Radiosurgery of Intracranial Lesions

by John S. Yu, Anne Luptrawan,
Robert E. Wallace, and Behrooz Hakimian

CEDARS-SINAI MEDICAL CENTER®
Gamma Knife Center at the
Samuel Oschin Comprehensive Cancer Institute

In 1951 Swedish neurosurgeon Lars Leksell coined the term radiosurgery to denote a noninvasive technique that precisely delivers a single high dose of radiation to a targeted area of brain through an intact skull. The desired biological effect of radiosurgery is the destruction of a targeted area in the brain while avoiding nearby normal tissue and critical structures. Leksell, along with biophysicist Dr. Borje Larsson, introduced the first gamma knife in Europe in 1968. Radiosurgery can be performed using two devices: gamma knife and linear accelerator. Photon and proton beam radiation are two forms of radiation sources used to perform stereotactic radiosurgery.

◆ Gamma Knife Radiosurgery

Gamma knife is a multisource photon-based device that houses 201 fixed cobalt-60 sources. Cobalt-60 emits gamma ray photons. These photons travel as high-energy beams and are delivered at a predictable and easily quantifiable rate. The gamma knife device allows precise delivery of radiation to a target. The cobalt-60 sources deliver 201 separate beams of radiation, which converge onto a predetermined central target. Only at the point where these beams cross is radiation delivered high enough to effectively destroy the cells of the abnormal brain lesion. The amplitude of radiation at this point of convergence is so high that it allows for “scalpel-like” precision. The targeted tissue absorbs the radiation, leading to cell death. This process of cell death occurs over time, usually weeks to months. The end result of treatment is typically shrinkage of the lesion, halting further growth of the lesion or causing total obliteration of the lesion. When used with a stereotactic head frame, the precision of radiation delivery is 0.3 mm.

The radiobiological effect of gamma knife radiosurgery is different from that of conventional fractionated radiotherapy. Conventional radiotherapy usually involves the delivery of large volumes of irradiation, which may deliver radiation to normal brain tissue. Conventional radiotherapy also includes fractionated radiotherapy, which involves fractionation or dividing radiation treatment into multiple smaller daily doses. Normal brain tissue can tolerate fractionated radiation but it is not tolerated by the brain tumor, which results in the control of tumor growth. Gamma knife radiosurgery, on the other hand, delivers the entire dose of radiation in a single sitting. In fact, a single given dose with the gamma knife produces three times the biological effectiveness as the same dose in fractionated radiation. Inhomogeneity of the radiation dose is another inherent characteristic of gamma knife radiosurgery. This results in the delivery of radiation at the center of the tumor that is twice the dose delivered at the tumor periphery.

◆ Modified Linear Accelerator Radiosurgery

The linear accelerator (linac) is another radiosurgery tool used to effectively treat brain lesions. Unlike a natural emission of gamma ray photons produced by the gamma knife cobalt-60 sources, photons are created via the linac by accelerating electrons along a linear path and colliding with a metal target. The single stream of photon radiation simulates multiple stationary beams by using multiple noncoplanar arcs around the patient’s head while the patient rotates on a turntable (couch) in each of four positions. Multiple beams of radiation can also be shaped with multileaved collimators to treat complex-shaped lesions.

Linac radiosurgery delivers very precise and uniform irradiation, but unlike the gamma knife, it allows for fractionation of treatment. Fractionation of treatment divides treatments into multiple sessions using smaller doses, or fractions, of radiation. This treatment strategy is referred to as stereotactic radiotherapy. Fractionation allows for treatment of larger lesions and lesions that are intrinsically part of a critical structure while minimizing effects on surrounding normal brain as compared with the gamma knife. Radiosurgery using the linac device can be more cost-effective as compared with gamma knife, particularly if institutions already use linacs for other applications.

◆ Patient Selection

Radiosurgery is considered an effective alternative treatment to conventional surgery and radiation therapy. It is an effective treatment option for patients who are considered highrisk candidates for conventional surgery. High-risk patients are those who are at high general anesthesia risk, too ill to undergo conventional surgery, or have lesions that are considered inoperable due to inaccessibility. Radiosurgery has been shown to safely and effectively treat patients with intracranial lesions that are considered inoperable using conventional surgery techniques. It is also an effective option for patients who have failed other forms of treatment, including conventional open surgery, conventional radiotherapy, and chemotherapy. At the same time, radiosurgery may be utilized in conjunction with conventional surgery and radiotherapy, especially for patients with aggressive conditions. Radiosurgery is increasingly used as first-line therapy for benign tumors, such as acoustic neuromas and meningiomas due to the efficacy in tumor control.

