RADIOSURGERY : A LITERATURE REVIEW

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ABSTRACT

Radiosurgery will be performed in Thailand soon, both in the government and private section. A literature review, concerning general introduction, physics and indication was presented.

INTRODUCTION

In 1951, Leksell first described stereotactic radiosurgery (1,2). He took his 1949 first generation stereotactic guiding device and coupled it to an orthovoltage x-ray tube capable of being rotated into arc planes around a patient's head (1-3). He irradiated the gasserian ganglion of several patients with trigeminal neuralgia. These patients maintained long-term successful pain control without the need for further surgery. Lars Leksell was a professor of neurological surgery at the Karolinska institute in Stockholm.

In 1954, John Lawrence, working with the California Berkeley cyclotron initiated charged particle irradiation of the pituitary gland to suppress pain in patients with metastatic breast cancer (1,4). The first thirty patients were treated using the Bragg peak principle of the proton beam, but all patients thereafter were treated using the helium ion beam.

In 1959, Raymond Kjellberg initiated Bragg peak proton beam stereotactic irradiation at the Boston (Havard) cyclotron unit (4).

The technical and time-consuming aspects of proton irradiation proved frustrating. In 1967, Leksell and his colleagues completed the development of the first neurosurgical stereotactic radiosurgical tool, the Gamma Knife (1,5,6). This prototype 179 multisource cobalt-60 unit was designed intentionally to produce small, discoid-shaped lesions in deep-seated white matter tracts or brain nuclei. The first reported patient treated in 1967 had a craniopharyngioma (5). The application of Gamma Knife radiosurgery to destroy vascular malformations or small brain tumors began in the Karolinska hospital in the 1970's (6). Leksell completed the installation of a redesigned second-generation gamma unit in the same hospital. The collimators produced a more spherical irradiation field. Radiosurgery for carefully selected vascular malformations, acoustic neuromas, pituitary tumors, and craniopharyngiomas (1,6) was then performed. Leksell hesitated to advocate radiosurgery for malignant neoplasms because he was concerned that the biological behavior of such tumors was inherently so poor that radiosurgery might not offer great hope and the number of patients with benign tumors, vascular malformations or functional disorders was large and access to the device was limited.

The 1980 saw an explosive growth in the development of stereotactic radiosurgical techniques at many sites around the world. Fabrikant in Berkely (1980) began to use the helium ion beam technique for vascular malformation (1,7). In 1980, radiosurgery was performed at two U.S. cyclotron units (Boston and Berkeley), at two gamma units and at a number of medical cyclotrons units in the Soviet Union.

The photon destruction or inactivation of a small brain tumor or vascular malformation, using

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newer generation stereotactic devices coupled with widely available medical linear accelerators, was pioneered by Betti and Derechninsky, working in Paris and Beunos Aires in 1982 (8), and by Columbo, working in Vicenza, Italy also in 1982 (9). Barcia-Salorio reported their modification of fractionated cobalt irradiation of carotid-cavernous fistulas (10). Winston and Lutz in Boston began to adapt their linear accelerator to a widely available stereotactic guiding device in 1987 (1,11).

In 1984, Bunge arranged for the construction in Switzerland of a newly designed third-generation gamma unit. It was subsequently installed in Buenos Aires. A fourth Gamma Knife was installed in Sheffield, England, in 1985 (12).

A commitment to undertake radiosurgery at a given center requires the dedication of time, personnel, resources, financing, and the expertise of a well-trained team (1). By mid-1992, more than 32 gamma units were in operation at a wide variety of medical centers in Europe, Asia, North America, and South America.

Stereotactic radiosurgery represents a merger of clinical disciplines (neurological surgery, radiation oncology, radiology, medical physics, and engineering).

RADIATION PHYSICS FOR RADIOSURGERY

Three general approaches to radiosurgery are employed today (1,13). The oldest utilizes positively charged particles like protons or helium ions from large accelerators that were originally built for nuclear physics research. The second approach, the Gamma Knife, makes use of the gamma radiation emitted from a fixed array of small cobalt-60 sources located within a large hemisphere that surrounds the patient's head. The third and most recent addition to radiosurgery techniques utilizes high energy x-ray radiation produced by the medical linear accerelator (LINAC) found in radiation oncology departments in most major hospitals.

Every radiosurgery system uses some type of sterotactic apparatus that is securely attached to the patient's head. This attached apparatus provides a coordinate system reference frame for determining the target location, a means of precise positioning for treatment, and a method of head immobilization during treatment.

Positively charged particle accelerators used for radiosurgery are generally either cyclotrons or synchrotrons. Both need the combined effects of electric and magnetic fields to produce beams of high-energy particles. Magnetic fields deflect charged particles and confine them to circular paths without changing their speed or energy. Once or twice in each orbit the charged particle passes through a strong electric field, which gives the particle a speed and energy boost.

The Gamma Knife utilizes 201 cobalt-60 sources distributed over the surface to a sphere 40 cm in radius. The sources, which emit gamma rays in all directions, are collimated and shielded, so that only the radiation directed toward the center of this spherical distribution of sources becomes the geometric focus of gamma rays from all 201 sources. The patient is positioned for treatment so that the center of the intracranial target and the center of the spherical distribution of sources coincide.

Cobalt-60 is an artifically made radioactive nuclide that is produced by exposing naturally occurring, stable cobalt-59 to neutrons in a nuclear reactor, where the cobalt-59 absorbs on neutron to become cobalt-60. The radioactive cobalt-60 decays to stable nickel-60 by emitting an electron from its nucleus followed by two relatively high-energy 1.2- and 1.3- Mev gamma rays (1 Mev=1 million electron volts and is a common unit of energy). The electron is absorbed within the source and plays no therapeutic role. Cobalt-60 has a half-life of 5.3 years. Gamma Knife unit therefore requires periodic replacement (i.e. every 5 to 10 years) of their radioactive sources.

