6 History of Stereotactic Neurosurgery in the Nordic Countries

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In the sixth volume of the classical and comprehensive textbook of neurosurgery by Olivecrona and Tönnis (1957), Lars Leksell contributed a chapter on "Targeted Brain Operations" (Gezielte Hirnoperationen). In the introduction he refers to the development of his stereotactic instrument – he always preferred to describe his stereotactic frame as a surgical instrument – that followed the pioneering work by Spiegel and Wycis in 1947–1948. The first presentation of Leksell's sterotactic apparatus dates from 1949 and already in the early 1950s he had gained experience in targeted lesional surgery using electrical current and different types of X-ray beams – radiosurgery. There is no doubt that this makes Leksell, together with a few others, one of the founders of stereotactic surgery. It should also be noted that the principal mode of function and general features of his original instrument have survived in the modern version that is still one of the most commonly used stereotactic systems in the world. That is why the advancement of stereotactic neurosurgery in the Nordic countries is so intimately associated with the name of Lars Leksell and his contributions.

Lars Leksell (1907–1986) started his neurosurgical training with Herbert Olivecrona in 1935 at the Serafimer Hospital, one of the oldest hospitals in Sweden founded in 1752. The Olivecrona neurosurgical service enjoyed a solid international reputation and attracted a large number of trainees from all over the world. For a short period Leksell served as a volunteer medical doctor in Finland when it was attacked by the Soviet Union in November 1939. Later he told that he during that war often speculated on the possibility of extracting bullets from the brain with minimal damage to the surrounding brain tissue using a mechanically guided instrument.

In the early 1940s Leksell joined Ragnar Granit, Nobel Laureate 1967, for experimental studies in neurophysiology. In 1945 he presented a PhD dissertation, a monograph on the motor gamma system titled "The action potential and excitatory effects of the small ventral root fibers to skeletal muscle." This was a major milestone in the understanding of muscle control and has now become part of basic neurophysiology. It should be noted that during these years he, together with Granit and Skoglund, made another major contribution by describing the phenomenon of ephapsis, "artificial synapses," caused by local pressure on a nerve, as a possible mechanism involved in trigeminal neuralgia.

After resuming clinical work, he started work on the development of a stereotactic instrument and in 1947 he visited Wycis in Philadelphia. Leksell described his instrument in a publication in 1949 and this was the first example of a stereotactic system based on the principle of "center-of-arc" in contrast to the Spiegel and Wycis orthogonal, rectangular frame (*Figure 6-1*). The use of a movable semi-arc with an electrode carrier implies that the tip of a probe can reach the target regardless of the position of the carrier or the angling of the arc relative to the skull

Figure 6-1
The first Leksell stereotactic instrument, based on the "center-of-arc" principle, was described in a publication from 1949

Figure 6-2
The first practical application of the stereotactic instrument was for puncture of craniopharyngioma cysts

fixation device, i.e., a frame or base plate with bars for bone fixation screws. This construction permits also transphenoidal, straight lateral and suboccipital probe approaches. Leksell was in many respects a perfectionist and for the rest of his life he continued to change and revise the design of virtually every small part of his instrument though the basic semicircular frame was retained. He focused not only on upgrading the function of the instrument but also on its aesthetic appearance. An important feature was that "the apparatus should be easy to handle and practical in routine clinical work" and "a high degree of exactitude is necessary."

An oft-cited quotation is "Tools used by the surgeon must be adapted to the task and where the human brain is concerned, no tool can be too refined."

The first, documented clinical application of Leksell's stereotactic system was a case of a craniopharyngioma cyst that was punctured and treated with injection of radioactive phosphorus – that patient was probably the first patient in the world to undergo this form of therapy (1948) (*Figure 6-2*).

Before the advent of modern imaging techniques (CT, MRI), ventriculography was, and in some centers still is, routinely utilized for target coordinate determination. Already in the late 1940s neuroradiology was a well-developed speciality at the Serafimer Hospital and angiography and pneumoencephalography were routinely practiced. Leksell performed pneumoencephalography, first in the sitting and then in the supine position to visualize the anterior and posterior commissures, respectively. In order to compensate for the divergence of the X-rays, he constructed a diagram of tightly packed concentric circles, approximated to spirals, geometrically related to the divergence and the distance between the X-ray tube and the film, and frame planes, for determining the target coordinates; it has to be admitted, however, that in contrast to Leksell's other inventions many surgeons found it difficult to understand and use this diagram.

Beside the passionate interest in the technical aspects of stereotaxy, Leksell was in the 1950s and 1960s very active in the operation theatre. He performed a large number of pallidotomies, and later also thalamotomies, in Parkinson's disease and capsulotomies in various forms of mental disorders (Figure 6-3). The results of a series of 81 patients subjected to pallidotomy was published in 1960, and 116 patients treated with capsulotomy were reported in 1961.

