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brain talk[®]

An Educational Publication

Acoustic Neuroma & Patient Choice

Our association receives patient inquiries from people with every type of brain tumor and brain dysfunction. With the acoustic neuroma patient there seems to be a wealth of myths and unreliable information about all treatment options. For this edition on acoustic neuromas, we asked a group of patients who had received different treatments (surgery, radiosurgery and fractionated radiotherapy) to work with us and research information on the web. Our group reported, and we agree, that there are only a few ethical web sites that did not try to persuade a patient to seek a certain type of treatment. Below we discuss more findings reported to us.

Acoustic neuroma associations provided very little information on their web sites, and what was provided was mostly about surgery. In providing this information, these associations failed to give in-depth information on the surgical approaches or the outcomes of surgery. Some members of our focus group called and asked for information to be sent to them from these associations. They felt they were provided with minimal materials and were asked to 'purchase' a membership or buy other materials to get more information. In the information provided there was a booklet on preparing for surgery. In another booklet, there was a small, somewhat misleading section entitled 'Radiation' that alluded to myths associated with radiosurgery. Local support group leaders reported to us that information about their groups is closely held by the associations and not readily provided to patients. We were told by several local support groups that the smaller groups are considered competitors for patient dollars by the national group.

Patient choice and informed consent...does it exist for acoustic neuroma patients?

The review of physician and hospital-based web sites resulted in somewhat better information. However, many of these sites are dedicated to the type of treatment the physician or hospital provides. One well-respected surgical institute in California provided erroneous information about radiosurgery. This same institute hosts a 'recent publications' web page as part of their web site. The published articles on this page date from 1990 to 1999. In the world of today's research this is old data, unless the surgical results are the same and have not improved in this period.

Patient-hosted web sites presented mostly information on the treatment they themselves had, but were on the whole more objective about all treatments and absolutely believed in the patient having a choice. Much of the information presented on these sites was technically incorrect and out of date.

Other findings reported to us were individual physicians' web pages that were masked as foundations, associations and brain tumor foundations. Some hospitals hosted web pages for a physician that performed one treatment and did not provide information on other available treatments at the same hospital. Members of our focus group reported that when they had visited the same physician while deciding which treatment to choose, they were not informed another physician in the same hospital provided a different treatment that might be of interest to them. This was true of many well-respected research institutions and universities.

Especially disheartening to our focus group were physicians who told horror stories about alternative treatments, or presented patients with old research articles that either promoted the physician's treatment choice or had out-of-date results for alternative treatments. Recently (2003), the issue of a physician providing a patient's with misleading research was upheld by the court as a violation of 'informed consent' and the patient right to have good information with which to make a choice.

By our mission, IRSA usually provides only information about radiosurgery and specialized radiation treatments. In light of problems encountered by our focus group in finding objective, and appropriate information we will present some material on all the accepted treatments for acoustic neuroma as well as evidence based (backed by research) management criteria.

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IRSA[®]

International
RadioSurgery
Association

Stereotactic Radiosurgery

Stereotactic radiosurgery is surgery using radiation as a scalpel. The skull is never opened. Radiosurgery involves the use of precisely directed radiation to create lesions within the brain or to treat tumors or vascular malformations with minimal damage to surrounding structures or tissues.

This works by delivering a relatively high dose of radiation in **one session** to the target with scalpel-like precision. The dose is designed to injure or kill the cells or their supporting blood vessels, while minimizing its effect on surrounding healthy tissue. The radiation distorts the cells' DNA, causing them to lose the ability to replicate themselves. The safety and clinical effectiveness of this technique has been established since 1968 in over 200,000 treated individuals.

The benefits include: no risks of infection or anesthesia reactions; virtually no pain; reduced costs; and an immediate return to normal activities.

Radiosurgery may or may not be appropriate for your condition. It may be used as the primary treatment or recommended in addition to other treatments you may need. Only a treating neurosurgeon can make the evaluation as to whether you can be treated. Some of the most common indications for treatment today are:

- Arteriovenous/vascular malformations
- Meningiomas
- Acoustic neuromas
- Pituitary and pineal tumors
- Metastatic tumors
- Glial and astrocytoma tumors
- All other malignant & benign tumors
- Trigeminal neuralgia
- Parkinson's tremors/rigidity
- Functional disorders

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What Is an Acoustic Neuroma?

An acoustic neuroma is really a vestibular schwannoma (also known as acoustic neurinoma, or acoustic neurilemmoma), which is a benign, usually slow-growing tumor that develops from the balance and hearing nerves supplying the inner ear. The tumor arises from an overproduction of Schwann cells—cells that normally wrap around nerve fibers in the fashion of onion skin to help support and insulate nerves. As the vestibular schwannoma grows it presses against the hearing and balance nerves, usually causing unilateral (one-sided) or asymmetric hearing loss, tinnitus (ringing in the ear) and dizziness or loss of balance.

As the tumor increases it can interfere with the nerve responsible for facial sensation (trigeminal nerve), causing facial numbness. Vestibular schwannomas can also press on the nerve responsible for the muscles of the face, causing facial weakness or paralysis on the side of the tumor. If the tumor becomes large, it will eventually press against nearby brain structures (such as the brainstem and the cerebellum) and become life-threatening.

Vestibular schwannomas usually affect only one ear. They account for approximately eight percent of all tumors inside the skull; 1 of every 100,000 individuals develops a vestibular schwannoma each year. Symptoms may develop at any age but usually occur between the ages of 30 and 60 years, and in women more often than men. Unilateral vestibular schwannomas are not hereditary. Small acoustic neuromas that did not cause any symptoms have been found on autopsy in 2.5% of the general population.

Acoustic neuroma was described for the first time in Holland in 1777. A comprehensive clinical description was presented in 1830. Although the first successful removal of an acoustic neuroma was performed in 1894, the mortality following surgery at the turn of the century was at

least 80%. Excision of the tumor was the standard treatment and the only available option for many years. Results improved gradually but were still far from satisfactory in the early 1960s, when microsurgical techniques were gradually introduced into this field in the USA.

Vestibular schwannomas arise from the VIII nerve (vestibulo-cochlear nerve). The VIII nerve is actually two separate nerves, the vestibular nerve and the cochlear nerve. The vestibular nerve is responsible for balance while the cochlear nerve is responsible for hearing. The facial or VII nerve, which is responsible for facial movement, along with important blood vessels, also passes with the VIII nerve in the canal. Acoustic neuromas usually grow very slowly over a period of many years.

