Clinical Images and Case Reports

Received 19 Jun 2024 | Revised 22 Jun 2024 | Accepted 05 Jul 2024 | Published Online 24 Jul 2024

vision publisher
Medical Journals
ISSN 2942-0776

Published By: Vision Publisher

CICR 02 (7), 56-66

Development of Stereotactic Ablative Radiotherapy: Radiotherapy Experience, Clinical Applications of the Stereotactic Method and Widespread Development of Stereotactic Apparatus and Techniques

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Abstract: Over the past half-century, stereotactic radiosurgery (SRS) has shown to be a successful method for treating both benign and malignant brain diseases. Stereotactic ablative radiotherapy (SAbR) in extracranial sites is currently challenging conventional wisdom in radiation oncology, much like SRS revolutionised neurosurgery. After William Coolidge created the high vacuum X-ray tube in 1913, "therapeutic radiology" took a giant leap forward. Therapy of deeper seated tumours would be possible within 10 years and for numerous decades to come with tube potentials exceeding 200 kV. It was well-known in the early days of radiation that low intensity X-rays couldn't penetrate very far. In response, several systems were developed to enable multi-beam delivery. Dosimetric compactness attained by aiming with numerous intersecting, non-overlapping beams is a basic idea in radiosurgery. These approaches lay the groundwork for this principle without using stereotactic localisation. Hence, ionising radiation's oncologic uses had little success during the first 30 years of the 1900s. Back then, we didn't know much about how time, dose, and radiation rate—three fundamental radiological parameters—impacted cell and tissue responses.

KEYWORDS: Radiotherapy Experience, Clinical Applications, Development of Stereotactic, Apparatus, Techniques

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Introduction

Stereotactic ablative radiotherapy (SAbR) was developed from the branches of surgical and therapeutic radiology and has been around for over a hundred years. Some began with stereotactic radiosurgery (SRS) and then progressed to extra cranial disease sites, stereotactic body radiation therapy (SBRT). It has been proven in clinical activities that SRS has applicability in the treatment of neurological diseases such as TN, brain metastases, cerebral vascular malformations and several primary brain tumors [1-3]. Today, outpatient cranial SRS can be performed without coming in contact with the brain tissue and the accuracy of the treatment can be extremely high. The current practice of extending SRS to lesions that lie beyond the CNS, for example, around the spinal cord, is now made possible due to development of newer technologies in tumor localization, imaging and better technology for repositioning the patient. But the same problems correlate with the high radiation dose to normal tissues and organs remain critical. The use of image guiding has emerged to be vital in the recent past in the applications of SAbR [7]. Therefore, what was once considered a radical/high dose-per-fraction delivery is now emerging as the new standard of RT treatment especially in organs such as the liver, the spine and the lungs, based on new clinical data.

