Review Article

An overview in stereotactic radiosurgery

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Abstract: Efficacy and utilization of radiation as a mode of management in neurosurgical lesions has increased radically as a consequence of improvements in appreciation of the concept of stereotaxis, progress in medical imaging, computer technology, and advanced delivery devices.[19,22] Primary management alternative in patients with cerebellopontine angle lesions, skull base tumours, meningiomas, paragangliomas, AVMs etc., is increasingly being used as also in secondary management of recurrent or planned residual disease patients where a part of the lesion is deliberately left behind to avoid loss of function and prevent iatrogenic injury.[22] Contemporary understanding with adequate and proper information of this resource along with understanding the controversies regarding the use of radiation for the management of several lesions is paramount. This article is intended to provide a concise basic introduction of the technology available and the pertinent applications in the management for several lesions with a basic understanding of the advantages and disadvantages of various available devices and the outcome in using various methods based on review of available literature. *(p1-13)*

Key words: *Radiation, radiotherapy, stereotaxis, 3D target localization, stereotactic radiotherapy (SRT), stereotactic radiosurgery (SRS), Gamma-knife radiosurgery, Linac radiosurgery, Cyber-knife radiosurgery, X-knife radiosurgery, external beam radiation therapy (EBRT), intensity modulated radiation therapy (IMRT), and fractionated radiotherapy*

Introduction

The way at the forefront for the advancement in the sphere of neurosurgery is to bring it into the lead and into the frontiers so as to explore and investigate ideas where there is still scope to get into the whole span of the disease spectrum to cover almost all the gamut of the diseases amenable for simple and less invasive treatment and for further perfection in areas where there is still room for improvement. The neuro-imaging directed radio-neuro-surgery is one such area which is currently being increasingly investigated progressively and over the decades has changed the landscape within the field of neurosurgery. The concept of stereotactic radiosurgery (SRS) came into being with the coupling of stereotaxy and radiation along with advanced neuro-imaging techniques like computed tomography (CT), magnetic resonance imaging (MRI) and digital subtraction imaging (DSI), in alliance with the advancements of the computer and information technology which reawakened the use of various non-invasive and more effective methods for the treatment of multiple lesions with probably increasing accuracy and efficiency.[24] It almost revolutionized the management of various disorders making it possible to treat even smaller tissues with great precision and with almost no injury to the surrounding normal brain tissue. Stereotactic radiosurgery has been used for more than 30 years to treat benign and malignant tumours, vascular malformations, and other disorders of the brain with minimal invasiveness. To date, more than 200,000 patients have been treated worldwide with radiosurgery.

Unlike standard external beam whole brain radiation therapy technique where in much or all of the surrounding brain is treated to the same dose of radiation, SRS is a precise and exact 3D radiation treatment planning technique where high level accuracy is maintained to treat small and minute intracranial lesions with specific targeting of a lesion, and are irradiated with high doses of radiation, in a single fraction, with specific lesion location in a well-defined target and treatment planning with computer imaging equipment and stereotactic techniques using precisely guided multiple collimated beams of focused radiation from a given source and without exceeding the radiation tolerance of the adjacent normal tissues. Stereotactic radiosurgery combines the principles of stereotaxy *(method for locating points within the brain using an external, 3D frame of reference based on the Cartesian coordinate system or 3D target localization),* with multiple cross-fired beams from a high-energy

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radiation source to precisely irradiate an abnormal lesion. Stereotactic techniques with various stereotactic apparatus can be used to accurately aim fractionated doses of gamma rays or x-rays to a target, administering the treatment in small doses over days to weeks which is a compromise between radiosurgery and conventional radiotherapy and is termed fractionated stereotactic radiotherapy.

With adaptation of Horsely and Clark's original apparatus,(19,20,22) the first practical stereotactic instrument was introduced by Spiegel and Wycis in 1947.[19.22] In 1950, Professor Lars Leksell at the Karolinska Institute in Stockholm, Sweden, by adapting the same principles conceived, developed and designed the first radiosurgical arc-radius design treatment device called Leskell Stereotactic System.[14,19-22,41] The Brown-Roberts-Wells (BRW) system was devised de-novo as a CT-guided apparatus and has an excellent accuracy of target localization where interlocking arcs generate the polar coordinate system and are fed into a portable microcomputer to assimilate the CT fiducial data and the entry point data to calculate the interlocking arc designs and for adjusting the arcs to obtain trajectories. Recently, the Cosman-Robert-Wells (CRW) stereotactic instrument was created to offer the advantage of the simple arc-radius design while interfacing with the existing, well proven fixation and fiducials components of the BRW system.

Professor Lars Leksell developed the Gamma-knife irradiation where gamma ray photons were used to radiate tissues using an orthovoltage radiation source around a stereotactic source.[19-22] He then worked with Bjorn Larsson, a radiobiologist at the Cyclotron Unit at Uppsala University and they together developed a proton based (charged particle) SRS system in the treatment of brain malignancies.[21,41]

Types of stereotactic radiosurgery

There are three basic types of radiosurgery. Each type uses different equipment and radiation sources. Cobalt 60 systems or Gamma-knife (Figs. 1 and 2) use cobalt as a source for gamma rays, Linear accelerator (LINAC) systems (Fig. 3) use high-energy x-rays to treat a tumour or other lesions. Proton beam therapy is a type of particle beam radiation therapy. Rather than using rays of radiation, such as gamma rays or x-rays, particle beam therapy uses particles such as protons or neutrons.

Lesions treated by radiosurgery: Although the indications for the procedure are many, lesions for which SRS is usually utilized are as detailed on the next page.