Once the tumor fully occupies the internal auditory canal, it often begins to erode the walls of the canal and enlarge it, which can be detected on X-rays or by MRI. However, this bony erosion does not always occur. The tumors typically remain within their capsule or lining and displace the surrounding nerves and brain tissue very slowly. This is why the body has ample time to accommodate the abnormal growth.

The tumor first distorts the VIII nerve, then presses on the adjacent VII nerve. The VII nerve is gradually stretched into a ribbon-like structure over the enlarging tumor. As the tumor slowly enlarges toward the brain, it protrudes from the internal auditory canal into an area of the skull called the cerebello-pontine angle. The tumor is now pear or mushroom shaped with the smaller end within the canal and the larger part extending toward the brain. It is at this stage that the tumor presses adjacent nerves such as the trigeminal or V nerve responsible for facial sensation. Ultimately, with increasing tumor size, it can press on the brainstem which can be life-threatening.

Fast Facts - ACOUSTIC NEUROMA

- ◆ An acoustic neuroma is a benign tumor.
- ◆ It is usually slow growing and expands at its site of origin.
- ◆ The most common first symptom is hearing loss in the tumor ear only.
- ◆ Continued tumor growth can be life threatening.
- ◆ The treatment options are surgical removal, radiosurgery, or observation.
- ◆ Observation in a growing tumor will result in more permanent problems.
- ◆ It may push on the surface of the brain but does not grow into the brain tissue.

Radiosurgery: The First Choice for Many with an Acoustic Neuroma

Stereotactic radiosurgery may now be the most commonly chosen treatment by patients with acoustic neuromas, also known as vestibular schwannomas. We estimate that there are approximately 2,000 new patients who receive treatment each year in the United States. In 2002, 931 patients had Gamma Knife® radiosurgery. This represented a 430% increase since 1993. Since the rest chose either fractionated radiotherapy, surgical resection or linear accelerator or charged particle radiosurgery, the most common treatment may be Gamma Knife radiosurgery.

What is responsible for the broad acceptance of this approach by both patients and physicians? In this report I will discuss the reasons why many patients choose radiosurgery. For others, the choice of observation, surgical resection, or fractionated radiotherapy may appear to be in their best interests.

Despite much opinion, particularly voiced on the Internet but also from support groups, physicians, and patient discussion, data exist in quality medical journals that can help patients decide between the various options. Some patients become confused by what they perceive as conflicting opinions amongst physicians. Many physicians provide only one kind of treatment and may appear to be biased toward their own approach. What we know from these reports is summarized in this article.

Surgical removal (resection) of the tumor is indicated for patients with larger tumors (>3 cm) which have caused major neurological deficits from brain compression. Surgeons perform stereotactic radiosurgery for small or medium-sized tumors (<3 cm) with the goals of preserving neurological function and prevention of tumor growth. The long-term outcomes of radiosurgery, particularly with the Gamma Knife, have proven its role in the primary or adjuvant management of this type of tumor. It is clear that results after radiosurgery are much more consistent than results following resection, **which is highly dependent on an individual surgeon's skill and experience**, among other factors. A 2003 report by Barker et al. in the journal *Laryngoscope* showed that better clinical outcomes were achieved by surgeons and hospitals that treat greater numbers of acoustic patients. Fractionated radiotherapy has been suggested as an alternative for selected patients with larger tumors for whom microsurgery or radiosurgery may not be feasible, or for some patients in an "attempt" to preserve cranial nerve function.

Why is radiosurgery a frequent choice for patients? The opportunity to avoid surgical complications is a major reason, including the risks of spinal fluid leakage, infections, cardiopulmonary complications, hydrocephalus ("water on the brain") and various cranial nerve deficits (facial weakness being the most important). Many patients feel radiosurgery is the best choice for maintaining nerve function and quality of life.

The Long-Term Tumor Response

Experience with radiosurgery now extends to over thirty years. During the late 1980s and early 1990s, patients and their doctors chose radiosurgery or resection based mainly on early outcomes data from limited patient series. In 1987 we began a prospective assessment of the response of patients with acoustic tumors to Gamma Knife radiosurgery.

At our last review, 827 patients underwent stereotactic radiosurgery for an acoustic tumor (vestibular schwannoma) at the University of Pittsburgh over a 15-year interval. These included 765 patients with solitary tumors and 62 with neurofibromatosis type II, a hereditary disease characterized by bilateral acoustic neuromas. Fifty percent of tumors were on the left side of the brain and fifty percent were on the right side, and half of the patients were female. The patient age range was 12 to 95 years (mean, 56 years).

Twenty percent had undergone prior surgery. "Useful" hearing before radiosurgery was noted by 33% of patients.

One hundred ninety-two patients had radiosurgery between 1992 and 1997 and were eligible for extended follow-up. The maximum follow-up in this cohort was 65 months. The median tumor margin dose was 13 Gy. Five-year actuarial rates of developing problems were: facial weakness, 1%; facial numbness, 2.6%; hearing level preservation, 71%; preservation of testable speech discrimination, 91%. At a tumor margin dose of ≤13 Gy, the rate of facial neuropathy was 0%, and above 13 Gy, 2.5% (usually mild and transient). Neuropathy refers to malfunctioning nerves, and symptoms can include weakness, numbness and pain. Tumor diameter did not significantly affect results.

We continue to evaluate a cohort of patients who were treated before 1992 who are a minimum of ten years out from their procedure (n=162). This study represented results of our initial techniques. Approximately 70% of irradiated acoustic tumors decreased in size over time. Nine patients had tumors that increased in size and all were identified within the first three years after radiosurgery. Enlargement represented either true neoplastic tumor growth (n=4) or tumor death (n=5) with an expansion of the tumor margins as the central portion of the tumor became necrotic. In the latter group, patients' subsequent imaging studies confirmed tumor volume regression. Four patients underwent resection. No further increase in tumor volume was identified in any patient with further follow-up. Patients returned to their routine activities immediately. In our five to ten year review, three patients developed hydrocephalus and required a ventriculoperitoneal shunt. All new or worsened post-radiosurgery deficits occurred within 28 months of radiosurgery and no patient described a treatment-related problem after the third year. We continue to tell patients that 2% of them may require tumor resection in the future, a number that is consistent with other groups.