First-Held Radiation Treatment

It is common knowledge that in late 1895 Wilhelm Roentgen was the first to notice that ionising radiation could be produced using a cathode ray tube. However, this process was actually the first time one obtained confirmed proof of the so called “X-rays”, yet it was probably not the first time these were made; several other contributors that were involved in experimenting with cathode tubes since the middle of the nineteenth century include Plucker, Crookes, and Lenard. Subsequent to Roentgen’s discovery, in January of the same year, Henri Becquerel found that certain chemical substances emit such invisible ‘X-rays’ as discovered and as observed, the relationship with fluorescence became one of the key driving forces. In the year 1901 Roentgen was awarded the first Nobel Prize in physics and in 1903 Becquerel was also rewarded the similar of Nobel Prize along with Marie and Pierre Curie. These breakthroughs were immediately considered of huge significance,('/')[end of the quote] The first time therapeutic applications of X-rays were done January 29, 1986, soon after Roentgen revealed it. Recognizing this date has now become general. Before the therapeutic suggestions for diagnosing a specific illness, there is the probability of the therapeutic uses being the initial ones established. In an unfortunate incident on March 14, 1896, shotgun was accidentally fired and doctors attempted to reconstruct the image of a child’s head as they were about to operate. This was perhaps the first time the method was used when it was applied for diagnostic purposes. However, it should be noted that the imaging process was unsuccessful In addition, three weeks after the surgery, the youngster went bald in the area receiving radiation exposure. For a long time, X-rays are considered only as a medical means, however, first observations are based on numerous anecdotes, and the history of discovering X-rays as a medicinal tool is rather confused. There was high incidence of TH, eczema, psoriasis, acne, ringworm, and portwine stain among the students. Furthermore, curing cancers especially those are observed on the surface of the skin was realized [8, 9]. The occurrence of fractionated distribution in the early 1920 led to an era of revolting change in the industry. Although the epochal idea of fractionation was first embodied and practiced by Claudius Régaud, it can be argued that the credit for having officially discovered it belongs to the Radium Institute of the University of Paris, You see, Régaud was not only a professor at Pasteur Institute but he was also the director of radio-physiological laboratory of the Radium Institute (now known as Curie Institute following the name of its founder and As a result of the fact that the overall effects of ionising radiation to spermatogenic cells that he was studying in testes of rabbits were found to be rather different if the exposure was slow like the case with radioactive raum, Régaud began to undertake a systematic study of the said effects. Consequently, it proved to be impossible to sterilise a rabbit’s testicles via a single exposure to a high dosage of X-rays without eliciting the onset of radio-dermatitis. Interestingly, if similar dosage is given in five divided doses, five to ten days apart, it is possible to sterilize this organ without producing skin lesion. “This biological technique has rendered it possible to achieve much higher percentages of cure than before in certain malignances like cutaneous cancer, cancer of cervix uteri, tumours of the mouth and pharynx, cancer of the larynx, tumour of High More, etc. and at the same time, the normal structures are given far better protection than was possible before,” Régaud took these observations further and related them to clinical usage On pages 10–12. In the later period, Henri Coutard adopted and especially actively promoted the principles of fractionation in therapeutic practice. Hence, individuals such as Régaud and Coutard among others are the ones that ensured that radiation continues to be utilized in therapeutic practices up to date. However, the reoxygenation of the tumour may be an exception On the whole, non-integrated radiation treatment is by no means the most effective means of curing cancer. The efficacy of the radiation modality with regards to the diseases being treated could be increased if an ablative dose could be safely given as shown in the earlier stereotactic methods. Where Stereotaxis Came From An act of neurological surgery that can be minimally invasive involves stereotaxis; this is a method that involves the help of a 3-D frame of reference from the outer part of the body to the inside part of the head. In the same way that radiation therapy had evolutionary tracks different and parallel to the tracks of its therapeutic radiation from the time it began to develop to the time when it is used for humans, stereotaxis also had the similar tracks from the time it began to develop to the time it is now being used for animal model. The two were invented around the early 1900s, but did not receive their major developments that made them applicable in the clinical practice until the middle of this century.

Stereotactic technique of Horsley and Clarke

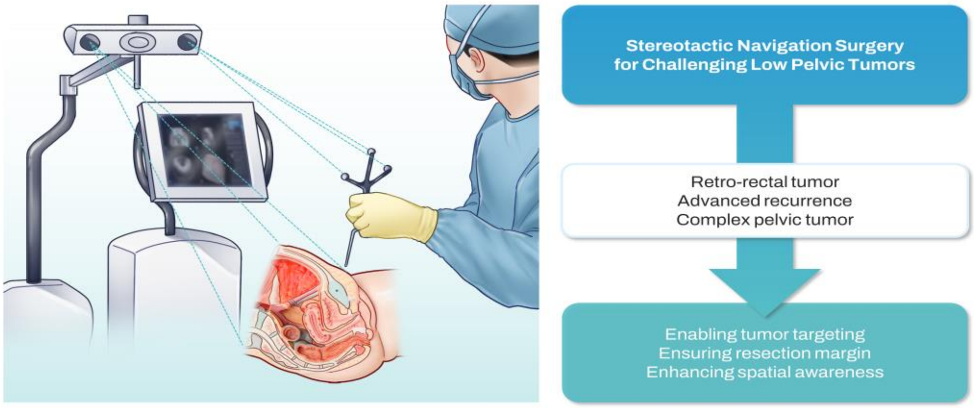
There are perfect tool for the simulation and the creation of lesions in accurate locations in the brains of experimental animals, known as stereotactic method which was developed by engineer, scientist, and surgeon Robert Clarke and neurosurgeon Victor Horsley. Subsequently, two more versions of Clarke’s frame were manufactured; one of them was imported to the United States by Ernest Sachs based on his earlier association with Horsely, is displayed today in the Division of Neurological Surgery UCLA School of Medicine Los Angeles, USA. Clarke-Horsley gadget was proposed decades later and attempts were made to optimize it so that it might be used by human [15, 16]. The most significant of such attempts were made by a neuroanatomist and physiologist Aubrey Mussen with whom Horsley and Clarke coincided for a short period. All these efforts have not produced any evidence that Clarke-Horsley-type device was ever used on humans. And thus, human stereotaxis was not put into practice for more than forty years after the basic work done by Horsley and Clarke.

