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Radiosurgery

A review of 3 current radiosurgery systems☆

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Abstract

Background: Stereotactic radiosurgery and fractionated stereotactic radiotherapy have become widespread techniques applied to the treatment of a variety of intracranial lesions. Rapid evolution of new technologies has now enabled clinicians to treat tumors outside the cranium and down the spinal axis. This review compares 3 commercially available systems in widespread use throughout the world.

Methods: Literature review and interviews with practitioners in the United States were performed to establish data for a comparative analysis of the Gamma Knife (Elekta, Sweden), Novalis (BrainLabs, Germany), and CyberKnife systems (Accuray, Sunnyvale, CA). Cost analyses were deliberately excluded because of the need for detailed cost-benefit analysis beyond the scope of the review.

Results: An unbiased comparative analysis was not possible because of the lack of objective data from a standard metric for these systems. Despite this shortcoming, disparate features of each system were compared and contrasted.

Conclusion: A careful assessment of each system, including its operational features, capabilities, and yearly capacity must be weighed against the composition of the radiosurgery team, the case mix of the practice, and the objectives of the clinical unit to yield the best fit.

Keywords: Gamma Knife; Novalis; CyberKnife systems

1. Introduction

Radiosurgery has become an important treatment alternative to surgery for a variety of intracranial lesions. As currently practiced, it has in fact replaced surgery as a standard of care in some instances, complements surgery as a postoperative adjunct in others, and most commonly represents an alternative to surgery or the only treatment option. Radiosurgery techniques have evolved quickly with the development of new technologies, enabling more complex yet more efficient treatment plans. As a consequence, these technologies have broadened radiosurgery applications and improved radiosurgery outcomes. This review will serve to provide the authors' assessment of the commercially available radiosurgery systems either rapidly growing or widely established in the world today. The systems under review will include the Gamma Knife, manufactured by Elekta based in Sweden; Novalis, manufactured by BrainLabs based in Germany; and CyberKnife, manufactured by Accuray based in the United States. We draw from our institutional experience with both a Gamma Knife and a Novalis unit as well as communicate the experiences shared by our colleagues with these units and the CyberKnife. Ideally, we wish this review to provide information about commercial products as much as a review in consumer reports would. Undoubtedly, some biases based on our experiences and lack of comparative data for all systems will limit our ability to achieve this. We will not provide cost figures and would rather refer the reader to the vendors. The cost of a radiosurgery unit must be assessed according to a variety of factors including cost per treatment, which should be weighed against the cost of alternative treatments, and measures such as QALY benefit.

☆ The authors have no conflict of interest with reviewed systems.

Abbreviations: CT, computed tomography; CT-3D, computed tomography three dimensional; IMRS, Intensity-Modulated Radiosurgery; IMRT, Intensity-Modulated Radiation Therapy; LINAC, linear acceleration; MLC, multileaf collimator; MR, magnetic resonance; QALY, quality of life; RTOG, Radiation Therapy Oncolgy Group; SRS, radiosurgery; SRT, radiotherapy; UCLA, University of California Los Angeles; X-Knife, stereotactic radiosurgery; XVI, X-ray Volume Imaging.

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2. Brief historical perspective

Radiosurgery was conceived and developed by the Swedish neurosurgeon Lars Leksell in 1952, and the first patients were treated in 1967. Originally designed as a noninvasive means of delivering small precise lesions for functional disorders, it evolved in its later applications to a broad variety of intracranial lesions including benign and malignant tumors and arteriovenous malformations. Its promise was recognized by the American neurosurgeon Dade Lunsford during his Van Wagonnen Fellowship with Leksell, and the first North American installation was completed in 1987 at the University of Pittsburgh, Pittsburgh, Pa [17]. Thereafter, with the rapid evolution of computing and imaging technology, the practice of Gamma Knife radiosurgery gained rapid and widespread acceptance worldwide. With a uniform dose delivery technique and treatment planning software, Elekta, with the coordinated efforts of the University of Pittsburgh, organized the Gamma Knife Users Group, and clinical data could be pooled to assess treatment results. Gamma Knife installations flourished but expenses limited most installations to large academic centers or large private referral hubs.