Figure 1 - Leksell Gamma-knife

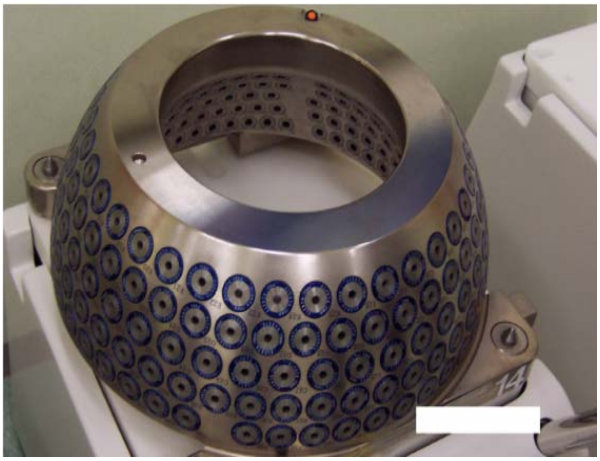


Figure 2 - Gamma-knife helmet

Figure 3 - Linac based stereotaxy

Brain tumours	Gliomas Astrocytoma Oligodendroglioma Ependymoma Pilocytic astrocytoma Anaplastic astrocytoma Glioblastoma multiforme Meningioma Pituitary tumours
Brain tumours	Pineal region tumours - acoustic neuroma and neuromas of the other cranial nerves Glomus jugulare tumour Metastatic brain tumours Craniopharyngiomas Residual lesions or recurrent small sized lesions of the brain
Vascular abnormalities	Arteriovenous AVMs Cavermous malformations Incidental cases including aneurysms
Functional problems	Trigeminal neuralgia Parkinson's disease Essential tremor Obsessive compulsive disorder
Ocular tumours	Uveal melanoma Orbital metastases Optic nerve sheath meningioma
Skull base tumours	Invasive squamous and basal cell carcinoma Chordoma Chondrosarcoma Esthesioneuroblastoma

***Procedure of administering stereotactic radiosurgery*:** The patient's head is attached to a head ring called stereotactic head frame (Fig. 4) which ascertains an orientation in the reference framework with a co-ordinate system for target determination and for precise patient positioning. A non-invasive fixation device with a meshed thermo-transformable mask moulded for each patient, or head immobilizers or fiducial markers used for localization with frameless equipment and aiding as co-ordinate systems placed on the bony skeleton of the patient, detectable by computer image detectors are used in frameless stereotactic technology. Mask system gives reproducible positioning with less than 1-2 mm variation. Real time online continuous updating of the patient's position during the treatment has made utilization of the stereotaxy based radiation to other parts of the body as well as in the spinal cord. The head, forehead, occiput, nasal bridge, maxilla and the upper jaw are the bony landmarks used to gain a secure fixation.

Next, a series of images with a specific reference coordinate attached to each is obtained by a CT, MRI, single-photon emission computed tomography (SPECT), and/or positron emission tomography (PET) (Fig. 5). Digital subtraction angiography (DSA)/CT/MR angiographic films are used as necessary. Images are obtained with the head ring in place and are transferred with the underlying coordinate system to the computer workstation. With advancement in the 3D visualization of the images that can be obtained in the scans, the lesion and the surrounding structures can be accurately localized and the critical structures can be avoided with a very small error margin delivering a high-precision dose to the lesion.[13] The virtual lesion is then outlined by the surgeon using computer software to analyze the cross-sectional anatomy, determine the tumour area to be treated, and to note the critical structures adjacent to the lesion that should be avoided.

Figure 4 - MR compatible head frame

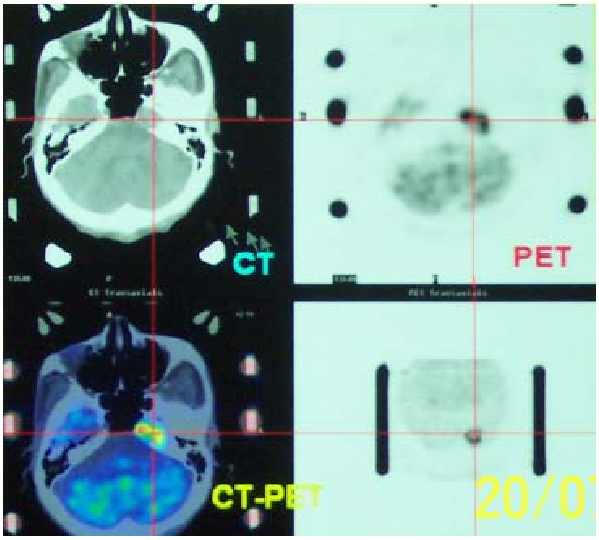


Figure 5 - Superimposed CT, MR and PET

The radiation oncologist with the collaboration of the radiation physicist and the neurosurgeon then prescribes an individual tailor-made treatment plan, the number of iso-centres required and the optimal dose to be delivered to the lesion.

The treatment planning session is called "simulation".

Simulation is mimicking the geometry of an iso-electric treatment machine, representation of the beam entry angle, beam trajectory, visualization of beam direction and treatment field with an understanding of the area of tissue at risk and tumour recurrence. The patient is positioned on the table. The laser beams coming from the ceiling and the lateral walls intersect and the axis of rotation of the gantry, the beam entry and the exit is determined and the intersecting line at the axis of rotation is called the iso-centre (Fig. 6). The position at simulation is recorded, which is called "triangulation" (Fig. 7).