Radiosurgery treatment of intracranial lesions is limited primarily by size. Patients with lesions measuring greater than 3.5 to 4.0 cm are not appropriate candidates for radiosurgery because treatment runs the risk of delivering an excessive amount of radiation to surrounding normal brain tissue.

The goals of stereotactic radiosurgery are to prevent tumor recurrence, maintain patient function, and prevent occurrence of new neurologic deficits or adverse radiation effects. Another aim of radiosurgery is to deliver a more localized sphere of high-dose irradiation than would be achieved with conventional radiotherapy. Radiosurgery reduces the risk to nearby healthy brain tissue and cranial nerves, allows for treatment near critical areas such as the brain stem and optic chiasm, and allows for safe treatment of large lesions up to 4.0 cm.

The most common clinical indications for the use of stereotactic radiosurgery include management of benign brain tumors such as meningiomas, acousticneuromas, craniopharyngiomas, and pituitary tumors; malignant tumors such as primary and recurrent gliomas, metastatic tumors, arteriovenous malformations (AVMs); functional disorders such as trigeminal neuralgia; and movement disorders.

Meningiomas

Radiosurgery is an effective alternative to surgical resection for the treatment of well–circumscribed, small, benign, intracranial meningiomas. After treatment with gamma knife, 53 to 74% of meningiomas decreased in volume, 17 to 40% had no enlargement, and only 7 to 9% had increased in volume.

Vestibular Schwannomas (Acoustic Neuromas)

Radiosurgery has been shown to effectively control the growth of acoustic neuromas. After gamma knife radiosurgery, tumor regression was 32 to 73%, no growth in tumor size was 25.5 to 59%, and only 1.9 to 3% of patients had increase in growth and underwent conventional surgery after radiosurgery. Overall tumor control rate after gamma knife radiosurgery was 92%.

Pituitary Tumors

Radiosurgery is safe and effective therapy for patients with pituitary tumors. After radiosurgery, 29 to 50% of patients had a decrease in tumor volume, 36 to 67% showed no change in tumor size, and 14% showed an increase in tumor size.

Craniopharyngiomas

Radiosurgery is being used increasingly as an adjunct to other therapies to treat craniopharyngiomas. In one series, volume reduction of residual tumor after treatment with bleomycin was noted in 74% of patients. In another series, tumor control was achieved in 87%, and 84% had fair to excellent clinical outcome in an average follow-up period of 36 months, when cysts were treated with adjuvant stereotactic aspiration and/or Ommaya reservoir implantation prior to radiosurgery. In a study of eight patients who underwent stereotactic neuroendoscopy and subsequent treatment with intracavitary bleomycin and radiosurgery, a reduction of the entire tumor volume of greater than 90% was observed in three of eight cases and reduction greater than 50% in four of eight cases.

Trigeminal Neuralgia

Radiosurgery is a safe and effective way to treat the pain associated with trigeminal neuralgia. After treatment with radiosurgery for medically refractory trigeminal neuralgia, 40 to 51.2% of patients reported excellent pain control and 17.1 to 30% reported good control. A decrease in pain medication usage was noted in 66% of patients. Recurrence of pain/treatment failure was reported in 23.9 13 to 30% of patients.

Arteriovenous Malformations

The treatment of AVMs using radiosurgery is both effective and well tolerated. Several series showed obliteration rates of AVMs to be between 77 and 81.3% on follow-up angiography. In a retrospective study of 118 patients treated with radiosurgery hemorrhage occurred in 6% of patients.

Malignant Primary Brain Tumors

Radiosurgery is typically adjunctive therapy for malignant primary brain tumors and has been shown to be clinically effective and safe in improving patient outcomes. Some publications have demonstrated increasing likelihood of local tumor control and prolongation in overall survival. Standard management of malignant primary brain tumors such as glioblastomas and grade 3 anaplastic astrocytomas is open surgical resection, with the goal of resecting as much tumor as safely possible, and subsequent postoperative external beam radiotherapy (EBRT). However, because of the aggressive nature of malignant gliomas (overall survival is 1 year for glioblastomas, and 2 to 3 years for anaplastic astrocytomas), patients continue to experience tumor recurrence even after high doses of EBRT. Brachytherapy and stereotactic radiosurgery are two approaches currently utilized to deliver higher doses of radiation to the tumor bed; controlling and slowing tumor growth in malignant gliomas. However, radiation boost via brachytherapy (temporary implants that deliver radiation to the tumor bed) is associated with prolonged hospital stay and higher rates of radiation necrosis. Because of increasing availability and less invasive means, radiosurgery is progressively replacing brachytherapy, with promising results.