Quality of Life

There have been a number of patient-based surveys to study outcomes after acoustic neuroma management. One of the first was a survey of 541 patient members of the Acoustic Neuroma Association who provided data on tumor resection between 1973 and 1983. Sixty-two percent reported facial weakness, 84% reported eye-related problems, and depression, sleep disturbance and speech or swallowing difficulties were reported by 38%, 26% and 16%, respectively. More recently, a larger survey of 1579 resections performed between 1989 and 1994 found improved results that included a 44% rate of facial weakness, an 11% rate of cerebrospinal fluid leakage, and persistent balance problems after one year in 9%. Approximately 8% had recurrent or residual tumor on follow-up imaging.



Continued on page 4

Better results following resection have been documented since that time. Samii et al. and Gormley et al. found that complete tumor removal was a frequent outcome. However, neurologic and systemic morbidity (complications) remained present with 1% mortality rates and cerebrospinal fluid fistula rates of 9.2% (Samii) and 15% (Gormley). The study by Barker et al. evaluated patient death following resection and found a rate of 1 in 200, even amongst surgeons with the most experience. However, for patients with large acoustic tumors (over 3 cm in extracanalicular diameter) and those with progressive neurologic deficits that require brainstem decompression, total or subtotal surgical resection is the preferred option. We believe that a complete resection should be performed in such patients if possible, but not at the expense of lost neurologic function. Stereotactic radiosurgery can be considered for patients with intracanalicular, small or medium-sized acoustic tumors since most such patients do not have a rapidly progressive neurologic syndrome. The initial symptoms caused by most acoustic tumors are not improved by resection.

A recent United Kingdom report by Martin et al. (Table 1) evaluated quality of life in patients after tumor resection. They found a disparity between the patient's report and the physician's assessment of function, with decreases in physical functioning, general health, and social functioning after surgery. More severe balance functions led to worse social functioning.

The long-term effects of both resection and radiosurgery must be documented to assist physician and patient decision making. Surprisingly little information has been published on long-term imaging-based outcomes after resection. Cerullo et al. noted a 10% recurrence rate after 10 years had passed following resection. In their series of over 100 patients in which hearing preservation was attempted during resection, Mazzone et al. reported that the overall tumor recurrence rate was 8.1%. These papers are often criticized for their results, but they represent an honest evaluation of longer-term imaging results. All groups should strive to obtain serial imaging studies on their own patients. Post et al. found that 4 of 56 patients (7%) had an incomplete resection when hearing preservation was attempted and that three had regrowth of the tumor within three years. In the largest series, Samii et al. reported a complete resection in 98% of patients and found later recurrence in 6 of 880 who did not have neurofibromatosis type II. In our radiosurgery

series, 98% of patients required no further surgery and 94% had imaging confirmation of persistent tumor control. Tumors that increased in size in the first year or two after radiosurgery did so usually in association with central tumor necrosis, with a small expansion of the tumor capsule. Most such tumors then regressed below baseline in size with longer follow-up. Such transient expansion may be associated with temporary ear region discomfort, perhaps from regional dural inflammation.

What Is Really Known About Fractionated Radiotherapy?

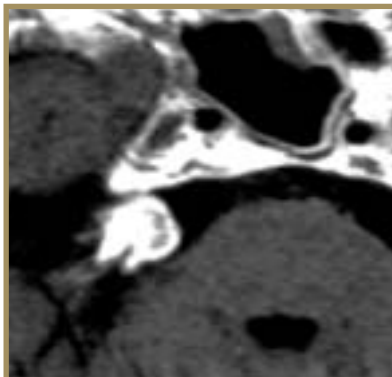
In the last several years, a number of groups have used fractionated radiation therapy to treat patients with acoustic neuromas. This technique developed when several centers who used linear accelerator irradiation technology were not satisfied with the results or accuracy of their devices after single 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 weakens the effect of the radiation on the tumor target.

Williams et al. reported 80 patients who had fractionated stereotactic radiotherapy. Median follow-up after radiotherapy was 2.9 years. Seventy patients received 25 Gy in five fractions and ten patients received 30 Gy in ten fractions. The treatment was delivered using CT targeting which is limited in evaluating the intracanalicular portion of the tumor. Only 19 of 80 patients had Gardner-Robertson grade 1 or 2 hearing ("serviceable" to "excellent" hearing) at the time of treatment. Hearing levels were preserved in 82% (actuarial data). Two patients had transient trigeminal neuropathies and no patient had a significant facial neuropathy. There is little data on this approach in the peer-reviewed literature that includes diligent outcomes and follow-up.

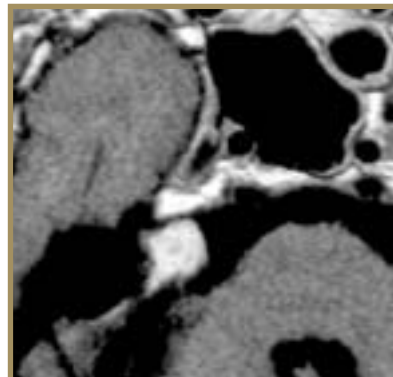
Standardization with linear accelerator machines, which are made by many manufacturers, does not exist. Therefore, research results with this technology are not as comparable among researchers as with Gamma Knife which is identical throughout the world.

Optimally, appropriate doses of radiation should be delivered precisely to the tumor and regional brain structures should be spared radiation. This is not the case with fractionated techniques where larger volumes of regional tissue are irradiated. We believe that any advantage of fractionation in limiting toxicity only makes sense if

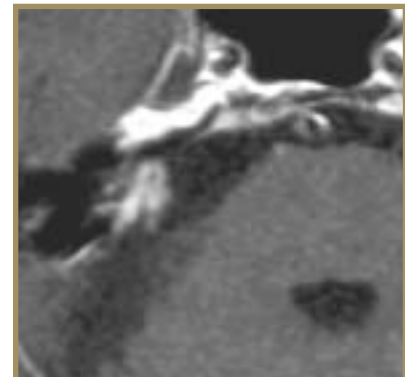
Gamma Knife® for Residual Acoustic Neuroma After Microsurgery



At Radiosurgery



5 years after Radiosurgery



12 years after Radiosurgery

Scans courtesy of University of Pittsburgh, Center for Image-Guided Neurosurgery.

The First Choice...

