IJMP

Review Article

Stereotactic Radiosurgery/Radiotherapy: A Historical Review

Mansoureh Nabavi[1,2], Hassan Ali Nedaie[2*], Narges Salehi[3], Mansour Naderi[2]

Abstract

"Stereotactic" is an exact radiotherapy treatment modality which implements invasive and non-invasive facilities for improving precise dose delivery. Stereotactic refers to three-dimensional localization of a specific point in space by a unique set of coordinates that relate to a fixed external reference frame. An accurate delivery of radiation is attainable using these techniques with high precision (1-2 mm) which leads to dose reduction in critical organs and adjacent normal tissues while delivering the highest dose to tumoral tissue. Stereotactic irradiation consists of two techniques of delivery: Stereotactic RadioSurgery (SRS) which is an accurate single fractionated delivery of radiation to intracranial lesions and is attained by converging series of radiation beams on a target from various angles. Stereotactic Radiotherapy (SRT) which is a fractionated irradiation of intra and extra cranial lesions. This review article intends to highlight the radiobiological and physical aspects of these techniques and also introduces three commercially available stereotactic machines systematically and functionally.

Keywords: Equipments; Stereotactic Radiosurgery; Stereotactic Radiotherapy.

1- Department of Engineering, Science and Research Branch, Islamic Azad University, Tehran, Iran
2- Radiotherapy Oncology Department, Cancer Research Centre, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran
* Corresponding author: Tel & Fax: +982166948673; E-mail: Nedaieha@sina.tums.ac.ir

3- Department of Medical Engineering, Tehran University of Medical Sciences, Tehran, Iran

1. Introduction

Stereotactic refers to three-dimensional localization of a specific point in space by a unique set of coordinates that relate to a fixed, external reference frame [1].

SRS is defined as an operation in which externally generated ionizing radiation in certain cases inactivates or eradicates a defined target(s) in the head or spine, defined by high-resolution imaging, performed in a limited number of sessions, up to a maximum of five [2]. Therefore, according to American College of Radiology (ACR) and American Society for Radiation Oncology (ASTRO), Stereotactic RadioSurgery (SRS) is an accurate single fractionated delivery of radiation to cranial lesions and SBRT is a hypofractionated irradiation of extra cranial lesions [3]. SRS has many indications in neuro-oncology, cerebrovascular neurosurgery, and functional neurosurgery, including the treatment of brain and spine neoplasm and vascular malformations [4].

SRS is based on a simple concept. Series of radiation beams converge on an intracranial target from various angles in just a single fraction by using a frame-based method [5, 6]. However, Stereotactic Radiotherapy (SRT) is a procedure which consists of high precision techniques that uses multiple, non-coplanar photon beams, and delivers a high energy fractionated dose of radiation to a localized lesion. It applies frame-based or frameless techniques. This division stands on radiobiological aim of the treatment. The intention to perform SRS is radio ablation (reduction or removal of the mass by use of radiation), an attempt to inactivate the growth potential of cells within a target volume using a single and high dose fraction of irradiation. SRT intends to preserve the function of normal cells within the target volume and surrounding normal tissues by using multiple, smaller dose fractions, with use of close margins around the tumor. In both cases, accurate positioning of radiation beams and rapid dose fall-off outside the target volume are the most important features. The first one is possible by operating with stereotactic device. The second one is attained either with secondary collimation or with a micro-multileaf collimator [1].

In fact, SRT allows radiation oncologists and neurosurgeons to suggest their patients a treatment method which includes the accuracy and treatment planning characteristics of SRS without the side effects and risks associated with the SRS treatment of larger lesions [7].

According to the radiobiological effect of irradiating a single dose, SRS indications are "1) a primary component of late responding cells surrounded by late responding normal tissues; 2) a minimum component of relatively radioresistant hypoxic cells; 3) acceptable local control rate and minimum morbidity reported following SRS" [8].

For many years, scientists have found that Central Nervous System (CNS) parenchyma is extremely sensitive to the dose per fraction. The sensitivity of neoplastic cells as the responding tissues, in brain radiosurgery to the fraction size is not similar to the paranchymal cells sensitivity. Fractionation of a large dose into many smaller doses imposes the inherent differences in cellular repair ability between late and acute cell response. It can lead to incurable damage in acute effect of tissues and relative protecting of late effect of tissues. Fractionated SRT combines the biological advantages with the dosimetric advantages of stereotactic irradiation in small targets. Physical advantages of the stereotactic approach and biological differences in radiation response are considered in therapeutic ratio. The result of normal brain tissues spared with fractionation might be greater focal doses delivered and a significantly larger margin of normal tissue in the treatment volume in comparison with SRS [9]. The aim of this review is to give an opinion to readers for finding out different SRS developments, equipments, applications as well as their advantages.

