Stereotactic radiosurgery for intracranial pathology: a review of treatment techniques and results

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Stereotactic radiosurgery techniques using the gamma unit and linear accelerator are reviewed. Both methods are employed in the treatment of a variety of intracranial lesions. Radiosurgery is particularly effective in the treatment of arteriovenous malformations and metastatic tumours. Results for the treatment of other tumours such as malignant gliomas, acoustic neuromas, meningiomas, and pituitary tumours are encouraging.

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Introduction

Stereotactic radiosurgery is a therapeutic option of growing importance for patients with malignant and benign brain lesions. It was first developed by the Swedish neurosurgeon Lars Leksell in 1951, to treat functional disorders of the brain.[1]

Stereotaxy refers to the accurate localisation of an intracranial target within a three-dimensional reference frame in terms of the X, Y, and Z coordinates. The method starts with fixing a base ring to the patient's skull. A frame is then attached to the base ring as shown in Figure 1. The rods in the frame act as markers for three-dimensional localisation. The patient then undergoes imaging studies, computerised tomography (CT), magnetic resonance imaging (MRI), or angiography, which give a two-dimensional description of the location of the intracranial target. Simple computer software then converts this planar two-dimensional imaging information into a three-dimensional stereotactic coordinate space.

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After imaging, the marker rods are removed and replaced by an arc system with scales for setting the target's X, Y, and Z coordinates. The system is devised in such a manner that the target to be reached stereotactically is located at the centre of the circular arc of the stereotactic instrument. Thus, a probe guide tube which points along a radius of the circular arc, will always pass a probe through the target, independent of the chosen approach angle (Fig 2). The intracranial target can then be reached from any direction. In stereotactic biopsy, a probe or biopsy device is then advanced to this unseen target via a burr hole, which can be placed at any convenient location of the head, then therapeutically manipulated.[2]

In radiosurgery, after stereotactic localisation of the target, the biopsy probe is replaced by sharply-focused beams of ionising radiation (gamma or X-rays). This permits a high dose of radiation to be delivered with precision in a single session to any intracranial lesion of a suitable size to achieve its biological effects, while reducing the dose to surrounding normal tissue.[3-5] If the radiation tolerance of normal brain surrounding the tumour is not exceeded, it may be possible to give a high dose to the tumour, without increasing damage to the normal tissue. Radiosensitivity of the lesion is not a major concern, because the single, high dose of radiation can cause direct damage to the abnormal tissues.[3,4]

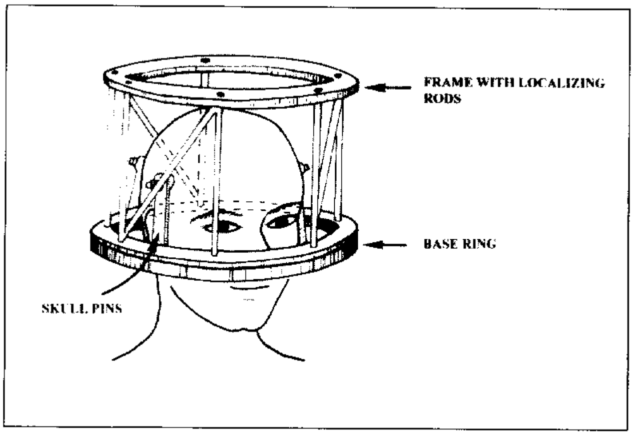

Fig 1. Diagram showing the attachment of a base ring to the patient's head using four pins. A frame with marker rods for stereotactic localisation is then attached to the base ring.