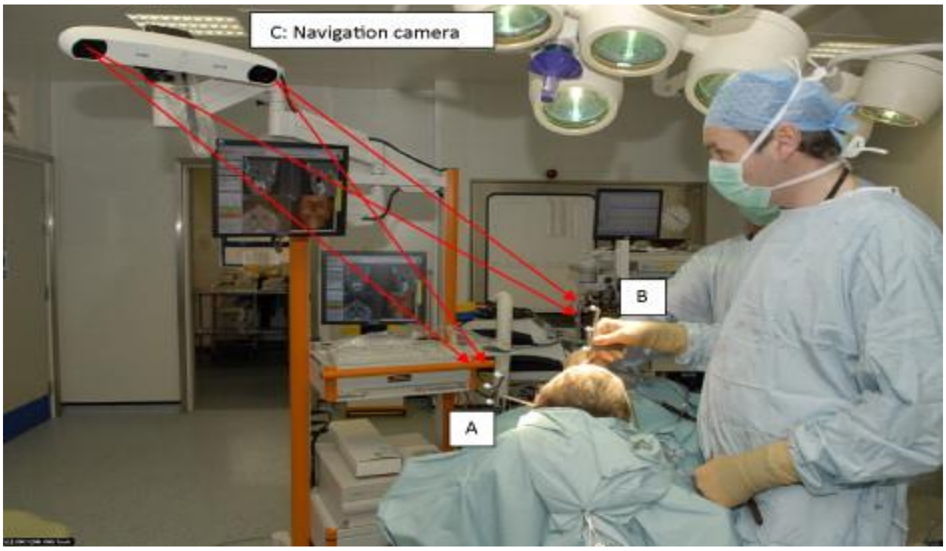
Stereotactic Techniques in Clinical Practice: In the course of Every Spiegel and Wycis discuss a variety of topics of this kind with their patients

Earlier model: The first model as mentioned earlier was slightly similar in design and working to Clarke Horsley device and operated by Cartesian co-ordinates, this piece of equipment was fixed to a patient’s skull by fixing it to a plaster cast. Since the cast and frame could be removed, then imaging and the surgeries could be carried out in different sessions. With contrast radiography, intracranial reference points could perhaps be viewed as and with subsequent ventriculography and then pneumo-/air encephalography for the localisation of target areas of interest. Especially, the prefrontal leucotomy that was a less extreme form of the procedure initially intended for use in psychosurgery as a means of diminishing emotional responsiveness was proposed [17, 18]. Other applications described by the authors for relief of pain (pallidotomy), for movement disorders (spinothalamic tract and Gasserian ganglion ablation), and for cyst evacuation were contemplated.

Stereotactic Equipment and Procedures Development for General Surgery

People’s interest surged in the formation of stereotactic devices and its use following the information provided by Speigel and Wycis. The Speigel-Wycis apparatus used Cartesian coordinates, but Leksell's frame used three polar coordinates: It includes several dimensions such as, angle, depth, and the position at the distance of anterior and posterior parts of the body. This “arc-quadrant” mechanism was much easier to operate because it gave maximum freedom of choosing the point of access of the probe and its trajectory. Despite undergoing some alterations since its establishment in 1949, the frame is as functionally and stylistically close to the original as could be imagined. In addition to the study of topographic epilepsy Talairach’s work contributed also to the development of stereotactic frames [19; 20]. The original stereotactic radiosurgery operation performed with the help of a linear accelerator is the Talairach frame which is very remarkable. Another structure that became a rather effective/sexy commercial frame was derived from modifications of the Todd-Wells mechanism. Integra Radionics (Burlington, MA) and BrainLAB both utilize modern frames that are based on BRW CSS or Brown-Roberts-Wells coordinate system.