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the target volume contains normal brain or nerves. Sophisticated stereotactic radiosurgical instruments allow regional brain or nerves to be spared through frame-based, single-session image guidance. We do not believe that fractionated radiotherapy provides any useful advantage over radiosurgical techniques that have been in use for the last 10 years.

What Would Neurosurgeons Choose for Themselves?

A survey was mailed to members of the Congress of Neurological Surgeons in July 2002. Six hundred sixty-three surgeons responded to the survey. The survey included two questions about acoustic neuroma. Forty-one percent of responders were between the ages of 40 and 50. Eighty percent of neurosurgeons surveyed had either performed radiosurgery on a patient with an acoustic neuroma or had referred a patient for neurosurgery (n=530).

Question Two

Question: You are a 50 year-old neurosurgeon who presents with mild decreased hearing on one side. You have tinnitus but no balance problems and facial function is normal. An MRI shows a 2.2 cm left acoustic neuroma. Which management strategy would you choose for yourself? (Observation, stereotactic radiosurgery, surgical resection or fractionated radiotherapy.)

Response: In this scenario, the neurosurgeon had a medium size acoustic tumor that indented the side of the brainstem but did not compress the fourth ventricle. The 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

Table 1. Comparison of Patient Survey Data For Vestibular Schwannomas

	Resection ¹	Radiosurgery ²
Year of Study	2001	1998
No Change in Employment	68%	69%
Offers Positive Recommendation about Treatment	74%	95%
Mean Tumor Size	25 mm	22 mm
New Balance Problems	78%	7%
New Onset Tinnitus	57%	3%
New Facial Nerve Dysfunction	63%	10%

¹ Martin HC, Sethi J, Lang D, et al. Patient-assessed outcomes after excision of acoustic neuroma: postoperative symptoms and quality of life. *J Neurosurg* 2001;94(2):211-216. ² Kondziolka D, Lunsford LD, McLaughlin MR, Flickinger JC. Long-term outcomes after radiosurgery for acoustic neuromas. *New Engl J Med* 1998;339:1426-1433.

Question One

Question: You are a 37 year-old neurosurgeon who presents with mild decreased hearing on one side. You have no tinnitus, no balance problems and facial function is normal. An MRI scan shows an intracanalicular acoustic neuroma and serial scans have shown a small amount of growth. Which management strategy would you choose for yourself? (Observation, stereotactic radiosurgery, surgical resection or fractionated radiotherapy.)

Response: The majority of surgeons (43%; n=283) stated that they would choose stereotactic radiosurgery for management of their small acoustic tumor. Only 122 surgeons (18%) stated that they would choose surgical resection of their tumor. Fractionated radiotherapy was chosen by 2% of responders. Interestingly, 240 surgeons (36%) stated that they would continue to observe their tumor rather than undergoing any specific treatment at the present time. It had been stated in the case presentation that serial scans had already shown a small amount of growth. This tumor had been observed and was increasing in volume. Nevertheless, approximately one-third of responders continued to choose observation for a 37 year-old patient with a small but growing tumor. This case reflected the care of an actual neurosurgeon who had Gamma Knife radiosurgery. He remains well 18 months after his procedure and maintains a full practice. He has had no facial weakness or change in hearing.

group, surpassing resection as the most popular choice when the neurosurgeon is over age 60. It appears that surgeons chose to have a resection because of the larger volume of the tumor with indentation of the lateral surface of the brain stem. This patient was also a real neurosurgeon who had radiosurgery. He remains well 18 months after the procedure with a decrease in the size of the tumor, and his facial function remains normal.

Some Common Patient Questions

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. Few patients have required resection after radiosurgery, and the opinions of the surgeons we have asked indicated that some tumors were less difficult, some were about the same, and some were more difficult to resect. 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 the eight patients had failed resection *before* they had radiosurgery. In a recent report, Regis et al. noted that most tumors were not more difficult to resect after radiosurgery than the typical untreated tumor.

Continued on page 6

Second, patients inquire about the risk of delayed malignant transformation. Malignant schwannomas are rare, but have been reported to occur spontaneously, after prior resection, and after irradiation. We answer that delayed malignant transformation is always a risk after irradiation, but the risk should be very low. We have not yet seen this in any of our 6400 patients during our first 17 years of experience with radiosurgery, but quote patients a risk of 1 in 1000 over the next 5–30 years of their life. We believe the risk of developing a tumor years after radiosurgery is much less than the risk of mortality immediately after a resection, and likely less than the risk of the patient developing another tumor on his own in another body location.

Neurofibromatosis Type II

We have conducted detailed evaluations for Gamma Knife radiosurgery in patients with tumors due to neurofibromatosis type II. Imaging studies of 45 tumors over a median 36-month follow-up (range, 6–120 months) found that 16 tumors (36%) had regressed, 28 tumors (62%) remained unchanged in size, and one tumor (2%) demonstrated progression. Loss of central contrast within the tumor was observed in some patients and was thought to reflect tumor necrosis.

At our last detailed review, the mean period of clinical follow-up was 41 months (range, 6–120). Thirty patients (67%) maintained a stable exam and 15 patients (33%) demonstrated some degree of clinical deterioration. Two patients (4%) died during the follow-up period due to unrelated illnesses. The median Karnofsky score after radiosurgery was 80. The Karnofsky score reflects a person's ability to perform common tasks. Thirty-five patients (78%) were able to carry out normal daily activities at the time of the last examination (Karnofsky score \geq 80).

Of the 14 tumors associated with useful hearing (Gardner-Robertson grades 1 or 2) at the time of radiosurgery, six (43%) demonstrated no change in hearing class during the follow-up period.

In tumors managed since 1992, nine patients with useful hearing underwent radiosurgery. Six of the patients (67%) had hearing preservation at the time of last examination. Thirty-one tumors (69%) were associated with intact facial nerve function (House-Brackmann grade 1) at the time of radiosurgery. Three patients (8%) experienced trigeminal distribution sensory loss at a mean five months (range, 4–5 months) after radiosurgery.

Summary

Patients with acoustic neuromas have several options available to them. Large tumors with significant brainstem compression usually require surgical resection. For patients with small or medium sized tumors, radiosurgery has become a common treatment with excellent long-term results. Patients must be comfortable with the concept of tumor control rather than tumor removal. Most seem to be satisfied with this concept, if it allows them to avoid brain surgery. Surgeons should strive to educate their patients with information from the peer-reviewed literature. Confusion amongst patients exists because information from Internet sources, newsletters, support groups and physicians has not always been validated and supported by outcomes data. The long-term results of radiosurgery from numerous centers support its important role in the care of patients with appropriate tumors.

