The History of Stereotactic Radiosurgery

1

Marina Kushnirsky, Vaibhav Patil, and Michael Schulder

Definition

Since its introduction in 1951, stereotactic radiosurgery (SRS) has become one of the most important technological innovations in neurosurgery. Hundreds of thousands of patients have undergone the procedure, which is now at the cutting edge of radiation therapy techniques. This modality originated as the minimally invasive stereotactic application of various energy sources—ultrasound, orthovoltage, X-rays, and accelerated subatomic particles—for the treatment of movement and pain disorders [1]. SRS has since evolved into a precise, cost-effective, and noninvasive therapy for a wide range of intracranial and extracranial pathologies. Advances in imaging enable highly accurate treatment planning, and radiobiological innovations have improved beam targeting. The evolution of SRS has allowed for the treatment of an ever-increasing range of oncological, cerebrovascular, and functional targets, while simultaneously improving patient comfort and diminishing harmful side effects.

Stereotactic radiosurgery was first defined in 1951 by the pioneering Swedish neurosurgeon Lars Leksell, who envisioned it as an alternative treatment during a time when mortality from open neurosurgery was close to 40% [2]. Leksell saw great potential in a technique that could use a single heavy dose of radiation to "destroy any deep brain structure without the risk of bleeding or infection" [3]. His invention predated advances in technology and radiobiology, which now enable frameless, fractionated stereotactic localization. As a result of these advances, the boundary between radiosurgery and fractionated stereotactic radiotherapy (FSRT) has become blurred. Sixty-two years since Leksell first treated a patient with trigeminal neuralgia using an orthovoltage dental X-ray tube [4], SRS has changed so radically that its definition has been reexamined. The argument in the first decade of the twenty-first century was framed thusly: the "purists" stated that the unique radiobiological advances of SRS were lost once fractionation was incorporated, while the "fractionators" claimed that it was overly rigid to not take advantage of the ability to fractionate, given the possibilities opened up by increased computer speed and power.

At a 2005 meeting of the American Association of Neurological Surgeons Stereotactic Radiosurgery Task Force, the members attempted to definitively separate fractionated stereotactic radiosurgery and FSRT. A related goal was to agree with organized radiation oncology (represented by ASTRO, the American Society for Therapeutic Radiation Oncology) on a definition of SRS as opposed to SRT. They dismissed radiobiological differences between the two modalities, stating they are unsubstantiated and theoretical at best [1]. Instead, the meeting chose to focus on the intent of treatments as the key distinction between hypofractionated SRS and FSRT. SRS uses steep radiation dose gradients to ensure that only the target lesion is destroyed while surrounding tissue is preserved. FSRT employs the differential responses of tumors and normal tissue to fractionated ionizing radiation. Thus, dose homogeneity is much more important for FSRT, in which abnormal and sensitive normal tissue may be in the same treatment field.

Ultimately, the task force defined SRS as "a distinct discipline that utilizes externally generated ionizing radiation in certain cases to inactivate or eradicate (a) defined target(s) in the head or spine without the need to make an incision. The target is defined by high resolution stereotactic imaging. Stereotactic Radiosurgery (SRS) typically is performed in a single session, using a rigidly attached stereotactic guiding device, other immobilization technology and/or a stereotactic image-guidance system, but can be performed in a limited

M. Kushnirsky, B.A. • M. Schulder, M.D. (✉)
Department of Neurosurgery, Hofstra North Shore LIJ School of Medicine, Manhasset, NY, USA
e-mail: mschulder@nshs.edu

V. Patil, M.D., M.S.
Department of Information Technology, Commonwealth Care Alliance, Boston, MA, USA

L.S. Chin and W.F. Regine (eds.), *Principles and Practice of Stereotactic Radiosurgery*,
DOI 10.1007/978-1-4614-8363-2_1, © Springer Science+Business Media New York 2015

number of sessions, up to a maximum of five" [1]. As FSRT's conformity and dose falloff improve, it may become necessary to rework the definition of SRS, perhaps including new information about radiobiological tissue response.