Presently, the most common role of the gamma knife in the treatment of malignant gliomas is to provide a radiation boost in addition to conventional radiation therapy. In a series of 31 glioblastoma patients treated with EBRT plus gamma knife radiosurgery boost, an overall survival of 25 months was produced, compared with an overall survival of 13 months when patients received EBRT alone.

Metastatic Tumors

Radiosurgery is effective in controlling metastatic brain tumors and is considered a safe and effective treatment option. Brain metastases are excellent targets for radiosurgery because these tumors are usually spherical, small, and well demarcated from the surrounding normal brain tissue, unlike primary brain tumors. Forty percent of patients treated with radiosurgery demonstrated no further growth, 30% of patients demonstrated a decrease in tumor size, and 20% of patients demonstrated virtual disappearance of the tumor. Treatment of multiple brain metastases with gamma knife radiosurgery produces median survival rates similar to patients treated for a single metastasis.

◆ Contraindications to Gamma Knife Radiosurgery

Gamma knife radiosurgery is contraindicated in a tumor or lesion size greater than 4.0 cm in maximum diameter and a tumor or lesion edge less than 3 mm from the optic chiasm.

◆ Alternatives to Radiosurgery

Alternatives to radiosurgery should be discussed with each patient. Taking into consideration the patient's neurological problem, these include conventional open brain surgery, conventional radiation therapy, and fractionated stereotactic radiotherapy using a linac or gamma knife. The option not to undergo any treatment should also be presented to the patient. These treatment options along with their risks and benefits should be discussed with each patient considering radiosurgery.

◆ Preoperative Management and Operative Procedure

Gamma Knife Radiosurgery

Gamma knife radiosurgery is typically performed on an outpatient basis. The procedure involves 3 to 4 hours. However, the age of cobalt-60 sources (decay with a half-life of 5 years), dose of radiation to be delivered, size of the patient's head, and tumor location play a role in the total actual treatment time. Duration of treatment usually ranges from 10 to 60 minutes. Large or irregularly shaped lesions usually require more than one gamma knife exposure. These "multiple isocenters" are delivered sequentially during a single sitting.

Linear Accelerator–Based Radiosurgery

Placement of Stereotactic Head Frame

If the patient is anxious a mild sedative 30 minutes prior to placement of the stereotactic head frame may be helpful. Placement of the stereotactic head frame is performed by a neurosurgeon. The neurosurgeon fits the patient for the appropriate-sized Cosman-Roberts-Wells (CRW) stereotactic head frame. The head frame provides regional immobilization holding the head still during the procedure and creating a fixed target. The stereotactic head frame also functions to provide the team with a set of exact coordinates to precisely target the lesion. The head frame is made of aluminum alloy and is relatively light in weight.

The head frame has four sites where it is attached to the skull with mounting pins. Before attaching the head frame, two frontal and two occipital sites are prepped with Betadine and injected intradermally with a local anesthetic. The patient will feel pressure as the pins are secured; however, if the patient complains of sharp pain, more local anesthetic should be administered. The neurosurgeon places two frontal and two occipital pins to immobilize the frame. Skull fractures have been known to occur if pins are secured too tightly.

Image Acquisition and Computerized Dose Planning

After the head frame is secured, image acquisition computed tomographic (CT) scan or angiography is performed. The type of study obtained is determined by the type of lesion: CT scan is indicated for tumors, angiography is indicated for AVMs or other vascular lesions. Image acquisition is necessary at this stage to identify the exact location and size of the intracranial lesion to be treated. These images are then fused with magnetic resonance (MR) images that were obtained previously. The following describes the process for stereotactic radiosurgery (SRS) in which high-energy x-ray treatment is delivered in one session. The course of events for multiple-session (on sequential days) stereotactic radiotherapy (SRT), follows the same steps over several days. On the treatment day, the surgeon affixes to the patient's head a rigid stereotactic frame (i.e., Brown-Roberts-Wells (BRW)/CRW for SRS) (**Fig. 15–1**). For SRT, this device is a relocatable frame (i.e., Gill-Thomas Cosman [Integra Radionics, Inc., Burlington, MA 01803] frame) allowing reproducible positioning for each of the sequential treatment sessions. The frame establishes the absolute coordinate system for treatment, to which all radiation beam orientations and motions are related. CT scans are taken in the position fixed by the connection of the rigid frame to the imaging couch, and prior MR (or other) images are fused to the CT using mutual information technologies. The three-dimensional (3-D) CT image set provides an accurate spatial description of the patient as well as the spatial distribution of electrons with which the high-energy x-rays interact to deliver the dose. MR images (and other image types) are used to discriminate radiation targets (benign and malignant tumors or other structures) from normal and eloquent anatomy. Fusion maps this MR information onto the spatially accurate CT images. To image tumors, typical MR specifications are 2 to 3 mm thick slices with no gaps, T1 weighting, and postcontrast image acquisition, and follow specifications particular to the neurosurgical interest. The CT image axial planes are imaged using a fiducial system that allows direct mapping of the location of CT (and MR) pixels into the stereotactic coordinate system of the rigid head frame. An attachment system, symmetrical to that on the CT, connects the rigid head frame to the therapy