How Stereotactic Radiosurgery Came to Be

Most sources agree that in the late 1940s, John Lawrence and Cornelius Tobias were the first to propose the idea of ablation or functional modification of cranial structures utilising tiny crossfiring beams of charged particles. A just few years prior, Nobel Laureate in physics Robert R. Wilson had noted that protons would possess a clear physical advantage when it came to curing human illness. During that period, the Radiation Laboratory in Berkeley, California was headed by John's brother Ernest O. Lawrence, who had already won the Nobel Prise for inventing the cyclotron. John Lawrence had been practicing nuclear medicine at the Radiation Laboratory since the mid-1930s, and he had already become famous for his groundbreaking work in the area after graduating from Harvard Medical School. While Tobias was a nuclear physics Ph.D. student at Berkeley, three Nobel laureates—Ernest Lawrence, Emilio Segre, and Luis Alvarez—served on his dissertation committee.

Stereotactic Radiosurgery in Its Early Days: Lars Leksell

Lars Leksell, a Swedish neurosurgeon who was familiar with the Berkeley research, suggested using the emerging technique of stereotaxis to better direct cross-firing radiation beams. According to Leksell's groundbreaking work in the field, stereotactic radiosurgery involves directing the radiation beam to the exact centre of the semicircular arch of the stereotactic instrument. The target is then irradiated through a multitude of small portals created by fixing the semicircular frame at various angles and mov[ing] the beam guide transversely along the frame. All of the convexity of the head can be employed as an entry for the beams that meet and cross in that structure. This brief three-page document has numerous noteworthy remarks. To begin, the term "radiosurgery" is absent from the book itself and only appears in the title [21–23]. Furthermore, Leksell acknowledges that ultrasound was examined before the use of "Roentgen radiation." Last but not least, Leksell saw the great potential for "radiation of a higher energy" than the existing 200 kV system right from the start. When exactly radiosurgery was initially used in a clinical setting is a topic of some debate. There is a picture of a patient in a stereotactic frame attached to an X-ray tube in Leksell's original publication, but no information about therapy is given. Uppsala, Berkeley, and Cambridge Particle Beam Radiosurgery The 185 MeV protons were quickly replaced with kV X-rays by Larsson and Leksell at the Gustaf Werner Institute in Uppsala, Sweden. Meanwhile, the Radiation Laboratory's 184-inch synchrocyclotron was producing 340 MeV protons, and the Berkeley group started systematically irradiating the pituitary gland in patients with advanced malignancies. Until the synchrocyclotron was deactivated in 1987 and the Bevalac in 1993, the radiosurgery programme at Berkeley flourished under the direction of Lawrence and Jacob Fabrikant. This was followed by the early 1990s. In 1961, neurosurgeon Raymond Kjellberg initiated a radiosurgery programme in Cambridge, Massachusetts, with the 165 MeV proton beam station. Prior to the first cyclotron's decommissioning in 2002, the Harvard programme treated thousands of patients with a variety of histologies, including arteriovenous[24,25] malformations and tumours of the skull base, including chordomas and chondrosarcomas. It is important to remember that the Uppsala, Berkeley, and Cambridge facilities were built for physics research and never meant for therapeutic usage. The development of radiosurgery programmes and the successful treatment of numerous patients is truly astounding and a tribute to the pioneers' efforts.

Welcome to the Gamma Knife's Debut !

