports (of variable reliability), and discussions between patients. A decision analysis study concluded that radiosurgery would be a more desirable choice for most patients [23]. We believe that information provided from the peer-reviewed medical literature is the most reliable for patient education. Nevertheless, some patients become confused by what they perceive as conflicting opinions amongst physicians.

We do not favor observation for younger patients with acoustic neuromas. Yamamoto et al. followed twelve patients who chose observation. A significant increase in tumor volume was found in seven patients during a mean observation period of 19 months [61]. Most schwannomas will show demonstrative tumor growth within five years of follow-up, although the growth rate during this period may be variable.

Resection is indicated for patients with larger tumors which have caused major neurological deficits from brain compression. Surgeons perform stereotactic radiosurgery for small or medium-sized tumors with the goals of preserved neurological function and prevention of tumor growth. The long-term outcomes of radiosurgery, particularly with gamma knife technique, have proven its role in the primary or adjuvant management of this tumor. Fractionated radiotherapy has been suggested as an alternative for selected patients with larger tumors for whom microsurgery may not be feasible, or for some patients in an attempt to preserve cranial nerve function. Some centers also offer radiosurgery, but most do not. Patients with neurofibromatosis type 2 pose specific challenges, particularly in regard to preservation of hearing and other cranial nerve function [56]. The primary clinical issues include avoiding tumor-related or treatment-related mortality, prevention of further tumor-related neurologic disability, minimizing treatment risks such as spinal fluid leakage, infections, or cardiopulmonary complications, maintaining regional cranial nerve function (facial, trigeminal, cochlear, and glossopharyngeal/vagal), avoiding hydrocephalus, maintaining quality of life and employment, and reducing cost. All treatment choices should strive to meet all of these goals. Several reports and surveys evaluated patient outcomes, particularly in regard to quality of life [37, 59]. Our single-center analysis of outcomes following radiosurgery or resection showed either equal or better results with gamma knife radiosurgery [48].

ISSUES IN DECISION MAKING

When we evaluate patients with acoustic tumors, many ask the following two questions. First, is the tumor more difficult to resect if radiosurgery fails? The answer to this is not clear [46, 47]. Few patients have required resection, and the opinions of the surgeons we have asked indicated that some tumors were less difficult, some about the same, and some more difficult. A tumor may be less difficult if it has lost much of its blood supply. In a report on this issue that included thirteen patients who had resection after radiosurgery, eight were thought to be more difficult. However, five of these eight patients had failed resection before they had radiosurgery [47]. Second, patients inquire about the risk of delayed malignant transformation. Malignant schwannomas are rare, but have been reported de novo, after prior resection [20, 55], and after irradiation. We answer that this is always a risk after irradiation, but that the risk should be very low [8]. We have not seen this yet in any of our 6,200 patients during our first 17 years experience with radiosurgery, but quote the patient an estimated risk of 1:1000, significantly less than the
risks for developing cancer on their own or for the risk of death after resective surgery. One report from Japan found a malignant tumor four years after resection, and six months following radiosurgery. The time interval after irradiation was too short to be causative [20]. A second report noted the development of a temporal lobe glioblastoma 7.5 years after radiosurgery for a nearby acoustic neuroma. The temporal lobe had received a low radiation dose [55]. In contrast, we have a patient who had initial resection and irradiation of a frontal lobe astrocytoma, and years later this patient developed an acoustic neuroma. Is there a relationship? Were these tumors related in some oncogenetic way, or were they radiation related?

A SURVEY OF NEUROSURGEONS ON ACOUSTIC NEUROMA MANAGEMENT

We surveyed members of the Congress of Neurological Surgeons in July 2002. Six hundred sixty-three surgeons responded to the survey (30%). Eighty percent of neurosurgeons surveyed had either performed radiosurgery on a patient with an acoustic neuroma or had referred a patient for radiosurgery (n=530). In the first clinical scenario, we asked the neurosurgeons how they would manage themselves, if they were a 37 year-old neurosurgeon who presented with mild unilateral decreased hearing, no tinnitus and no balance problems. An MRI scan showed an intracanalicular acoustic neuroma and serial scans showed a small amount of growth. In the survey, the majority of surgeons stated that they would choose stereotactic radiosurgery for management of their small acoustic tumor (n=283; 43%). Only 122 surgeons stated that they would choose surgical resection of their tumor (18%). Fractionated radiotherapy was chosen by 2% of responders. Interestingly, 240 surgeons stated that they would continue to observe their tumor (36%) rather than undergoing any specific treatment at the present time.

In a second clinical scenario, we asked fellow neurosurgeons about management recommendations if they were a 50 year-old neurosurgeon who had mild decreased unilateral hearing, mild tinnitus and no balance problems. An MRI showed a 2cm left acoustic neuroma. To this question, a minority of surgeons recommended continued observation for a tumor of this size (6%). Surgical resection was recommended by 347 surgeons (52%), whereas radiosurgery was chosen by 261 surgeons (39%). Fractionated radiotherapy was only chosen by 3%. When the results were stratified by age, resection was the most popular choice across the groups between the ages of 30 and 60. However radiosurgery became more popular with advancing age of the survey group, passing resection as the most popular choice when the neurosurgeon was over age 60. Both of these scenarios represented the presentations of real neurosurgeons managed with gamma knife radiosurgery who have done well with no new neurological deficits more than two years after the procedure.