High-energy-x-ray or photon beams produced by medical LINACs are available in virtually all radiation oncology departments. Production of these high energy x-rays, called bremsstrahlung radiation, by LINACs can be viewed as a two-step process. First electrons are accelerated to fixed high energy (e.g. 6 Mev) by strong electric fields generated by microwave power. This monoenergetic electron beam is focused onto a heavy metal (e.g. tungsten) target. The incident electrons are abruptly slowed down and stopped by collisions with the electrons and nuclei of the tungsten atoms in the target. During a collision with a nucleus, all or part of the incident electron's energy may be converted into a photon (called a bremsstrahlung x-ray). Most of the bremsstrahlung x-rays produced are directed nearly parallel to the original direction of the electron beam.

Collimation distal to the target determines the size of the treatment field.

The goal of radiosurgery is to deliver a high dose of radiation to the target while sharply minimizing the dose to the surrounding tissue. This is accomplished by firing multiple beams at the target that are incident from different directions. This strategy is most effective for small targets. As the targets, and treatment beams, increase in size, the dose fall-off immediately outside the target becomes more gradual. This is inescapable and applies to all radiosurgery techniques.

The concentration of dose within a radiosurgery target by the Gamma Knife is accomplished by directing 201 well-collimated individual cobalt-60 gamma ray beams toward a common point called the isocenter. These beams enter the head over an area covering approximately half of the upper hemisphere of the skull. Circular fields with four diameters are available: 4,8,14, and 18 mm. The shape of the isodose lines can be altered somewhat to provide better target coverage by selectively blocking some of the 201 beams. When all beams are used, the isodose surfaces are egg-shaped, elongated in the patient's superior-inferior direction. With the central one-third of the beams blocked, the isodose surfaces near the target become more spherical. Other isodense surface shapes may be produced by selective beam blocking. Beams may also be selectively blocked to minimize the dose delivered to critical structures that lie outside the target. For targets too large to be accomodated by the 18-mm beams or that are irregularly shaped, multiple isocenters are needed. Ideally, if one isocenter is to be used, the dimensions of the target should be slightly less than the diameter of the beam. In multiple-isocenter treatments, successive courses of radiation are directed to different points within the target. Up to 12 isocenters have been used. Large and irregularly shaped targets can be well covered this way. The potentially difficulty with this technique, apart from the increased treatment time, is that the individual sphere-like isodose surfaces do not stack together evenly, resulting in very nonuniforming dose deposition within the target.

For medical LINACs, the patient is supported supine on the treatment couch. By making use of two intersecting axes of rotation and by putting the center of the target at this intersection point, beam entry points over the entire upper hemisphere of the skull can be accessed. The turntable axis rotates the couch (patient and target), whereas the gantry axis rotates the x-ray beam. If x-rays are directed into the head while the gantry is rotating at each of four stationary couch positions, the central line of the beam might trace out paths. These paths and the radiation intensity along them can be altered to help the dose distribution conform better to the target and to reduce the dose to critical structures outside the target. This procedure is directly analogous to the blocking of beams in the Gamma Knife. Circular beams ranging from 10 to 50 mm in diameter have been in common use with LINAC radiosurgery. Because of the large field sizes available, multiple isocenters are used much less frequently than with Gamma Knife. Multiple isocenters are reserved primarily for irregularly shaped targets. Nonuniform dose deposition within the target is a natural consequence of multiple-isocenter use. On the other hand, using large diameter beams and a single isocenter to treat irregularly shaped targets will generally result in more normal tissue receiving higher doses than if well planned, multiple isocenters with smaller diameter are used. It is possible that the use of five or six individually shaped, fixed direction beams, similar to the charged partical strategy, will be the best way to treat relatively large, irregularly shaped targets.

Overview of treatment planning tasks and comparison between the different technique (1).

Task	Heavy Particles	Gamma Knife	LINAC
Imaging	CT, MRI, and angiography, PET, SPECT (mathematically correlated with spatially high-resolution images), and MEG for localization of functional abnormalities and metabolic activity.		
Fixation	Cranially fixated headframes: BRW, Leksell, Fischer, etc.		
	Cranial head frame or bite block		Repeat localization headframes and cranial markers
Patient positioning	Relative to markers or mechannically calibrated to headframe.	Mechanically calibrated positioning of focal or isocenter point to headframe	
Patient verification	X-ray verification of cranial landmarks or markers in treatment position	Patient position occluded by device treatment position	Port film or mechanical verification in treatment position
Beam alignment	Calibrated with respect to headframe		
Field shaping	Multiple static fields. Customized three-dimensional shaping to target volume possible	Multiple shots or targets positioned in target volume. Aperture size adjustable per treatment position. Treatment at a single position results in a nearly spherical treatment volume.	
Normalization	90-95%	50 %	80%
		Poor dose uniformity for multiple shots	
Software	Custom	Commercial/custom	
Entrance dose	Depends on number of static fields, $\leq$ 30%	Negligible except for superficial lesions	

Abbreviations: PET = positron emission tomography; SPECT = single photon emission computed tomography; MEG = magnetoencephalography.