2. Historical background

Stereotactic technique was used on human brain by Spiegel and Wycis in 1947. Their

research led to the development of multiple stereotactic neurosurgical devices during the 1950s [10]. SRS was conceptualized by Lars Leksell in 1951. The first patient was irradiated with X-ray spectrum of 200kV energy, produced via bremsstrahlung radiation while he was fixed in a stereotactic ring with a precisely guided roentgen-ray tube [11]. Gamma knife, the first clinical stereotactic radiosurgery machine, was founded by Lars Leksell and Borje Larsson to treat intracranial lesions in a noninvasive method [12]. The Gamma Knife application is based on gamma emitter sources such as cobalt 60 radiation which are arrayed on the hemispherical shell.

Development of imaging techniques and rising of frameless techniques instead of rigid head fixation for immobilizing the patients as well as new approaches in stereotactic targeting made the extra-cranial stereotactic irradiation possible [4].

Since 1968, many stereotactic systems have been evolved. The main differences of these machines are: radiation and radiation source type (γ, X-ray and proton beams), delivery system, target localization, and frame requirement. SRS by using charged particles was first introduced in decade between years 1950 and 1960 when Tobias et al. started irradiating brain tumors with high energy protons accelerated from synchrocyclotron [13]. Bragg-peak studies with protons began in Uppsala, Boston, and Berkeley. In Berkeley, Bragg-peak radiosurgery using helium ion beams was also developed [11]. Proton therapy can be used for single-fraction brain stereotactic irradiation, since it suggests proper dose distribution and optimal dose homogeneity in the treatment volume with minimized integral dose [14]. According to its high cost and special shielding, there are a few proton therapy systems worldwide [15].

Linear accelerator (Linac) based SRT was initiated in the early 1980 by a Swedish physicist who proposed to use the linac instead of cobalt-60 or protons [11]. Same as the Gamma Knife systems, linac employs accelerated photons but its application is based on different software and hardware compared with the Gamma knife. Linac has the ability to operate as both frame-based and frameless systems which makes it efficient for fractionated SRT which is not applicable with the Gamma Knife [16].

Stereotactic brachytherapy is applicable by implementing 125I seeds in the irregular target with neurosurgical needle guidance. Since this approach is similarly as invasive as conventional surgery and in spite of SRS it is only operable on inpatients and it is considered as a drawback [14].

3. Procedures of SRT

Fixation and immobilization, imaging, treatment planning, treatment verification, and quality assurance which are mechanical and dosimetric, are main steps in stereotactic irradiation [11].

3.1. Stereotactic neurosurgical/relocatable frames

Fixation of stereotactic items (localizer and positioner) and definition of the reference point (0,0,0) of the stereotactic coordinates rely on stereotactic frame. There is a constant geometrical relationship between the stereotactic frame and anatomical structures, such as Planning Target Volume (PTV) which is achieved by fixation of the frame to the patient's head. During the whole treatment procedure, from the first step (imaging) to the last (irradiation), stereotactic frame must remain on patient's skull. In SRT technique in which the fixation is applicable by use of relocatable frames, the reproducibility of the patient positioning must be ensured[11,15].

In SRS the frame system is neurosurgically fixed onto the patient's skull with three or four pins, under local or general anesthesia which is much invasive for patient (Figure 1)[1,15].

Figure 1. Brown-Robert-Wells (BRW) frame with fiducial system [15].

For SRT, the head is fixed non-invasively in a relocatable thermoplastic mask attached on the stereotactic frame (Figure 2)[1,15].
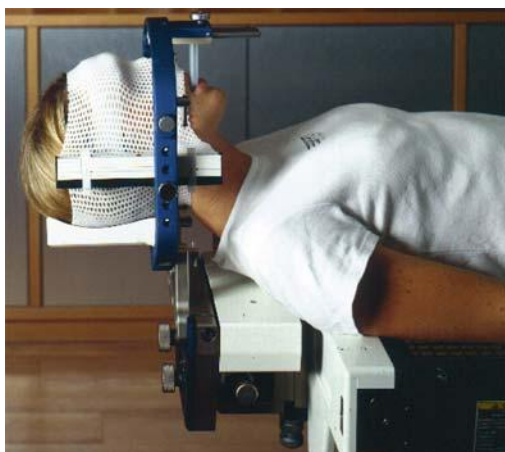

Figure 2. Non-invasive repeat head fixation with the mask system and upper jaw support [11].

There are different stereotactic frame systems which are used widely in different centers: Brown-Robert-Wells (BRW) system, Cosman-Robert-Wells (CRW) system, Leksell system, Leibinger Fischer system, and the Brainlab system. These systems are made up of different materials of the stereotactic frame, design, and connection with the localizer and positioned and accuracy of repositioning [11].

3.1.1. BRW frame
BRW stereotactic head frame is typically used for single fraction SRS. The frame is pinned to the skull with three or four screws through a procedure followed by anesthesia.