Early Roots

Lars Leksell's 1951 development of stereotactic radiosurgery was preceded by a multitude of technological innovations in both stereotactic surgical fixation and medical physics. The first stereotactic apparatus was described in 1908 by Sir Victor Horsley and Robert Clarke [5]. It utilized Cartesian coordinates to locate structures within the brain, using bony landmarks for reference. Their work also included the first stereotactic atlas, which contained illustrated cross sections of the monkey brain registered to distinguishing features on the skull. The major issue with Horsley and Clarke's system was that intracranial anatomical structures vary significantly between individuals in their relationship to bony landmarks of the skull, making accurate targeting impossible. Interestingly, one of the engineers who worked on the apparatus designed a frame for human use. Unable to persuade his neurosurgical colleagues to use it, he stored it in a closet until his family discovered it, almost 60 years later [6].

The first stereotactic device accurate enough for use in humans was developed in 1947 by Ernest A. Spiegel and Henry T. Wycis (Fig. 1.1). This new stereotactic frame needed an improved method of intracranial targeting, and by this time X-ray technology had sufficiently advanced to be practical and quick enough for use in the operating room. Spiegel and Wycis employed X-ray ventriculography to identify where a target lesion was in relation to any cerebral structure. Imaging techniques combined with advances in physiology allowed for recognition of select target pathways: the dorsomedial nucleus for psychosurgery, the lemniscal system for pain, and the extrapyramidal pathways for movement disorders [7]. In spite of these developments, the Spiegel–Wycis frame, which consisted of a Horsley–Clarke device attached to patients' skulls with a ring secured by a plaster of Paris cap [5, 8], was not without drawbacks. During pneumoencephalography, cerebrospinal fluid was drained so that air would enter the cerebral ventricles and allow for targeting of brain structures using X-rays. The side effects were so severe that patients were unable to undergo surgery on the same day their imaging and measurements were taken. However, when positive contrast became available, the procedure became more easily tolerated. The Spiegel–Wycis frame spurred the invention of at least 40 other stereotactic devices [5], including Leksell's.

Fig. 1.1 Henry T. Wycis holding Spiegel–Wycis stereotactic frame with Horsley-Clarke frame on the table. From *Textbook of Stereotactic and Functional Neurosurgery*. Lozano, Andres M.; Gildenberg, Philip L.; Tasker, Ronald R. (Eds.) 2nd ed. 2009; used with permission

Concurrent radiobiological innovations played an equally important role as stereotactic ones in the development of SRS. Ionizing radiation was used for therapeutic purposes soon after it was discovered; three months after Wilhelm Konrad Roentgen published his report in 1895, X-rays were used to treat skin and breast cancers [3, 9]. The discovery of radioactivity by Becquerel in 1896, and of radium by the Curies soon after, opened the door for the medical use of radioisotopes. X-rays were used to treat patients with pituitary tumors as early as 1906, and radium brachytherapy was applied to treat similar conditions at about the same time [10]. Harvey Cushing, the father of American neurosurgery, had extensive experience with both X-ray and brachytherapy treatments, although he remained skeptical of the utility of either [11]. Dosimetry was poorly understood, and treatments were not standardized. Nonetheless, some neurosurgeons continued to explore the uses of ionizing radiation, and new methods continued to be developed through the 1950s.

Emergence of Radiosurgical Practice

Lars Leksell conducted his earliest work with SRS while serving as head of the neurosurgery department at the University of Lund [12]. His preliminary work with a 250 kVp X-ray unit attached to a single beam port resulted in the successful management of pain control in trigeminal neuralgia patients (Fig. 1.2) [2, 5]. A ceaseless innovator, Leksell noticed that if he used higher energy radiation, depth dose and beam definition could be improved, especially in smaller treatment fields [12]. He then began working with Borje