Three-dimensional treatment planning for stereotactic radiosurgery: device properties (1)

<table>
<tr><th>Property</th><th>Heavy Particles</th><th>Gamma Knife</th><th>LINAC</th></tr>
<tr><td>Beam</td><td>Protons, π - mesons, or helium and neon ions</td><td>Photons</td><td></td></tr>
<tr><td>Energy</td><td>70-250 MeV (range, 5-32 g/cm^2, protons)</td><td>Cobalt 60 ($\approx$ 1.2 MeV)</td><td>4-to 20-MV photons.</td></tr>
<tr><td>Focusing</td><td>Multiple Bragg peaks superpositioned in target volume per beam. Multiple beams at different entry positions. Sharp distal fall-off beyond Bragg peak. Sharp lateral penumbra</td><td>201 fixed sources distributed over upper cranial hemisphere and focused at a single spot. Focal spot to source distance is 55 cm.</td><td>Gantry-based source sweeps out an are in a plane around the LINAC isocenter. Patient-plane intersection adjusted by pivoting patient treatment couch around isocenter.
Dynamic, noncoplanar, treatments.
Focal spot to source distance 100 cm.</td></tr>
<tr><td rowspan="2">Field sizes</td><td rowspan="2">Arbitrary shape and size.</td><td>Circular 4-18 mm.</td><td>Circular, 5-50 mm. Dynamic collimation devices.</td></tr>
<tr><td colspan="2">Treatment volume is spherical around a single target point. Field shaping accomplished through placement of multiple shots/targets inside the target volume and differential dose per target.</td></tr>
<tr><td>Sparing</td><td>Small number of static beam portals geometrically chosen to avoid critical structures</td><td>Selective plugging of individual source apertures whose field of view includes critical structures. Standard patterns available</td><td>Customized gantry rotation intervals at specific couch angles.</td></tr>
<tr><td>Dose rate</td><td>Variable per beam portal. Arbitrary beam weighting.</td><td>Fixed source output.
Dose rate inhomogenicity across target from individual sources, per shot weighting.</td><td>Variable per arc and target.</td></tr>
</table>

CLINICAL INDICATIONS AND RESULTS (14)

(datas from Gamma Knife radiosurgery)

1. Arteriovenous malformations

Gamma Knife surgery has proven highly effective in the treatment of AVMs. More than 8700 patients have been treated since 1971. The complete obliteration rate for AVMs is satisfactory (most of which were considered unsuitable for microsurgery). This success rate underscores the importance of Gamma Knife treatment as an alternative to microsurgery.

Multiple studies show that the clinical efficacy and the non-invasive procedure makes it advantageous for patients medically unable or unwilling to undergo conventional surgery. The non-invasive nature of the Gamma Knife treatment also helps when treating centrally located lesions and those close to critical structures such as the brain stem. In a recent study comparing hemorrhage in non-obliterated AVMs during the first two years following Gamma Knife surgery with the incidence in untreated patients, it was noted that the risk for permanent neurological deficit or death due to AVM rupture between the treatment and total nidus obliteration was less than 0.5% for small AVMs and 2-4 % for larger ones during the first two years. This compares to 4-6 % for an untreated AVM.

2. Acoustic neuromas

Several published studies indicate effective management of acoustic neuromas while still perserving cranial nerve function. According to a recent study, a permanent growth control rate after Gamma Knife surgery of 90-95 % was achieved with facial nerve function perservation of nearly 100 % and preservation of serviceable hearing of approximately 80 %. With enhanced diagnostic imaging technique, a growing number of previously undetected acoustic neuromas are being identified. In addition, noteworthy studies indicate that most of these tumors enlarge within 1 or 2 years. The challenge is to treat these tumors totally while preserving full cranial nerve function and hearing. Results in a study by the University of Pittsburgh comparing microsurgery with Gamma Knife surgery, indicate that microsurgery is associated with a greater

