

Stereotactic radiosurgery and the linear accelerator: accelerating electrons in neurosurgery

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The search for efficacious, minimally invasive neurosurgical treatment has led to the development of the operating microscope, endovascular treatment, and endoscopic surgery. One of the most minimally invasive and exciting discoveries is the use of targeted, high-dose radiation for neurosurgical disorders. Radiosurgery is truly minimally invasive, delivering therapeutic energy to an accurately defined target without an incision, and has been used to treat a wide variety of pathological conditions, including benign and malignant brain tumors, vascular lesions such as arteriovenous malformations, and pain syndromes such as trigeminal neuralgia. Over the last 50 years, a tremendous amount of knowledge has been garnered, both about target volume and radiation delivery. This review covers the intense study of these concepts and the development of linear accelerators to deliver stereotactic radiosurgery. The fascinating history of stereotactic neurosurgery is reviewed, and a detailed account is given of the development of linear accelerators and their subsequent modification for radiosurgery. (DOI: 10.3171/2009.7.FOCUS09116)

KEY WORDS • linear accelerator • radiosurgery • stereotactic radiotherapy

MODERN neurosurgery has witnessed a surge of new technologies and minimally invasive techniques that attempt to minimize tissue damage and patient recovery times after neurosurgical interventions. With improving accuracy of imaging techniques, neurosurgeons are capable of delivering targeted treatment that causes little damage to surrounding tissues without compromising efficacy. The search for minimally invasive neurosurgical treatment has led to the development of the operating microscope, endovascular treatment, and endoscopic surgery. One of the most exciting discoveries made during this search is the use of targeted, high-dose radiation for neurosurgical disorders.

Lars Leksell,³¹ a Swedish neurosurgeon, coined the term “radiosurgery” to describe any method for stereotactically focusing multiple beams of radiation on an intracranial target. Leksell collaborated in the development of the Gamma Knife to deliver radiosurgery. At the time, LINACs were the most commonly used machines for conventional radiotherapy. Because of the costs associated with the Gamma Knife, LINACs were modified for radiosurgical use.³⁷ The LINAC is now the most frequently used device for delivery of conventional radiotherapy and radiosurgery.

Radiosurgery is truly minimally invasive, delivering therapeutic energy to an accurately defined target without an incision. It has been used in the treatment of a wide variety of pathological conditions, including benign and malignant brain tumors, vascular lesions such as arteriovenous malformations, and pain syndromes such as trigeminal neuralgia. Radiosurgery is also being studied for the treatment of movement disorders and epilepsy. A tremendous amount of knowledge has been garnered in the last 50 years about lesion targeting and as well as about radiation delivery. In this review, we discuss the intense study of these concepts and the development of the LINAC to deliver radiosurgery. In the present study, we reviewed the fascinating history of stereotactic radiotherapy, and gave a detailed account of the development of LINACs and their subsequent modification for radiosurgery.

Regardless of the source of radiation, the fundamental concepts of radiosurgery include the following¹¹: 1) the delivery of a very high dose of radiation (usually in a single treatment); 2) the use of a steep dose gradient with minimal dose delivered to the surrounding structures; 3) stereotactic localization of the target; 4) the use of computerized dosimetry planning; and 5) a highly accurate radiation delivery system.

Radiosurgery refers to a single-session surgical procedure in which ionizing radiation is delivered to a target volume with accurate preplanning of 3D isodose surface

Abbreviation used in this paper: LINAC = linear accelerator.

TABLE 1: Early history of LINAC radiosurgery

| Date | Primary Authors | Location | Event |
|------|---------------------|-------------------------|---|
| 1928 | Wideroe | Baden, Switzerland | developed photon beam radiation w/ high-frequency generator |
| 1938 | Hansen | Stanford, US | description of "rhumbatron" using a resonant microwave unit to accelerate electrons |
| 1939 | Boot & Randall | Birmingham, UK | creation of "magnetron" using resonant microwave for radar during WWII |
| 1939 | R. & S. Varian | Stanford, US | creation of "klystron" using resonant microwave for radar during WWII |
| 1948 | Hansen | Stanford, US | development of microwave LINAC |
| 1953 | Miller & Fry | Great Malvern, UK | development of microwave LINAC |
| 1957 | Leksell | Stockholm, Sweden | treatment of patients w/ Gamma Knife |
| 1983 | Betti & Derechinsky | Buenos Aires, Argentina | LINAC radiosurgery w/ Talairach stereotactic localization |
| 1984 | Heifetz | Los Angeles, US | description of high-dose radiation w/ LINAC to small targets in the brain |
| 1984 | Colombo | Vicenza, Italy | description of LINAC radiosurgery system |
| 1985 | Hartmann | Heidelberg, Germany | modified stereotactic localization to deliver multiple arc radiosurgery treatments |
| 1985 | Ginsberg | Miami, US | first description of LINAC radiosurgery in US |

contours.^{25,26} These concepts require precise knowledge of both the target volume and the behavior of the therapeutic energy beam.⁶