Figure 15–1 Patient after placement of stereotactic head frame and undergoing stereotactic radiosurgery treatment with linear accelerator.

radiation machine and thereby establishes the mapping between the stereotactic coordinate system and the orientation and motion of the radiation beams used in treatment. So the use of rigid attachment of the patient's head to a frame, a CT scanner, and a treatment machine allows the development of a plan for therapy that will be as precise as these connections allow. Using specialized equipment, the mechanical stability of the frame attachment to the patient's head is evaluated upon its placement and just prior to treatment to establish that there had been no movement of the frame while the patient waited for treatment. The mechanical accuracy of the fiducial device is subpixel size for a modern CT scanner. The mechanical accuracy of the aim of the treatment machine is verified prior to treatment and has magnitude depending on the radiation system in use. Typically, this is on the order of one fourth to one third of a millimeter. This is done using a system of film and a precise mechanical apparatus. Similarly, the accuracy of the image fusion is important in defining the radiation targets. Modern mutual information algorithms can reduce the imprecision to submillimeter pixel dimensions. The net uncertainty in the position, or more important, the border of a target or an important normal tissue structure, is then on the order of 1 mm with attention paid to technique. Mechanical alignment and its quality assurance are integral to maintaining the integrity of the stereotaxy. Other sources of uncertainty in target position derive from the ambiguity in target definition in the images, particularly with regard to different image interpretation among a group of observers/ readers.

The CT and MR images, and identified targets and normal anatomy (to "miss"), having been established in the stereotactic space, a computer-aided radiation therapy design system is used to plan the treatment. The orientation and possible motions of radiation beams to treat the target(s) are evaluated interactively. The 3-D distribution of the radiation dose is predicted for a given proposed beam arrangement and the doses to identified structures can be evaluated in 3-D detail. To do this, a radiation and mechanical model of the treatment machine and adjunct stereotactic accessories are maintained in the treatment planning program. The relationships among the head frame stereotactic coordinates, those of CT and MR images, and those of the treatment machine are captured in the planning program via the CT fiducial device. The accuracy of the treatment planning software in predicting dose is maintained through standardized and legally mandated quality assurance of the radiation-producing machines. Furthermore, an independent method is used to certify the calculations for each particular treatment.

Once the planning is completed, the information that describes the steps to administer the radiation is transferred to a database/control system to ensure that treatment occurs as planned. Prior to treatment, the patient is attached to the treatment machine couch using the rigid frame attachment, reproducing that of the CT and planning. During treatment, radiation therapist downloads the parameters stored for the patient under treatment, checks that these are for the correct patient, makes adjustments for the direction and motion of the machine, and engages radiation for the radiation fields dictated by the plan. After treatment, the patient is detached from the treatment couch, and the rigid head frame is removed.

The use of modern linacs in radiosurgery allows the treatment of odd-shaped tumors using shaped fields. More traditional spheroidal targets, common in gamma knife therapies, are also possible using circular field "cones" that move about the target at a fixed distance, along an arc of a circle. An example of shaped fields is shown in **Fig. 15–2A–C**, where a meningioma is shown treated with 10 conformal radiation fields. **Fig. 15–2A** shows the 3-D volume of the prescription dose in the upper left panel, and the 3-D dose distributions in each of three principal planes through a central point in the tumor. **Fig. 15–2B** depicts the planned shape of one of the 10 fields and **Fig. 15–2C** is a predicted transmission x-ray with the target and field indicated. Each of these figures is used in planning, either to shape the field or to evaluate the planned distribution of radiation dose. In particular, aside from the directions and relative intensity ("weight") of planned treatment fields, the display in **Fig. 15–2B** allows the manipulation of the beam-shaping leaves of the treatment machine (shown as the yellow and blue bars in the figure). By moving these, a planner can evaluate the effects of leaf position on desired/ desirable dose to the target. Noncoplanar arcs or radiation using circular beams of radiation are used for smaller and more spherical targets such as metastatic brain tumors.