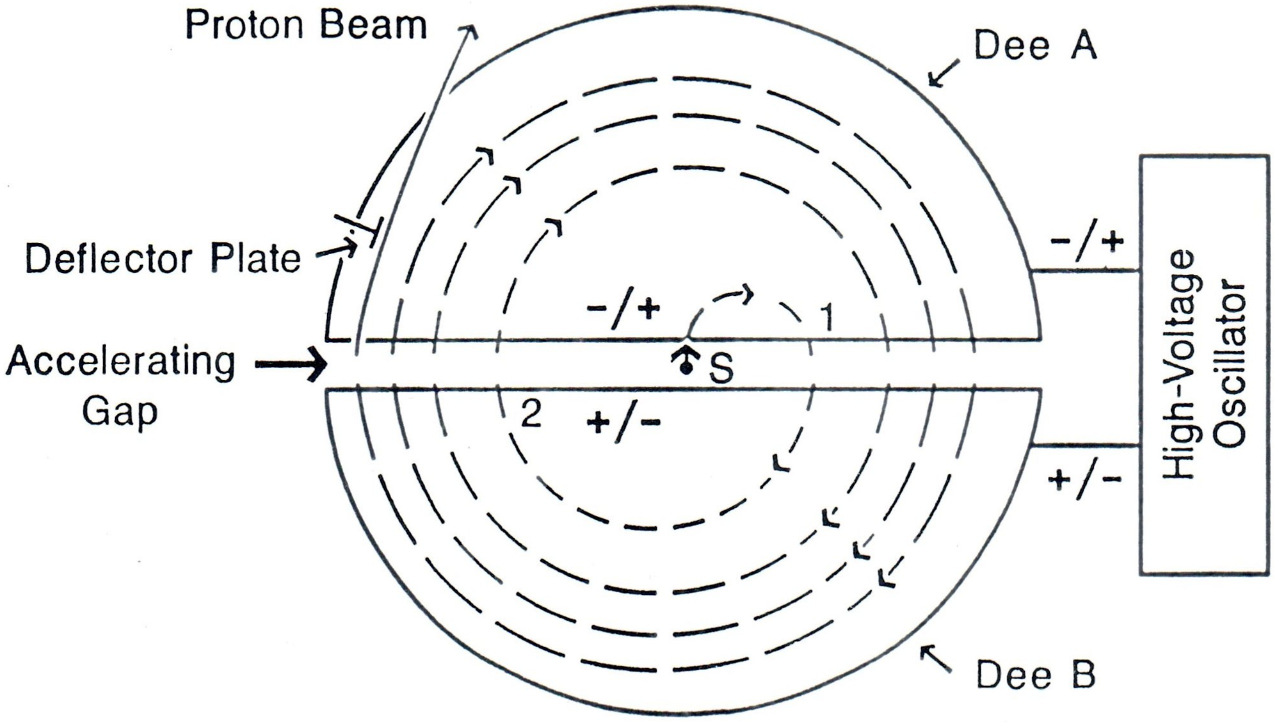

Fig 1 Schematic of the cyclotron, used primarily for the acceleration of protons.

incidence of peri-operative or delayed facial dysfunction and a decreased rate of preservation of the preoperative level of serviceable hearing. This further indicates the importance of Gamma Knife surgery for acoustic neuroma patients.

3. Mastastatic tumors

It is currently estimated that around 20-30 % of all patients harbouring malignant disease develop metastases to the brain. The established treatment modality for cerebral metastases has been craniotomy and whole brain radiation therapy. The convenience and efficacy of Gamma Knife procedures, however, has given rise to an increasing use of this treatment for both single and multiple metastases. Excellent results have been achieved with the Gamma Knife, even for such traditionally radioresistant tumors as melanoma.

4. Meningiomas

Although the accepted first line of treatment for meningiomas is microsurgical removal, Gamma Knife surgery is being increasingly used as a valuable adjunct, particularly in cases of subtotal tumor removal. Morbidity from intracavernous surgery may be markedly decreased by planning in advance for a less aggressive intracavernous surgical resection followed by delayed radiosurgery to the intracavernous tumor residual.

Additionally, Gamma Knife surgery can result in a significant reduction in recurrence rates and prevents reoperation in up to 87.5 % of patients with relatively low complication rates. This includes tumors close to important structures such as the brain stem and cranial nerves.

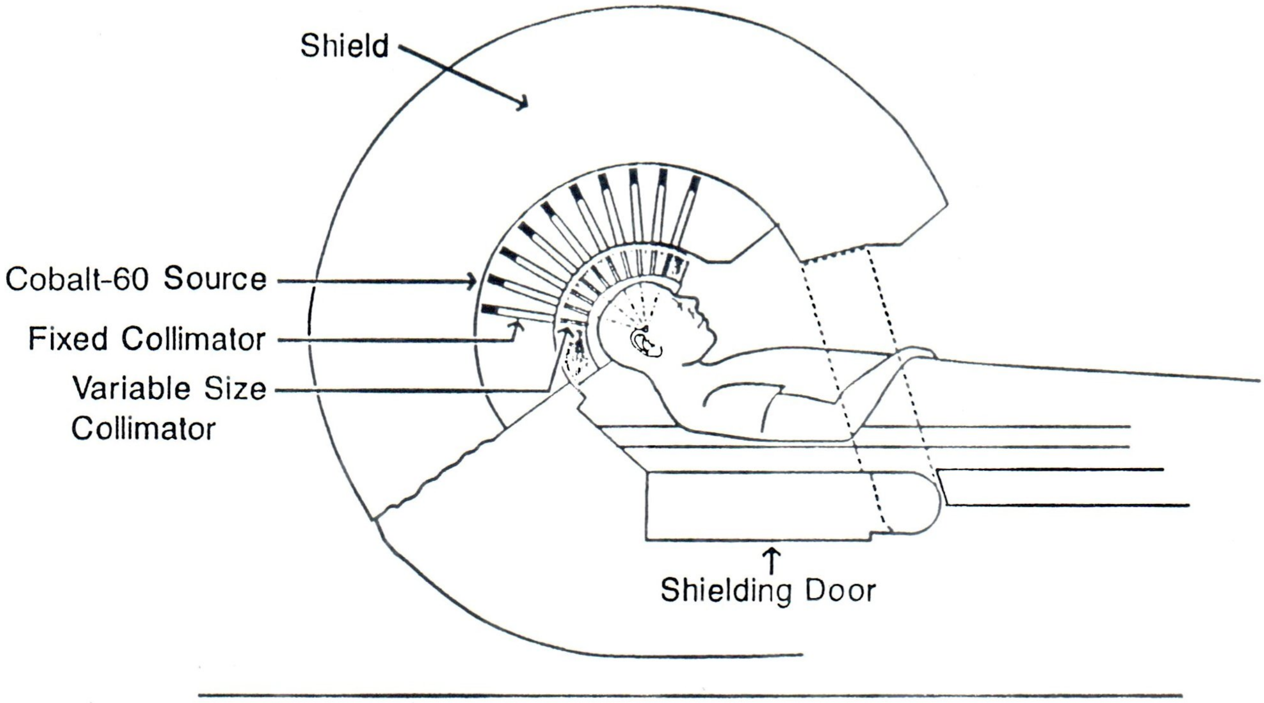

Fig. 2. A cross-sectional schematic of a Gamma Knife showing the location of the cobalt-60 sources, their collimators, and the point at which all gamma ray beams are aimed. The patient is positioned within the Gamma Knife so that the focal point of the beams and the center of the intracranial target coincide.