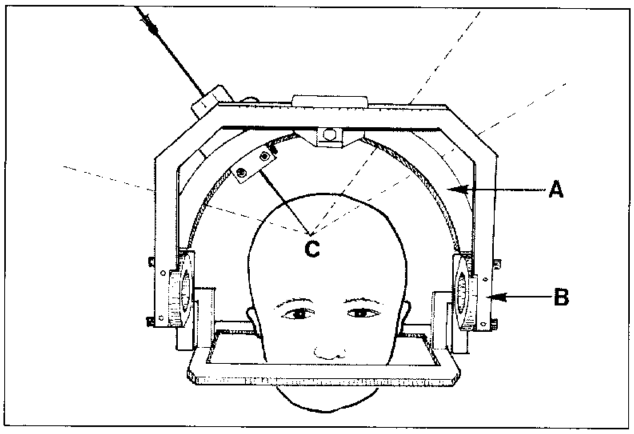

Fig 2. A stereotactic system with a semi-circular arc (A) for introduction of the guide probe (black line) or biopsy device. The arc can be turned forward or backward through a device (B) and the probe can be slid towards the left or right, so that the target (C) is always at the centre of the circular arc. All radial probe tracts (dotted lines) pass through the target.

Radiobiological principles

Radiation beams act by directly damaging nuclear DNA, giving rise to cell necrosis. The dose required to produce radionecrosis depends strongly on the rate of mitosis of the cell population. The higher the proliferative activity of the pathological cell populations, compared with healthy brain tissue, the lower the dose needed to achieve necrosis.[6] Another important factor that affects cellular destruction is the volume of tissue being irradiated. The larger the target volume, the higher the incidence of complications.[7]

How is radiosurgery performed?

At most centres, radiosurgery is performed on an outpatient basis. The procedure begins in the morning with fixation of the stereotactic frame to the patient's head under local anaesthesia. The patient then undergoes CT and/or MRI with the head frame in place. Angiography is performed for vascular lesions.

The lesion defined by imaging is then outlined manually. Computer reconstruction of the images allows three-dimensional display of the target and the surrounding critical brain structures. The X, Y, and Z coordinates of these structures with respect to the frame can then be determined.

Treatment planning is carried out by defining the centre of the target (isocentre) on stereotactic coordinates. With the aid of an interactive display of isodose lines (lines joining points of equal radiation dose in a particular plane) superimposed on the isocentre, radiation delivery is contoured to the tumour margin (Fig 3). Irregularly-shaped or different-sized lesions can be well covered.

When treatment planning is completed, the patient is positioned within the radiation source and therapy begins. Actual treatment time varies greatly, depending on the technique used. Following radiosurgery, the frame is removed and the patient returns home. The entire procedure usually takes five to eight hours.

The radiosurgery team

According to the consensus statement on quality improvement of stereotactic radiosurgery issued jointly by the American Association of Neurological Surgeons and the American Society for Therapeutic Radiology and Oncology, the radiosurgery team should comprise a neurosurgeon, radiation oncologist, radiation physicist, and radiation technologists.[8]

Methods of delivering radiation

Three main types of radiation technique are used for radiosurgery: heavy charged particles such as protons generated by a cyclotron, photons produced by cobalt^{60} sources from a gamma unit, and high energy X-rays produced by a linear accelerator. The first method is too complicated and expensive for general use. In this review, only the gamma unit (Gamma Knife) and linear accelerator (Linac) based systems are discussed. The two systems are different in design and generate photons using different sources.

Fig 3. Treatment planning with isodose lines contoured to the lesion margin (an arteriovenous malformation), shown in a stereotactic CT scan. The surrounding brain receives a much smaller radiation dose.

The Gamma Knife

The concentration of dose within an intracranial target by the Gamma Knife is accomplished by directing 201 cobalt^{60} gamma ray beams towards the common centre of the target (isocentre). These beams enter the head over an area covering approximately half of the upper hemisphere of the skull. The size of these beams can be changed to produce spherical isodose surfaces. The resulting shape of the isodose lines can be altered to provide better target coverage, by selectively blocking some of the 201 beams or using multiple isocentres. By this means, non-spherical and irregularly-shaped targets can be covered. The potential drawback of this technique, apart from the increased treatment time, is that individual, sphere-like, isodose surfaces do not stack together evenly, resulting in very non-uniform dose deposition within the target.[4,9,10] It remains unknown, whether dose inhomogeneity affects treatment results in different pathological conditions.