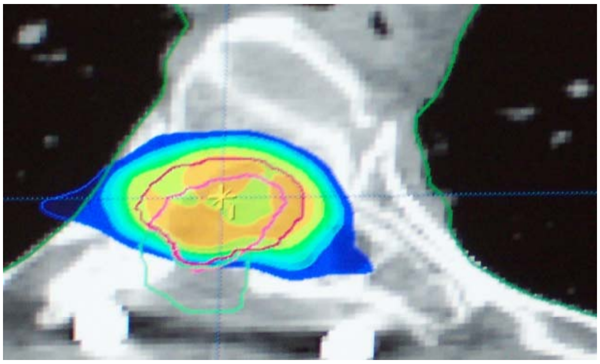


Figure 6 - Isodense curves in planning

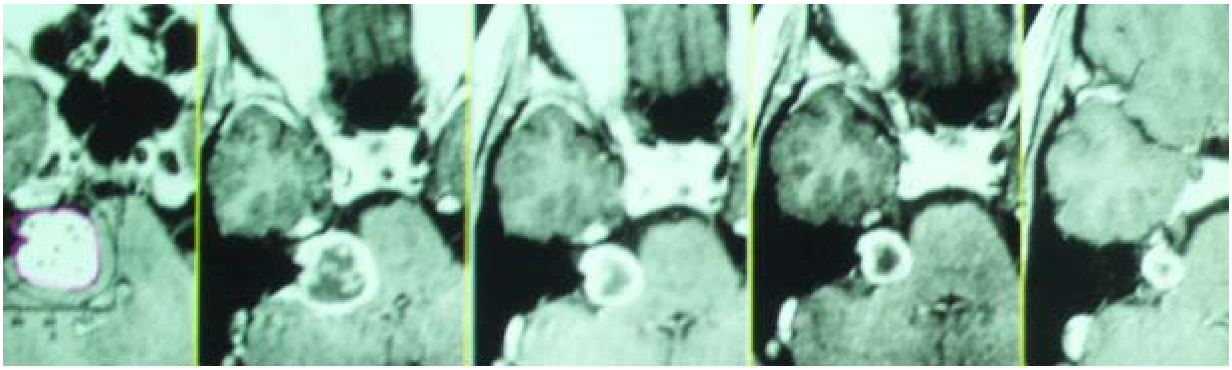


Figure 7 - Acoustic neuroma serial films with reduced size of lesion

Immobilization aids include, head holders, chin supports and thermo plastic masks. The dosimetrist and the radiation physicist, simulate the patient, after immobilizing the patient and planning the treatment. The CT and MRI are done in the treatment position, target area localized; target position registered and the relation with anatomical landmarks assessed with half to one cm cuts. The target volume is defined by contouring with target volume curves and a dose specification given for the margins. The initial treatment field includes the tumour area with the oedematous area and the boost treatment field includes only the tumour and/ or the tumour bed. After simulation, patient is re-simulated with mask and the beam trajectory visualized. The portal online printer is obtained and compared with the simulation filter.

The treatment planning is computerized, defines the target, and analyzes the dose distribution in 2D and 3D aspects (Fig. 8) or dose-first (inverse planning). In beam-first or forward planning, the beam angle and the beam orientation is made from any angle using multiple static coplanar and non-coplanar fields which form the basis of dynamic treatment modality. The dose can be escalated without complications and delivery of radiation with more conformal radiation fields. The target volume which may be a gross tumour volume, which is the actual tumour, or a clinical tumour target volume, which includes the tumour with oedema or the planned target volume which also includes other margins to counteract uncertainties, is defined. In dose-first or inverse planning or the Peacock plan, especially in irregularly shaped lesions or in lesions around highly radiosensitive structures like the optic apparatus, brainstem region etc., the safe dose for the surrounding healthy tissue is determined first, and then the required beam intensity and shape for each portion of the field is planned. Dose volume histograms provide quantitative display of the portion of defined volume that receives a given dose. This is automatically done by multi leaf, macro and micro collimators, (Figs. 9 and 10) where multiple pairs of thin beams that alternate each other, with each leaf moving independent of each other, helps in field shaping, which improves treatment efficiency.

Accuracy of the beam angle and dose is then ascertained. Quality control and final verification is performed more so

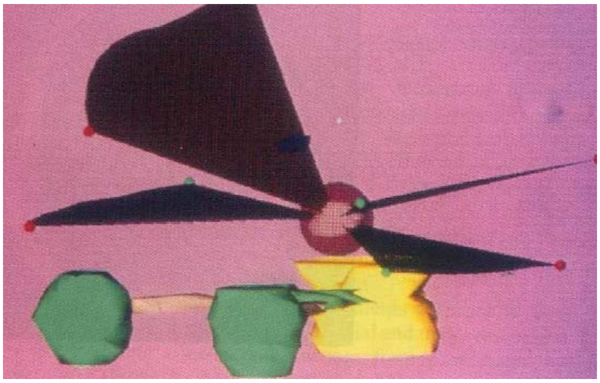


Figure 8 - Three-dimensional planning

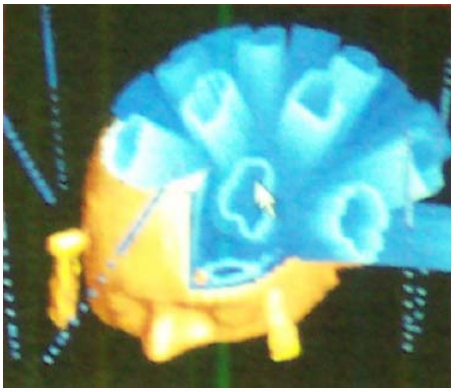


Figure 9 - Multimicroleaf collimeter superimposed on the brain

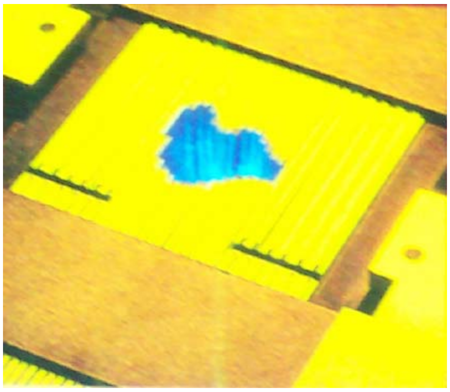


Figure 10 - Multimicroleaf collimeter

with LINAC based systems than with Gamma-knife on a target positioner such as stereotactic hardware with radiographic film, laser-guided systems or newer electronic detector systems and a trial run is then performed on the positioner or the phantom base before treating the patient. Collimators are then selected and attached to the radiation unit depending on the type of system that is used by the hospital. Conformal blocks to further silhouette the lesion are placed inside the collimator beam. Patient is placed in the radiation unit, the head frame and the patient's head are secured into position, and necessary monitors are applied. The planned radiation treatment is then administered. Recently, advanced radiosurgical frameless positioning system utilizing a micro-multi-leaf collimator allowing repeated treatments without surgical insertion of skull pins, and is more feasible for treatment in small children, patients requiring fractionation and in uncooperative patients refusing skull pin fixation.[1]