With the inauguration of radiosurgery in Pittsburgh, the Harvard neurosurgeon Ken Winston was well underway in a collaborative effort with medical physicist Wendell Lutz to retrofit a standard linear accelerator for radiosurgery treatments [23], as was Florida neurosurgeon Bill Friedman working with medical physicist Frank Bova [10]. Similar efforts were underway with the Italian neurosurgeon Federico Colombo in Vincenza [7] and the Argentinian neurosurgeon Oswaldo Betti in Buenos Aires [5]. Together, these clinicians established the feasibility of radiosurgery practice with linear accelerators and, given the ubiquity of linear accelerators in the world, expanded the practice of radiosurgery beyond the Gamma Knife. Initially, however, there existed a number of shortcomings to linear accelerator–based practices. Because these were general-purpose units, they had to be retrofitted and used only at specified times, usually once a week. Quality assurance was onerous and treatment planning systems were often institution specific and awkward. Linear accelerators varied, each with their own specifications, which differed with respect to important variables such as monitor units, gantry sag, and collimation systems. It was difficult to pool outcome data among active linear accelerator–based programs.

A remarkable and somewhat rancorous meeting was held in Boston at Pine Manor Junior College in June of 1990 at which the merits of these emerging technologies were discussed and debated. Three years later, the first International Stereotactic Radiosurgery Society convened in Stockholm, Sweden, where initial clinical series for institutions around the world were shared and debates about competing technologies continued.

The early limitations of radiosurgery units were overcome by the mid-1990s. The more cumbersome KULA treatment planning software was replaced with the Leksell Gamma Plan, which was both more effective and user-friendly. The University of Pittsburgh reported refinements in Gamma Knife outcomes for acoustic tumors by increasing the number of isocenters [9] and switching from CT-based to MR-based treatment data. Downward dose iterations were reported worldwide, which improved treatment-related cranial neuropathies while preserving tumor control rates.

The greater limitations of linear accelerator–based units were later overcome by more formative developments in the mid-1990s. Treatment planning software became more uniform, and the first linear accelerators designed for and dedicated to radiosurgery emerged. The group at the Joint Center for Radiation therapy at Harvard developed a robust 3-dimensional (3-D) treatment planning software called *X-Knife*. In a close collaborative effort with the Radionics Corporation (Burlington, MA), the medical physicist Hanna Kooy [14], working with radiation oncologist Jay Loeffler [16] and neurosurgeon Eben Alexander [2], developed the first user-friendly treatment planning tool that would provide a common platform for LINAC-based radiosurgery programs. In a collaborative effort with the Varian Corporation (Palo Alto, CA), the initial success of X-Knife was followed by the construction of a prototype linear accelerator designed for and dedicated to radiosurgery with features that included tighter tolerances for isocentric rotation, 360° of gantry rotation with a couch mount apparatus, and fixed primary and secondary collimation units that minimized gantry sag. Rapid evolution of X-Knife software followed with features adapted to the prototype and improvements that included automated tasks. These tasks included accurate fusion of MR and CT data into 1 composite image [15], automated placement of the initial isocenter at the geometric center of the target, and later, automated treatment planning. The design of linear accelerators also invited the capability of fractionating treatment, and the Radionics Corporation developed a reliable relocatable frame based on a dental mold of the upper arch [13], inspired by the design of the prototype by the talented British neurosurgeon Stephen Gill, collaborating with David Thomas [11].

After much discussion among ourselves, we chose to initiate radiosurgery at Temple University (Philadelphia, PA) with the first commercial use of X-Knife in August of 1991. By 1992, we had acquired the relocatable frame and initiated fractionation in a patient with a clival chordoma. After a move to Thomas Jefferson University, Philadelphia, Pa, in 1994 and with an opportunity to build a radiosurgery program with new capital equipment, we purchased both a Gamma Knife and the first commercial dedicated linear accelerator, the Varian 600SR [8]. Over the ensuing 10 years, we built a program around the complementary application of both units and exploited the opportunity to contrast single fraction and fractionated techniques for particular lesions when feasible [4].