The Linac technique

Most modern linear accelerators can be relatively easily adapted for stereotactic radiosurgery.[11] Circular collimators of various sizes are fitted to the head of the machine to allow small field sizes to be used. The stereotactic frame is fitted either to the treatment couch or directly to the floor via a floor stand. Treatment is delivered using multiple arcs of movement of the gantry of the Linac machine, as illustrated in Figure 4, to achieve treatment fields of equivalent dose distribution to the gamma unit.[9,10]

Comparison of the Gamma Knife and Linac-based radiosurgery

The advantage of the gamma unit is its simplicity of use. There are relatively few moving parts and alignment of the collimator helmet to the hemispherical radiation sources is precise. The disadvantages are the high initial equipment cost, the radiation shielding problems encountered during initial installation and at source replacement, and the inflexibility of the equipment in terms of field size and shaping.[4,9]

The advantages of the Linac technique are its flexibility and low cost. There is no limitation in field size and beam shaping can be carried out for the treatment of pathologies with irregular volumes.[12] Treatment times of 30 to 40 minutes allow the technique to be performed with minimal disruption to the regular workload of the machine. The moving parts, and the sophistication of the set up and radiation delivery require an intensive quality assurance programme.[13] The inherent inaccuracy of the linear accelerator system has been improved by Friedman et al, from the University of Florida, who incorporated high-precision bearings into the machine, which control all patient and gantry movements.[14] As a result, the radiation beam accuracy has been improved to 0.2 mm, similiar to that of the gamma unit.

The main limiting factor in the efficacy and precision of radiosurgery is the inaccuracy of the imaging methods. Biplane angiogram and CT scan give the most accurate location of the intracranial target. However, the resolution of CT is not as good as that of MRI, as the latter gives excellent resolution of intracranial lesions and is therefore good for diagnostic purposes. When MRI is used for treatment, the exact location and size of the target can be distorted as a result of the inhomogeneity of the magnetic field and the chemical shift generated by the body tissues.[15,16] An error in localisation of the lesion of up to 4-5 mm

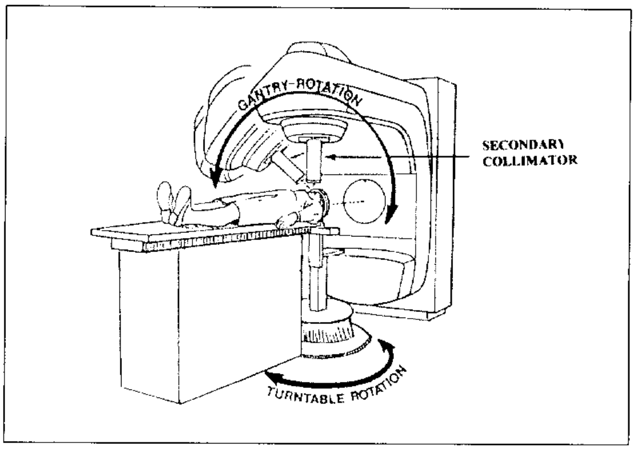

Fig 4. Diagram showing how a linear accelerator can be adapted for use in radiosurgery. A secondary collimator is fitted for focusing of the radiation beam. Multiple arcs of rotation of the gantry and couch positioning can be used to achieve treatment fields of equivalent dose distribution as the gamma unit.

can result, and critical areas of the brain, instead of the lesion, may be injured by the radiation beam. Since radiation-related injury is usually delayed, this may not manifest itself until months later. Despite differences in technique, the biological effect of Gamma Knife and Linac-based treatment is identical and dependent on dose/volume distribution and the proximity of critical structures. The major determinant of accuracy of therapy is not the technique of radiation delivery and the machine, but the clarity and precision as well as the interpretation of CT or MRI images.[3] New computer software allows the fusion of CT and MRI images, thereby combining the accuracy of CT localisation and the excellent image resolution of MRI.[17]