Gamma-knife

The Gamma-knife contains 201 small cobalt sources of gamma rays arrayed in a hemisphere within a thickly shielded structure. A primary collimator aims the radiation emitted by these sources to a common focal point which is comparable to focusing the radiant energy of the sun with a magnifying glass to a hot focus. Near the glass there is not much heat, but the energy is intense at the focal point Optical lenses cannot focus gamma rays, rather individual beams are allowed to summate by overlapping at the focal point of the collimator, achieving the same effect. A second collimator, which fits within the primary collimator, allows the beam focus size to be adjusted from 4 to 18 mm. This modality is good for intracranial tumours such as acoustic neuromas, pituitary adenomas, pinealomas, craniopharyngiomas, meningiomas, chordomas, chondrosarcomas, metastases glial tumours, AVMs, functional disorders such as trigeminal neuralgia, obsessive-compulsive disorders, intractable pain, Parkinson's disease, essential tremors and epilepsy (Figs. 11 - 14).[37,43]

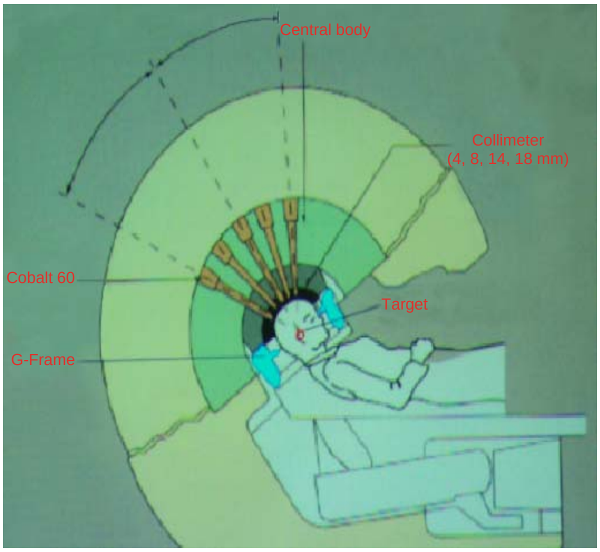


Figure 11 - Treatment progress in Gamma-knife

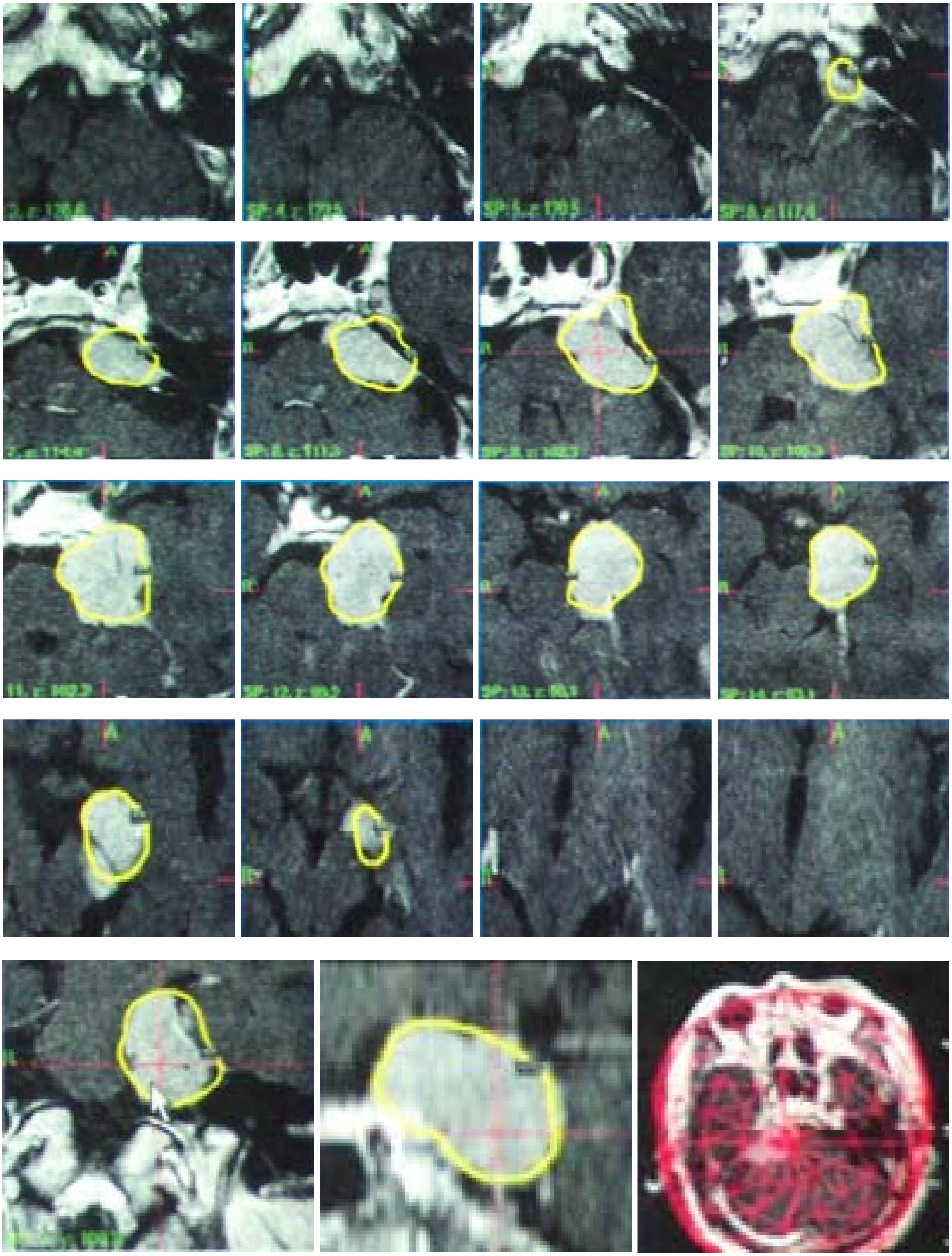


Figure 12 - Treatment planning for acoustic neuroma

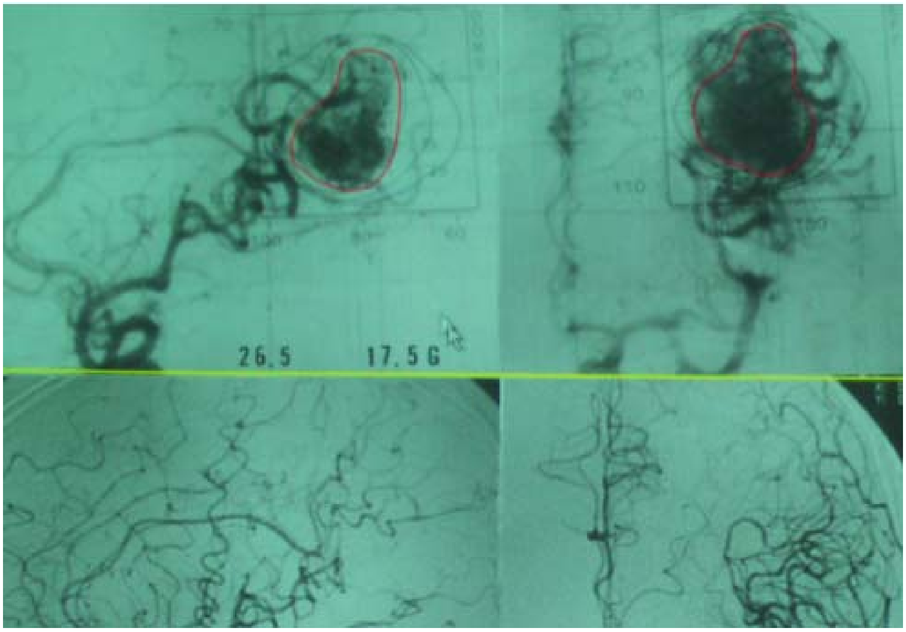


Figure 13 - Treatment planning in AVMs

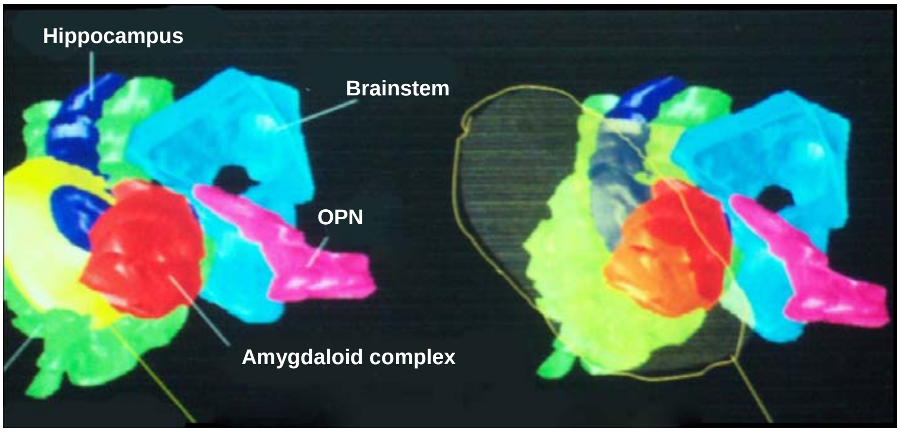


Figure 14 - Treatment planning for mesial temporal lobe epilepsy

Advantages of the Gamma-knife include:	Disadvantages of the Gamma-knife include:
1. Boasts over 30 years of clinical use with a large number of studies published in the medical literature 2. Simple treatment planning, better field shaping and rapid treatment per isocentre, even for treatment for lesions located near nerves and other sensitive structures 3. Multiple targets in the brain are easily treated during a single treatment session with a targeting precision within 2 mm 4. The cost is often 25 - 30% less than traditional neurosurgery. 5. Hospitalization is short, typically an overnight stay or an outpatient surgical procedure and the patients can immediately resume their previous activities. 6. Allows treatment of inoperable lesions and offers hope to patients formerly considered untreatable or at very high risk during open skull surgery	1. The basic design limits use exclusively for the treatment of brain disorders. 