3.1.2. GTC frame
Gill-Thomas-Cosman (GTC) relocatable frames for stereotactic radiation consist of a standard head ring to which an individualised dental impression of the upper teeth and a moulded occipital head support are attached (Figure 3). The advantages of this method are its convenience of use and quick release in emergency situations such as a seizure or claustrophobia. They can be used for multi-fractionated treatments. It is better for patient's in need of relocatable head frames to have good dentition for the use of the mouth blocks [17]. The localizer unit consists of a dental piece fixed between two positioning plates. These components are provided as individual pieces made of perspex. They are accumulated and bonded together at the time of patient fixation and are specific to that individual [18].
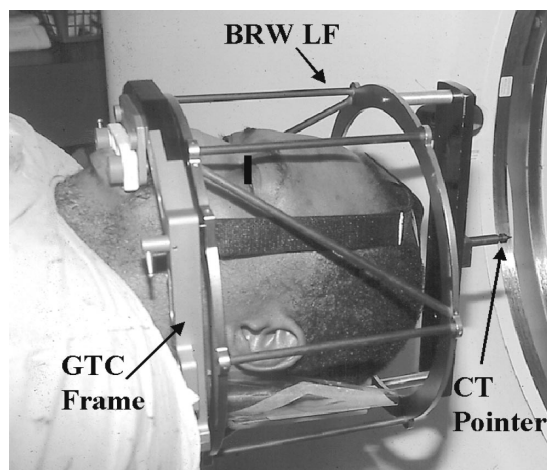

Figure 3. The GTC relocatable frame contains fiducial system.

3.1.3. Fiducial system
Fiducial systems are regularly in different shapes such as rod elements attached to support rings, etchings, or steel balls on the sides of plastic fiducial boxes or wires stretched between rigid spacers. The ideal stereotactic fiducial systems have no significant artifacts or obscuring the anatomical images, precise conformity to the patient's immobilization system, an apparent simple marker arrangement, and ability of correcting the effect of imaging slices that are not perpendicular to the cantilever of scanner couch [14].

3.2. *Imaging*

Computed Tomography (CT) is commonly used for stereotactic system localization. During CT scan, the localizer is attached to the frame. The localizer box has CT-compatible fiducial markers on each plane that are visualized on CT. Therefore, stereotactic coordinates are related to imaging coordinates by localizer. The localizer and positioner system have to be adaptable to the radiological work-ups and offer an accurate image of the tumor and of the critical structures, without artifacts. When Magnetic Resonance Imaging (MRI) is used for localization and positioning, high homogeneity of the magnetic field is necessary to prevent spatial distortions artifacts, which may disturb the geometrical relation between the stereotactic coordinates system and imaging coordinates system [11].

Various imaging techniques are used for treatment planning, these are different methods and have a complementary nature: 1) MRI describes the anatomical structures of soft tissue with a high accuracy, 2) CT is important for description of bone and soft tissue, 3) angiography is essential for the visualization of the arterio-venous malformations, 4) positron emission tomography (PET) and single photon computed emission tomography (SPECT) offer additional information about tumor extension and biology, 5) Digital Subtraction Imaging (DSI), and 6) Computed Tomography Angiography (CTA). So, the definition of tumor extension and critical structures is characterized by the use of correct merging information of multiple imaging systems and image fusion method[11]..

Most of the planning systems use CT images for calculating the correct dose in three dimensions. The Hounsfield number of the CT is exchanged to an electron density by treatment planning software. Some planning software programs can use MRI information only, with regard to homogenous soft tissue density for the dose calculation. Since no large-density inhomogeneities are in the brain, the stereotactic planning systems use simpler and quicker algorithms [11].

3.3. *Treatment Planning*
3.3.1. **Target definition**

The description of the target volume is associated with all of the imaging data and clinical information (operation, histopathology, other treatment approaches, etc). "The tumor specific morphology, the growth pattern of the tumor, and the anatomical relationship to the normal tissue are essential parameters in defining the target volume" [11]. The most important step in SRT is definition of critical structures. For applying this technique, target point should be defined in the target volume and must be positioned in the linac isocentre exactly. Related to the shape of the tumor, one or more target points can be specified. Position of target points in stereotactic coordinate is obtained by the planning system. Before delivery of radiation, these coordinates are used for patient positioning by positioner, a device attached to the frame, which connects the stereotactic coordinate system to the room coordinate system in linac isocentre [11].

The stereotactic radiation is defined by a very steep dose fall-off on the peripheral organs of the target volume. This is achieved using appropriate collimators and some of various radiation directions [11].

Stereotactic treatment planning needs facilities to plan multiple noncoplanar arcs focused to a single or several isocentres, and requirements for using multiple fixed noncoplanar conformal beams specified by either conformal blocking or multileaf collimators (MLCs). Tumors adjacent to critical structures, such as the brain stem and optic apparatus, ought to be treated by Intensity Modulated Radiation Therapy (IMRT). These treatments are mostly designed by an inverse planning. The physicists must prevent overlapping of beam entrance and exits and should consider the maximum separation according to the expression 1800/N in arc planes (as defined by the couch angle) where N is the number of arcs to be used[1,11].

Prevention from reirradiation and irradiation of critical structures manifests the importance of optimization softwares and Tumor Control

Probability (TCP)/ Normal Tissue Complication Probability (NTCP) modeling [8,9].