In radiosurgery, each step in the planning and treatment process affects the ultimate accuracy of radiation delivery. Regular programmes should be established in each centre to check for inaccuracy of the entire treatment process. This includes the stereotactic system, imaging methods, image data transfer, and radiation delivery system. Error in any step can have a significant impact on treatment results.[18]

Clinical applications and results

Arteriovenous malformations

Most arteriovenous malformations (AVM) present with either haemorrhage or convulsion. Regardless of the mode of presentation, AVM carry an annual risk of rebleeding of 2% to 3% and an associated overall mortality of 12% to 29%.[19]

The treatment of choice for AVM is microsurgical resection, but a substantial number of these lesions are located in deep or critical structures and are not surgically resectable. Surgery, if successful, offers an immediate cure to the patient. Evidence suggests that AVM can also be cured after radiosurgical obliteration. However, during the latent period for radiation to obliterate an AVM, which may take up to two years, the risk of rebleeding is unaffected.

Treatment results obtained using either the Gamma Knife or Linac are comparable.[19-22] The major determinants of outcome and complications after radiosurgery are the size of the AVM and the dose of radiation given.[19,21,22] The overall cure rate of AVM approaches 90%, using modern radiosurgical techniques.[19,22] The use of radiosurgery on the treatment of cavernous haemangioma is controversial.[19] Further research is required to define the optimal treatment dose before radiosurgery.

Malignant brain tumours

a) Malignant gliomas

Malignant gliomas are the commonest primary brain tumours in adults. Despite optimal treatment with surgery, external beam radiotherapy, and chemotherapy, the median survival is only nine months for patients with glioblastoma, and 24 months for anaplastic astrocytoma.[3]

Normal brain tolerance limits the maximum amount of radiation that can be delivered by external beam irradiation. Stereotactic brachytherapy by direct implantation of iodine[125] sources into the tumour has been used to increase the dose of radiation delivered to the tumour site while sparing surrounding brain. Using this technique, survival of selected patients with glioblastoma can be increased to 18 to 27 months.[23] Radiosurgery can achieve the same effect as brachytherapy with the additional advantages of being non-invasive and allowing the treatment of tumours in surgically inaccessible or eloquent areas. Results using Linac are encouraging, and its outcome, as measured by survival, is comparable to that of brachytherapy.[23]

b) Brain metastases

Metastases comprise almost 50% of all intracranial tumours.[24] Untreated brain metastases are fatal, with an associated survival of one month. Central nervous system malfunction is the usual cause of death.[25] Patients treated with whole-brain radiotherapy, the current mainstay of palliation, have a median survival of three to six months.[25] Those with a solitary metastasis who undergo surgical resection and whole-brain radiotherapy have longer survival and functional independence than do patients treated with radiation alone.[26]

An important consideration in the treatment of these patients is to provide a comfortable means of palliation so that they can stay out of hospital for as long as possible. This is of particular importance for patients with metastatic cancer, who are often debilitated and face limited life expectancies.

Metastases are usually spherical in shape and are prime candidates for radiosurgery. The results of stereotactic radiosurgery are broadly comparable to those of surgical resection series, which report an average local control rate of 75% to 80%.[25] Both the Linac and Gamma Knife series report similar local control rates of 80% to 90%, with complete disappearance of the tumour on imaging.[27-30] Radioresponsive and radioresistant tumours have similar control rates. Results of these studies indicate that radiosurgery is an effective, minimally invasive, outpatient treatment option for intracranial metastases. Radiosurgery not only provides local control rates equivalent to those from surgical series, but is also effective in treating patients with surgically inaccessible lesions, with multiple lesions, or with tumour types that are resistant to conventional therapy.