2. The procedure for radiation targeting requires the placement of a stereotactic head frame 3. It can be difficult to treat patients with lesions located in certain areas (e.g. the periphery) of the brain 4. High cost of initial acquisition 5. Difficulty with fractionation as it can not be used for staged radiosurgery for delivering the radiation dose in more than one fraction or treatment session 6. Necessity to replace the Gamma-knife radiation source every five to ten years

Linacs or linear accelerators

In the year 1982, a substitute to Gamma-knife utilizing LINACS was developed by two groups, Betti with Derechinsky and Colombo which was followed in 1987 by Winston and Lutz of Boston. Linear accelerators were adapted to stereotaxy, to provide a precise high dose. Linac-based systems use x-ray beams generated from a linear accelerator (Fig.15) and require no radioactive material. X-rays are produced upon the electrons striking a target. The beam goes through primary collimator, platinum filter, secondary collimator, wedges and blocks, to shape the beam to the required form. Utilization of microwave accelerated electrons for mega voltage radiotherapy with high energy electro magnetic waves, to accelerate electrons, is the basic phenomenon in Linac. The parameters helping in complex field shaping in the Linacs, include the patient's couch angle, gantry, arc angle, iso-centre position, collimator size, beam weighing and tissue depth. Multiple iso-centres are used to optimally and safely shape a lesion to deliver maximum dose at the target volume and rapid dose fall-off outside the target volume and control of the dose adjacent to critical structures. The four jaws in the Linacs provide conformal treatment planning, both for spherical and non-spherical lesions. This is mounted on a rotating gantry with the centre of rotation, the table is movable in the X, Y and Z axes. The axes between the cable and the gantry is called the iso-centre. Linacs move in arc shaped paths and crossfire various radiations to a well-defined target. The number, orientation and the lengths of the arcs can be modified by the treatment strategy and the diameter of the beam is regulated by utilization of the secondary collimators for each iso-centre. The patients need to use a head frame in all cases. The other ways of treatment process is in many ways similar to the Gamma-knife. There are both dedicated and non-dedicated (temporarily modified to perform radiosurgery) Linac-based radiosurgery devices (Fig. 15). Common brand names for modified linacs include X-Knife (Radionics Inc).[36]