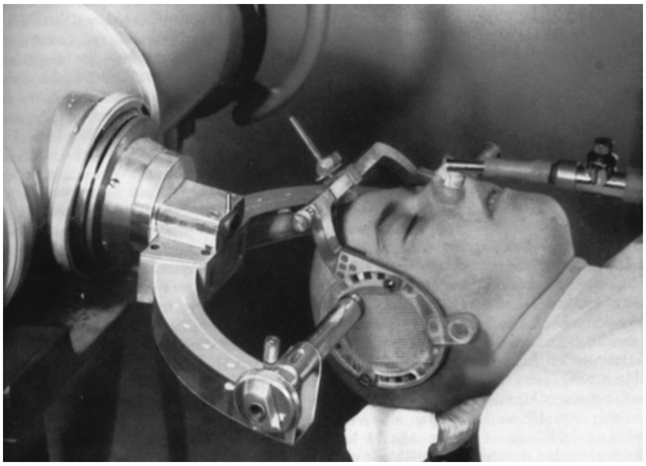

Fig. 1.2 First stereotactic instrument for radiosurgery using 280 kV X-rays, early 1950s. From *Textbook of Stereotactic and Functional Neurosurgery*. Lozano, Andres M.; Gildenberg, Philip L.; Tasker, Ronald R. (Eds.) 2nd ed. 2009; used with permission

Fig. 1.3 Lars Leksell and his physicist colleague, Borje Larsson, preparing a patient for SRS with a particle beam accelerator in 1958. (Photo courtesy of L. Dade Lundsford, MD)

Larsson, a radiobiologist at the Uppsala University cyclotron unit, to investigate the use of converging proton beams for neurosurgery (Fig. 1.3). When these beams proved too complicated and difficult to use in a hospital setting, Larsson and Leksell began collaborating with Kurt Liden, a medical physicist at Lund.

After experimenting with particle beams and linear accelerators, Leksell and his colleagues ultimately designed the

Fig. 1.4 Lars Leksell treating the first case of acoustic neurinoma with first version of gamma knife, 1968. From *Textbook of Stereotactic and Functional Neurosurgery*. Lozano, Andres M.; Gildenberg, Philip L.; Tasker, Ronald R. (Eds.) 2nd ed. 2009; used with permission

gamma knife (GK), containing 179 cobalt sources in a hemispheric array (Fig. 1.4). The first unit was operational in 1968; Leksell's first patient was immobilized using a molded plaster headpiece and treated for a craniopharyngioma [4]. The potential of the GK to treat neoplasms and vascular anomalies, as opposed to functional targets such as lesioning for control of pain and movement disorders, was recognized by Leksell early on. In the precomputed tomography (CT) era these treatments were mostly limited to patients with arteriovenous malformations (AVMs) [13] and acoustic neuromas, which could be imaged either on angiography or by polytomography, respectively [3].

At the same time, work was continuing elsewhere with focused heavy particle irradiation. John Lawrence, whose brother Ernest won the 1939 Nobel Prize for his invention of the cyclotron, began experimenting with charged particle radiation in 1954. He treated patients with pituitary and other intracranial disorders (Fig. 1.5) [14, 15] using proton and helium ion beams. He initiated the use of the Bragg peak principle according to which proton beams deposit their energy at a distinct point, with minimal exit dose. In practice, heavy particle beams must be carefully shaped and spread in order to treat patients with intracranial lesions.

After visiting Stockholm in 1959, Raymond Kjellberg, a neurosurgeon at the Massachusetts General Hospital, began the use of Bragg peak proton beam treatments in the USA [16]. He amassed a large series of patients with arteriovenous malformations and pituitary tumors. Similar efforts were carried out in California with helium ions [17]. For decades, the expense of building and maintaining a cyclotron has limited the use of heavy particle SRS to a few centers. In the last few years, new technology has decreased the size and cost of proton beam irradiation devices, and the number of such facilities has grown.

Fig. 1.5 Raymond Kjellberg with a frame for proton beam therapy of a patient with an AVM. (Photo courtesy of Richard Wilson, Mallinckrodt Research Professor of Physics, Harvard University)

Acceptance

When SRS was first invented, stereotactic localization relied on atlases, ventriculography, and angiograms. The advent of the computerized tomography (CT) scanner in the mid-1970s, and MRI some 10 years later, opened up the possibility of direct targeting of tumors and other "soft tissue" targets inside the skull. Image-guided stereotaxy became available for brain biopsy, craniotomy, tumor resection, and functional neurosurgery. Due to this, the 1980s saw the evolution of SRS from an esoteric technique, available at the original GK in Stockholm (and as fractionated treatments at the few heavy particle accelerators around the world), to an emerging technology of increasing utility.

