The History of Stereotactic Radiosurgery and Radiotherapy

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KEYWORDS

- Stereotactic radiosurgery • Stereotactic radiotherapy
- Gamma knife • Linear accelerator (LINAC) • Cyberknife
- Historical review

Stereotactic radiosurgery evolved from the pioneering work reported in 1908 by Horsley, a neurophysiologist and neurosurgeon, and his associate Clarke, a mathematician. Horsley and Clarke[1] developed a tool that could localize an intracranial structure in three dimensions, enabling the insertion of a needle electrode for studying a desired locale within the monkey brain. These early investigators developed a stereotactic atlas of the monkey brain based on a cartesian coordinate system relative to landmarks (the inferior orbital rim and internal auditory canal) on the monkey's skull.[2,3] Similar to today's stereotactic head frames, their stereotactic apparatus was fixed to the monkey's skull. Using this apparatus, Horsley and Clarke were the first to describe the stereotactic destruction of an intracranial target using electrode electrocoagulation.[2,3] Despite the fact that Clarke patented the use of this device in humans, it was never applied outside the animal model.[4,5]

Spiegel, a neurologist and director of experimental neurology at Temple Medical School in Philadelphia, began developing the first stereotactic device for human use. Spiegel and colleagues,[6] a neurosurgeon who worked in Spiegel's laboratory as a medical student, reported on their human stereotactic apparatus in 1947. Their device was fixed to the patient's head in much the same way as Horsley and Clarke's simian model; however, intraoperative radiographs were used for localizing intracranial structures during the procedure. By 1952, Spiegel and Wycis[7] had developed

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a stereotactic atlas of the human brain, and they coined their technique stereoencephalotomy. Their methods paved the way for functional human stereotactic neurosurgery. By this time, it was understood that sectioning the extrapyramidal system could be used to treat movement disorders such as Parkinson's disease; however, open neurosurgical operative mortality was quite high at the time. Russell Meyers,[8,9] a neurosurgeon at the University of Iowa and a leader in functional neurosurgery for movement disorders, reported that his open neurosurgical techniques carried a 15.7% mortality rate. By 1958, Spiegel and colleagues[10] were reporting the operative mortality for stereotactic surgery for movement disorders to be 2%. Their methodology and reduced mortality rate were met with enthusiasm by the worldwide neurosurgical community. Multiple stereotactic apparatus designs were developed in the 1950's, and it was estimated that nearly 25,000 functional stereotactic procedures were done worldwide before the introduction of L-dopa therapy for movement disorders.[11,12]

Lars Leksell is known as the father of stereotactic radiosurgery for his pioneering work applying the stereotaxic technique to radiation delivery. Leksell was born in Fassberg, Sweden, in 1907, and attended medical school at the Karolinska Institute. By 1935, he began his neurosurgical training under Herbert Olivecrona, and ultimately succeeded him as chairman of neurosurgery in 1961. Leksell understood that much of the morbidity and mortality associated with neurosurgery during this time was a consequence of invasive procedures, and therefore, he dreamed of developing a minimally invasive approach to treat intracranial lesions. Building on the principles produced by Horsley and Clarke and applied by Spiegel and Wycis, Leksell[13] developed his arc-centered stereotactic apparatus for intracerebral surgery in 1947. The device enabled the precise placement of a needle or electrode into a desired location within the human brain. Leksell first described the concept of stereotactic radiosurgery in 1951.[14] The initial device used a collimated x-ray beam (gamma rays) that could move along the semicircular arch of his stereotactic apparatus to strike an intracranial target.[14] Leksell[14] discussed the potential of using stereotactic radiosurgery to produce a lesion within the human brain, and noted the technology might be well-suited for functional neurosurgery. As exciting as the concept was, the effect of radiation on the central nervous system was poorly understood. Further research was needed, and Leksell[14] developed a feline stereotactic radiosurgical device to determine the effects on the cat brain.

During the late 1950s and early 1960s Leksell searched for an ideal form of radiant energy convenient for clinical stereotactic radiosurgery. Physicists Liden and Larrson of Uppsala University in Sweden were integral in the development of a system that used a cyclotron to direct proton beams at a target.[15–17] These physicists determined in the animal model that a sharply delineated stereotactic lesion was produced with high-energy protons.[15] In 1960, Leksell and colleagues[16] performed their first human stereotactic proton beam operation (a bilateral anterior capsulotomy) at the Gustaf Werner Institute in Uppsala. About the same time, Woodruff and colleagues[18] at University of California at Berkeley introduced a similar cyclotron-based radiosurgery system and began irradiating pituitary lesions. The cyclotron ultimately was determined to be too cumbersome and impractical for clinical use. Leksell eventually settled on gamma rays as a practical compromise for stereotactic radiosurgery. The first gamma unit was installed in the Sophiahemmet Hospital in Stockholm, Sweden, in 1968. The device used 179 sources of cobalt-60 distributed with collimators to create a sharply circumscribed disc-shaped lesion, and the device initially was intended for use during functional neurosurgery.[19–21] The second gamma unit was installed at the Karolinska Hospital in Stockholm, Sweden, in 1974 (**Fig. 1**). This