Particle radiosurgery has a lot of problems, even though it was very successful in the clinic in the '50s and '60s. Particle accelerators were primarily designed for physics research, which meant that biological studies and patient treatment had limited access. Practitioners had it tough already, and patients were understandably worried that none of the centres were hospital-based. Leksell inspired a joint effort to develop a radiosurgery device "fit for use in a hospital" by the Physics Unit at the University of Lund's Radiation Physics Department, Kurt Lidén's Department of Physical Biology at Uppsala's Gustaf Werner Institute, and Rune Walstam's Department of Clinical Radiation Physics at Stockholm's National Institute of Radiation Protection.26 and 27. Also, Walstam replaced Rolf Sievert and Anders Brahme as heads of Medical Radiation Physics at the Karolinska Institute, which is a noteworthy historical footnote. In an earlier presentation, Lidén had proposed an initial study that advocated for the utilisation of high-energy (10-20 MV) Roentgen radiation (X-rays) and proposed a design that positioned the collimator near the patient to reduce geometric penumbra. A beam with a 2.5 9 7.5 mm cross-section and a 0.5 mm penumbra width at the beam focus was produced by the collimators. It is worth noting that a 6 MeV linear accelerator (Varian) was utilised for the majority of the initial collimator design and optimisation work. Together with Hans Dahiln, Bert Sarby of the National Institute of Radiation Protection conducted the initial dosimetry experiments and developed a technique for determining the dose distribution due to the 179 superimposed beams; he was also responsible for collimator design. Before relocating to the Hospital Sofiahemmet, the first two patients were treated in December 1967 in an experimental hall at the Atomic Energy Corporation in Studsvik, Sweden. Initially intended for the therapy of functional impairments, the device found use in the early stages for the treatment of vascular malformations, benign and malignant tumours, and tumours of various types. Cobalt supplies in Gamma Knife I had depleted considerably by the mid-1970s. The first Gamma Knife was donated to UCLA by the Karolinska Institute and the Swedish government, based on the personal relationships between Leksell, Ned Langdon, and Robert Rand, who are professors of neurosurgery and radiation oncology at UCLA, respectively. In 1976, Langdon went to the Karolinska Institute to get the go light to use the Gamma Knife. A prominent American research institution was Leksell's first choice to employ the unit [29–31]. It wasn't until 2 in the morning on July 21st, 1980, after being loaded onto a truck and hauled 29 miles to UCLA, accompanied by police, that it arrived (UCLA 1980). Returning to Elekta in the early 1990s, the unit saw minimal clinical and research use before being taken away. The first Gamma Knife, which was used at UCLA, is shown in Figure 3a. For their PerfexionTM gamma unit, Elekta debuted it in 2007. With 192 cobalt sources organised in a conical rather than spherical arrangement, the Perfexion's design and functioning are significantly different from the Gamma Knife variants. Furthermore, the 192 sources are partitioned into eight separate sectors, and each of these sectors has the capability to dynamically alter collimation between 16, 8, and 4, mm circular apertures, in addition to a completely blocked position. More than half a million patients across the globe have benefited from Gamma Knife treatments as of 2008. In Chapter 2 of this book, you will find more information about the strategy, operation, and design of Gamma Knife. The crew from Spain's University of Valencia also made an outstanding effort. In order to treat a carotid cavernous fistula, neurosurgery professor Juan Luis Barcia-Salorio and physics professor Gregorio Hernández created a stereotactic head frame and a specialised collimator that could be attached to a stationary cobalt device. The device was subsequently rotated around the patient's head. Radiosurgery's early use in treating epilepsy and vascular disease was spearheaded by BarciaSalorio. There have been other efforts to recreate the Gamma Knife's success over the years. Among them, OUR New Medical Technology Development's Rotating Gamma System from Shenzen, China stands out. Although just a small number of units have been sent outside of China, the first American installation took place in 2002 at the UC Davis Cancer Centre in Sacramento, California. The gamma units developed for cranial and extracranial radiosurgery by GammaStar Medical Group, the successor to OUR and led by Shipeng Song, have achieved remarkable success in China .

Miniature X-Ray Surgery

Linacs from that time didn't have the precision qualities needed for that kind of work. The groundbreaking work that led to the first Gamma Knife was clearly inspired by this idea: "The choice between the two alternatives, i.e. roentgen or gamma radiation, should be based on technical, clinical and economical rather than physical considerations [33, 34]." Larsson and colleagues clearly understood this. It seems like a very appealing alternative to use upgraded electron accelerators for roentgen synthesis specifically for radiation surgery if that becomes the norm.

The First Time I Had Linac Radiosurgery

The first patient was treated in 1982 by neurosurgeon Osvaldo Betti and engineer Victor Derechinsky in Buenos Aires, Argentina, who adapted a Varian Clinac 18 for radiosurgery. The couch was the most vulnerable mechanical component, therefore Derechinsky created a unique chair to support the patient and attach a Talairach stereotactic frame. To provide multiple convergent beam delivery, the original "Betti chair" physically rotated the patient along a horizontal axis while the gantry rotated perpendicularly. A chair that could spin on its vertical axis was later installed in place of the first. The original Betti-Derechinsky system was located in Buenos Aires, but two more were set up and utilised in Lille and Paris, France. To add intrigue, Bordeaux, France also built and used a Betti-Derechinsky system replica.