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Commentary: Radiosurgery and Acoustic Neuroma

It is an amazing development of acoustic neuroma treatment Dr. Kondziolka presents in his article. Not many years ago, most doctors found the concept of treating these very benign tumors with radiation as very strange and even opportunistic. Acoustic neuroma has long been defined as a surgical disease and should be treated surgically.

From a handful of patients treated annually with radiosurgery in the U.S. in the late 1980s, we now are approaching a situation where almost half of all patients decide to have their acoustic neuromas treated with radiosurgery. How was this development possible?

Radiosurgery as a concept was presented in 1951, more than 10 years before surgery with microscopic technique was introduced into neurosurgery. However, treatment of tumors with radiosurgery became feasible only when the Gamma Knife was presented in 1968. Even then there was a long way to go to prove that the precise cross-firing of acoustic neuromas with focused radiation really stopped the growth, not only for some time, but permanently. There is now an abundance of peer-reviewed scientific publications demonstrating the short and long term efficacy of Gamma Knife radiosurgery in the treatment of acoustic neuromas and other intracranial tumors.

Almost as important as the 97–98% chance of permanent growth control is the fact that this can be achieved with a minimum of side effects. The risk of facial weakness, temporary or permanent, now is 0% at many Gamma Knife centers. The incidence of temporary facial numbness is approaching the 0% level as well. The focus now is on increasing the preservation of hearing.

So, how was this development possible? The answer is simple. Who wants his or her head cut open if a non-invasive, equally effective method in terms of tumor control is available with much lower risks and almost immediate recovery from the treatment? As pointed out by Dr. Kondziolka, a majority of neurosurgeons now realize the advantage of radiosurgery when they happen to be the patients themselves. Isn't that the ultimate "proof of the pudding"?

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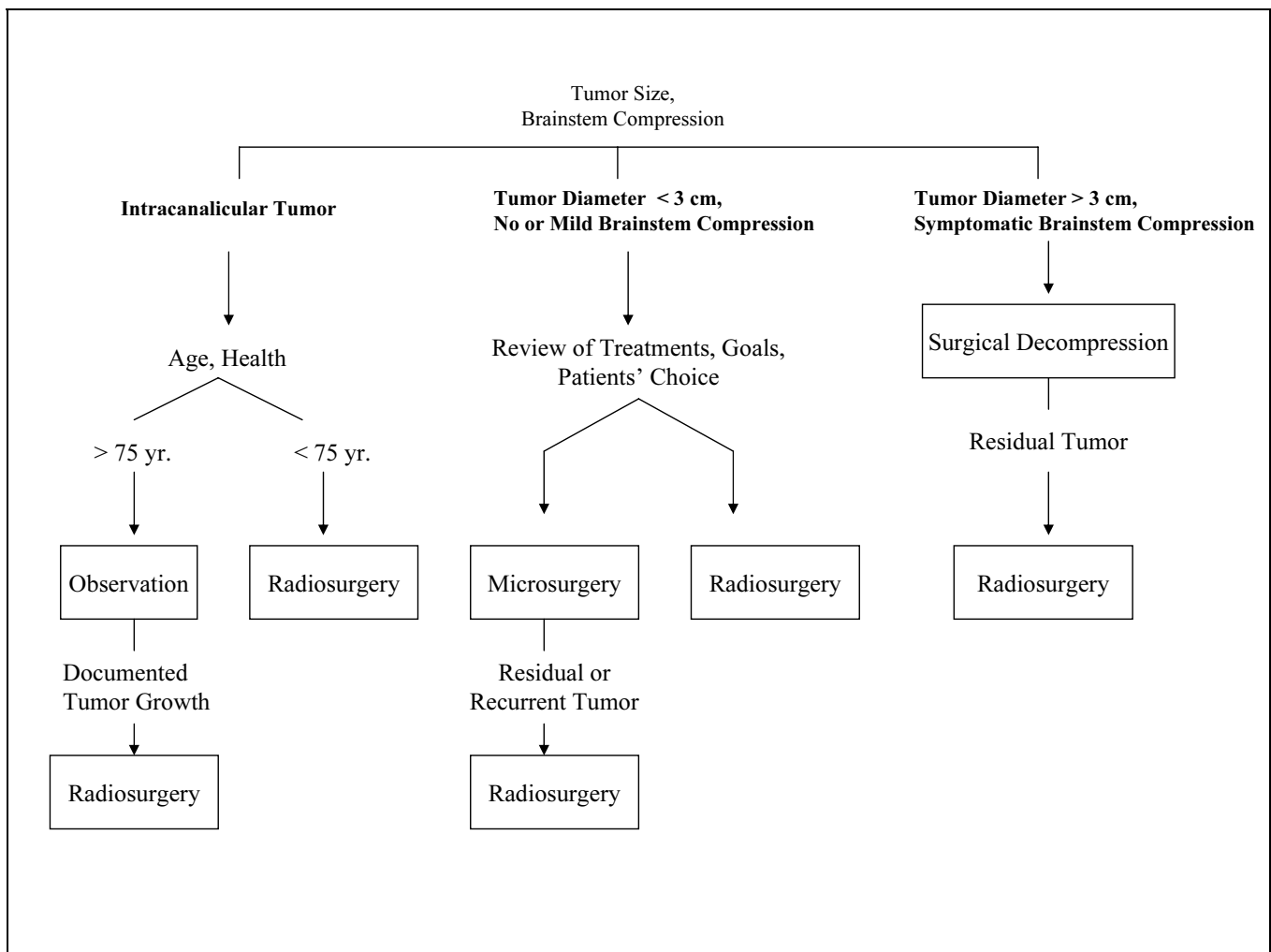
Acoustic Tumor Management

A number of factors are considered in making a recommendation. These factors include:

1. Patient's Age
2. Patient's Medical Condition
3. Tumor Size
4. Presenting Symptoms
5. Brain Stem Compression
6. Patient's Goals and Choice*
7. Prior Procedure and Response
8. Current Neurological Status

A broad outline of management algorithm is shown; however, the final recommendation is usually influenced by the recommending neurosurgeon's experience and availability of technology along with patient preference.