Cyber-Knife

In frameless stereotaxy or Cyber-knife, the main advantages include precision irradiation, development of image guidance instead of external frame, easy fractionation, and treatment of young children without general anaesthesia. Cyber-knife is a Linac based highly manoeuvrable, real-time image guided robotic manipulator (Fig. 16), which acquires the images automatically through computer and registers the images to determine the treatment site co-ordinates with respect to Linac and the manipulator and transmits the co-ordinates through the manipulator which then directs the beam to the lesion. The significant part is movement of the target is detected, the aim of the beam corrected in near real time and the re-targeted area treated. The patient's skeletal frame work and rigid anatomy itself is a stationery frame of preference. The treatment of spherical and non-spherical lesions can be done with equal accuracy with the Cyber-knife. Non iso-centric beams within a volume of any target is allowed to be delivered at various points within the target that may not be the centre of the sphere. Even for complex lesions, the treatment time is very short and fractionation is possible even with minimal patient discomfort.[28]

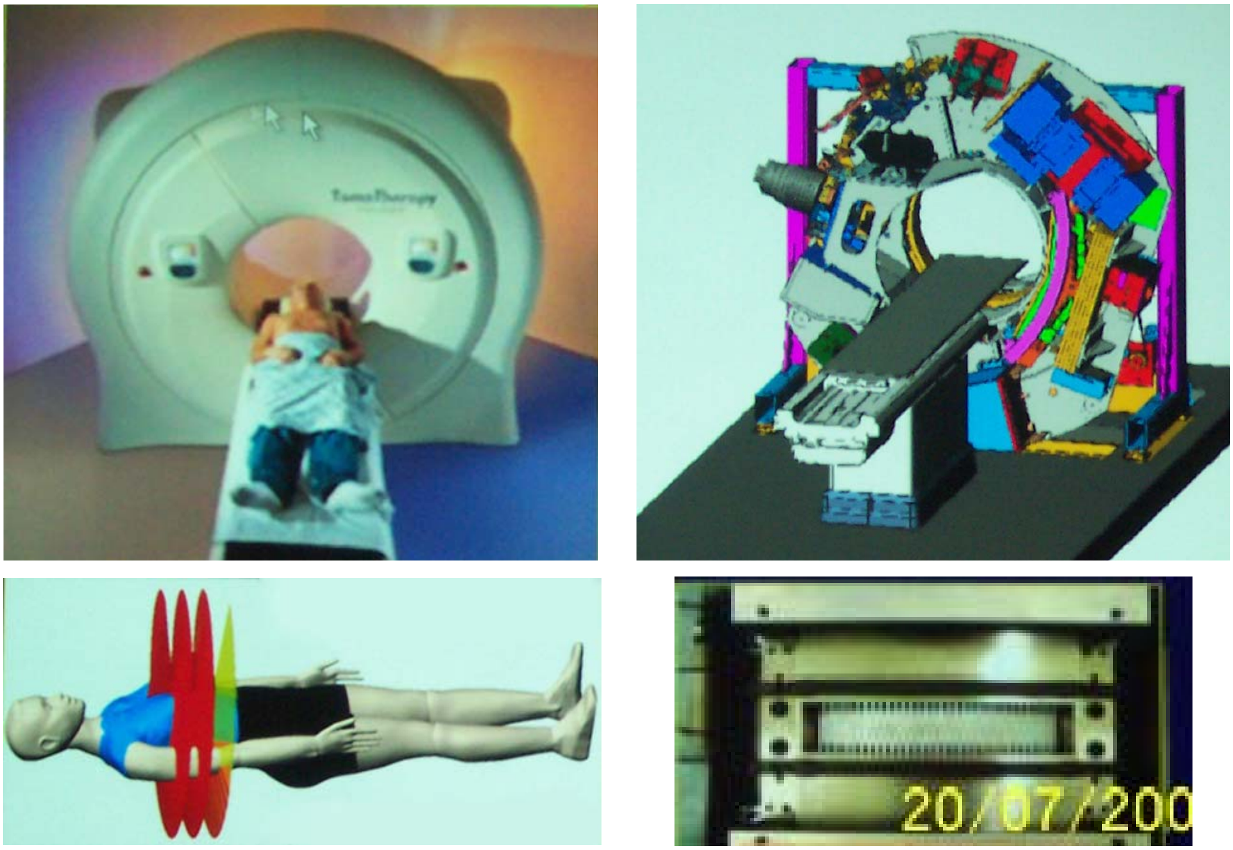
Figure 15 - Linac whole body radiosurgery

Figure 16 - Cyber-knife

Advantages of the Linac radiosurgical system :	Disadvantages of the Linac radiosurgical system :
1. More common place technology in hospitals with low cost of installation 2. Minor modifications required for the standard medical Linacs 3. Great flexibility in photon delivery 4. Lack of field size limitation and easily fractionated 5. May be dedicated or non-dedicated for multi-purpose use in various hospitals. Dedicated systems are calibrated for added spatial accuracy and optimized for radiosurgical efficiency	1. Less accurate than Gamma-knife 2. Less efficient than dedicated systems, which results in longer treatment time 3. Frame-based targeting only works for brain lesions 4. Requires more extensive quality assurance procedures to ensure safety and reliability

Intensity Modulated Radiation Therapy (IMRT)

Intensity Modulated Radiation Therapy is a Linac-based advanced radiation therapy that uses modern medical linear accelerators and computer-controlled "beam-shaping" in multi-fraction radiation therapy which conforms the radiation dose to the shape of the lesion and can be utilized at virtually any location in the body by a mechanical device called a multi-leaf collimator which dynamically reshapes the outlines and intensity of the radiation field during cancer treatment (Figs. 9 and 10). IMRT utilizes non-uniform small multiple beams of variable intensity to get a conformal dose distribution. The rate of photon delivery can be varied both in static and dynamic collimated fields. In the Nomose Peacock system, IMRT uses arc therapy where the photon beams are shaped by collimators called MIMiC (Multivane Intensity Modulating Collimator) which is linac based. IMRT along with sophisticated planning software fits the dose of radiation to a target much better than conventional radiation therapy, minimizes the volume of surrounding normal tissue that receives radiation there by producing fewer side effects but is not as spatially precise as radiosurgery and therefore, treatment is typically administered over multiple treatment sessions. The most well-recognized manufacturers by brand name at this time are the Trilogy® (Varian Medical Systems, Inc.), SynergyS® (Elekta, Inc.), X-Knife® (Radionics, Inc.), Novalis® (BrainLAB, Inc.), and CyberKnife® (Accuray, Inc.). All of these machines are image-guided and can perform IMRT (Figs. 17).