Interpersonal correspondence. Neurosurgeon Federico Colombo oversaw the development of a stereotactic frame and linac-based SRS system in Vicenza, Italy, shortly after the "Betti chair"' was built. The Vicenza group had a humorous way of calling the Betti chair a "Cyclothrone." Heidelberg, Montreal, Boston, and Gainesville were the four academic centres that were at the forefront of linac radiosurgery in the late 1980s; Table 1 summarises the early linac SRS practitioners and the procedures they used. Radiation was administered in one or more arcs at specific couch positions using specially built circular collimators in the majority of cases. A commercial Reichert-Mundinger stereotactic frame was adjusted to fit on the Siemens linac couch by the Heidelberg group at the German Cancer Centre (DKFZ). A sizable team at Harvard Medical School and the Joint Centre for Radiation Therapy in Boston, headed by Drs. William Saunders and Jay Loeffler, was working on a system that would have a significant influence on the spread of linac radiosurgery at the same time. The main obstacle to the frequent use of linacs for radiosurgery at the time was the mechanical properties of the various moving components. The linac couch was at the centre of all of them. Wendell Lutz built a floor stand to fix this problem; it allows patients to have their heads immobilised and positioned precisely away from the radiation couch, and it does it without the need for room lasers or light fields. A patient-specific quality assurance procedure was built into the system. It involved attaching a radio-opaque [35-38] ball to a BRW ring, which was then fastened to the floor stand. The patient's goal coordinates on the floor stand were established, and then a sequence of films were acquired at eight typical gantry and couch configurations. Without the need for external markings or room lasers, patients may be precisely located in this way. Nowadays, everyone uses the term "Winston-Lutz" to describe the process of getting isocenter ball shots; nevertheless, this term is most commonly used in reference to machine QA and not patient QA, which was the original intent. Several scientists from Harvard University who work on localisation, dosimetry, and treatment planning supplemented the floor stand development efforts. It was Bob Siddon and Norman Barth who came up with the idea of utilising two radiographs to pinpoint intracranial targets. Because of its submillimeter accuracy, this approach is still considered the best for localising AVMs. Roger Rice did a lot of the early cone dosimetry. Barth and Rice were both postdocs at Harvard University back then. A specialised graphics computer was used to rewrite the initial treatment planning system that Siddon had created on a Mac II [39, 40]. Numerous eminent international scientists and physicians attended a 1987 Boston linac radiosurgery meeting. Although the linac couch was eliminated by the floor-stand method, the gantry rotation properties of the linacs that were available at the time were also fairly subpar. Frank Bova and Bill Friedman of the University of Florida in Gainesville took up the cause, building on the work of a group at Harvard. Their isocentric arm improved the accuracy of gantry rotation by connecting the source and collimator to the floor stand through a high precision bearing. A gimble-type bearing was designed to support the tertiary circular collimators, thereby preventing torque from acting on the linac head.

Micro-Multileaf Collimators Just Arrived !

Circular collimators were used for radiosurgery up until the mid-1990s, regardless of whether the beam was provided by linac, particle, or cobalt. Due to the non-spherical nature of the majority of tumours, a trade-off between plan quality, treatment time, and dose heterogeneity was frequently required when circular collimators were used. The trimmers could move in and out, revolve around the beam axis, and be controlled by motors. The authors showed that compared to just using circular collimation, using a single isocenter significantly enhanced conformality. Later on, Hacker et al. (1997) created and used a comparable method, but one that was static. The XKnife planning system made this methodology commercially available. Consequently, the first micro-multileaf collimators used for cranial radiosurgery were developed by a group at the German Cancer Research Centre (DKFZ) in Heidelberg, who had previously achieved a number of noteworthy advancements [41, 42]. We built two versions with 3-millimeter-wide leaves: one with manually-positioned leaves and another with computer-controlled, motorised leaves. They are both attached to the linac's auxiliary device holder. A DKFZ offshoot, MRC Systems of Heidelberg, Germany, commercialised the ModuLeaf MLC technology and later sold it to Siemens Medical Solutions of Malvern, Pennsylvania (Fig. 8a). For tiny field cranial radiosurgery, Shiu et al. (1997) detailed the design and features of a compact multileaf collimator. With a maximum field area of 6,96 cm2, the MLC was composed of 15 pairs of leaves that projected a width of 4 mm at isocenter. The XKnife system was used to facilitate treatment planning. Following this, Radionics brought to market a 27-leaf-pair variant with a maximum field area of 13.4 9 10.8 cm2. Maximum field size was 10.2 9 10.0 cm2 with 14 pairs of 3 mm leaves in the centre, 6 pairs of 4.5 mm leaves in the middle, and 6 pairs of 5.5 mm leaves on the periphery. Radionics and BrainLAB microMLC were integrated onto numerous linacs in the years that followed, and they are still utilised today to treat a large number of patients annually .