Acoustic Tumor Management Algorithm



* Patient Goals:

Patient goals are specific to the individual and must be clearly outlined with your treating neurosurgeon. Patients who have small to medium tumors (<3 cm) and would be comfortable with tumor growth control, low rates of facial dysfunction and high rates of hearing preservation should consider radiosurgery. Patients who have large tumors (>3 cm), or that believe it would be better to have the tumor removed and are prepared to accept higher short term and permanent complication rates should seek surgery with an experienced neurosurgeon who routinely performs removals of acoustic neuromas for best results.

SRS and FSR

Current Radiosurgery and Fractionated Stereotactic Radiotherapy Results



Patients should be aware that research articles that are more than five years old in the field of radiosurgery and radiotherapy do not represent current outcomes and methods of treatment. Researchers are constantly refining the techniques and lowering the radiation dose to allow the least amount of permanent side effects and the most preservation of useful hearing, along with maintaining a high tumor growth control rate. Therefore this table has been designed with recent research articles (2001–2003) from well-respected researchers in the field who treat an abundance of acoustic neuroma patients. Long term results exist for Gamma Knife with a range from 17 years in the USA to 30 years world-wide. Fractionated treatments do not have long-term results at this time.

A review of this table shows the following:

- ◆ Gamma Knife or LINAC radiosurgery (one-session) appear to have good useful hearing preservation rates (70–71%).
- ◆ Fractionated radiotherapy with LINAC or Proton Beam have much lower rates of preservation of useful hearing (31–61%).
- ◆ Proton Beam did not provide good results for useful hearing, whether treatment was in one session or fractionated (31–33%).
- ◆ Gamma Knife had substantially lower rates of facial weakness (1–4%) and facial numbness (0–0.5%) compared to permanent facial problems presented in research from one-session radiosurgery LINAC groups (8–18%), Proton Beam groups (9–11%) and fractionated LINAC groups (2–12%).

Conclusion: At this time, the best overall results are obtained with Gamma Knife surgical technology. There appears to be no advantage to fractionated treatments for the patient unless radiosurgery (one-session) with Gamma Knife, or alternatively Linac, is not available.

	Number of Patients	Radiation in Gy	Median Follow-up (Months)	Tumor Growth Control	Facial Weakness (Permanent)	Facial Numbness (Permanent)	Useful Hearing Preserved
Gamma Knife Surgery	190 ¹	12–13 Gy	30	97.1%	1%	0.5%	71%
	97 ²	12–14 Gy	36	97%	4%	0%	70%
LINAC Radiosurgery	44 ³	11–20 Gy	32	98%	8%	18%	71%
	139 ⁴	12.5 Gy	36	93%	12%	10%	Not Reported
Proton Beam Radiosurgery	88 ⁵	12 Gy	38.7	93.6%	9%	11%	33.3%
Fractionated Stereotactic Radiotherapy (FSR), LINAC or Proton Beam (Multiple Sessions)	65 ⁶ LINAC	44–50 Gy (20–23 Fractions)	37	92%	12%	5%	47%
	80 ⁷ LINAC	20 Gy (4–5 Fractions)	33	94%	2%	3%	61%
	29 ⁸ Proton Beam	54–60 Gy (30–33 Fractions)	34	100%	0%	0%	31%

¹ Flickinger JC, Kondziolka D, Niranjan A, Lunsford LD. Results of acoustic neuroma radiosurgery: an analysis of 5 years= experience using current methods. *J Neurosurg* 2001;94(1):1-6. ² Regis J, Pellet W, Delsanti C, et al. Functional outcome after gamma knife surgery or microsurgery for vestibular schwannomas. *J Neurosurg* 2002;97(5):1091-100. ³ Spiegelmann R, Lidar Z, Gofman J, et al. Linear accelerator radiosurgery for vestibular schwannoma. *J Neurosurg* 2001;94(1):7-13. ⁴ Foote KD, Friedman WA, Buatti JM, et al. Analysis of risk factors associated with radiosurgery for vestibular schwannoma. *J Neurosurg* 2001;95(3):440-449. ⁵ Weber DC, Chan AW, Bussiere MR, et al. Proton beam radiosurgery for vestibular schwannoma: tumor control and cranial nerve toxicity. *Neurosurgery* 2003;53(3):577-586. ⁶ Sakamoto T, Shirato H, Takeichi N, et al. Annual rate of hearing loss falls after fractionated stereotactic irradiation for vestibular schwannoma. *Radiother Oncol* 2001;60(1):45-8. ⁷ Meijer OW, Vandertop WP, Baayen JC, Slotman BJ. Single-fraction vs. fractionated linac-based stereotactic radiosurgery for vestibular schwannoma: a single institution study. *Int J Radiat Oncol Biol Phys* 2003;56(5):1390-6. ⁸ Bush DA, McAllister CJ, Loreda LN, et al. Fractionated proton beam radiotherapy for acoustic neuroma. *Neurosurgery* 2002;50(2):270-273.

12 Years After Gamma Knife for Acoustic Neuroma



Editor's note: this story was submitted by Joe, who persevered in his search for treatment alternatives, and whose search for information was the beginning of IRSA. Joe has remained physically active by mountain climbing and building his own cabin with no noticeable deficits from his Gamma Knife surgery. His serviceable hearing is good and he functions without hearing aids.

On April 9, 1992, I was treated with the Gamma Knife for a 2.9 cm acoustic neuroma tumor which was diagnosed by an MRI on February 28, 1992. Over twelve years and two months after radiosurgical intervention, the quality of my life as well as the health of my life are both quite remarkable. However, the road I traveled from pre-treatment to post-treatment intervention was equally as frustrating and challenging.

As acoustic neuromas develop, their growth patterns are slow and, for most patients, symptoms are undetected until such time that the tumor mass is so large that it compromises surrounding healthy tissue. In my case, a slight loss of unilateral hearing was my only symptom which, for years, I reasoned was simply a sign that I was aging. This was reinforced by a number of routine visits to my primary care physician over a two to three year period. As the years went by, additional troublesome symptoms arose, such as vertigo, tinnitus, and an occasional numbness in my right leg. Finally, I convinced my primary care physician to order an MRI which confirmed the presence of the acoustic neuroma. After a brief explanation of the physiology of an acoustic neuroma by my primary care giver, my first reaction was to ask him what treatment intervention should be procured. He responded without hesitation—microsurgical intervention—and provided me with a referral to a local neurosurgeon.