Figures 17 - Treatment with IMRT

Figure 18 - Fiducial placement in IMRT

Advantages of IMRT:	Disadvantages of IMRT:
1. The capacity to treat most regions of the body with IMRT and also extracranial (non-brain) tumours than standard radiation therapy 2. When coupled to an invasive stereotactic frame, precision targeting for brain tumours that approaches but can not equal the accuracy of Gamma-knife 3. An ability to deliver fractionated intracranial or extracranial treatment	1. The need for an invasive head frame (similar to the Gamma-knife) to assure treatment accuracy when used for brain radiosurgery (single fraction) 2. Less treatment accuracy when multiple fractions are used and lesser degree of targeting accuracy when treating extracranial tumours compared to brain radiosurgery

Research has found no benefit as to how radiation is delivered or the biological affect and probable outcome which is the same regardless of gantry or robot delivery.[3]

***Side effects*:** Side effects of radiation therapy will depend on the type of radiation received, the amount of the surface of the brain targeted, the site targeted, and the total dose of radiation. In general, there will be hair loss, skin irritation, possible hearing problems, nausea, vomiting, loss of appetite, and neurologic effects. The most prevalent side effect is fatigue which may last through treatment and for many months afterwards.[11] The neurologic effects most affecting quality of life are eventual permanent memory and speech problems.[4,5,31] These are just a few of the problems that can develop.

Radiobiology in SRS

In G1 and G2 phases of the cell cycle, the G2 phase is delayed which accounts for radiation resistance. Likewise, rapidly dividing cells respond acutely to radiation, whereas, late dividing or slowly dividing or non-dividing cells of the nervous system, the response is much delayed. Single large dose of radiotherapy causes more injury to the nervous system, than to the tumour, which is biologically undesirable. Therefore, multiple small doses are becoming more acceptable. The dose which is one unit equivalent to one gray which is 1 Joule of energy absorbed per Kg of tissue is variable in different parts of the brain which is called brain tolerance to radiation. In children, optic apparatus, brainstem area etc., toleration to radiation is very less (not more than 1.9 gray per fraction). This has brought in various treatment modalities like hyper fractionation which is division of one dose into two, with time interval of 4 – 6 hours for repair, between each treatment. In accelerated fractionation, the same dose is divided into two doses and given in a still shorter time.

The process of radiobiology: When a beam enters the body, the radiation to the skin subcutaneous tissue etc., causes a "*build-up region*" and after entering the brain tissue, there is a "*fall-off region*" and when it reaches the tumour, the dose is maximum which is a narrow tissue width where the energy is dissipated, called the "*Bragg-peak effect*".[6,7] The interaction of particle with matter causes a large amount of energy to be dissipated into the atom in a short path length which is produced at a predictable, specific depth in the tissue.[15] The radiation dose damages even the normal adjacent tissue which repairs faster than the abnormal tissue because the lesion or the tumour cells have abnormal cell cycle mechanism, diffusion of genetic features, abnormal metabolic patterns which delay the repair mechanism. The photon beams utilize x-rays or gamma rays where as particle beams utilize protons or electrons. The radiation interaction with the tissues may be of a photo-electric type where the energy is dissipated with the transfer of the photonic energy to the electron or a pair production occurs when a high energy photon and the nucleus of a target atom interacts and transforms into a positron and an electron. In the Compton effect the photons dissipate the energy to the Compton electron which forms the dominant effect in the therapeutic range utilizing photonic energy.[8]

The critical concept in the radiobiology of SRS is the ratio of alpha to beta α/β which is the survival of cells in relation to the dose of radiation that it receives. The biological equivalent dose (BED) is determined by the alpha to beta ratio α/β. Allowing radiation fractionation schemes to be compared depending on the number of fractions and the dose per fraction. A low alpha to beta ratio α/β is seen in normal brain, slowly growing and benign neoplasms which translates into a higher BED i.e., slowly growing lesions can receive a low dose of radiation and yet have the biological effect equivalent to that targeting on a malignant lesion which receives a conformal high dose of targeted radiation. Optimal dose range of each tumour is determined by the α/β of the tumour, tumour volume, the proximity to important structures like the optic apparatus, brainstem, facial nerve, eloquent brain, previous radiation, future radiation etc. An important biological rationale for understanding therapeutic effect of radiotherapy is repair, repopulation, re-oxygenation, and re-assortment. Compared with tumour, late-responding tissue with slow cell turnover like central nervous system tissue has a higher capacity for repairing the sub-lethal damage caused by radiation.[9] In radiobiological principles, the depth dose analysis, which is the analysis of the penetration of the radiation beams, after impacting a tissue, require to be made. In high energy photons, there is an increased depth of penetration in superficial tissues. The depiction of points of equal dose on the lesion is called an iso-dose line, which provides a dose distribution pattern in a single plane. The shape can be changed with the source size, beam energy, flattening filter, field size, source to skin and wedges.[10]

Multi-fraction radiotherapy balance increase in destroyed tumour cells by minimizing tumour cell repair and repopulation. Re-oxygenation of hypoxic areas can occur between each fraction of radiation as oxygenated cells around the periphery of the tumour are eradicated. Treatment with multiple fractions over time also allows re-assortment of cells into more sensitive phases of the cell cycle.

