CyberKnife Radiosurgery for Spinal Neoplasms

Peter C. Gerszten, Steven A. Burton, Cihat Ozhasoglu

Departments of Neurological Surgery and Radiation Oncology, University of Pittsburgh Medical Center, Pittsburgh, Pa., USA

Abstract

The role of stereotactic radiosurgery for the treatment of intracranial lesions is well established. Its use for the treatment of spinal lesions has been limited by the availability of effective target immobilization and localization technologies. Conventional external beam radiotherapy lacks the precision to allow delivery of large doses of radiation near radiosensitive structures such as the spinal cord. The CyberKnife® (Accuray Inc., Sunnyvale, Calif., USA) is an image-guided frameless stereotactic radiosurgery system that allows for the radiosurgical treatment of spinal lesions. The system utilizes the coupling of an orthogonal pair of X-ray cameras to a dynamically manipulated robot-mounted lightweight linear accelerator which has 6 d.f. that guides the therapy beam to the intended target without the use of frame-based fixation. Real-time imaging tracking allows for patient movement tracking with 1 mm spatial accuracy. Cervical spine lesions are located and tracked relative to skull bony landmarks; lower spinal lesions are tracked relative to percutaneously placed gold fiducial bone markers. Spinal stereotactic radiosurgery using a frameless image-guided system is now both feasible and safe. The major potential benefits of radiosurgical ablation of spinal lesions are short treatment time in an outpatient setting with rapid recovery and good symptomatic response. This technique offers a successful therapeutic modality for the treatment of a variety of spinal lesions as a primary treatment or for lesions not amenable to open surgical techniques, in medically inoperable patients, lesions located in previously irradiated sites, or as an adjunct to surgery.

Radiotherapy for Spinal Lesions

Standard treatment options for spinal tumors include radiotherapy alone, radionuclide therapy, radiotherapy plus systemic chemotherapy, hormonal therapy, or surgical decompression and/or stabilization followed by radiotherapy [1]. If a spinal tumor causes compression of the spinal cord or other neural
elements, surgical decompression is often necessary with or without spinal fixation based on the extent of spinal column destruction and instability of the spine. The role of radiation therapy in the treatment of tumors of the spine has been well established. The goals of local radiation therapy in the treatment of spinal tumors have been palliation of pain, prevention of pathologic fractures, and halting progression of or reversing neurological compromise.

A primary factor that limits radiation dose in this tumor control with conventional radiotherapy is the relatively low tolerance of the spinal cord to radiation. Conventional external beam radiotherapy lacks the precision to deliver large single-fraction doses of radiation to the spine near radiosensitive structures such as the spinal cord. It is the low tolerance of the spinal cord to radiation that often limits the treatment dose to a level that is far below the optimal therapeutic dose [2–4]. Precise confinement of the radiation dose to the treatment volume, as is the case for intracranial radiosurgery, should increase the likelihood of successful tumor control at the same time that the risk of spinal cord injury is minimized [5].

**Spinal Radiosurgery**

Lars Leksell introduced the term ‘radiosurgery’ in 1951 to refer to single-fraction, high-dose irradiation of a limited target volume of tissue [6]. Stereotactic radiosurgery was conceived to be more analogous to conventional surgery than to conventional radiotherapy [7]. Stereotactic radiosurgery offers a method for delivering a high dose of radiation in a single or limited number of fractions to a small volume encompassing the tumor while minimizing the dose to adjacent normal structures [8]. The use of multiple beams of radiation requires extremely precise control of position and movement of the linear accelerator. In the past, stereotactic radiosurgery was limited to intracranial disease because precise localization could be achieved only by neurosurgical frames fixed to the patient’s skull. The frame acts as a fiducial reference system to provide accurate targeting and delivery of the radiation dose. As a corollary, treatment is typically limited to single-fraction treatments. Intracranial radiosurgery is practical because the lesions are fixed with respect to the cranium, which can be immobilized rigidly in a stereotactic frame. Spinal lesions also have a fixed relationship to the spine. However, stereotactic radiosurgery techniques developed for spinal lesions using standard linear accelerators require the placement of an invasive rigid external frame system directly to the spine and therefore have not been adopted for general use [9].