In 1984, after several years of intense regulatory reviews and logistical battles, Dade Lunsford and colleagues completed the installation of the first American GK at the University of Pittsburgh [18]. This group was instrumental, via an ongoing series of peer-reviewed publications, in placing the technique and clinical indications for SRS on a sound scientific basis. Since then, several new models of GK units have become available. The most current high-end model, the GK Perfexion, enables automated collimator changes and improves access to intracranial targets.

As the potential horizons of SRS broadened, other investigators were able to adapt linear accelerators (LINACs) for SRS (Fig. 1.3) LINAC units create X-rays by accelerating electrons to almost the speed of light, then directing the electron beams to a heavy metal alloy. The resulting X-ray is collimated and focused onto a target. Before inventing the GK, Lars Leksell and his colleagues at the Karolinska Institute experimented with LINAC, but abandoned the system due to low photon energies and mechanical inaccuracy [4]. However, the ability to use CT imaging for lesion localization and beam targeting greatly increased the accuracy of LINACs. These systems were a cheaper alternative to GK or heavy particle accelerators [19] and were quickly adapted. Working independently, in Buenos Aires and Vicenza, Italy, respectively, Betti and Colombo reported the successful use of LINACs for SRS [20, 21] in 1982. Their systems allowed for the rotation of the LINAC gantry in a single plane.

At about the same time, Winston and Lutz described the use of a commercially available stereotactic frame for LINAC radiosurgery [22]. Following in their footsteps, Loeffler and Alexander demonstrated how a LINAC dedicated to SRS could be a practical alternative to a GK [23]. In the late 1980s Friedman and Bova elected not to install the second American GK unit, preferring to develop a new LINAC SRS system [24]. Other advantages of these LINAC systems, besides ubiquity and lower cost, included the availability of collimators in a much greater variety of diameters than provided with the GK. This allowed for the use of single isocenters when treating patients whose targets were over 18 mm in diameter, the width of the largest GK collimator. However, at around the same time several GKs were installed in several sites around the world.

As clinical experience increased, publications appeared, indications broadened, and vendors became increasingly interested, a debate emerged regarding the merits of the Gamma Knife versus LINAC-based SRS. By now, clinical and physics studies indicate that SRS can be delivered effectively and accurately with either method [19, 25]. Numerous reports demonstrating the efficacy of SRS with few if any short-term complications and lower costs led to the proliferation of GK and LINAC units around the world.

Fractionation, Extracranial Radiosurgery, and Other Advances

As the Gamma Knife and LINAC systems continued to improve treatment outcomes, it became clear that both technologies had promise for wider application. Rapid advances in neuroimaging, robotic technology, and beam targeting soon followed. John Adler, a neurosurgeon who trained at the Brigham and Women's Hospital in Boston, spent a fellowship year with Lars Leksell in 1985 (Adler JR, personal communication). Excited by his exposure to the GK, Adler saw the potential of SRS being extended to other areas of the body. This required a method of delivering focused

Fig. 1.6 The first Cyberknife treatment, 1994. (Photo courtesy of John R. Adler, MD)

radiation without a stereotactic frame. Partnering with engineers at Stanford University and with private financial backing, the Cyberknife ultimately came into being in 1994 (Fig. 1.6).

The Cyberknife delivers SRS via an X-band LINAC with an output of 6 MV. It is nonetheless small enough to be mounted on an industrial robot, allowing for a theoretically infinite number of beams to be aimed at the target. For treatment of intracranial targets, the patient is immobilized using a customized, molded plastic mask system that offers a high degree of reproducibility between multiple fractions. Treatments are fashioned using an inverse planning method; to allow for practical computation times, the number of beam origins ("nodes") and robot angles are limited. Various other LINAC-based systems have been developed to improve dose planning and delivery through beam shaping and intensity modulation. These systems include XKnife (Radionics), Novalis (BrainLAB), and Peacock (NOMOS Corporation). Single fraction SRS technologies have also been evolving; a rotating Gamma Knife system (RGS), invented in the 1990s, changes beam diameters during treatment without interchanging collimator helmets, which increases the system's flexibility and decreases treatment time.