According to classical radiobiology, stereotactic radiosurgery should be less effective for metastatic tumours of the central nervous system. However, the medical literature has repeatedly disproved this supposition.[6] In general, stereotactic radiosurgery is more effective for control of metastatic lesions, especially the histologic types classically believed to be radio-resistant. The current assumption is that single high-dose treatment overcomes the radio-resistance of hypoxic cells as well as cells in the less-sensitive phase of the cell cycle. Another important observation to consider is that classic radiobiologic principles do not account for the gliosis and proliferative vasculopathy which occur from radiosurgical treatment. These and other events may also account for the enhanced biologic effectiveness of single-fraction treatment.[40]

A newer approach developed in recent years is the use of fractionated stereotactic radiotherapy (FSRT). This treatment allows use of the same precision techniques as SRS but improves the therapeutic ratio for treatment in eloquent areas of the brain. An increase in the therapeutic gain is seen when progressing from 1 to 10 fractions and is seen only incrementally beyond ten fractions. Increasing the "margin" of normal tissue around the target for daily setup error reduced potential biological gains. Fractionated stereotactic radiotherapy has been shown to be an important tool for treatment of tumours. By the use of multiple fractions, the total treatment dose can be kept below the radiation tolerance of this structure while still achieving effective tumour control.[13] Fractionated stereotactic radiotherapy has traditionally been confined to use of modified linear accelerators and generally is not compatible with a Gamma-knife system. In recent years, the technique has been improved by the development of more precise relocatable frame systems.

The protons and heavy particles are produced by cyclotrons or synchrotrons and utilize the protons for radiotherapy.[7] Of late, neutrons which have no charge interact directly with the nucleus and cause nuclear death, irrespective of cellular oxygen dependence. These are more toxic, have a Bragg-peak effect with increased dose localization and no exit dose.

Discussion on specific common issues(18,27,29,33,34,38)

***Meningioma*:** It is mainly indicated for small lesions, as adjunctive treatment for residual lesions, recurrent lesions and malignant transformations. There is a definite freedom from progression of the disease and actuarial tumour control and survival probability varies between 90 – 68% with 1 - 5 year survival rate. More complications like peri-lesional oedema, involvement near critical structures, should be borne in mind, but, still it is relatively safe and effective, more as a means of control than treatment

***Vestibular schwannomas*[12,17,30,32]:** Micro neurosurgery and SRS, both have equal incidence in various studies as regards to sensory neural hearing loss. Fractionated stereotactic radiotherapy is more commonly advocated in vestibular schwannomas. Involvement of facial nerve, trigeminal nerve and symptoms of hemi-facial spasms are much less with SRS. Five-year local control rate of 90 – 95% with a 66% hearing preservation (in previously hearing patients) and 97% five-year no trigeminal toxicity, is claimed, in several studies. Facial nerve complications are in the range of only 1 – 2%. The volume of treatment in radiosurgical principles is up to 6 cms and quasi spherical centres are better treated with Linac. The end point of treatment to see for tumour progression and availability of serviceable hearing seems to be better with SRS.

***Malignant astrocytoma*[2]:** The focal target dose and a dose volume have an inverse relation. Acute complications like oedema, worsening of symptoms, seizures, aphasia and motor deficits are more ideally a target of less than 30 mm, which is discreet and focal, is desirable. Acute toxicity increases with larger lesions. Dynamic enhanced MRI and dual isotope thallium-technetium SPECT helps to differentiate radiation necrosis and active lesion. The dual isotope SPECT data, co-relates with histo-pathological findings and at pre-operation and with survival in patients with malignant gliomas after surgery or high dose radiotherapy.

Brain metastases[25,35,39]**:** Ideal for SRS because of quasi spherical lesions which are usually less than 3 cms. They grow rapidly and respond quickly and clear efficiently after the necrosis with no residual vasogenic oedema and have radiographically discreet targets, with no cellular infiltrations. Single Mets are ideal for local control and the disease free survival is comparable to surgery. Stereotactic radiosurgery can reverse neurological deficits and is a good alternative to surgery.

Functional radiosurgery**:** Evolution of functional SRS began with Gamma-knife and still is more precise than Linac. The thalamus targets, globus phallidum, Parkinsonism, pain syndromes secondary to trigeminal nerve root entry zone involvement and capsulotomy for behavioural disorders are still utilized for functional radiosurgery. Very small volume of functional target requires special caution. Dosages are in the range of 120 - 140 gray, much higher than required for other pathological lesions. Since fiducial errors up to 6 mm are produced, localization errors with real spatial position at a given point are encountered. A lesion of 5 cms is ideal.

Conclusion

Linac is the most widely available SRS technology, requiring rigorous quality control and assurance programmes. The variability in quality and technique causes significant difference in outcome. Gamma-knife precisely delivers doses to small and moderate size lesions and lesions > 3 cms require cumbersome combinations of multiple iso-centres.

Proton, helium and carbon nuclei, heavy particle radiotherapy systems require expensive cyclotron and synchrocyclotron technology which is scarcely available in the world.[42] The main advantage is the Bragg-peak physical property of the radiation. The entry and exit points are unwieldy and the overall volumetric dose distribution can be very precise with an advantage in trimming to the critical tumour margin. In very small targets of 8 mms, there is a physical limitation of Bragg-peak method.

Experience and attention to detail are critical and utilization of multiple technologies to enable to push the frontiers beyond simplistic approaches is based on the given technology. Neuro-imaging, robotic technology, stereotactic techniques etc., have improved results in radiosurgery and more patients opt for radiosurgery, rather than microsurgery. The derived effect depends on the neurosurgeon's ability to detect normal from abnormal.

Cell specific radiation response modifiers, enhance radiation response, of the target cells, which may be helpful in managing problems with pituitary micro adenomas. Mircoscopic infiltration, causing recurrence, may be dealt by viral vector based gene transfer technology, with additional chemo- and radiotherapy. Gene transfer, to sensitize tumour cells to radiosurgery, is another option. Dynamic MRI with open box magnet is a promising method of localizing potential sites of active tumour growth, in patients with malignant astrocytomas and metastatic lesions. With the increasing availability of PET work by a variety of groups has started to integrate PET with conventional static, anatomical CT/MRI into the Gamma-knife treatment planning process.[23] Early results suggest that these combined methods of imaging improve target definition, particularly for infiltrating tumours whose boundaries are not so specifically defined on MR alone.

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