The term and concept of radiosurgery were introduced by Leksell already in 1951 when he reasoned that the "center-of-arc" principle and his first stereotactic instrument were suitable for replacing a probe (needle electrode) by *cross-firing* intracerebral structures with narrow beams of radiant energy. X-rays were first tried but both gamma rays and ultrasonics were included as alternatives (Figure 6-4). Initial experiments were performed on cats and then a few patients with pain and chronic psychosis were treated with a 280 kV X-ray tube attached to the arc. Of particular interest is that in 1953 two cases of trigeminal neuralgia were treated and at follow-up in 1971 they were still free of pain.

In 1946 Leksell was appointed head of a neurosurgical unit in Lund in southern Sweden where he became professor in 1958 and remained so until 1960. In those days there were very few neurosurgeons around the world who were active in stereotactic surgery and the international network was very small; it is of interest that the Schaltenbrand and Bailey's Stereotactic Atlas was partly based on some brain specimens supplied by Leksell. While in Lund, Leksell was apparently able to evade many of his clinical obligations because he was able to initiate a close collaboration with a team of physicists led by Börje Larsson at the University of Uppsala (north of Stockholm) where a synchrocyclotron was available. They conducted experiments with stereotactic high-energy proton irradiation in goats resulting in a seminal publication in Nature in 1958 (Figure 6-5). This technique was also applied in a few patients with Parkinson's disease (pallidotomy), psychiatric disorder (capsulotomy) and pain (mesencephalotomy).

Although precisely placed and well-limited lesions could be produced by the focused proton beams, as demonstrated in a few autopsy cases, the synchrocyclotron proved to be too complicated for general clinical use. This compelled Leksell to consider other radiation sources and he started designing the ^{60}Co Gamma Unit that was fully integrated with the stereotactic system. The

Figure 6-3
Leksell in the early 1960s with the second generation of his stereotactic frame

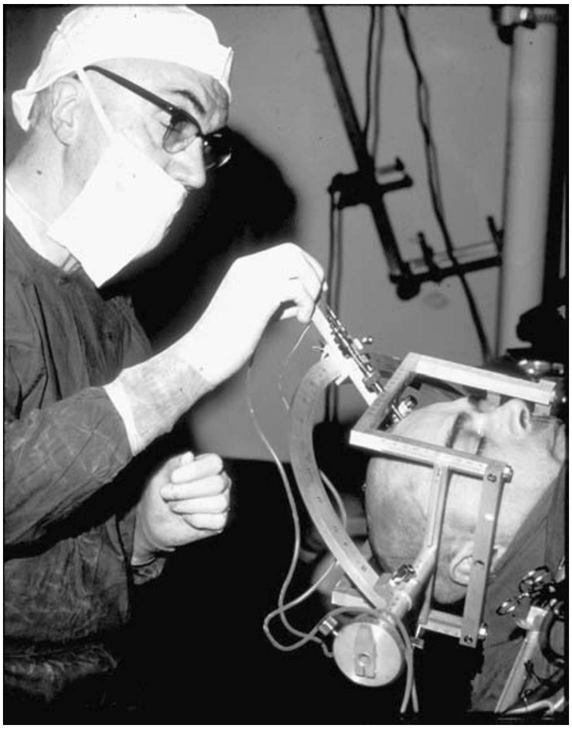


Figure 6-4
Application of the first stereotactic instrument for radiosurgery using cross-firing of 280 kV X-rays. Photo from the early 1950s

Figure 6-5
The first clinical trials with radiosurgery using proton beams from the cyclotron at Uppsala University were performed in the late 1950s

Figure 6-6
Leksell treating the first case of acoustic neurinoma with the first version of the Gamma Knife in 1968

development of the "Beam-knife" took place after Leksell had been appointed successor to Olivecrona in 1960 and the first unit was inaugurated in 1967 (*Figure 6-6*). Later the same year reports of the two first cases, patients with cancer related pain subjected to radiosurgical thalamotomy, were published.

Originally, radiosurgery and the Gamma Unit were developed with the hope that it would offer a bloodless, and less risky, method to be applied principally in functional neurosurgery, for example in thalamotomy for Parkinson's disease. On the other hand, Leksell had always considered his sterotactic instrument a surgical tool that should also be utilized in general neurosurgery in order to enhance precision and minimize hazards. This idea had to some extent been realized by the extensive use of stereotactic technique in puncturing cysts and also in performing biopsies in critical regions. However, the Gamma Unit soon proved to be very useful in the treatment of some typical diseases requiring neurosurgery, such as pituitary adenomas, acoustic neurinomas and arteriovenous malformations. This successful application of radiosurgery has indeed revolutionized the management of these conditions but was also met with much skepticism from the neurosurgical community.