In addition, CT scanners are now being incorporated into LINAC-based systems. The Tomotherapy Hi-Art system, invented in the 1990s, provides integrated treatment planning, patient setup, and CT-guided treatment. The newest Novalis TX system includes an on-board imaging cone beam CT scan to improve visualization of soft tissue targets during treatment and an ExacTrac image-guidance system to adjust for minute patient movements. These developments allow for real-time updated imaging during treatment to ensure positioning accuracy. Perhaps more significantly, this improves intrafraction targeting accuracy as well. Peer-reviewed publications have demonstrated the acceptance of the Cyberknife and Novalis frameless systems [26–29]. These and other articles have fostered a useful debate regarding the concept of hypofractionation in SRS and indeed if such treatments are still "radiosurgical" [30, 31].

Extracranial SRS

With frameless LINAC-based SRS and SRT, it became possible to further step outside the bounds of traditional radiosurgery and treat targets outside the brain. The first radiosurgical moves out of the intracranial compartment were in the logical direction of the skull base and past that into the paranasal sinuses, using either GK [32, 33] or LINAC units [34]. Creative modifications of standard stereotactic systems, such as the vacuum pillow stabilizer described by Lax in 1994 [35], were designed to allow for treatment of targets throughout the body. Hamilton and colleagues described the first truly extracranial radiosurgical unit in 1995. This prototypical system relied on a skeletal fixation frame and was designed to provide spinal SRS [36]. The need to surgically place a clamp on a spinous process and to treat the patient in a prone position limited the appeal of this groundbreaking concept. Non-CNS targets were later treated using newer stereotactic technologies such as the Elekta Stereotactic Body frame. However, with the advent of new frameless techniques and improvements in beam targeting, such external devices for rigid fixation and localization are no longer necessary. Table 1.1 summarizes the historical landmarks in the development of SRS.

The Role of Industry and Future Advances

The convergence of image-guidance and radiation delivery technologies initially encouraged the entry of multiple vendors into the SRS marketplace. This reflected the undeniable advantages of stereotactic localization and the resulting ability to focus radiation treatments on the smallest possible volume. While GK was historically the gold standard in SRS, a variety of frame-based LINAC systems were designed to provide single fraction SRS beginning in the 1980s. Vendors included Radionics (X-Knife), Zmed (the University of Florida system), BrainLab, and Fischer-Leibinger. As radiation oncologists accepted the concept of SRS, and neurosurgeons accepted fractionation, the industry's focus shifted toward frameless systems. As a result, Radionics and BrainLab adapted their LINAC-based SRS devices for frameless use, and Elekta created a frameless system that can be used to fractionate GK treatments.

Additional technological advances in stereotactic devices, imaging modalities such as PET scans, and diffusion tensor imaging (DTI) are rapidly altering methods for tumor analysis and surgical planning. DTI helps visualize nerve tracts,

Table 1.1 SRS landmarks

Year	Author	Device/event
1947	Spiegel/Wycis	First human SRS frame developed
1951	Leksell	Invention of SRS with rotating orthovoltage unit
1954	Lawrence	Heavy particle treatment of pituitary for cancer pain
1962	Kjellberg	Proton beam therapy of intracranial lesions
1967	Leksell	Invention of gamma knife
1970	Steiner	GK SRS of AVMs
1980	Fabrikant	Helium ion treatment of AVMs
1982	Betti/Colombo	LINACs adapted for SRS
1984	Bunge	Installation of commercial GK
1986	Winston/Lutz	LINAC SRS based on common stereotactic frame
1992	Loeffler/Alexander	Dedicated LINAC for SRS developed
1993	Mackie	First tomotherapy system developed
1994	Adler	First Cyberknife treatment
1997	DeSalles, Solberg	First Novalis shaped beam RS unit installed
2011	Sheehan et al.	First Gamma Knife extend case studies