5. Chordoma and Chondrosarcoma of the cranial base

Kondziolka et al (15) attested to the value of stereotactic radiosurgery as an adjuvant or primary treatment for selected patients with chordoma or chondrosarcoma and demonstrated its potential advantages over standard fractionated irradiation.

6. Movement disorders, pain and psychological disorders (16)

Radiosurgery was applied to movement disorders, pain and psychological disorders such as obsessive compulsive neurosis. Disorders treated were tremor in Parkinson's disease, intractable pain with cancer, trigeminal neuralgia, and obsessive compulsive neurosis. Today, the Gamma Knife is used for making thalamotomies to arrest the tremor of Parkinson's disease, to ameliorate dyskinesia and rigidity of the same disease by pallidotomy, to stop intractable cancer pain by thalamotomy or hypophysectomy to eradicate the excruciating pain fo trigeminal neuralgia by radiation of the trigeminal root at its exit zone from the brain stem, and to make bilateral lesions of the anterior internal capsule for remedying obsessive compulsive disorder. Efforts have been made recently to use Gamma Knife surgery also as a treatment for focal epilepsy.

7. Other pathologic processes

The following conditions had been treated by radiosurgery; craniopharyngiomas (17,18), pituitary adenomas (19), pinealomas (20), primary glial tumors (21), hemangiopericytomas of the meninges (22), radiosurgery to the pituitary gland in Cushing's disease (23), refractory anxiety disorders (24), squamous cell carcinoma of the nasopharynx (25), Nelson's syndrome (26), human ACTH producing pituitary tumors (27), and eye melanoma (28).

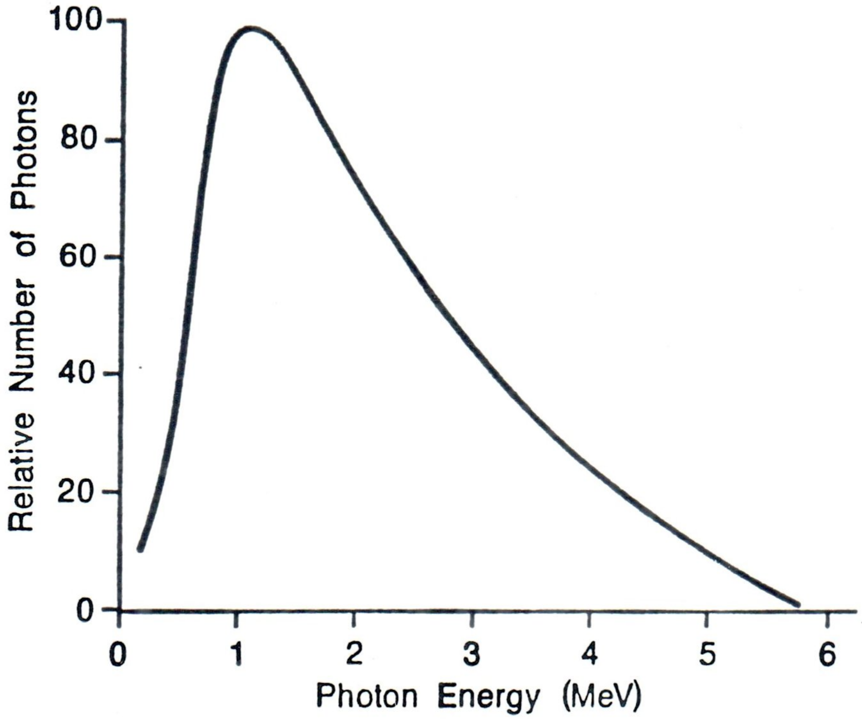

Fig. 3 The distribution of photons (bremsstrahlung x-rays) from a 6-MeV LINAC. The average energy of the x-rays produced is approximately 2 MeV, while the maximum energy is 6 MeV.