My consultation with the neurosurgeon confirmed the diagnosis and he immediately scheduled the operation which would surgically remove the tumor. The surgeon then referred me to an upcoming meeting of the local chapter of the Acoustic Neuroma Association while reassuring me that the surgical removal of my tumor would be routine and, in all probability, without complications. As I was leaving the exam room with the neurosurgeon I asked if there were any other options that I should consider relative to the treatment of my acoustic neuroma. The surgeon's response was NO... microsurgical intervention was my only option!

Although I was frightened of the unknown, I felt confident in my initial decision to procure surgical removal of the tumor. Everything changed for me, however, as I walked into the conference room two days later where the local chapter of the Acoustic Neuroma Association was conducting its quarterly meeting. Since the surgeon never mentioned the "down side" of open skull intervention—facial palsy, eye problems, total hearing loss—I was unprepared to see a majority of the members in the room exhibiting the above adverse effects of microsurgical inter-

vention. At that moment, I reached a psychological state of mind which best could be defined as a "fight or flight response." I wanted to leave the meeting room, yet I somehow knew that I had to stay and learn from other patients' experiences. On the one hand, I felt I had to maintain an open and rational perspective relative to any and all treatment options, nationally or internationally, if treatment alternatives could potentially improve my odds of avoiding such adverse events. On the other hand, I had the urge to



Joe Mountain Climbing

simply allow others in the group to make the decision for me.

Fear and uncertainty of illness is a powerful response to psychological and/or physical trauma. In such situations, it helps to be with people who have gone through similar experiences. However, the social dynamics of group interaction can sometimes resist new approaches that are counterproductive to the group norms. As I interacted with the members of the

Association they assured me that I would survive, which was not what I wanted to hear. My response was immediate and direct: "What about the quality of my life?" It was clear for those who responded in the group that from their perspective the quality of my life was about to change FOREVER. This was unacceptable to me. I was 44 years old, fully employed, and a single parent with an eight-year-old son who needed a healthy father with an income. Suddenly, the world became my stage. My life revolved around a 24-7 search to find a treatment option that would ensure survival while maintaining the quality of my life. It was apparent to me that the answer would not come from the members of an organization who all had experienced microsurgical intervention. As I continued to seek out a broader representation of post microsurgical patients through the Acoustic Neuroma Association, I became even more frustrated in my search to find balanced information on alternatives to microsurgical intervention.

Within two weeks of my initial diagnosis and meeting with the neurosurgeon, my "fight" response paid off. I learned about the Gamma Knife. I quickly identified and talked with as many people as I could who were treated with the Gamma Knife, both nationally and internationally. For most of these patients, their post radiosurgical intervention stories were much different from those patients who received microsurgical intervention. The quality of these patients' lives, in most cases, was maintained. I concluded after talking with these patients that there was life after being diagnosed with an acoustic neuroma! As I mentioned above, I elected to have radiosurgical intervention on April 9, 1992—one of the single most important decisions of my life. Although the first year post intervention was difficult, I managed to continue to work full time while simply experiencing the joy and challenges of being a father to my eight-year-old son.

The past twelve years have been the most productive in my life. Although no one would ever want to be diagnosed with an acoustic neuroma, the experience has been life changing for me. My attitude and outlook on life was changed forever on February 28, 1992! Survival is temporary for all of us in this world. The ultimate challenge in life is to maintain the quality of our lives within the narrow window of survival that we are granted. I came to the realization through my experience that the quality of my life was equally as important as survival... compromising one over the other was not an option!

Those interested in contacting Dr. Joseph Anderson may call him at 717-732-0611.



Joe with his wife Zella.

The Type of Scan Makes a Difference: MRI Versus CT

CT Scan

Computed tomography (CT) uses X-ray technology to scan a tumor by taking a series of detailed pictures of areas within the brain from different angles. The pictures are then created by a computer linked to an X-ray machine. With CT scanning, the body receives a mild dose of radiation. The resulting CT scan will show bones, bony structures and subtle outlines of some organs.

There are several downsides to using CT scanning technology to perform radiosurgery for an acoustic neuroma. First, the tumor borders cannot be seen well due to artifact from the petrous bone which obscures the tumor image. There can be blurring of the CT images near bone. Second, the tumor within the auditory canal cannot be imaged with CT. Thus, the actual extent and shape of the tumor is not properly identified. Compared to MRI, the precise details of soft tissue (including some deep parts of the brain) are less visible on CT scans. Computed tomography is not sensitive in detecting inflammation of the meninges, which are the membranes covering the brain.

MRI Scan

Magnetic resonance imaging (MRI) is an imaging modality which is primarily used to construct pictures of the signal from the hydrogen atoms in an object. With MRI, the scanner can pick out a very small point inside the brain and determine what type of tissue it is. MRIs provide an unparalleled view inside the human body. Magnetic resonance imaging is the method of choice for the diagnosis of many types of injuries and conditions because of its ability to "see" soft tissue.

Within the brain, the cranial nerves and brain stem are soft tissue and best viewed with MRI. MRI systems can also image flowing blood within the brain. The downside to MRI is that it cannot be used on patients with pacemakers or defibrillators or metal implants in the head (clips, screws, plates, etc.).

CT or MRI Based?

When radiosurgery and radiotherapy use CT scans as the basis of treatment planning and delivery, there will always be some loss of accuracy over using MRI with stereotactic immobilization. If planning occurs on one day and the patient is treated on another, there is loss of precision compared to treatment that is stereotactic, uses MRI and is completed in one session, as with the Gamma Knife. This may contribute to linear accelerator results for tumor growth control, facial deficits and hearing preservation that are not as good as with Gamma Knife technology.

Cobalt⁶⁰ Gamma Knife[®] – MRI based, requiring stereotactic frame immobilization.

LINAC Technology:

CyberKnife[®], Novalis[®], Synergy[®], Trilogy[®] and X-Knife[®] all use CT-based planning and may or may not use stereotactic immobilization and CT MR fusion.

Understanding Terminology

Cerebrospinal Fluid (CSF) Fistula: An abnormal passage permitting the cerebrospinal fluid to leak from the inner spaces of the brain, called ventricles. A CSF leak is usually caused by the trauma of surgery to remove an acoustic neuroma and may leak through the ears, nose, or surgical site, into the body.