Table 1.2 Peer-reviewed publication on SRS

Year	Papers	Citations
1951–1960	1	7
1961–1970	0	0
1971–1980	17	402
1981–1990	122	4,707
1991–2000	1,024	20,056
2001–2010	1,563	19,051
2011–present	505	477

while PET produces three-dimensional images of processes in the body. Together with fMRI, these technologies will likely improve the precision of SRS and SRT and may be incorporated into the imaging suites of current units. Nanotechnology, which can be used to detect tumor margins or as a tool for radiation guidance [37], is also a major source of excitement in the industry. The advancement of SRS and related techniques has been integral in defining the modality as a new standard in patient care.

Organized Radiosurgery

Stereotactic societies have been critical in disseminating information about radiosurgical advances. While today's organizations host international symposiums with extensive membership and attendance, their origins are much more humble. After Spiegel and Wycis created their stereotactic device, neurosurgeons who were interested in learning the technique visited the inventors at their lab at Temple Medical School in Philadelphia [38]. To facilitate the exchange of this information, the International Society for Research in Stereoencephalotomy was created in 1961.

Interestingly, the word stereotactic is a relatively recent product of organized neurosurgery. Originally, Horsley and Clarke labeled their technique "stereotaxic," meaning "three-dimensional arrangement" in Greek. However, when the International Society for Research in Stereoencephalotomy voted on a new name in 1973, it was decided that the object of the technique was to touch the desired structure with a probe or electrode. Hence, the group chose the word "Stereotactic," a mongrel of the Greek *stereo* meaning "three dimensional" and the Latin *tact* meaning "to touch."

Neurosurgeons' interest in SRS was slow to develop but increased exponentially over time. In 1987, the year that the first American GK was installed at the University of Pittsburgh and early work on LINAC SRS had been published, there were no SRS-related presentations at the annual meeting of the American Association of Neurological Surgeons (AANS). By 1998 there were 31 such abstracts in addition to practical course and seminars devoted to the topic. SRS has remained a key item of interest at the major annual meetings of the AANS and of the Congress of Neurological Surgeons. In addition, the meetings of the American and World Societies for Stereotactic and Functional Neurosurgery feature SRS as one of the main topics. The number of peer-reviewed publications on SRS has grown tremendously as well. From 1981 to 1990, 122 such papers were published; in 2011 alone, that number was 532 (Table 1.2) [39].

As the field grew more interdisciplinary, the International Stereotactic Radiosurgery Society (ISRS) was founded in 1993 and held its first biannual meeting that year in Stockholm. At first the papers presented dealt entirely with the treatment of intracranial conditions. As SRS has moved below the skull base, studies regarding patients with such conditions as tumors of the spine, lung, pancreas, and prostate have been included in the ISRS program. Thus, the expertise of clinicians in fields completely unrelated to neurosurgery is being applied to the study of SRS. Neurosurgeons comprise the single biggest specialty group in the organization, followed by radiation oncologists and medical physicists. As interest in extracranial and non-neurosurgical SRS inevitably increased, the membership of ISRS will evolve to reflect this. The ISRS publishes a peer-reviewed collection of selected manuscripts from each meeting, entitled *The Journal of Radiosurgery and SBRT*. The growth of SRS and its widespread acceptance have been such that yet another organization, the Radiosurgery Society, has begun to hold annual meetings.

Conclusion

In the 60 years since it was invented, it is clear that stereotactic radiosurgery has become a mainstream treatment for a wide variety of conditions. This is not surprising; due to innovations in stereotactic immobilization, imaging, and radiobiology, the technique is now extremely precise, noninvasive, well tolerated, and effective. Invented more than 60 years ago, SRS is over half the age of its main "parent" specialties, neurosurgery and radiation oncology. It is no longer considered an experimental or new treatment, but rather a continuously growing and advancing field. Acceptance by neurosurgeons, surgical specialists, and radiation oncologists means that as SRS evolves it will not be a technique for "radiosurgeons," but one of the methods available to treat patients.