It is proper if the final dose distributions can be shown in any required plane, such as adjacent structures. For Plan comparisons, dose volume histogram (DVH) analyses are required for choosing the ideal treatment plan. DVH analyzing for various arc collimated techniques has shown that 3-5 arcs for SRS or SRT has spared sufficient normal tissue, although for benign tumors, it would be better to increase the number of arcs for reduction of exit doses from each arc[11].

Although MLC aperture are mostly used for SRT to produce conformal beams, since the 10-mm MLC system is often too coarse, more conformal dose distribution in target can be attained using lead blocks. Moreover, this conformity is gained using micro MLC but is limited to field sizes below 100 mm. Localization of the target volume is the greatest concern and therefore it is important to have an accurate stereotactic treatment[14].

For attaining sufficient coverage of the target with isodose curves between 80 and 95% of the central dose, desired margin to PTV is required. Using multiple isocentres with arcing circular beams, dose uniformity is lost to achieve more conformal target coverage. To evaluate optimized plan dose volume, histograms and radiobiological considerations can be administered to the PTV and organs-at-risk (OARs) [14].

3.3.2. Beam data measurement

For small photon beams with tertiary collimator, following data must be measured: up to five profiles, a central axis depth dose or Tissue Maximum Ratio (TMR) curve, output factors in air and water, and build-up curves. In order to obtain exact measurement, small detectors with high spatial resolution are required due to lack of lateral electronic equilibrium in pencil beams. Profiles are often measured using X-ray verification film, such as Kodak XV2 or EDR2, and other films such as EBT, EBT2, and EBT3that are improved for dose/density nonlinearity[11,14].

To measure the depth-dose or TMR data for small fields (down to 20 mm diameter), small-volume (<0.2 cm3) ionization chambers are generally advisable. In depth-dose measurements of pencil beams should be avoid of the beam divergence. This cause a significant distort in the depth-dose curves. Another way is using a water tank system in conjunction with a p-type electron diode or diamond detector for measurements down to about 15 mm diameter collimators. For such measurements, the set up should indicate the mean isocentre depth and scatter geometry of the patient. If the detector resolution is about 2 mm or less, the beams, below 20 mm diameter, should be measured with film, (Thermo Luminescent Dosimeter (TLD), and a small diode. It should be noted that tertiary collimators can also increases build-up depth [14].

3.3.3. Dose specification

Dose distribution in stereotactic is delineated as absolute or normalized dose distribution. The prescribed dose is defined as the isodose surface surrounding the PTV. Evaluating the treatment plans, same as the conventional 3D radiation, is based on the isodose curves, DVHs, conformity index, or mathematical models for the NTCP and TCP. Finally the best plan is accepted by physician, using clinical awareness [11].

3.4. Treatment Verification

The set up can be done in two ways. 1) Bringing the plan isocentre into linac isocentre by setting three X, Y, and Z vernier scales. This system is not reasonable for fractionated stereotactic treatments because it is not repeatable, but generally can be used in single-fraction radiosurgery. 2) Using the setup boxes with specific plates of each patient or hard copies with the isocentre intersections and beam projections signed for room laser set up. This method is proper for daily set-up in fractionated stereotactic treatments [14].

Patient positioning on the linac is performed using a stereotactic positioner. This device can be used to project the coordinates of the target point onto orthogonal planes fixed to the stereotactic frame. In this process, the patient

can be positioned so that the target point locates on the isocentre of the linac [11].

In linac-based stereotactic treatments, stability and accuracy of the device in comparison with conventional treatments is more desirable. In this regard, for using isocentric treatment in SRS and SRT, the accuracy of the isocentre point has the most importance. Therefore, the axis of the gantry rotation, the central axis of the beams, and the rotation axis of the treatment coach must be adjusted into one point. Since these conditions cannot be achievable in practice, it is appropriate that the three axes, gantry rotation axis, central axis, and coach axis, meet each other in a sphere including isocentre with 1 mm diameter[11].

After the patient positioning, the positioner is removed and radiation is delivered [11].

3.5. Quality Assurance

The clinical use of the linac is provided by categorical and well-defined protocols such as Task Group 42 in 1995[19]. The quality necessities in stereotactic are different from conventional radiotherapy agreements. Following quality assurance (QA) protocols, the exact location of the target volume and target point using various imaging modalities, dosimetry, the planning of the irradiation, and specially using the absolute dose calibration and dose application can be obtained. In the QA process, it is essential to provide appropriate phantoms and specialized dosimetric equipments [11]. Generally, QA tests relate to the exact technique used [14]. Documentation of quality-control requirements have been published by Hartman (1995) [11].

4. Specification of the Radiosurgery Units

In this article, the main focus is on the cobalt-based and linac-based systems, since particle-based devices are only available in a few medical centers.

4.1. Gamma Knife

The only cobalt-based system is Gamma Knife that was designed by Lars Leksell in 1968.