Albeit the topic of this chapter is the history of stereotaxis, two other examples of Leksell's exceptionally innovative mind deserve to be mentioned. He was the first to apply ultrasound in neurosurgical diagnosis by the development of echoencephalography as early as 1955. Moreover, his elegantly designed, double action rongeur has become an indispensable tool in the hands of most neurosurgeons.

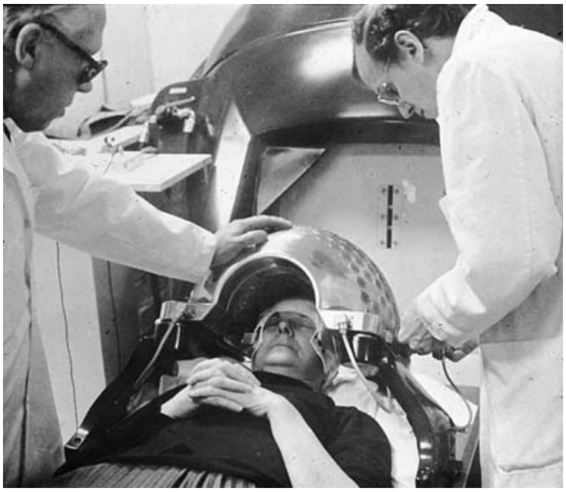
Leksell's Disciples

Erik-Olof Backlund (1931) started his neurosurgical training in 1960 at the Serafimer Hospital and he soon became a pupil and a close associate of Leksell.

At that time neuroradiology could visualize pathological mass processes only indirectly, and therefore stereotactic biopsy was rarely performed, the exceptions being trials to obtain specimens of the cystic wall when performing craniopharyngioma cyst punctures. This became part of Backlund's doctoral thesis and to facilitate biopsy sampling he constructed a new device consisting of a spiral that could be screwed into the often quite tough craniopharyngioma tissue from which a specimen could then be harvested by using an outer sharp cutting needle as a sleeve punch. This biopsy needle proved to be very useful and is still routinely used. Backlund also contributed other innovative needle instruments for aspiration biopsy, hematoma evacuation, and aqueduct reconstruction. Backlund's interest in craniopharyngiomas led him to reconsider the choice of radioactive phosphorus for cystic intracavity irradiation and he demonstrated that a colloid ^{90}Y was more effective. Subsequently, he developed a multimodal treatment program for craniopharyngiomas, and the evacuation of cysts and installation of radioactive substances were in some cases supplemented by radiosurgery of the solid parts (*Figure 6-7*). This treatment strategy is still practiced at the Karolinska University Hospital. Another contribution was the application of radiosurgery for capsulotomy in patients with anxiety and OCD; this was first published, with Leksell as co-author, in 1978.

As noted by Backlund himself in an autobiographical vignette, the most spectacular phase of his career was the first neurotransplantation of adrenal chromaffin cells in a patient with Parkinson's disease. This trial was initiated by a group of researchers in basic sciences at the

Figure 6-7
Erik-Olof Backlund (*right*) and the research engineer Bengt Jernberg (*left*) preparing a patient for capsulotomy. Note, at that time the head was fixed with a Orthoplast cap. Photo from the mid 1970s



Karolinska Institute and Backlund developed the stereotactic technique for precise depositing of the cellular specimen.

Ladislau Steiner (1920) is presumably the most well known of Leksell's pupils. From 1962 he first trained with Olivecrona who was then still active in spite of retirement. His prime interest was vascular and tumor microsurgery rather than endeavors within the stereotactic and functional field. His first exposure to radiosurgery was when he took part in a major study thalamotomy for cancer-related pain. It then appeared that radiosurgery might be useful for some common neurosurgical diseases also, and together with Leksell he became the first to demonstrate that centrally located arteriovenous malformations, otherwise inaccessible to surgery, could be miraculously obliterated. Steiner, along with *Christer Lindquist* (1944) who later became one of the leading names in radiosurgery with many important publications, subsequently performed a large number of AVM treatments. Following the first publication many patients from all over the world were referred to him. The AVM experiences triggered a surge of trials on new applications for radiosurgery (acoustic neurinomas, pituitary adenomas, pituitary hormone suppression in Cushing's disease, pinealomas, meningiomas, and later cerebral metastases). In 1987 Steiner left the Karolinska University Hospital and became professor and director of the Lars Leksell Gamma Knife Center at the University of Virginia. There he created a very active team that has made this center one of the leading ones for radiosurgery. Scientifically also, he has continued to be very active and is co-author of numerous publications covering the entire field of radiosurgery.