Since Hamilton et al. [9] first described the possibility of linear-accelerator-based spinal stereotactic radiosurgery in 1995, multiple centers have attempted to pursue large-fraction conformal radiation delivery to spinal lesions using a
variety of technologies [10–16]. Treatment of spinal lesions by stereotactic conformal radiotherapy and intensity-modulated radiotherapy (IMRT) have shown promising clinical results [15]. Others have demonstrated the effectiveness of protons for spinal and paraspinal tumors [17]. Recent studies using hypofractionated or single-dose treatments for spinal metastases reported results that were comparable to conventional fractionation [12–14, 18]. With advances in conformal treatment techniques using multileaf collimators such as IMRT, Chang et al. [11–16] found that intensity-modulated, near-simultaneous, CT image-guided stereotactic radiotherapy is a feasible and highly precise technique for the noninvasive treatment of spinal metastases. Bilsky et al. [11–16] found successful tumor control in 13 of 15 patients with spinal metastases using an IMRT technique. Milker-Zabel et al. [11–16] achieved tumor control in 95% of patients. Nevertheless, conformal radiotherapy and intensity-modulated radiation therapy (IMRT) are limited by problems with target immobilization as well as localization. This limitation of IMRT precludes large single-fraction treatment to spinal lesions.

The image-guided frameless stereotactic radiosurgery delivery system known as the CyberKnife® Stereotactic Radiosurgery System (Accuray Inc., Sunnyvale, Calif., USA) was developed by Dr. John Adler, Jr., and colleagues at Stanford University. It was approved in 2001 by the United States Food and Drug Administration for use throughout the body [19]. The CyberKnife was first developed for treatment of brain tumors at Stanford University. Since 1994, the device has been used at a number of sites around the world to treat a variety of benign and malignant intracranial lesions [20, 21]. As expected, treatment outcome has closely mirrored the results of conventional frame-based radiosurgery [3]. With the ability to treat lesions outside of the skull using fiducial tracking, a growing interest in the treatment of spinal lesions using the CyberKnife has emerged [3, 22–24]. The CyberKnife technology is now being adopted worldwide as a feasible method to perform spinal radiosurgery. Our work with the CyberKnife at the University of Pittsburgh has demonstrated both the feasibility as well as the clinical efficacy of spinal radiosurgery for a variety of both benign and malignant lesions [5, 22, 24, 25].

**The CyberKnife System**

The CyberKnife is a frameless image-guided stereotactic radiosurgical system that uses X-ray radiographic imaging to locate and track the treatment site while controlling the alignment of radiation beams via a robot-mounted linear accelerator [19]. The CyberKnife system consists of a lightweight linear accelerator (weight, 120 kg) mounted on a robotic arm (fig. 1). Real-time imaging tracking
allows for patient movement tracking with 1 mm spatial accuracy [3, 21, 26]. Dosimetry compares favorably with other intracranial radiosurgery devices [27].

The CyberKnife was developed as a noninvasive means to precisely align treatment beams with targets. It differs from conventional frame-based radiosurgery in three fundamental ways [3]. First, it references the position of the treatment target to internal radiographic features such as the skull or implanted fiducials rather than a frame. Second, it uses real-time X-ray imaging to establish the position of the lesion during treatment and then dynamically brings the radiation beam into alignment with the observed position of the treatment target. Third, it aims each beam independently, without a fixed isocenter.

Changes in patient position during the treatment are compensated for by adaptive beam pointing rather than controlled through rigid immobilization. This allows the patient to be positioned comfortably in the treatment room without precise reproduction of the position in the treatment planning study. Because of the spatial precision with which the CyberKnife can administer
radiation, it is theoretically feasible to administer a tumorcidal radiation dose in a single outpatient treatment. By minimizing the irradiation of surrounding healthy tissue, it should also be possible to decrease the rate of complications. The design of the CyberKnife makes it intrinsically capable of treating sites anywhere in the body in either a single-fraction or multifraction manner [28].