The most current model, the Leksell Gamma Knife (LGK) Perfexion, was introduced in 2006 with a redesigned machine from previous models [20]. The previous model, the LGK 4C, is still in wide use [21, 22].

The Gamma Knife was designed to provide highly accurate radiation treatment of intracranial targets. According to fabricator, overall treatment accuracy is 0.3 mm. The system consists of three basic components: spherical source housing, four collimator helmets, and a couch with electronic controls. Various models of the Gamma Knife are different mainly in the pattern of the source distribution within the housing, the couch path, hydraulic or electric motor driven couch movement, and whether the treatment is computer controlled with automatic patient positioning. 201 Co-60 gamma-ray emitting sources are distributed in a semi-hemisphere array in the source housing. The Co-60 half-life is 5.26 years and radiates 2 photons with an average energy of 1.25 MeV. Therefore, for avoidance of long treatment time, the sources must be replaced every 5 years. Each Co-60 pill is wrapped by a welded stainless steel tube, which is put inside a stainless steel bushing[1,15].

All beams focalize to a point known by unit center point (UCP) which has 40 cm distance from each source. The UCP is similar to the linac isocentre and is a point that the target volume must reside in treatment duration. This is attained by the three-dimensional coordinate system on the Leksell frame. At installation, the activity of each source is approximately 30 Ci, and total dose rate of sources is about 300 cGy/min at the UCP[1].

Enroute to the UCP, the radiation beam from each source is collimated by a primary collimator and then by a secondary collimator helmets (there are 4 secondary collimators). 201 tungsten collimators specify circular apertures that project a specific beam diameter of 4, 8, 14, or 18 mm at the UCP. The radiation dose deliver to the patient when the primary and secondary collimators adjust and the couch fixes the helmet in the source place. Adaption of dose similar to the target, is

possible by the difference in conformation of aperture diameters, plugging, irradiation times, and head positions that defines a ″shot″ in Gamma Knife[1, 15].

Gamma Knife is not suited for extra cranial targets, because it does not have adequate space within the helmet. The Gamma Knife requires the use of an invasive stereotactic frame, which is pinned to the patient's skull, so it is not suitable for fractionated treatments [1].

An improved design of Gamma Knife is defined with computer control of the treatment steps. Prior to irradiation, the automatic positioning system (APS) moves the patient's head into a desired location. In SRS and SRT, patient positioning can often be performed without human interposition. On the other hand, when there are multiple separate targets, it is necessary to monitor the patient in the treatment duration by the therapist. Computerized Gamma Knife also allows merging of an R&V system. In Gamma Knife model C, with its present software version, the therapist can monitor several treatment parameters such as: helmet aperture, patient position with gamma angle, and treatment time; but now checking helmet plugging is performed only manually [1].

4.2. Linac based SRS/SRT systems

Linac-based SRS and SRT systems are specialized machines which use fixed Co-60 sources or a particle-beam source[23,24]. This equipment generates low-energy megavoltage beams (1–6 MeV) focusing through multiple paths to a specific point in space. The CyberKnife is an exception, that uses a compact linac on a robotic arm and a defined isocentre is not required [1].

4.2.1. Conventional Linac

Conventional linac is worldwide radiation equipment in every radiation therapy departments so that it can be used as a source for SRS and SRT. For utilizing the conventional linac for SRS and SRT, special stereotactic accessories are needed including secondary collimator system, a patient positioning and immobilization system, and a stereotactic device [1].

Circular or oval target volumes are treated using tertiary stereotactic collimators attached to the tray holder of the linac. The diameter of the irradiated area is specified by the size of the circular collimators that are available between 1 to 35 mm. For irregular target volumes, different individual apertures, and in some cases micro multileaf collimators can be used. In spite of traditional multileaf collimators, the resolution of micro-multileaf collimators is optimized (between 1 to 3 mm) which is beneficial[11].

Dynamic field adjustment during irradiation can be applicable using computerized micro-multileaf collimators and using dynamic arcs we can shape our fields [11].

4.2.2. Novalis

The Brainlab Novalis system (BrainLAB, Heimstetten, Germany) is a developed project from collaboration between Varian Medical Systems, Inc. and Brainlab, AG. Novalis is an integration of Brainlab's m3 MLC collimator and head of a Varian 600C Linac. Novalis is confined to 10 cm2 field size like conventional systems with m3 MLC collimator, while in order to obtain larger radiation field they must be patched together. Dynamic intensity-modulated radiotherapy can be provided by Novalis since it has an m3 MLC collimator[1].

Novalis system is equipped with various positioning, tracking, and immobilization devices for the patient, such as on-board stereoscopic kilovoltage X-ray imaging with additional infrared video motion-tracking systems. An overall treatment accuracy of 1–2 mm has been claimed by the manufacturer. A specialized treatment-planning system is also included [1].

With increase in stereotactic knowledge and advanced radiosurgery equipment and softwares, Novalis has been built specifically for radiosurgery over the past decades. As other stereotactic systems, Novalis delivers the radiation precisely and accurately to the lesion according to its size, complexity, type, and location [1].