◆ Postoperative Management

After the treatment is complete, the head frame is removed. Bleeding from the pin sites is common. Applying gauze and pressure should halt the bleeding. Occasionally, patients may experience headaches or nausea. Analgesics such as acetaminophen and antiemetics may be given before the patient is discharged home. The use of steroids is case- and physician-specific.

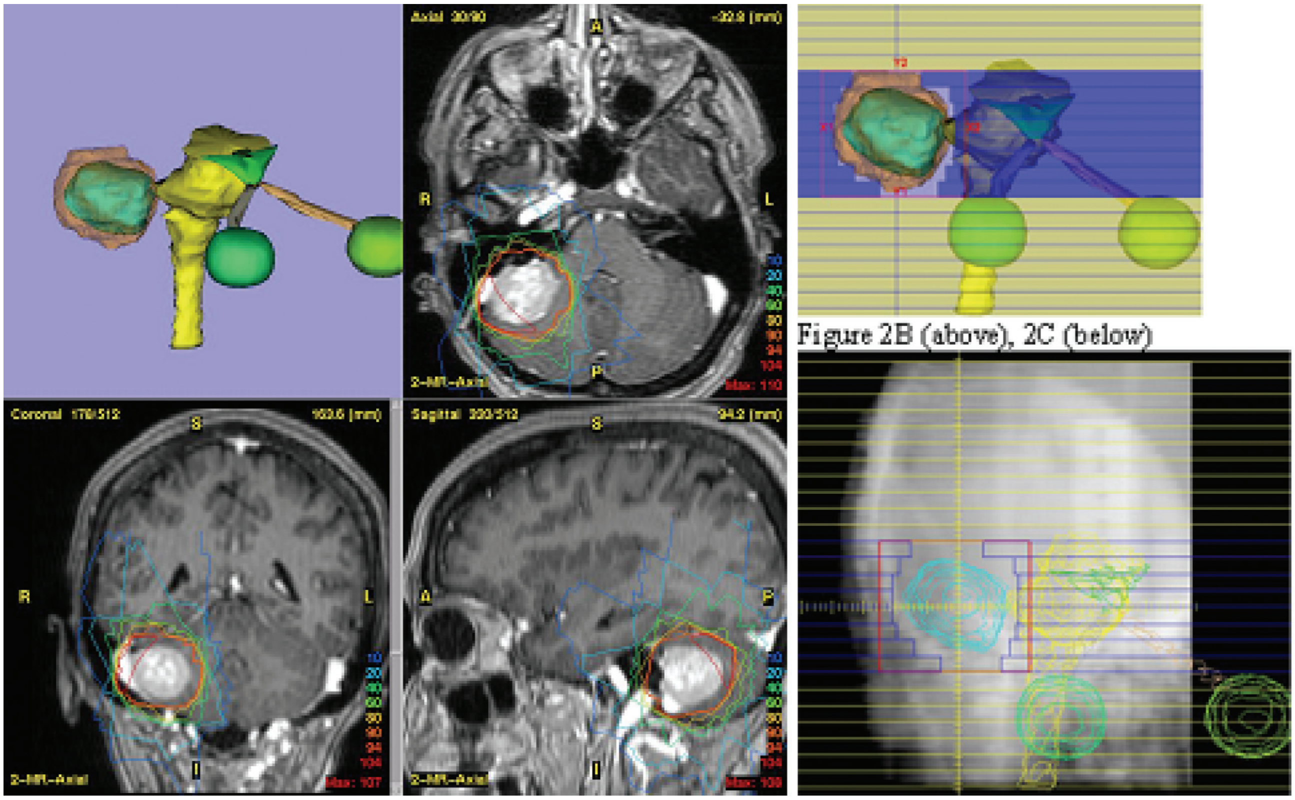

Figure 15–2 An example of shaped fields where a meningioma is shown treated with 10 conformal radiation fields. (A) The three-dimensional (3-D) volume of the prescription dose in the upper left panel, and the 3-D dose distributions in each of three principal planes through a central point in the tumor. (B) The planned shape of one of the 10 fields. (C) Predicted transmission x-ray with the target and field indicated.