In response to meet the need for better technology to treat increasingly more complex geometric targets, BrainLabs partnered with the Varian Corporation to develop an

Table 1

Features	Unit		
	Gamma Knife[a]	Novalis	CyberKnife
Photon source	Gamma ray	X-ray, s-band/6 MV	x-ray, x-band/6 MV
Output (monitor units) /variable	~3. 5 Gy/min, at installation	800/yes (100-800 MU/min)	300/no (400 for CK Express)
Penumbra of circular collimators	2.2 to 8 mm—*f* (helmet size and x, y, z planes)	<3 mm for all cones	<7 mm for all cones
Collimation system	Circular, donut type array	Circular or micro-multileaf	Circular
Flattening filter	NA	Yes/promotes homogeneous dose across beam profile	No/inhomogeneous dose across beam profile
Bunker requirements	Shielding for standard Co-60	Standard LINAC bunker	Requires 4-m ceiling height
Dose delivery	Static point of convergence	Isocentric dynamic or circular arc rotation Static segmented fields (IMRS/IMRT)	Isocentric and nonisocentric circular rotation
Extracranial treatment	No	Yes	Yes
Complex target method	Multiple shots High conformality Low homogeneity Less efficiency	IMRT/IMRS/dynamic arc High conformality High homogeneity Highest efficiency	Nonisocentric High conformality High homogeneity Less efficiency
Fractionation capability	No	Yes	Yes
Dedicated radiosurgery unit	Yes	Yes	Yes
Patient throughput			
Maximum no. of new points per site per year	600 (Pittsburgh 2005, per Gamma unit)	490 (UCLA 2004)	380 (Stanford 2003)
Average treatment time per SRS case	Dependent on cobalt half-life	20-40 min	40-60 min
Average treatment time per SRT case	NA	10-30 min	30-50 min
Software features	Image fusion Automated treatment planning Automatic positioning system Plan comparisons	Image fusion Automated treatment planning Arc and intensity modulation capabilities Forward and reverse planning capabilities Plan comparisons	Image fusion Automated treatment planning Nonisocentric treatment planning Forward and reverse planning capabilities Plan comparisons
Advantages	Ideal for functional lesioning Minimal preventive maintenance Simple quality assurance	Versatility in treatment planning (SRS vs SRT vs IMRS vs IMRT) Efficient, single isocenter solutions highest daily patient volume, 20-25 patients/d) Most dose homogeneity Extracranial targets Fractionation Robotic couch Infinite source of photons	Versatility in treatment planning (isocentric vs nonisocentric) Higher daily patient volumes Infinite source of photons Extracranial targets Fractionation More dose homogeneity
Disadvantages[b]	Cobalt reload Cobalt decay a dose rate variable Geometric constraints of fixed frame application More limited patient base Lower daily patient volume (5-7/d)	More preventive maintenance More quality assurance High output required for IMRS/IMRT	More preventive maintenance Most quality assurance Longer treatment times with lower output

NA indicates not applicable.

[a] 4C model.

[b] Patient throughput will depend on a number of variables, including the dose prescribed, the complexity of the plan (how many isocenters), and whether robotics are used (all latest models under review have robotics).

automated tertiary microleaf collimation system, which adapted to the shape of the target with each 10° of gantry arc rotation through the beam's eye view. This dynamic arc technique was interfaced with the Varian 600SR, which was renamed the Novalis Shaped Beam Radiosurgery Unit, and the first installation was inaugurated at UCLA under the direction of neurosurgeon Antonio DeSalles in collaboration with medical physicist Tim Solberg [22].

Two other important technologies were emerging during this period. The neurosurgeon Mark Carol saw the utility not only in focusing radiation with radiosurgery technique, but also in modulating the intensity of the radiation beam within the field of radiation, and thus initiating the technique of intensity-modulated radiation therapy [6]. For the first time, focused radiation could be shaped to conform to irregular concave surfaces to produce invaginations in dose distribution with doses, which were both effective while sparing circumscribed normal tissues. Tim Solberg recognized the utility of IMRT technology and convinced BrainLabs to include IMRT as a treatment planning platform in the Novalis software. Also, during this period, the Stanford neurosurgeon John Adler foresaw the importance of robotic technology and, with a team of engineers, developed the first robotic linear accelerator capable of the precise delivery of radiation to targets [1] not only within but also for the first time beyond the cranium and down the spinal axis. The CyberKnife became the third dedicated linear accelerator after the Varian 600SR and its successor, the Novalis, and the first robotic linear accelerator available for commercial purchase. The Gamma Knife had also evolved to include a robotic automatic positioning system in the B model, further refined in the C model, thus allowing for faster treatments and a greater patient capacity.