4.2.3. Cyberknife

Radiosurgery is one of the best approaches for treating intracranial lesions and arteriovenous malformations (AVM). This technique requires rigid cranial fixation which makes patient uncomfortable during the treatment, and treatment degrees are limited and it is not able to be used for extra cranial lesions. The Cyberknife is a frameless conformal radiosurgery delivery system which is a combination of advanced approaches in robotics and computerized image processing that makes image guided radiosurgery applicable [25-27].

Cyberknife consists of a lightweight linear accelerator (130 kg) 6-MV linac (for the administration of radiation), designed for radiosurgery and mounted on a highly flexible robotic manipulator capable of positioning and guiding the linac with an accuracy of <0.6 mm [28]. The second approach is real-time image guidance, which declines skeletal fixation requirements for either positioning or invasive immobilization of the treated volume. The imaging hardware consists of two fixed silicon detectors elucidated by X-ray sources placed orthogonally toward the patient (installed in the ceiling of the treatment room) and they are attached to digital image collectors for providing an image guided treatment [25,27,29]. They afford a stable reference frame for patient localization. This imaging system attains digital radiographs of bony landmarks or implanted fiducial markers in the treatment site and uses image registration techniques to specify the target's coordinates with regard to the Cyberknife treatment head. The robot administers these coordinates to aim the photon beam to the target. This process detects the variations and corrects beam localization in real-time while the target is moving. The table (remotely controlled) can move around different axes and thus adjust the position of the patient [29]. Figure 4 shows a layout of Cyberknife components.

The Cyberknife characterizes the skull location, spine, or other radiographic landmarks in the machine coordinate frame according to digitally reconstructed radiographs (DRRs) given by the treatment planning CT using X-rays projection from the real-time imaging system. A computer algorithm is used for measuring both anatomic interpretation and rotation by repeated changes in the position of structures to adjust the CT radiographs and DRRs [30]. Once skeletal position is attained, the coordinates depend on the robotic arm, which matches the localization of the beam and delivery. When linac position is changed, this process would be repeated. Total system error for the Cyberknife is less than 1.2 mm [25,27]. Motions limit conventional radiosurgery machines to isocentric-based (Source-Axis Distance (SAD)) treatments in which all beams converge on a single point in space, but the Cyberknife enables more complex treatments whereby beams originate at random positions in the room, and target is pointed from different positions with beam. "During the actual patient treatment, the linac stops at each of approximately 100 equally spaced nodes, at each of which, the beam can be aimed anywhere within a volume around the center (non-isocentric beams)" [31].

For determining a satisfying dose distribution, optimization techniques such as beam weighting can be used. Complexity of the plan and delivery approaches determine the total treatment time; its length is comparable to standard radiosurgery with more than one isocentre. As rigid fixation is not required, fractionation is possible[31].

The CyberKnife system is mostly followed by dynamic tracking software which is a subject for identification and measurements of the treatment volume, and transmits this information to the robotic arm. The image guided treatment assures the optimization of the patient's position so that allows precise irradiation of treatment volume. The CyberKnife has also a dynamic tracking system (the Synchrony system) which is used for tumors that have intrafraction movement by breathing or organ movements. (e.g., tumors in the lung, pancreas or liver). Tumor location and the respiratory movements are followed continuously, the robotic arm can compensate them and the radiation beams will be fixed on the target [31]. Characteristics of three radiosurgical systems are compared in table 1.
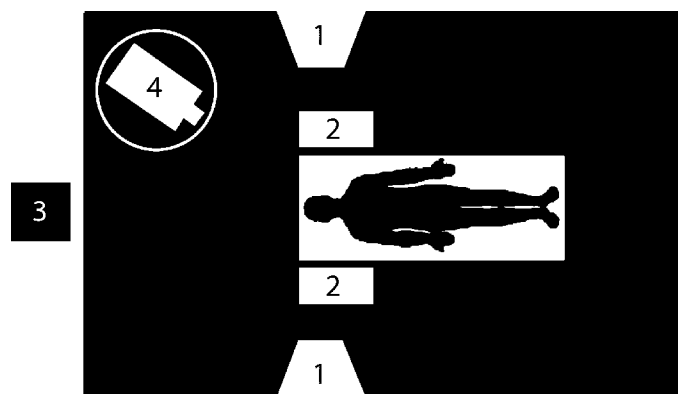
Figure 4. CyberKnife component layout: *1:* X-ray tubes, *2:* flatpanel imagers, *3:* modulator cabinet, and *4:* linear accelerator [1].

Table 1. Comparison between 3 radiosurgery systems [32,33].