The Early LINAC

Photon beam radiation was proposed by Swedish physicist Gustav Ising and subsequently developed by Rolf Wideroe, a Norwegian physicist working in Switzerland in 1928 (Table 1).^{39,41} Wideroe described a series of colinear tubes connected to a high-frequency generator. This apparatus became widely used in experimental physics for heavy particles, in which the increase in velocity is modest. However, because of their tiny size, electron velocity increased so rapidly that the tubes could not be long enough and the system was impractical for medical applications.³⁹

World War II drove the need for microwave technology for military radar equipment. Innovations in this field led to the development of the modern LINAC. Linear accelerators produce photon beams very differently from the Gamma Knife. Instead of using the decay of cobalt, LINACs use a microwave generator to accelerate electrons within a waveguide. The waveguide bunches the electrons onto a portion of the wave, where they can be efficiently accelerated up to 99.9% of the speed of light. Once the electrons reach their full accelerating potential, they collide with a heavy metal target. The energy generated from this collision is mostly lost as heat. However, a small percentage of electrons pass near the large nuclei of the metal target, are deflected, and undergo a change in acceleration. This interaction results in emission of a photon from the electron, electromagnetic radiation.⁷ "Bremsstrahlung," German for "braking radiation," is used to describe the production of radiation from decelerating or "braking" electrons. Once the photon beam is produced, it is limited by a primary collimator, passes through a flattening filter to improve the spatial uniformity of the beam, passes through 2 independent monitoring ionization chambers, and can then be collimated by a set of secondary and tertiary collimators.⁷ The photon then

transfers energy and ionizes atoms within tissue; these ionizing events lead to molecular changes. Photon beam radiotherapy differs from particle beam radiation, which propagates particles such as protons, neutrons, pions, and heavy charged particles through tissue. These charged particles directly disrupt the atomic structure of the material they are traverse, thereby causing biological change.²⁰ The expense of particle beam units has partly driven the development of LINACs for radiosurgery.

In 1938, William Hansen at Stanford described the concept of accelerating electrons by passing them repeatedly through a resonant microwave cavity, gaining velocity with each pass. He called this a "rhumbatron."¹⁶ The improvements in microwave generators, necessitated by World War II, enabled this concept to become a reality. These discoveries, along with Harry Boot and John Randall's creation of the "magnetron" in the UK and the Varian brothers' development of the "klystron" in the US (Fig. 1), both in 1939,³⁹ led to the development of microwave LINACs in both countries by 1945.³ All of these devices worked similarly to accelerate electrons. The groups lead by Don Fry at the Atomic Energy Research Establishment and Hansen at Stanford both described clinically workable LINACs. Interestingly, the groups had little knowledge of each other's work until the late 1940s.³⁹

Linear Accelerator Technology and Radiosurgery

Leksell first used the term radiosurgery shortly after World War II.³¹ This concept sprouted from an idea he had discussed with Sir Hugh Cairns at the first Scandinavian neurosurgical meeting in Oslo after the war. He discussed his concerns about then-available neurosurgical techniques, and his plans to mechanically direct a probe or narrow beam of x-ray or ultrasound into the brain to ablate pathways for pain alleviation. Cairns responded positively to this idea, and Leksell began his systematic investigation of ionizing beams.¹⁴ Leksell and his colleagues tested an orthovoltage x-ray tube and proton beam produced by the cyclotron in Uppsala.²⁷ They also considered the LINAC as a potential radiation source.

Accelerating electrons in neurosurgery



FIG. 1. Photograph of the Varian brothers with the klystron.

Ultimately, they constructed the Gamma Knife using cobalt radiation.³⁰ Leksell began treating patients with this device in 1957, calling the technique “stralkniven” (ray knives).^{11,27} Other investigators worked with particle beam radiosurgery systems at the University of California at Berkeley and in Boston.^{23,33}

Early radiosurgery researchers were aware of LINAC’s potential in delivering targeted radiation. In 1974, Larsson, the head physicist in the collaborative group at Uppsala University with Leksell, wrote:

The choice between the 2 alternatives, such as roentgen or gamma radiation, should be based on technical, clinical and economical rather than physical considerations. If radiation surgery will reach a position as a standard procedure, improved electron accelerators for roentgen production, adapted for the purpose, would seem a most attractive alternative.²⁸