3. Specification of the radiosurgery units

Table 1 summarized the features of each of these units, along with perceived advantages and disadvantages. For institutions initiating a radiosurgery program, the choice of system will depend on a variety of factors. The present and future treatment goals of the radiosurgery team, the biases or clinical research interests of the clinicians within the team, the available space and cost constraints, and the nature of both the patient population and referral base all represent important variables that should be considered in the purchase. For institutions with an established radiosurgery program, rapidly evolving technology may provide an impetus for an upgrade or replacement with an entirely new system.

A cardinal new feature of radiosurgery (SRS) or fractionated stereotactic radiotherapy (SRT) systems is the ability to shape the dose to target with a much higher conformality than that achievable with circular collimators. The radiation dose can be wrapped around normal structures using an inverse planning algorithm and either an intensity-modulated or nonisocentric beam delivery. A typical example would be a spinal axis metastasis surrounding the spinal cord. Both the Novalis and the CyberKnife are capable of spinal axis radiosurgery, whereas Gamma Knife cannot, although Elekta has diversified into linear accelerator units with the acquisition of Philips in Europe and more recently cone-beam technology (discussed hereinbelow).

For a radiosurgery program driven predominantly by neurosurgeons, the patient mix will traditionally include a broader variety of lesions, benign and malignant and neoplastic and nonneoplastic. For a radiosurgery program driven predominantly by radiation oncologists, the patient mix will traditionally include a much greater number of patients with primary and metastastic malignant disease and, in the latter case, both intracranial and spinal axis metastases. We will create scenarios with particular variables at play and configure a unit best suited for a radiosurgery team.

In 1 scenario, the radiosurgery team is composed of a clinically active radiation oncologist with a focus on brain tumors and a neurosurgeon who has a strong interest in noninvasive approaches to functional disorders. The radiation oncologist treats a large volume of patients with brain metastases, and the neurosurgeon gets a large number of patient referrals for treatment of trigeminal neuralgia. Any one of the systems under review would serve this team, but the Gamma Knife, originally designed for noninvasive functional lesions, might best fit this program. Brain metastases are usually spherical lesions and, thus, are ideal targets for a circular collimation system such as the Gamma Knife. Radiosurgery boost treatment has gained widespread acceptance as a standard treatment of brain metastases [3]. Because functional lesions necessarily involve the delivery of a high single fraction dose (70-120 Gy), the static cobalt array, 4-mm collimation helmet, and MR-based imaging data together provide the simplest treatment planning solution with the greatest assurance of achieving an accurate functional lesion.

In another scenario, the patient population includes a predominance of cancer patients with metastatic disease including spinal axis metastases. The team also includes a radiation oncologist who has an interest in applying radiosurgical techniques to primary lung cancers. The CyberKnife would best serve this team with these interests. For spinal column metastases, the ability to shape the radiation beam around the spinal cord with reverse planning capability and nonisocentric dose delivery would provide a reliable platform for a spine radiosurgery program. The robotic capability of the CyberKnife would also provide the opportunity to treat a lung cancer. The CyberKnife would continuously track the location of the target, in this case, a lung mass, without the need to deliver the radiation with a complex gaiting mechanism adapted to the patient's respirations. The robotic accelerator moves synchronously with the chest wall movement, and the radiation dose is delivered seamlessly to the target.

At our institution, our program has evolved in many directions because of the acquisition of both a Gamma Knife and a dedicated linear accelerator. After treatment of more than 150 trigeminal neuralgia cases, we would recommend without hesitation the Gamma Knife for all patients with functional disorders. We would like to expand the clinical indications for Gamma Knife treatments to other functional disorders including intractable epilepsy limited to small periventricular heterotopias and movement disorders. We have developed a large patient population with benign tumors, typically acoustic schwannomas and skull base meningiomas, now having treated more than 300 acoustic tumors and

400 meningiomas. The conversion of the Varian 600SR to a Novalis Unit has doubled our daily treatment capacity treatment from 8 to 12 patients a day to 16 to 24 patients a day. This census is predominantly patients with benign tumors who are being treated with fractionated treatment regimens using a conventional dose of 1.8 Gy per fraction. We have established the indications for the conventional fraction treatments to include tumors near or involving the special sensory cranial nerves (vision or serviceable hearing) or tumors that are either large or geometrically complex. We have found that laterally placed single metastases or widely dispersed metastases result in either a collision with the collimator helmet or treatment of only those lesions within the Leksell stereotactic space, in either case requiring frame reapplication. The Novalis unit enables the treatment of multiple and widely dispersed intracranial metastases (median of 3 with a maximum of 6) with 1 frame application.