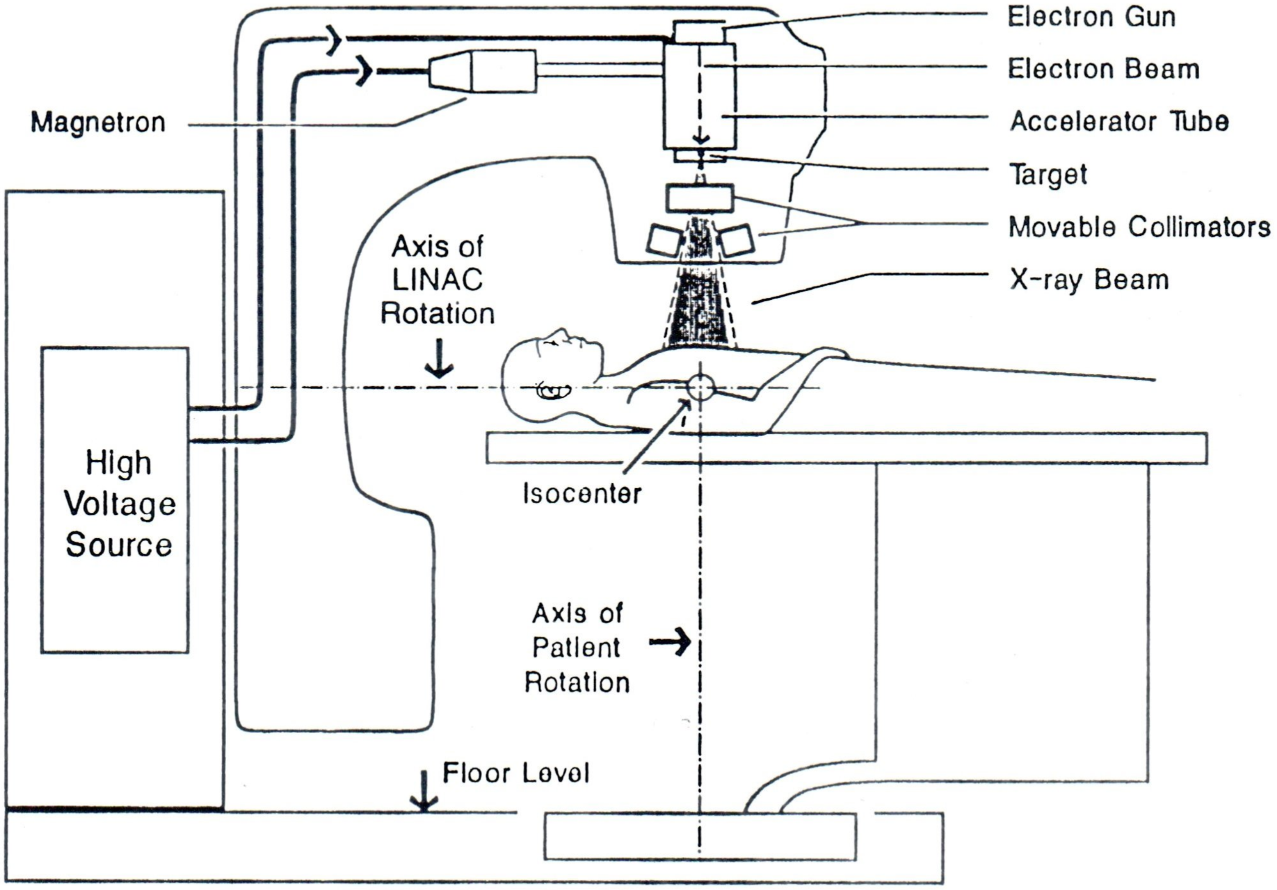

Fig. 4 Diagram of a common type of medical LINAC. The high-voltage source supplies high-voltage pulses simultaneously to both the electron gun and the magnetron, which converts them to microwave pulses. Thus a microwave pulse and electrons from the gun are simultaneously injected into the accelerator guide. The microwaves accelerate the electrons to high energy. The high-energy electrons strike a tungsten target, producing bremsstrahlung x-rays. The size of the x-ray beam is defined by two pairs of movable collimators. The entire x-ray producing unit can rotate about a horizontal axis passing through a point called the isocenter. The patient can be rotated about a vertical axis through the isocenter point. If the center of the larget to be treated is placed at the isocenter, then x-ray beams can be directed at the target from a variety of directions by utilizing different combinations of LINAC and patient rotations. When a LINAC is used for radiosurgery, it is fitted with a secondary collimator located downstream of the standard movable collimators.

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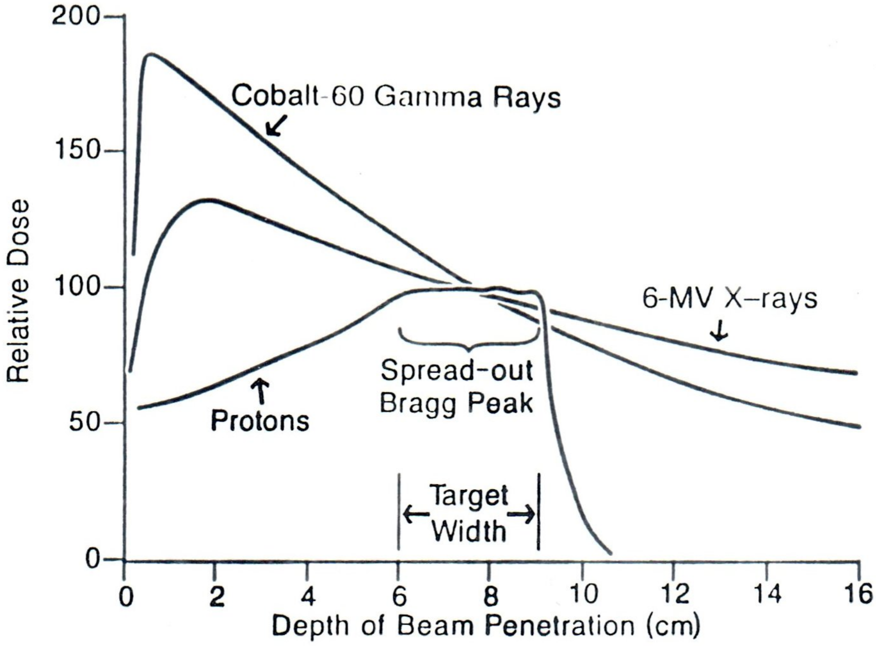

Fig. 5 Comparison of dose deposition for single beams of radiation measured from the head surface through the region of the target. In this example, the center of the target is 7.5 cm from the surface: If single beams were used for treatment, gamma rays and x-rays would be unsatisfactory because they deposit more dose outside the target than to the normal tissues along its entry path. The “single” proton beam is actually a composite beam.