End-Use Linac Radiosurgery Equipment

The use of linacs in radiosurgery was contentious during the 1990s, with some practitioners arguing that the accuracy of gamma units was superior to that of linac-based systems due to the complexity of the former. Even though Friedman and Bova's research disproved this reasoning, many still held this view. In response to this argument, there were a number of noteworthy initiatives to create linacs specifically for use in radiosurgery. The linacs that were developed as a result of their efforts include a robot-mounted model, a C-arm multi-rotation-axis model (made by Mitsubishi Electric Ltd., Tokyo, Japan), a conventional linac model (600SR, Varian) with a fixed 10-centimeter primary collimator, and a linac model (Novalis, BrainLAB) with an integrated micro-multileaf collimator. A brief description is provided for each of these .

Adler sought advice from Schonberg Radiation Corporation of Santa Clara, CA, on how to construct a linac meeting all specifications (dimensions, mass, power, dosage rate, etc.). Peter and Russell Schonberg started SRC. Russell was a medical linear accelerator developer at Varian Associates and the manager of electrical systems before that. The Mobitron, a portable electron linac developed by Russell and later marketed by IntraOp Medical of Santa Clara, California, was another invention of his. Accuray was issued patent number 5,207,223 in 1993, which had been awarded to Adler and the Schonberg brothers. A picture of the Stanford prototype and a schematic from the patent document. An industrial robot (GMF, Auburn Hills, MI) was equipped with a 300-pound (6 MeV x-band, 9.3 GHz) SRC linac in the initial system, which was referred to as the Neurotron 1000. The isocentric limitation of radiation delivery was removed by the robotic arrangement. The original goal of the technology was to make stereo X-ray-based frameless radiosurgery more accessible, and the Accuray creators were trailblazers in the field of image-guided radiation therapy (IGRT) [43, 44]. The Food and Drug Administration gave the CyberKnife the green light to treat symptoms all over the body in 2001. Submillimeter accuracy has been shown in cranial and spinal applications using anthropomorphic phantoms. For stereotactic procedures both inside and outside the skull, CyberKnife has become an indispensable tool.

A New Approach to Stereotactic Body Radiation

After cranial SRS proved to be an effective and efficient technique to treat tumours in the skull, other groups began to look into applying similar high dose-per-fraction treatments to tumours outside of the brain and other areas not directly related to the nervous system. Several groups in Sweden, Arizona, New York, Houston, and elsewhere initially attempted to localise extracranial targets using a paradigm based on frames and fiducials, which was heavily influenced by Leksell's use of a rigid frame to stabilise the head during cranial SRS. As in-room image guidance has become more commonplace, frame-based techniques have fallen by the wayside [46, 47]. The field owes a great debt of gratitude to the pioneers who used frame-based methodologies to determine the clinically achievable doses of radiation that were necessary for the effective treatment of many patients .

Frame-Based SBRT with Image Assistance

Early SBRT practitioners developed image-based methods for target verification due to the clear inaccuracies of frame-based methodologies. Portal imaging was definitely a part of the first methods. In their 2003 study, Yenice et al. detailed SBRT that used frames in conjunction with daily CT scans taken right before each treatment. First, the patient was set up to stand; next, the patient and frame were tilted backwards into a horizontal treatment position to help with increased repeatability. With a precision of 1 mm (1r) in all directions, the authors proved their localisation accuracy. With little loss of aiming accuracy, localisation based on electronic portal imaging finally replaced daily CT. The UCLA team began developing and manufacturing a line of body frames in 1993 with the goal of treating spinal injuries as their driving force. Following this, a minimally invasive localisation technique was suggested by Medin et al. (2002) with the purpose of irradiating tumours close to the spine with high doses of a single fraction. With the use of local anaesthesia, three tiny radioopaque markers were securely attached to the spinous processes and vertebrae. Biplanar radiographs taken during the planning CT allowed for the localisation of the implanted fiducials. In order to construct a coordinate system, imaging processes made use of an external localisation box. While receiving treatment, a mobile radiography unit was used to take additional biplanar radiographs in the same room. Using the geometric relationship between the target and implanted markers obtained during CT imaging, the isocenter position was estimated once the implanted fiducials were discovered [48]. Even if (a) the patient had moved since the first CT and (b) the target could not be immediately seen in the treatment room, precise target localisation could still be done in this way. The maximum targeting inaccuracy that was recorded in phantoms designed specifically for the purpose of assessing the overall accuracy of the system was 1.17 mm. After that, a pig model was used to assess the process. Radionics explored making the approach available for purchase for a short time. Two groups have successfully utilised linac delivery in conjunction with in-room CT imaging to achieve stereotactic irradiation of both intra- and extra-cranial targets. Before treatment, patients had localization/verification CT scans while immobilised in a full-body stereotactic frame. A CT on rails was set up in the treatment room to make this possible. Using CT scans taken every day, the researchers found that, throughout all treatments, the total deviation from the target isocenter was less than 1 mm. Later on, capabilities were built to make it easier to automatically register digitally reconstructed radiographs (DRRs) made from pretreatment CT scans with DRRs made from planning CT scans. Eight patients with primary or metastatic brain tumours were treated and reported on by Uematsu et al. (1996). Traditional face masks and a dental impression were used to immobilise the patient. To achieve localisation, the target was first aligned with the CT gantry's axis, then little metallic balls were used to designate the respective axes, and finally, the lasers of the linear accelerator were used to align the balls. The localisation uncertainty, according to phantom investigations, was about 1 mm. The technology has since seen substantial use in the stereotactic targeting of malignancies outside of the brain.