FRACTIONATED RADIOTHERAPY

In the last several years, a number of groups have used fractionated radiation therapy to treat patients with acoustic neuromas [1, 5, 17, 36, 39, 58]. This technique developed when several centers who used linear accelerator irradiation technology were not satisfied with the results or accuracy of their device after single fraction irradiation (radiosurgery). In order to decrease the cranial nerve morbidities they were observing, they began to deliver radiation over multiple sessions (fractionation). The goal of this approach is to weaken the effect of each radiation administration and try to maintain brain or nerve function. Correspondingly this also weaknesses the effect of the radiation on the tumor target. There is little data on this approach in the peer reviewed literature that includes diligent outcomes and follow-up. Linskey et al. conducted an anatomic study of tissues irradiated during a gamma knife procedure and concluded that the dose received by inner ear structures was likely too low to cause any symptoms [34]. This is likely not the case in fractionated radiotherapy where more regional tissue is irradiated.

Williams et al. reported 80 patients who had fractionated stereotactic radiotherapy [60]. Median follow-up after radiotherapy was 2.9 years. The treatment was delivered using CT targeting, a poor technique to evaluate the intracanalicular portion of the tumor. In a later report, Williams published their experience in 125 vestibular schwannoma patients with >1 year follow-up (out of 249 treated between 1996 and 2001). Tumors <3.0cm in diameter received 25 Gy given in 5 consecutive 5-Gy fractions (111 patients), while tumors ≥3.0cm in diameter received 30 Gy in 10 fractions (14 patients). With early median follow-up of 21 months, tumor control and facial nerve preservation were both 100%. However, we have subsequently evaluated two patients from this series with enlarged tumors who are seeking re-treatment of some kind. Two patients developed transient decreases in facial sensation. Hearing preservation was approximately 70%.

In a separate oral report, Lederman et al. provided results from the Staten Island group at the 2001 meeting of the International Stereotactic Radiosurgery Society. They provided no treatment
planning images, no cranial nerve outcome data using the accepted grading systems, and they did not define “hearing preservation”. They did describe that hearing was preserved at a rate “above” 90%, but the quality of hearing was not reported.

In another report, Andrews et al. reported 69 patients who had gamma knife radiosurgery and 56 patients who had linear accelerator based radiotherapy [1]. Tumor control rates were high (97%) in early follow-up and cranial nerve morbidity were low in both groups. With their technique, they found a higher rate of early hearing preservation after radiotherapy, but both treatments had median follow-up times of less than 10 months. Their rate of hearing preservation after radiosurgery (33%) was lower than reported by others. The main drawback of this report is the lack of randomization. Patients were allocated to either treatment according to “strong physician preferences”. Sawamura reported the experience of Hokkaido University in Sapporo, Japan with stereotactic fractionated radiotherapy to 40-50 Gy in 20-25 fractions in 101 patients with a median follow-up of 45 months [54]. The 5-year actuarial tumor control rate was 91.4%. Transient facial nerve trigeminal nerve palsy developed in 4% and 14% of patients. A ventriculoperitoneal shunt was subsequently required in 11%. In our own experience using radiosurgery, the need for a shunt is less than 1%.

Fractionated radiotherapy has been touted by some as the “best way to save hearing”. However, the published outcomes do not confirm this opinion, with hearing deterioration rates in the 20-50% range. The results will vary depending on tumor size, radiation dose, conformality, and the unknown factors of nerve related ischemia or regional tumor effects. Most untreated patients will lose hearing from an acoustic tumor, with or without progressive tumor growth. Patients who receive low biologic doses of irradiation may have low rates of early side effects, but should be expected to have higher rates of later tumor growth, and concomitant neuropathy. Chang et al. reported two provocative cases of acute hearing loss following fractionated irradiation of acoustic neuromas [7].

Optimally, appropriate doses of radiation should be delivered precisely to the tumor and the regional brain structures should be spared of radiation. This is not the case with fractionated techniques where larger volumes of regional tissue are irradiated. We believe that any advantage in fractionation in limiting toxicity only makes sense if the target volume contains normal brain or nerve. Sophisticated stereotactic radiosurgical instruments allow regional brain or nerve to be spared through frame-based, single-session, image guidance. We do not believe that fractionation provides any useful advantage over radiosurgical techniques that have been in use for the last 10 years. In order to confirm a significant difference, a prospective trial likely would require hundreds of patients in each are to detect a difference.

FUTURE DEVELOPMENTS

It is clear that more and more patients are choosing radiosurgery for their acoustic neuroma [49]. The technology is becoming increasingly available and patients in many countries are demanding it [52]. We believe that as more outcomes studies are published, fewer patients will choose to undergo surgical resection of their tumor.

The clinical results following radiosurgery could be improved in several ways. First, studies that define the lower dose limit may enable us to better meet the goal of tumor growth arrest with functional preservation. Although there is now much data for the tumor margin dose of 12 Gy, future studies will evaluate the 10-11 Gy range. Second, pharmacological radioprotection during irradiation has been evaluated in normal brain and experimental tumor models, but has not reached the clinical setting. Agents such as the 21-aminosteroid family of drugs work through membrane stabilization and free radical scavenging effects, particularly in endothelial cells. The drug tirilizad has been tested in subarachnoid hemorrhage and spinal cord injury and is free of significant side effects. It should be tested in tumor radiosurgery.

Third, can we halt an adverse radiation effect once it occurs? We should test new anti-inflammatory agents such as the cyclooxygenase-2 inhibitors to see if they are as effective in the brain as they are with joint inflammation. Fourth, we should work to develop new management strategies for patients with large tumors that include planned tumor resection followed by radiosurgery for the residual mass. This would hopefully lead to improved neurologic outcomes in patients with the most difficult tumors.

REFERENCES