Characteristic	Unit		
	Gamma Knife	Novalis	Cyberknife
Radiation type	Gamma (1.25 MV)	X-ray (6 MV)	X-ray (6 MV)
Collimation system	Circular (4, 8,14,and 18 mm aperture)	Circular/micro-multileaf	Circular (5-60 mm aperture
Number of beams	201	Infinite	Infinite
Dose fall off	Sharp	Sharp	Sharp
Image guidance/ Tracking	No	Infrared cameras, Orthogonal kV X-ray	Orthogonal kV X-ray
Fractionation capability	No	Yes	Yes
Average treatment time per SRS case	Dependent on cobalt half-life	20-40 min	40-60 min
Average treatment time per SRT case	NA	10-30 min	30-50 min
Advantages	Effective on functional lesions Simple quality assurance	Constant out-put Most dose homogeneity Extracranial targets Fractionation Robotic couch Non invasive frame	Constant out-put More dose homogeneity Extracranial targets Fractionation Frameless
Disadvantages	Reload of Co-60 sources Alteration of dose rate in order of Co-60 decay curve Invasive frame	More QA	Most QA

4.2.4. Other stereotactic systems

Another system that is applicable for stereotactic use is the Varian Trilogy system. Trilogy has a kilovoltage orthogonal imaging system on board in addition to its megavoltage imaging system and the Millennium 120 multileaf collimators. Cone beam reconstruction of target volume is produced while imaging during the gantry rotation which is beneficial in patient positioning and provides the acquired stereotactic accuracy [1]. Cone-beam CT is obtained using a cone-shaped beam X-ray instead of fan beam for a slice and the different way of target volume calculations by its imaging. Elekta has a sophisticated approach in cone-beam technology application in Elekta synergy. Elekta synergy offers various ranges of precise

field cones which promote performing SRS and SRT by optimizing stereotactic field shaping which are variable in size from 5 to 50 mm and there are three dynamic micro multileaf collimators to choose from providing a 3, 5, and 7 mm leaf width at isocentre[33].

Another discernible stereotactic system is TomoTherapy system which its application is based on a small 6 MV linear accelerator fixed on gantry that constantly rotates and the patient is transited concurrently toward the beam by couch movement. There are Mega Voltage CT (MVCT imaging detectors placed on the gantry in counter direction from radiation source. As another linac-based stereotactic system, HT has MLC collimation system which dynamically modulates irradiation in transverse and cranial-caudal plane. In contrast to SRS, HT systems do not require surgically fixed head frames [34].

5. Conclusion

The Gamma Knife is a foundation for other SRS systems since it has been used for clinical SRS studies for a long time. It is a proper system for SRS treatment of cranial lesions, especially functional lesions. It is a fixed device with high accuracy in patient immobilization which is considered as an advantage. The disadvantage of the Gamma Knife is using an invasive head frame that should be pinned to the skull. The head frame is attached with local anesthesia and has an irritation for patient. Only limited number of patients can be treated in a day, because the frame is usually attached to the skull in the same day and planning cannot be done earlier.

The Gamma Knife is not suitable device for peripheral cranial as well as large lesions and it can only be used for head and upper cervical neck tumors. The Cobalt-60 sources must be replaced every couple of years according to their half-life. In comparison, the linac dose rate is be constant.

The flexibility of the linac based system in treatment of tumors with various shapes and implementation of their related plans is another advantage of these machines. Using non-invasive frames makes the linac a proper device for fractionated stereotactic treatments, but there are some inherent movements in frameless systems which makes the radiation delivery less accurate, albeit with aid of image-guided facility any changes in patient positioning may be corrected. Image-guided systems also compensate the physiological movement during respiration in extra-cranial lesions. Moreover, treatment can be planned in previous days of the procedure and number of patients in a day may be increased.

Clinical outcome has a considerable importance. In multivariate analysis of a multi-institutional trial, it was shown that single-dose SRS treatment of previously irradiated cranial tumors with linac systems had greater risk of recurrence than those treated with Gamma Knife.

Acknowledgment

References

1. Levitt SH, Purdy JA, Perez CA, Vijayakumar S. Technical basis of radiation therapy. 4threvised Edition. Springer-Verlag Berlin Heidelberg. 2006.p.234-249.
2. Barnett GH, Linskey ME, Adler JR, Cozzens JW, Friedman WA, Heilbrun MP, et al. Stereotactic radiosurgery — an organized neurosurgery-sanctioned definition. J Neurosurg 2007; 106:1–5.
3. Practice guideline for the performance of stereotactic radiosurgery. ACR Practice Guideline. Reston: 2006 [cited 2010 April 20]. Available from: http://www.acr.org/Secondary Main Menu Categories/quality safety/
4. Kondziolka D, Lunsford LD, Flickinger JC. The application of stereotactic radiosurgery to disorders of the brain. Neurosurgery 2008; 62:707–719.
5. Seung SK, Larson DA, et al. ACR–ASTRO. Practice guideline for the performance of stereotactic radiosurgery. Revised 2011.