A few others of Leksell's disciples who were active in the field of radiosurgery and have made important, more or less independent contributions should be mentioned. *Georg Norén* (1943) was the first to demonstrate, in an extensive and long-lasting study, that the outcome of radiosurgical treatment of acoustic neurinomas is at least as favorable as that with open surgery performed by the most experienced neurosurgeons. Since 1992, Norén has been director of the Gamma Knife Center at Brown University, Providence.

Tiit Rähn (1940) became involved in stereotactic techniques and radiosurgery in the late 1960s and he pioneered the management of hormone secreting pituitary adenomas. His career, until retirement, has been entirely devoted to radiosurgery.

The senior author of this paper (*B.A.M* 1933), Meyerson joined Leksell's team in 1968, shortly after the inauguration of the first Gamma Unit. He soon became involved in "gamma-thalamotomy" for cancer-related pain and the preliminary results were published in 1969. Because of the relatively unsatisfactory outcome of this form of surgery a project with intracerebral electrical stimulation (deep brain stimulation, DBS) for pain was initiated in 1974, and with electrodes of our own design stimulation was applied simultaneously in several brain targets. This was the beginning of a life-long career in pain research. At an early stage Meyerson was also introduced to surgical treatment of mental disorders and subsequently he performed the great majority of capsulotomies, as well as a large number of interventions for movement disorders, at the Karolinska University Hospital.

The second most prominent stereotactic neurosurgeon in the Nordic countries was *Lauri Laitinen* (1928–2005) and it is notable that he pursued his own career independent of Leksell. He had his basic neurosurgical training in Helsinki and was confronted with stereotactic surgery when working in London, and visiting Gillingham in Edinburgh. He started operating on Parkinsonian patients in 1961 using first the Cooper instrument and later a Riechert-Mundinger frame. He was, however, dissatisfied with both these instruments and towards the end of the 1960s he had constructed his own system that was later acquired by many stereotactic centers (*Figure 6-8*). This instrument has the Leksell center-of-arc design combined with some features of the Riechert-Mundinger frame. Throughout his career he was very active in clinical practice and performed about 200 thalamotomies annually. During these operations he made extensive trials with impedance monitoring which he found very helpful for differentiating white from grey matter, for example to identify the border between the internal capsule and pallidal tissue. In 1963 Laitinen published his first paper in the field of stereotactic surgery, on the treatment of torticollis. Later he joined with a young neuropsychologist, Juhani Vilkki, and in a series of papers they documented, for the first time, the deterioration of motor, verbal, and visuospatial functions that may occur after thalamotomy. Laitinen was also very interested in pain, and inspired by Gabriel Mazars in Paris, he performed the first trial of implanting a stimulating electrode in a patient with phantom limb pain already in 1968.

In 1980 Laitinen moved to Umeå, a university town in northern Sweden, where he revived stereotactic and functional neurosurgery to such an extent that Umeå became a center of excellence. There he developed a device (the "Stereoadapter"), a light frame that in a reproducible way could be repeatedly attached to the skull during CT and MRI examinations and then utilized for coordinate determination together with the original frame. In 1984 he, along with Marwan Hariz (who later became his successor) and Tommy Bergenheim, began to test Leksell's old and almost forgotten version of pallidotomy from the early 1950s. For many of the younger neurosurgeons this endeavor is directly associated with the name of Laitinen. It should be recalled that with the advent of L-dopa in the early 1970s the use of surgery for movement disorders, in particular for Parkinson's disease, was reduced to just a few cases each year even in the major centers. The first presentation in 1992 of the favorable outcome of Laitinen's pallidotomy cases resulted in a dramatic change in attitude toward surgery among the neurologists. A contributing, important factor was that this type of intervention had proven to be effective for L-dopa induced hyperkinesias also, which by that time had become a major problem. No doubt, the acceptance of pallidal surgery following Laitinen's reports paved the way for the ensuing development of stimulation of central brain areas (DBS) as a novel mode of therapy for Parkinson's disease.

Figure 6-8
Lauri Laitinen standing by a case displaying his own frame and stereoadapter. Photo from 2003

During the 1960–1970s stereotactic surgery was practised occasionally in a few other neurosurgical units in the Nordic countries but these activities cannot be regarded as pioneering or innovative. One exception was the contributions made by *Kjeld Vaernet* (1920–2006) in Copenhagen who in 1974 reported on a trial with "stereotactic stimulation and electrocoagulaton of the lateral hypothamus" in five patients with gross obesity. He also performed many stereotactic surgeries for epilepsy and mental disorders.

Even though the contributions of Leksell are exceptional and outstanding, the importance of the achievements of his disciples and of Laitinen in making the Nordic countries strong in stereotactic open neurosurgery and radiosurgery should not be underestimated.

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