The X-Ray Stereophotogrammetry Method for Orthogonal kV Localisation

For the precise visualisation of internal anatomical features required for stereotactic applications, the concepts of stereophotogrammetry can be easily applied to X-ray imaging. Selvik and colleagues were the first to describe the use of X-ray imaging in stereophotogrammetric analysis, which is also called Roentgen stereophotogrammetry. For tumour tracking and localisation, Shimizu et al. (2001) detailed a system that used three pairs of room-mounted X-ray tubes—image intensifiers. Despite the gantry's ability to hide only one pair of images at a time, continuous 3D imaging was made possible by employing three imaging systems. A pattern matching algorithm enabled the automatic recognition of an implanted gold marker, allowing for continuous tracking. While the imaging system was in sync with linac, there was a discrepancy of around 1 mm between the planned and delivered targets. At this time, room-mounted stereophotogrammetry capabilities coupled to their respective SRS/SBRT linacs are offered by both the CyberKnife and Novalis commercial systems. There is no need for extra "localisation boxes" to conduct targeting when the imaging system is permanently installed in the treatment room. On one side of the CyberKnife are two amorphous silicon detectors set up in the floor of the treatment room, while on the other side are two diagnostic X-ray units mounted on the ceiling that beam images through the patient. Early uses of the CyberKnife included fractional or single-fraction therapy of cranial diseases, made possible by the biplanar imaging system's capacity for frameless stereotactic radiosurgery. Nevertheless, the CyberKnife is also well-suited for stereotactic irradiation of extra-cranial tumours because to its integrated image guidance system. According to Murphy et al. (2000), the original CyberKnife was modified to make stereotactic irradiation of tumours next to stiff bony structures, including spinal tumours, easier. A growing number of researchers have documented CyberKnife's clinical use in a variety of extracranial locations, including the spine, lungs, liver, and pancreas. In a similar vein, the Novalis system uses stereoscopic X-rays to pinpoint extracranial targets and infrared (IR) to help with patient setup and position tracking. The kV X-ray component differs from the CyberKnife in that it uses two X-ray tubes located on the floor and two amorphous silicon (aSi) flat panel detectors mounted on opposite sides of the ceiling. At the linac isocenter, each set of X-ray tubes and detectors is set up to produce images with a coronal field of view of about 18 cm in the S-I and L-R directions. Two modes of operation are available for the X-ray localisation system: automatic registration of X-ray and digitally reconstructed radiographs (DRRs) by an iterative edge matching algorithm, and matching of implanted radio opaque markers .

Last thoughts

The use of stereotactic radiosurgery, which has been around for more than a century, has now become the norm for treating disorders affecting the head and neck. Extracranial illness sites have been encouraged to apply SRS as a result of its success. The SBRT movement is shaking up radiation oncology like SRS did to neurosurgery: by questioning established norms and expectations. The ongoing advancement of technology has played a significant role in enabling this shift in perspective. The continued importance of SRS and SBRT in cancer treatment is assured by future advancements, a deeper knowledge of the biological response to massive doseper-fraction irradiation, and molecular methods to response optimisation.

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