What remains to be seen is how the field will evolve in response to developments in imaging and nanotechnology. SRS has already seen one major revolution: once the genie of hypofractionation was let out of the radiosurgical bottle, fractionation became the norm among LINAC users, and GK created a frameless immobilization device in order to fractionate treatments. The impetus toward more focused and less invasive treatments is likely to spur other such changes in the future. Clinical and technological advances will continue, and SRS will play an increasingly important part in the management of patients with a range of tumors and disorders.

References

1. 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):1–5. Epub 2007/01/24.
2. Alexander E, Loeffler JS, Lunsford LD. Stereotactic radiosurgery. New York: McGraw-Hill; 1993. p. 254.
3. Leksell L. Stereotactic radiosurgery. J Neurol Neurosurg Psychiatry. 1983;46(9):797–803. Epub 1983/09/01.
4. Niranjan A, Lunsford LD. Radiosurgery: where we were, are, and may be in the third millennium. Neurosurgery. 2000;46(3):531.
5. Gildenberg PL, Krauss JK. History of stereotactic surgery. In: Lozano A, Gildenberg P, Tasker R, editors. Textbook of stereotactic and functional neurosurgery. Berlin: Springer; 2009. p. 1–33.
6. Olivier A, Bertrand G, Picard C. Discovery of the first human stereotactic instrument. Stereotact Funct Neurosurg. 1983;46(1–4): 84–91.
7. Gildenberg PL. Spiegel and wycis—the early years. Stereotact Funct Neurosurg. 2001;77(1–4):11–6.
8. Schulder M. Overview of radiosurgery technology. In: Lozano A, Gildenberg P, Tasker R, editors. Textbook of stereotactic and functional neurosurgery. Berlin: Springer; 2009. p. 867–96.
9. Schulder M, Rosen J. Therapeutic radiation and the neurosurgeon. Neurosurg Clin N Am. 2001;12(1):91–100. viii. Epub 2001/02/15.
10. Hirsch O. Uber methoden der operativen behandlung von hypophysistumoren auf endonasalem wege. Arc Laryngol Rhinol. 1910; 24:129–77.
11. Schulder M, Loeffler J, Howes A, Alexander III E, Black P. The radium bomb: Harvey Cushing and the interstitial irradiation of gliomas. J Neurosurg. 1996;84:530–2.
12. Benedict SH, Bova FJ, Clark B, Goetsch SJ, Hinson WH, Leavitt DD, et al. Anniversary paper: the role of medical physicists in developing stereotactic radiosurgery. Med Phys. 2008;35(9): 4262–77.
13. Steiner L, Leksell L, Greitz T. Stereotaxic radiosurgery for cerebral arteriovenous malformations. Acta Chir Scand. 1972;138: 459–64.
14. Kirn TF. Proton radiotherapy: some perspectives. JAMA. 1988; 259(6):787–8.
15. Skarsgard LD. Radiobiology with heavy charged particles: a historical review. Phys Med. 1998;14 Suppl 1:1–19.
16. Kjellberg RN, Abe M. Stereotactic Bragg peak proton beam therapy. In: Lunsford LD, editor. Modern stereotactic neurosurgery. Boston: Martinus Nijhoff; 1988. p. 463–70.
17. Fabrikant J, Lyman J, Frankel K. Heavy charged particle Bragg peak radiosurgery for intracranial vascular disorders. Radiat Res Suppl. 1985;104:8244–58.
18. Lunsford LD, Flickinger JC, Linder G, Maitz A. Stereotactic radiosurgery of the brain using the first United States 210 cobalt-60 source gamma knife. Neurosurgery. 1989;24:151–9.
19. Podgorsak E, Pike G, Olivier A, Pla M, Souhami L. Radiosurgery with high energy photon beams: a comparison among techniques. Int J Radiat Oncol Biol Phys. 1989;16:857–65.
20. Betti O, Derechinsky V. Hyperselective encephalic irradiation with a linear accelerator. Acta Neurochir Suppl. 1984;33:385–90.
21. Columbo F, Benedetti A, Pozza F, Avanzo RC, Marchetti C, Chierego G, et al. External stereotactic irradiation by linear accelerator. Neurosurgery. 1985;16(2):154–60.
22. Winston KR, Lutz W. Linear accelerator as a neurosurgical tool for stereotactic radiosurgery. Neurosurgery. 1988;22:454–64.
23. Loeffler J, Shrieve D, Wen P, Fine H, Kooy H, Adessa A, et al. Radiosurgery for intracranial malignancies. Semin Radiat Oncol. 1995;5:225–34.
24. Friedman W, Bova F. The University of Florida radiosurgery system. Surg Neurol. 1989;32:334–42.
25. Luxton G, Petrovich Z, Joszef G, Nedzi L, Apuzzo M. stereotactic radiosurgery: principles and comparison of treatment methods. Neurosurgery. 1993;32:241–59.
26. Rahimian J, Chen JT, Girvigian M, Miller M, Rahimian R. Frame-based and frameless accuracy of novalis® radiosurgery. In: De Salles AAF, Gorgulho A, Agazaryan N, Slotman B, Selch M, Burwick AJ, editors. Shaped beam radiosurgery. Berlin: Springer; 2011. p. 37–46.
27. Chang SD, Murphy M, Geis P, Martin DP, Hancock SL, Doty JR, et al. Clinical experience with image-guided robotic radiosurgery (the Cyberknife) in the treatment of brain and spinal cord tumors. Neurol Med Chir (Tokyo). 1998;38(11):780–3.
28. Mehta VK, Lee QT, Chang SD, Cherney S, Adler Jr JR. Image guided stereotactic radiosurgery for lesions in proximity to the anterior visual pathways: a preliminary report. Technol Cancer Res Treat. 2002;1(3):173–80.
29. Ishihara H, Saito K, Nishizaki T, Kajiwara K, Nomura S, Yoshikawa K, et al. CyberKnife radiosurgery for vestibular schwannoma. Minim Invasive Neurosurg. 2004;47(5):290–3.
30. Pollock BE, Lunsford LD. A call to define stereotactic radiosurgery. Neurosurgery. 2004;55(6):1371–3.
31. Adler Jr JR, Colombo F, Heilbrun MP, Winston K. Toward an expanded view of radiosurgery. Neurosurgery. 2004;55(6):1374–6.