4. Future directions

4.1. Emerging technologies

We have reviewed popular systems in widespread use, but new platforms based on novel strategies are emerging.

Cone-beam CT refers to the way data are acquired (using a cone-shaped beam of x-rays rather than a fan beam for a slice) and the way the imaging volume is calculated. Elekta has taken a lead in the development of cone-beam technology with the Elekta Synergy system, and we are currently evaluating its spinal axis targeting accuracy in a comparison with the Novalis ExacTrac localization system. Elekta's approach integrates large area of flat-panel detectors and a kilovoltage imaging source with a linear accelerator, creating a novel treatment platform that enables radiography, fluoroscopy, and XVI immediately before treatment and in the treatment position [12]. X-ray volume imaging builds on the techniques used in cone-beam CT. Accordingly, an XVI-based treatment system does not produce slices; it images and reconstructs the entire volume in 1 operation. What makes the cone-beam technology so interesting is its ability to create a kilovoltage CT 3-D image of the patient just before radiation treatment and in a reasonable amount of time. This means that one can now view a full 3-D image of a patient's anatomy and adjust the patient position and, perhaps, the size, shape, and intensity of the radiation beam to the precise location of the patient's tumor. The cone-beam technology is a step-up from the BrainLabs ExacTrac system, which uses 2 kilovoltage x-ray tubes with opposed amorphous silicon panels to acquire 2 orthogonal planar x-ray images. Other major manufacturers recently started to offer their own cone-beam systems (Varian's Trilogy system [Varian Corporation] and Siemens ARTÍSTE system [Siemens AG, Munich, Germany]).

Tomotherapy is yet another technology that offers both IMRT dose delivery and online imaging for patient positioning [18]. The tomographic radiotherapy abandons the standard static treatment arm and couch platform in lieu of a helical CT platform. The radiation source (linear accelerator) is miniaturized to a height of 18 in, allowing it to be placed on a CT gantry and thus used for both imaging and treatment. This megavoltage radiation source can travel in multiple circles all the way around the gantry ring. The source movement is synchronized with the movement of the MLC. The computer-controlled MLC has 2 sets of interlaced leaves that move in and out very quickly to constantly modulate the radiation beam as it leaves the accelerator. Meanwhile, the couch is also moving, guiding the patient slowly through the center of the ring, allowing the treatment of different areas. The tomotherapy unit also has the ability to create a CT 3-D image just before radiation treatment, but it uses a megavoltage rather than a kilovoltage radiation to produce the CT study.

4.2. Comparative analysis

The MD Anderson Cancer Center (Houston, TX) has provided a universal phantom available to any radiosurgery program for a standardized quality assurance assessment. With the systems presently under review, objective data should become available, which are derived from a common phantom. These data would serve to guide consumers or qualify centers participating in multi-institutional trials. The same standardized approach should be applied to new and emerging treatment systems.

Cost and performance specifications remain important variables, but perhaps the most important variable is the clinical outcome. A number of institutions with extensive experience have reported their single institution experience with a single system. Comparisons of different units within a single institution are rare because acquisition of different units serving 1 purpose is for most institutions impractical and cost prohibitive. Early and multi-institutional prospective data compared treatment outcomes between Gamma units and LINAC-based units in patients with brain metastases and primary brain tumors. Although the earlier RTOG 90-05 study suggested an advantage with better local tumor control [21] with Gamma Knife treatment, this was not borne out in the later RTOG 95-08 study in which no significant difference was noted in the treatment of brain metastases [3].

The practice of modern radiotherapy sets forth 3 principal goals: dose homogeneity, target coverage, and normal structure sparing, achieving the latter 2 with dose conformality. The RTOG guidelines for radiosurgery were established for single fraction treatments with circular collimators [20]. Pirzkall et al [19] felt it was necessary to modify these criteria to be more broadly applicable to fractionated treatments or targets with complex shapes. An organization such as the RTOG would provide an ideal structure in which to design comparative studies of these different units with updated standard metrics. Comparisons would include treatment outcomes including radiographic responses based on central review of MR and/or CT data.

5. Conclusions

In summary, this review has compared 3 currently popular radiosurgery systems. The need for standardized comparative data is clear and should be a future mandate for organizations such as the RTOG. Technology devoted to the delivery of focused radiation, which is changing rapidly, and careful research with an eye toward the future will benefit new and established radiosurgery programs.

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