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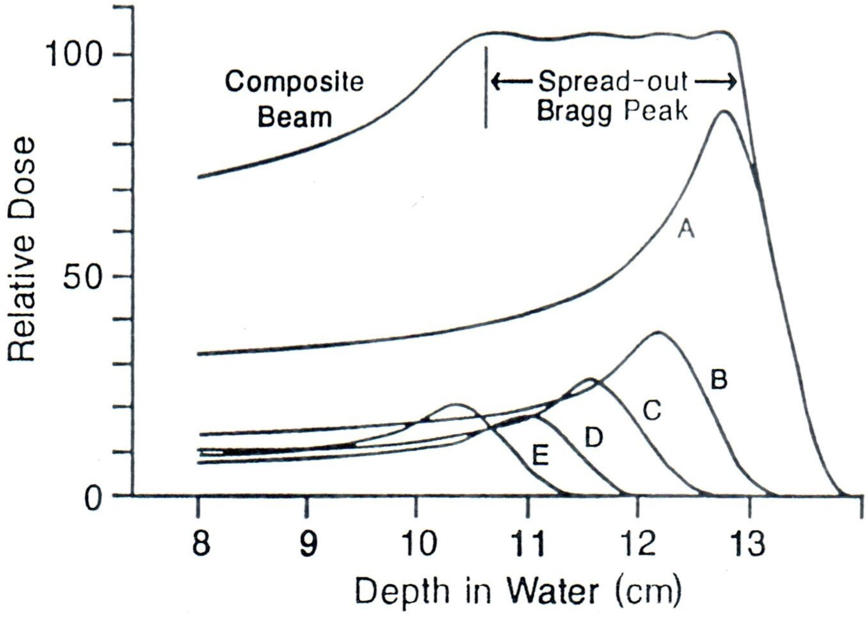

Fig. 6 The spread-out Bragg peak is formed by adding together beams of different penetrating ability (energy) and intensity (beams A,B,C,D and E) to form one composite beam. Beam A consists of 160-MeV protons. Beams B, C, D and E are various lower-energy beams formed from the 160 MeV beam by passing it through attenuators of different thicknesses. The high-dose, flat region of the composite beam is designed to have a width approximately equal to the width of the target in the beam direction. In this example, the flat region of the composite beam is approximately 2.5 cm.

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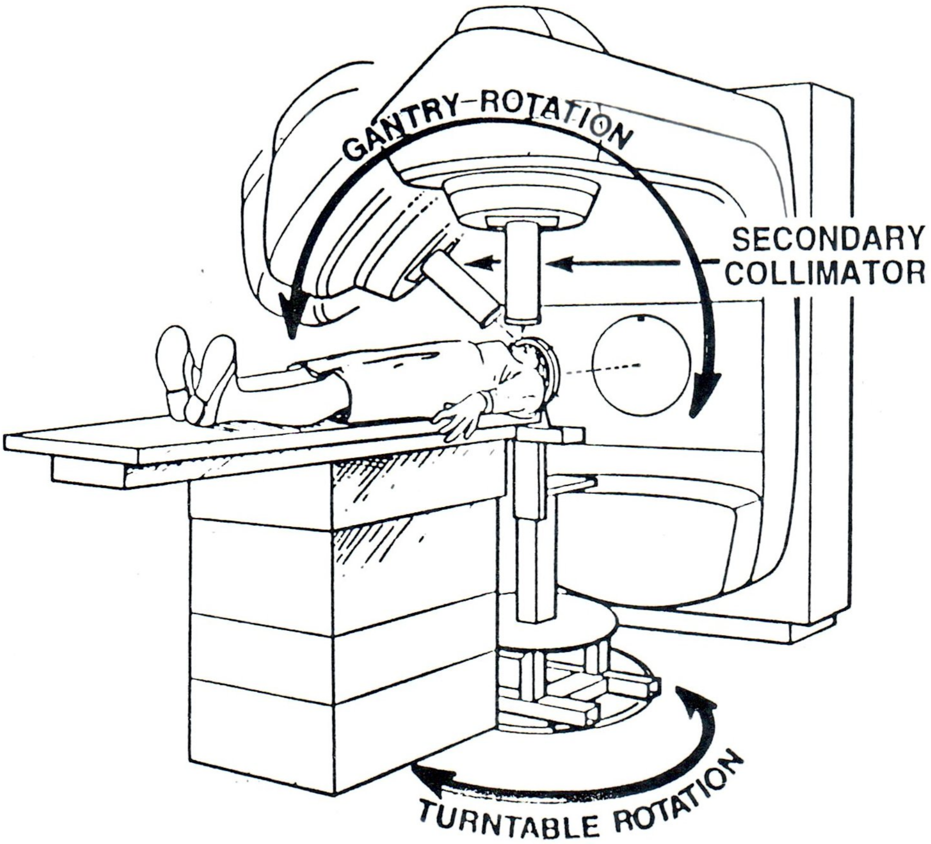

Fig. 7 Medical LINAC showing the two principal axes of rotation relevant for radiosurgery. Combinations of both rotations permit beams to be directed at an intracranial target from many different directions. A secondary collimator positioned close to the patient's head defines the shape of the x-ray beam.