6. Larson DA, Gutin PH. Introduction to radiosurgery. Neurosurg Clin N Am 1990;1(4):897-908.
7. Bellerive MR, Kooy HM, Loeffler JS, M.D. Linac radiosurgery at the joint center for radiation therapy. Medical Dosimetry.1998; 23(3):187-199.
8. Larson D, Flickinger JC, Loeffler JS. The radiobiology of radiosurgery. Int. J. Radiat. Oncol. Biol. Phys. 1993; 25:557–561.
9. Solberg TD, Selch MT, Smathers JB, Desalles AF. Fractionated stereotactic radiotherapy, rationale and methods. Medical Dosimetry. 1998; 23(3):209-219.
10. Lasak JM, Gorecki JP. The history of stereotactic radiosurgery and radiotherapy. Otolaryngol Clin North Am 2009; 42:593–599.
11. Schlegel W, ortfeld T, Grosu AL. New technologies in radiation oncology. Springer-Verlag Berlin Heidelberg 2006.p.267-274.
12. Jayarao M, Chin LS. Robotics and its applications in stereotactic radiosurgery. Neurosurg Focus 2007; 23.
13. Pannullo SC, Yama C, Wernicke AG. Stereotactic Radiosurgery for Brain Tumors. Diagnostic Techniques and Surgical Management of Brain Tumors. 2011
14. Lunsford L, Alexander E, Chapman P, Coffey R. Consensus Statement on Stereotactic Radiosurgery: Quality Improvement.Neurosurgery.1994. Available from: http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:Consensus+Stat
15. Mayles P, Nahum A, Rosenwald JC. Handbook of radiotherapy phys-theory and practice. Taylor & Francis Group. 2007.p.987-1003.
16. Goetsch SJ. Linear accelerator and gamma knife-based stereotactic cranial radiosurgery:challenges and successes of existing quality assurance guidelines and paradigms. International journal of radiation oncology, biology, physics. 2008; 71:S118-21. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18406908
17. Chelvarajah R, Leighton B, Martin B, Wayne et al. Cranial Immobilization – Is There A Better Way? Department of Radiation Oncology.Westmead Hospital, Sydney, Australia
18. Gill SS, Thomas DGT, Warington AP, Brada M. Relocatable frame for stereotactic external beam radiotherapy. Radiation Oncology Biol.Phys. 1991; 20: 599-603.
19. Report of Task Group 42, Radiation Therapy Committee, AAPM Report no.54, Published for the American Association of Physicist in Medicine by American Institute of Physics. 1995.
20. Novotny J, Bhatnagar JP, Niranjan A, Quader MA, Huq MS, Bednarz G, et al. Dosimetric comparison of the Leksell gammaKnife Perfexion and 4C. J Neurosurg 2008; 109:8–14.
21. Sahgal A, Ma L, Chang E, Shiu A, Larson DA, Laperriere N, et al. Advances in technology for intracranial stereotacticradiosurgery. Technol Cancer Res Treat 2009; 8:271–80.
22. Nguyen T, Hsu W, Lim M, Naff N. Delivery of stereotactic radiosurgery, a cross-platform comparison. Neurological Research 2011; 33:8-787.
23. Walton L et al. Development of a relocatable frame technique for gamma knife radiosurgery. Technical note. J Neurosurg. 2000; 93: 198-202.
24. Yamamoto M. Gamma knife radiosurgery: technology, applications and future directions. Neurosurg Clin. 1999; 10:181-202
25. Adler JR, Murphy MJ, Chang SD, Hancock SL. Image-guided robotic radiosurgery. Neurosurgery. 1999; 44:1299–1307.
26. Chang SD, Adler JR. Robotics and radiosurgery-the CyberKnife. Stereotact Funct Neurosurg. 2001; 76:204–8.
27. Ryu SI, Chang SD, Kim DH, Murphy MJ, Le QT, Martin DP, Adler JR. Image-guided hypo fractionated Stereotactic radiosurgery to spinal lesions. Neurosurgery. 2001; 49:838–846.
28. Murphy MJ, Cox RS.The accuracy of dose localization for an image-guided frameless radiosurgery system. Medical Physics. 1996; 23:2043–2049.
29. Kuo J, Cheng Y, Zbigniew P, Apuzzo M. The Cyberknife stereotactic radiosurgery system. description, installation, and initial evaluation of use and functionality. Neurosurgery. 2003; 53:1235–9.
30. Murphy MJ. An automatic six-degree-of-freedom image restoration algorithm for image-guided Frameless stereotaxic radiosurgery. Medical Physics. 1997; 24:857–866.
31. Stieber VW, Bourland JD, Tome WA, Mehta MP. Gentlemen (and ladies), choose your weapons.gamma knife vs. linear accelerator radiosurgery. Technol Cancer Res Treat 2003; 2:79–86.
32. Andrews DW, Bednarz G J, Evans JJ, Downes B. Review of 3 current radiosurgery systems. Surgical Neurology .2006; 559– 564.
33. Pamela J, Ross BS, Hani Ashamalla, Sameer Rafla. Advances in Stereotactic Radiosurgery and Stereotactic Radiation Therapy. Radiation Therapist. Spring. 2010; 1:63.
34. Sanghera P. Fractionated Helical Tomotherapy as an alternative to radiosurgery in patients unwilling to undergo additional radiosurgery for recurrent brain metastases. The British Journal of Radiology. 2010; 25–30.