The CyberKnife consists of a computer controlled, compact 6-MV linear accelerator, that is smaller and lighter in weight than linear accelerators used in conventional radiotherapy [23, 29, 30]. The smaller size allows it to be mounted on a computer-controlled six-axis robotic manipulator that permits a much wider range of beam orientations than can be achieved with conventional radiotherapy devices (fig. 2). The CyberKnife system utilizes image-guided frameless robotic radiosurgery. Two ceiling-mounted diagnostic X-ray cameras are positioned orthogonally (90° offset) to acquire real-time images of the patient’s internal anatomy during treatment. The images are gathered using two amorphous silicon X-ray screens capable of generating high-resolution digital
images [31]. The images are processed automatically to identify radiographic features and then registered to the treatment planning study to measure the position of the treatment site. The measured position is communicated through a real-time control loop to a robotic manipulator that aims the linear accelerator. The system can adapt to changes in patient position during treatment by acquiring targeting images repeatedly and then adjusting the direction of the treatment beam. If the patient moves during treatment, the change is detected during the next imaging cycle and the beam is adjusted and realigned with the target [28]. The target to be treated is identified prior to treatment on planning images. Between 100 and 200 beams are commonly used to irradiate the target in a stereotactic fashion. The treatment beam can be maneuvered and pointed nearly anywhere in space. Treatment beams are also not confined to isocentric geometry, so they can be arranged in complex overlapping patterns that conform irregularly shaped tumor volumes [3]. An analysis of the accuracy of the CyberKnife radiosurgery system found that the machine has a clinically relevant accuracy of $1.1 \pm 0.3$ mm using a 1.25-mm CT slice thickness. Hence, the CyberKnife precision is comparable to published localization errors of other current frame-based radiosurgical systems [31].

### Indications for Spinal Radiosurgery

The indications for spine radiosurgery using the CyberKnife are currently evolving and will continue to evolve as clinical experience increases. This is similar to the evolution of indications for intracranial radiosurgery which occurred in the past. Table 1 summarizes the candidate lesions for CyberKnife spinal radiosurgery. Similar to intracranial radiosurgery, candidate lesions may

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<thead>
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<th>Candidate lesions for CyberKnife spinal radiosurgery</th>
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<td>Well-circumscribed lesions</td>
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<td>Minimal spinal cord compromise</td>
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<td>Radioresistant lesions that would benefit from a radiosurgical boost</td>
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<td>Residual tumor after surgery</td>
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<td>Previously irradiated lesions</td>
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<td>Recurrent surgical lesions</td>
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<td>Lesions requiring difficult surgical approaches</td>
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<td>Relatively short life expectancy as an exclusion criteria for open surgical intervention</td>
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<td>Significant medical comorbidities precluding open surgical intervention</td>
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<td>No overt spinal instability</td>
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be of either benign or malignant histology. Spinal vascular malformations are also amenable to spinal radiosurgery [3].

This new technique is an important treatment modality whose clinical role has not yet been fully defined. The most frequent indication for the treatment of spinal tumors is pain, and spinal radiosurgery is most often used to treat tumor pain. Radiation is well known to be effective as a treatment for pain associated with spinal malignancies. Our clinical experience has found a 92% improvement in pain after CyberKnife therapy. We have found CyberKnife spinal radiosurgery to be highly effective at decreasing pain in this difficult patient population. Spinal radiosurgery was also found to successfully alleviate radicular pain caused by tumor compression of adjacent nerve roots.

Another indication for spinal radiosurgery might be to halt tumor progression that could lead to spinal instability or neural compromise. The ideal lesion should be well circumscribed such that the lesion can be easily outlined (contoured) for treatment planning. Our initial experience has found that many of our cases have already received irradiation with significant spinal cord doses or have lesions that recurred after open surgical removal. Currently, it appears that CyberKnife radiosurgery is often being used as a ‘salvage’ technique for those cases in which further conventional irradiation or surgery are not appropriate.

Other candidate lesions are those that would require difficult surgical approaches for adequate resection. Spinal radiosurgery can deliver radiation to anywhere along the spine. Candidate patients may have significant medical comorbidities precluding open surgical intervention or a relatively short life-expectancy that would deem them inappropriate for open surgical intervention. We have treated several radioresistant tumors (e.g. renal cell carcinoma, melanoma, sarcoma) that have completed external beam irradiation with or without IMRT, and we have used CyberKnife radiosurgery for a boost treatment. Other lesions have been treated with CyberKnife radiosurgery as their sole radiation treatment. The benefits for this treatment option include a single treatment with minimal radiation dose to adjacent normal tissue. In addition, a much larger radiobiologic dose can often be delivered compared to external beam irradiation. With greater clinical experience, upfront radiosurgery perhaps will become more commonly used in certain cases such as patients with a single symptomatic spine tumor of a radioresistant histology.

If a tumor is only partially resected during an open surgery, fiducials can be left in place to allow for radiosurgery treatment to the residual tumor at a later date. Given the steep falloff gradient of the CyberKnife target dose, such treatments can be given early in the postoperative period as opposed to the usual significant delay before standard external beam irradiation is permitted by the surgeon. With the ability to effectively perform spinal radiosurgery, the current surgical approach to these lesions might change. Open surgery for