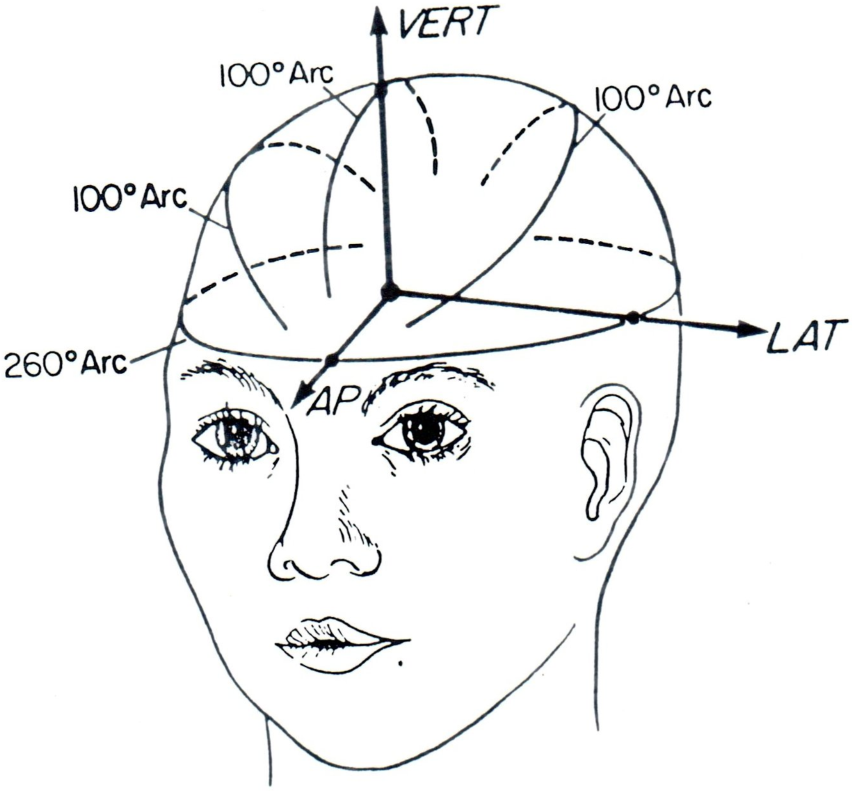

Fig. 8 Head schematic showing the paths traced by the central line of the x-ray beam on the surface of the head for a hypothetical treatment. Great flexibility exists in selecting these paths, or arcs, to optimize the dose distribution for a given patient's treatment.

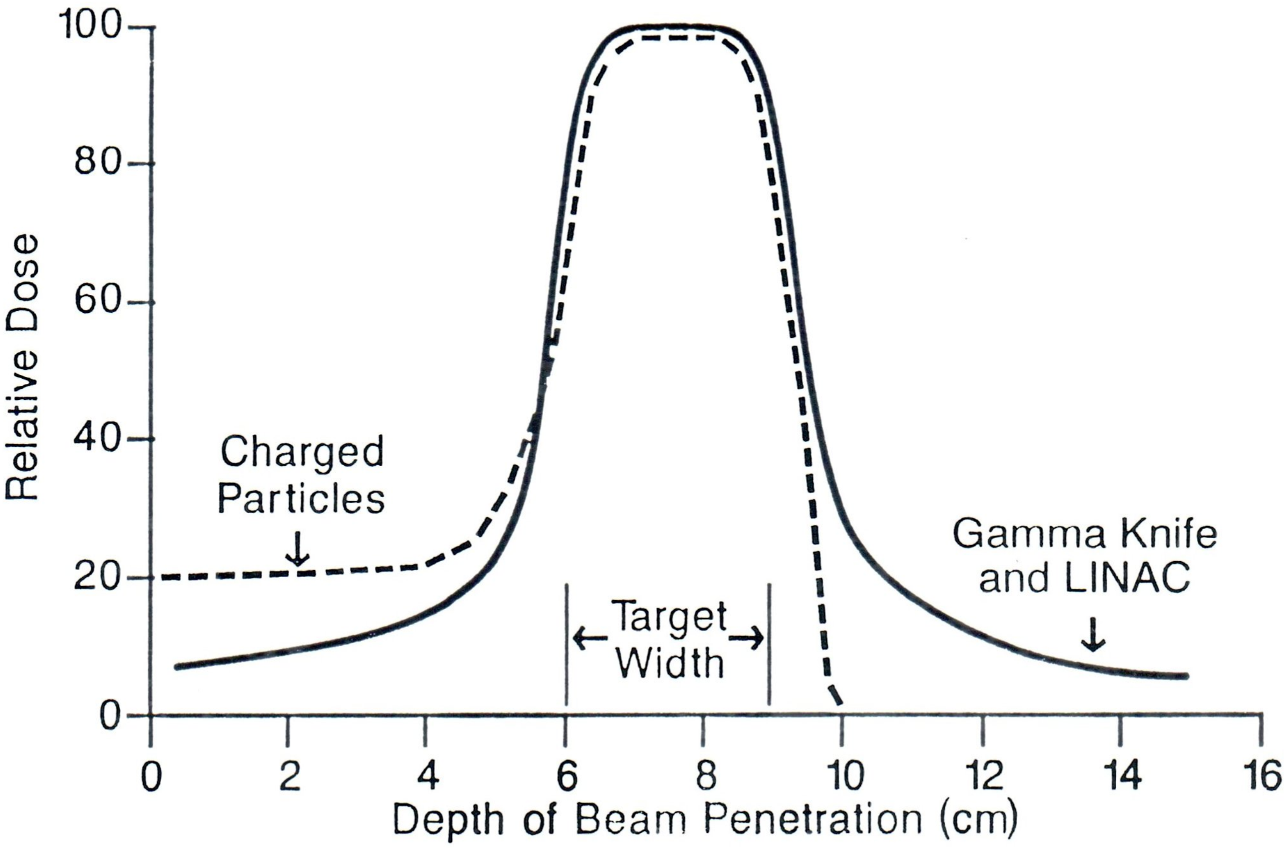

Fig. 9 Treatment dose measured along the center line of one beam from the head surface through the region of the target for a single isocenter. The dose values were generated by using a complete set of representative beams for each of the three treatment approaches. Each technique is capable of concentrating the dose within the target region. Entry doses appear to the left of the target and exit doses to the right. Note that charged particle beams have a finite range and hence deposit very little dose distal to the target. Entry and exit doses are essentially the same for both LINAC and Gamma Knife treatments. A charged particle treatment (e.g. four beams) deposits more dose (about 20 percent of the target dose) along each of its entry paths than the dose deposited along each entry path for either a LINAC (e.g., the four arcs or a Gamma Knife (201 beams) treatment. However, the typical charged particle treatment deposits dose to normal tissue only along four paths.