FSR: Fractionated stereotactic radiotherapy is where the radiation dose to a tumor is divided into fractions, that are delivered over days or weeks to minimize damage to healthy tissue, nerves, and at-risk structures of the brain. This occurs when limitations of the technology being utilized, or the method of localization for treatment, may allow for overlap of radiation to healthy tissue or other at-risk structures near the tumor area. FSR may be directed by a radiation oncologist without benefit of a neurosurgeon.

Intracanalicular: Within the internal auditory canal.

Radiation: Radiation destroys or slows the development of abnormal cells. Tumor cells will eventually lose the ability to reproduce. This will happen at the rate of the growth of the tumor. A slow growing tumor, such as an acoustic neuroma will die and decrease in size slower than a highly malignant tumor which will react quickly to radiation. Radiation also disables the tumor cell's ability to regulate fluids which may cause edema (swelling).

Resection: Resection is the surgical removal of all or part of a tumor. A conservative resection may be performed on a large acoustic neuroma to 'debulk' the tumor to a smaller size. This would be done to spare damage to one or all of the surrounding cranial nerves allowing radiosurgery to treat the residual tumor that is left.

Residual: Residual is the amount of tumor remaining after a surgical resection.

Stereotactic: This word describes using a computer and a scanning device to create three-dimensional pictures.

SRS: Stereotactic radiosurgery is surgery which involves the use of precisely focused radiation that allows for minimal radiation to healthy tissues, nerves, or at-risk structures of the brain. SRS is always directed by a neurosurgeon.

Acoustic Neuroma Recurrence Rates

Surgery: 10% (Cerullo et al.)
8% (Mazzoni et al.)
16% (Cerullo et al.) Where preservation of the facial and cochlear nerve is a priority

Gamma Knife: 3% (Flickinger et al.)
3% (Regis et al.)

The Myths about Radiosurgery

Surgery will be harder if radiosurgery fails:

Research has been published of the review of 13 cases where the patient had delayed microsurgery at a median of 27 months after radiosurgery. The conclusion was that there was no clear relationship between the use of radiosurgery and the subsequent ease or difficulty of delayed microsurgery, as surgeons' reports found some tumors easier to remove, some were considered about the same and others were difficult. The need for resection following radiosurgery tends to occur when large tumors (>3 cm) with brainstem compression are treated; therefore, a partial resection followed by radiosurgery should be considered for these patients rather than initial treatment with radiosurgery.

Malignant tumor will develop from having radiosurgery:

There is always the risk of development of a malignant schwannoma and this has been known to occur spontaneously, after prior microsurgery, and after irradiation. In the Pittsburgh experience of treating 6400 people with Gamma Knife over 17 years this has not occurred. There are three case reports in world literature that qualify for the criteria of radiation induced malignant tumor after radiosurgery. This makes the actual risk 3 in 20,000 to 50,000. However, the patient is told that there is a risk of 1 in 1000 over the next 5–30 years of life. It is believed that the risk of developing a tumor years after radiosurgery is less than the risk of death (1 in 200) or severe side effects after microsurgery. (Microsurgery: 1:200 risk of death after surgery; Radiosurgery: 1:1000 risk of cancer formation in 20 years.)

Edema from radiosurgery will cause problems:

Edema or swelling (the taking on of fluids) routinely occurs after a trauma to soft tissues. After microsurgery for an acoustic neuroma, there is swelling which will resolve over time. If the edema causes problems for the patient, medications can be used to reduce the swelling. With radiosurgery, the radiation given to the acoustic neuroma disrupts the ability of the tumor cells to continue dividing and growing. This will occur at the rate of the tumor growth—which in the case of an acoustic neuroma is usually very slow. The radiation also disrupts the tumor cells ability to regulate fluids. This can cause edema to be seen on imaging and will appear as an 'enhancement' of the tumor. Not everyone will have edema. Edema is a sign that the radiosurgery treatment is working. The same as with surgery, a course of medications can be given if the swelling is causing the patient to have problems.

Necrosis from radiosurgery will require another surgery:

Necrosis is the death of living tissue, usually from injury. Radiosurgery treatment will cause the cerebral blood vessels and capillaries within the acoustic neuroma to grow thicker and eventually close off, sometimes leaving a mass that is referred to as necrosis. This new dead tissue is carried away over time by an inflammatory reaction of the body. Necrosis will usually occur over six months to two years after radiosurgery for an acoustic neuroma. With proper selection of the patient (tumor size, location, etc.) and the radiation dosage, necrosis is seldom an issue in radiosurgery. In rare cases, the shrunken dead tissue may be an irritant or cause problems to the patient. If the problem does not resolve naturally over time, or cannot be medically managed, then surgery may be required.

Observation?

Acoustic neuromas are usually very slow growing and benign. They are found in a percentage of people upon autopsy who did not have symptoms. The rate of growth may vary (1–2 mm/year, no growth for initial few years then sudden growth, or initial growth of 1–2 mm then no growth for few years). However, if observed for 5–10 years almost all show evidence of growth. Thus observation may be appropriate in the elderly age group or for people with significant medical problems.

- ◆ Age >75: No or mild brain stem compression.
- ◆ Age <75: No documented tumor growth, No or mild brain stem compression, Incidental finding of intracanalicular tumor.

After Treatment Imaging Schedules

After surgery or radiosurgery, patients should be closely followed to assess swelling, regrowth, and residual tumor issues. Many surgical patients state they are not rescanned for 2–3 years after tumor removal. If there is tumor growth or problems with the residual tumor, a long wait may mean that the patient has lost the chance to choose radiosurgery and must undergo surgery again. More permanent side effects can also result from regrowth that is not followed closely. Centers of Excellence have provided the following imaging schedule as a standard regardless of the type of treatment chosen.

MRI: 6, 12, 24, 48 and 96 months

Five Most Common Presenting Symptoms

- ◆ Hearing Loss 98%
- ◆ Tinnitus 70%
- ◆ Balance or Vertigo 67%
- ◆ Headaches 32%
- ◆ Facial Problems 39%



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(The International RadioSurgery Association) is an independent 501(c)3 non-profit organization dedicated to providing information to patients, physicians, insurers, and government agencies through education about radiosurgery treatment and its availability.

The Association is instrumental in promoting the development of evidence based guidelines that have appropriate recommendations for radiosurgery treatment options. Currently, IRSA receives over 180,000 inquiries annually.

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