Benign brain tumours

The optimal treatment for most benign brain tumours is surgical excision. Radiosurgery, however, provides an increasingly valuable alternative as primary treatment for selected patients with these lesions. Several features of benign tumours make them especially suitable for radiosurgery. These features include well-demarcated borders, failure to invade surrounding brain, and the widespread availability of MRI, which has enabled these lesions to be detected at an earlier stage when they are still small.[4] Radiosurgery may also be used as adjunctive therapy to surgery; either to treat residual tumour after a subtotal resection or to treat tumours that have recurred after surgery.[31]

The primary goal of radiosurgery is primarily to prevent further tumour growth. The lesion may persist after treatment. Between 30% and 60% of tumours show regression, but it is uncommon for these tumours to completely resolve, as is often seen with metastases.[4] Radiosurgical experience has been most extensive with acoustic neuromas, meningiomas, and pituitary adenomas.

Acoustic neuromas are benign tumours that arise from the Schwann cells of the eighth cranial nerve. Early results using the gamma unit in Stockholm, Sweden, showed that treatment results of radiosurgery compared well with those of open surgery. The study, however, reported treatment results over a long period before modern imaging techniques for pre-operative and follow up documentation of tumour size were available.[32]

Experience with the Gamma Knife in Pittsburgh, Pennsylvania, USA, in the treatment of this tumour showed a 94% local tumour control rate; 34% of patients had a decrease in tumour size and 60% had no change.[33] Radiosurgery using the Linac has been shown by Mendenhall et al to have a 100% local tumour control rate; 78% had tumour regression and 22% had unchanged tumour size on follow up.[34]

Radiosurgery may be used alone to treat meningiomas if they are small, or as an adjunctive treatment in the partial surgical resection of large tumours. It also has a role in the treatment of recurrent tumours, and those in elderly or debilitated patients. Early results using the Gamma Knife and Linac are comparable and promising, although in most cases, follow up is limited.[31,35]

The primary treatment for pituitary adenomas is surgery. Radiosurgery is useful in the treatment of recurrent tumours that are endocrinologically active, are not compressing the optic apparatus, and tumours that have involved the cavernous sinus.[3]

Paediatric tumours

Radiosurgery is an attractive therapeutic option for the treatment of intracranial lesions in children. Limiting the radiation dose to surrounding brain tissue potentially reduces the long term neuropsychological impairment associated with conventional radiotherapy.[25] There is only limited experience with radiosurgery in children, apart from in the treatment of AVM. This reflects physicians' reluctance to refer patients for treatment, as well as the difficulty in fitting the stereotactic frame to children.

The development of the relocatable stereotactic frame has enabled this device to be applied repeatedly with a high degree of accuracy.[36,37] This has led to the development of stereotactic fractionated radiotherapy. Initial experience using the Linac device and the relocatable system in Boston, Massachusetts, USA, has been encouraging. Lesions treated included malignant gliomas, primitive neuroectodermal tumours, and craniopharyngiomas. With a short follow up period, 25% of the patients had up to a 50% reduction of the original tumour volume and less than 10% had a complete response. The remaining patients had stable disease. There were no in-field recurrences.[38] Similar studies are ongoing at the Royal Marsden Hospital in London, UK. Prospective studies to evaluate neurocognitive and neuroendocrine effects are underway. This innovative approach may make a significant impact on the treatment of intracranial neoplasms in children.

Skull base/Head and neck tumours

Patients with locally recurrent, malignant head and neck tumours that involve the skull base benefit from re-irradiation. A major barrier to successful palliation or cure is dose limitation, secondary to normal brain tissue tolerance.

Stereotactic radiosurgery has recently been used to treat these lesions. Due to physical constraints, the gamma unit cannot treat skull base lesions that extend beyond the foramen magnum.[39] With the Linac, lesions that extend down to the level of the second cervical vertebrae can be treated in conjuction with any intracranial lesions.[40] Preliminary results using both methods have been reported.[39,40]

Conclusion

Stereotactic radiosurgery by Linac, though a relative newcomer to this field, has proved to be as effective as the Gamma Knife in the treatment of a wide variety of brain, skull base, and head and neck pathologies. The low capital cost of the Linac and potential technological improvements make it an attractive tool to acquire for radiosurgery.

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