The initial LINACs developed in the UK and the US used traveling-wave technology.³⁹ These devices were limited by a relatively low beam energy, low radiation output because of an inefficient waveguide design and limited microwave power, and a restricted range of movement. These systems were also large, with the top of the gantry being ~4 m off the floor, to accommodate the accelerating waveguide. The next generation of devices achieved full isocentric rotation by mounting the accelerating structure to a gantry, allowing the radiation source to be rotated in a vertical plane about a single point. Also, by mounting the waveguide horizontally with magnetic beam deflection (beam bending), the next generation of LINACs had more manageable heights. The next major improvement came in 1968 when Knapp et al.²⁴ developed the side-coupled standing-wave structure which improved shunt impedances so that the total length of the accelerating structure could be greatly reduced. This development did away with the need for beam bending (which had its own problems), while still allowing for full isocentric rotation at a practical height.³⁹ Currently, US and Japanese manufacturers use standing-wave technology, while UK manufacturers continue to use traveling-wave technology.

All LINAC radiosurgery systems focus a collimated x-ray beam on a stereotactically identified target. The gantry of the LINAC rotates over the patient, producing an arc of radiation focused on the target. The patient couch is then rotated in the horizontal plane, and another arc is performed. In this manner, multiple noncoplanar intersecting arcs of radiation are produced. As in the Gamma Knife, the intersecting arcs produce a high target dose with minimal radiation delivered to the surrounding brain tissue.¹¹ Along with the LINAC rectangular colli-



FIG. 2. Photograph of LINAC collimators.

mator, a set of secondary circular collimators of varying sizes is used to conform the beam (Fig. 2).¹⁹ Modifications to LINACs were necessary for performing radiosurgery have included a system to rotate the couch in synchrony with the gantry, collimator development, and stereotactic localization.¹⁵ Several factors have made the LINAC desirable for radiosurgery delivery. Linear accelerators have been widely in the US for conventional radiotherapy, and modifying the LINAC for radiosurgery was much more cost effective than purchasing a Gamma Knife. Gamma Knife units at the time were only capable of delivering radiosurgery, and could not deliver conventional radiotherapy when not in use for radiosurgery. Additionally, extracranial radiosurgery treatment was believed to be more feasible using LINACs. The theoretical benefits of LINAC as discussed by radiosurgery leaders in the past have now become a reality.

Within 10 years of LINAC development, reports appeared of the use of external beam radiation for radiosurgery.³ In 1983, Oswaldo Betti and Victor Derechinsky reported the development of a multibeam LINAC coupled with a Talairach stereotactic localization system in Buenos Aires.^{3,4} They used circular collimators that could be oriented in multiple coronal planes in a patient sitting in a moveable chair while attached to a rotating head frame.⁴⁻⁶ Their system uniquely had the patient in a sitting position.¹¹

In 1984, a standard LINAC with small modifications was used by Heifetz et al.¹⁸ (with Marilyn Wexler’s physics contributions) to deliver high-dose radiation to small targets sparing normal brain, similar to Leksell’s Gamma Knife. Simultaneously, a neurosurgeon, Federico Colombo, and a group of physicists lead by Renzo Avanzo in Vicenza, Italy, reported on their stereotactic LINAC radiosurgery system.² They wrote about radiosurgical dose schemes of 40–50 Gy given over 2 fractions separated by 8–10 days for various intracranial targets 2–4 cm in diameter.^{8,9} The dose gradient achieved compared well with Gamma Knife data.^{9,10} Hartmann et al.¹⁷ in Heidelberg, Germany, followed these achievements with the description of a modified stereotactic localization and positioning system to deliver multiple arc radiosurgery treatments. They modified a Riechert-Mundinger stereotactic device, using laser lights to position the frame within the isocenter.

The first published work on LINAC radiosurgery in the US came from the University of Miami in 1985.²¹ However, the system the authors described relied on the



FIG. 3. Photograph of modern LINAC with a rotating gantry.

jaws of the treatment machine for beam collimation instead of the secondary collimation system described by Larsson and colleagues.²⁸ The Miami group's technique was regarded as fractionated, rather than single fraction.

One of the first solutions for the requirement to spread out the radiation entrance path and minimize treatment delivery time was described by Ervin Podgorsak and colleagues at McGill University.³⁵ These investigators modi-



FIG. 4. Photograph of the CyberKnife: a LINAC with a robotic arm.