32. Kondziolka D, Lunsford LD. Stereotactic radiosurgery for squamous cell carcinoma of the nasopharynx. Laryngoscope. 1991; 101(5):519–22.
33. Firlik KS, Kondziolka D, Lunsford LD, Janecka IP, Flickinger JC. Radiosurgery for recurrent cranial base cancer arising from the head and neck. Head Neck. 1996;18(2):160–5. discussion 6.
34. Kaplan ID, Adler JR, Hicks Jr WL, Fee WE, Goffinet DR. Radiosurgery for palliation of base of skull recurrences from head and neck cancers. Cancer. 1992;70(7):1980–4.
35. Lax I, Blomgren H, Näslund I, Svanström R. Stereotactic radiotherapy of malignancies in the abdomen: methodological aspects. Acta Oncol. 1994;33(6):677–83.
36. Hamilton A, Lulu B, Fosmire H, Stea B, Cassady J. Preliminary clinical experience with linear accelerator-based spinal stereotactic radiosurgery. Neurosurgery. 1995;36:311–9.
37. De Salles AAF, Sedrak M, Lemaire JJ. The future of radiosurgery and radiotherapy. In: De Salles AAF, Gorgulho A, Agazaryan N, Slotman B, Selch M, Burwick AJ, editors. Shaped beam radiosurgery. Berlin: Springer; 2011. p. 305–9.
38. Gildenberg PL, Krauss JK. History of the stereotactic societies. In: Lozano A, Gildenberg P, Tasker R, editors. Textbook of stereotactic and functional neurosurgery. Berlin: Springer; 2009. p. 35–44.
39. Harzing AW. Publish or Perish. 2007. Available from http://www.harzing.com/pop/htm.