◆ Complications

Radiosurgery is designed to deliver a high dose of radiation to a small area in the brain. It has been successfully used in the past 40 years, treating many benign and malignant brain tumors successfully. The use of linac– and gamma knife–based radiosurgery has made this modality more popular and the utility has significantly increased. With this in mind, one should use radiosurgery judiciously because many patients with benign tumors will live a normal life, and complications can be devastating if they happen. Delivery of excessive amounts of radiation to normal brain tissue is a potential complication of radiosurgery. Radiation reactions and radiation necrosis are two primary types of complications that may occur after treatment with radiosurgery. Radiation reactions appear as hyperintense signal areas surrounding the originally treated lesion (perilesional) on T2-weighted MR images and are more suggestive of a glial inflammatory response rather than true edema. Clinical symptoms of perilesional radiation reactions usually occur with reactions in eloquent areas of the brain such as in speech areas and the internal capsule. Treatment for symptomatic radiation reactions is corticosteroids such as dexamethasone. Radiation reactions rarely produce neurological deficits because most subside over time. The occurrence of radiation reactions is largely dose dependent, with an increased likelihood of complications occurring with higher doses of radiation.

A more serious reaction to radiosurgery is radiation necrosis. Radiation necrosis is a result of either death of tumor cells and associated reaction in surrounding normal brain tissue, or necrosis of normal brain tissue surrounding previously treated metastatic brain tumor. Twenty to 25% of patients with primary malignant brain tumors treated with gamma knife radiosurgery experienced radiation necrosis. If significant clinical symptoms persist despite treatment with corticosteroids, surgical resection of the area of severe radiation reaction or necrosis would be indicated to improve the patient's quality of life.

In general, one should decrease the total dose delivered in a single fraction as the irradiated volume increases. The dose-volume histogram should be looked at to decide whether the dose intended to an area is safe or even warranted. The reported data indicate that the risk of necrosis is anywhere from 1 to 7% in the patients treated for brain metastasis. Most studies indicated a range of 3 to 4%. Of course not everyone with radiological abnormality of necrosis requires treatment. Gerosa et al reported a necrosis rate of 7% for treatment of variably sized and histological metastatic disease. They also reported some of the longer median survivals for patients with metastatic diseases. In addition many of these patients may require whole brain radiation therapy, and with no doubt this could explain the risk of this magnitude. As indicated, this risk is dose and volume dependent. With the aggressive nature of metastatic tumors, even this high risk should be acceptable.

Although the risk of necrosis for malignant tumors may be acceptable, it would be difficult to justify this risk in patients with benign diseases. Fortunately, benign diseases, in general, require a lower dose of radiation for optimal control. Although acoustic neuromas were being treated with doses of 15 Gy in the past with gamma knife, the doses used are now on the order of 12.5 to 13 Gy. It is invariably noted that meningiomas close to the optic nerve or skull base may require doses that will exceed the tolerance doses of the cranial nerves. Single-fraction radiosurgery often limits the dose to these structures and could potentially underdose these most critical areas. Fractionated stereotactic radiotherapy is being used to treat these regions with excellent control and minimal risk to these structures. More conventional dose regimens of 1.8 to 2 Gy/fraction for a total of 50 to 54 Gy have shown excellent control of the tumor without any significant morbidity. Selch et al, in review of 45 patients treated with fractionated stereotactic radiotherapy, reported minimal acute side effects. They also reported one patient with cerebrovascular accident 6 months after completion of the treatment. None of the patients in this publication reported long-term neuropathy, tumor edema, cognitive dysfunction, endocrine dysfunction, or secondary malignancy.

◆ Conclusion

As described here, radiosurgery can be utilized successfully to treat numerous neurosurgical conditions. Its induction into the neurosurgical armamentarium has largely replaced conventional microsurgery and radiotherapy with documented clinical efficacy. The utilization of radiosurgery for the treatment of intracranial lesions as we have discussed is effective, safe, and cost-effective and has been shown to improve patient outcomes and prolong overall survival. However, radiosurgery should be used judiciously because many patients with benign tumors will live a normal life, and complications can be devastating if they occur.

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CEDARS-SINAI MEDICAL CENTER®

Gamma Knife Center at the
Samuel Oschin Comprehensive Cancer Institute

Cedars-Sinai Medical Center
8700 Beverly Blvd
Los Angeles, CA 90048
Phone: (310) (310) 423-9888
Fax: (310) 659-3332
www.cedars-sinai.edu/gammaknife