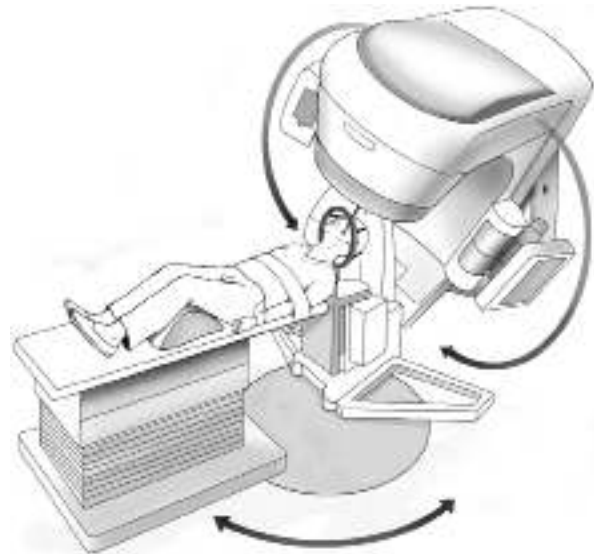


FIG. 5. Illustration of the Trilogy system with inline CT scanner for target localization prior to treatment.

fied a LINAC using extra collimators to define small circular fields and simultaneous gantry and couch rotations. Additionally, the couch and gantry were monitored from the control area, eliminating the need to enter the room during treatment.³⁶ Because of increased error rates with simultaneous gantry and couch rotation, most institutions have not adopted this system. Concerned with error and quality control, Winston and Lutz⁴² published their work on multiple arc LINAC radiosurgery in 1988. Their system included a phantom target device that could easily be used to check the accuracy of each treatment as well as to evaluate sources of error. These authors found the mechanical accuracy of their system to be 0.5 ± 0.2 mm, and suggested that the major error in any radiosurgery system was the error of localization and not mechanical error.¹¹ In 1989, Friedman and Bova¹² reported on the LINAC radiosurgery system in use at the University of Florida. A portable add-on stereotactic device was coupled to the LINAC, and high-precision bearings in the device controlled all patient and gantry movements. As a result, the radiation beam accuracy was improved to 0.2 ± 0.1 mm (Fig. 3). The accuracy of treatment delivery was further increased with imaging software improvements, and the ability to fuse CT and MR imaging images.¹²

As LINAC radiosurgery became more prevalent, increasingly larger targets were being treated. Circular collimators were initially developed for targets < 3 cm in diameter; when used in the treatment of larger targets, unacceptable volumes of normal tissue were included.³ This dilemma was addressed by Dennis Leavitt, who built the first dynamic field shaping collimator for radiosurgery in 1989.²⁹ The circular collimators were supplemented with independent rectangular vanes that trimmed the circular radiation field. This and other discoveries eventually led to the development of a micromultileaf collimator from Varian and Brainlab.⁴³ These collimators have changed treatment delivery from multiple noncoplanar arcs to

Accelerating electrons in neurosurgery

fixed static fields and dynamic arcs, and allow for treatment of larger and more geometrically complex lesions.

Linear accelerators are continuously being modified to improve radiosurgery delivery. For example, John Adler and Richard Cox at Stanford University reported the development of an industrial robot combined to a LINAC, called the Cyberknife (Accuray Inc.).¹ This system can position a circularly collimated beam of x-rays to a target from a range of positions and angles. Moreover, the Cyberknife uses room-mounted imaging to localize the treatment isocenter before treatment (Fig. 4).³⁴ Other systems such as the Trilogy (Varian Medical Systems, Inc.) also localize the isocenter prior to treatment (Fig. 5).²² Real-time imaging of patients can be used to readjust beam coordinates for the target, making treatment of extracranial sites such as the spine and abdomen possible.^{3,19} Spinal radiosurgery is being implemented for benign and malignant tumors, overcoming the tremendous difficulty of target localization in an area with movement of multiple joints.^{13,32,38,40} In addition to modifications to collimation and target localization, LINACs have been modified to deliver radiosurgery with intensity-modulated radiation therapy.³ Linear accelerators provide tremendous possibilities for unique approaches to treatment. These systems demonstrate the versatility of LINAC for radiosurgery.

Modifications of LINACs for radiosurgery have led to close collaboration between neurosurgeons, medical physicists, and radiation oncologists. Such collaborations have increased cross fertilization for each of these fields. Increasing the use of LINAC in radiosurgery has helped neurosurgeons to gain a more in-depth understanding of radiotherapy and the challenges of delivering radiation to patients. Radiosurgery has become an essential part of neurosurgical education.

Conclusions

The development of LINAC has led to widespread availability of radiotherapy for patients. Linear accelerators are found in almost every major medical center in the US. With affordable modifications to the LINACs, radiosurgery is also now widely available, and are currently the most common devices used to deliver radiotherapy and radiosurgery. Linear accelerator radiosurgery is currently in use for the treatment of brain tumors, vascular malformations, pain syndromes, and for other functional indications. Linear accelerator technology is continually being improved, and will continue to play a major role in clinical delivery of radiosurgery for patients.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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