Medilux Healthcare Ltd

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Information for doctors and patients considering the application of CyberKnife® radiosurgery for

Spinal Tumours

IMPORTANT NOTE

The following is drawn from information provided by Accuray Inc., USA, the manufacturers of CyberKnife® and providers of a range of supporting medical software and is offered for general guidance. Medilux Healthcare Ltd. takes no responsibility of the accuracy or otherwise of statements contained herein. To check for the most recent guidance on treatment protocols for any particular conditions visit www.accuray.com

CyberKnife® treats a range of cancers and other medical conditions and there are now many CyberKnife® centres around the world, but not all countries yet have one and some centres specialise more in certain areas than in others or only accept international patients for specific types of treatment. CyberKnife® is a remarkably effective tool for certain cancers and medical conditions but cannot be used for others.

Based on our practical experience in handling a great many enquiries for the European CyberKnife Centre in Munich, Germany, Medilux Healthcare Ltd. provides information to doctors and patients worldwide as to the range of conditions treated, the parameters which generally apply to assessment of cases and how to apply for treatment. We continue our close co-operation with Munich but we now also handle new patient and doctor enquiries for a growing number of CyberKnife centres worldwide.

What is spinal radiosurgery? Why is it difficult to perform radiosurgery outside of the brain?

Radiosurgery is the term used to refer to a class of radiation techniques that are spatially very precise and enable the dose to very rapidly fall-off in the immediately surrounding anatomy. This approach makes it possible to administer aggressive, and even ablative, doses of radiation without damaging adjacent normal tissue. To achieve the above objectives, radiosurgery is delivered in a small number (typically 1 to 5) of daily treatments.

Radiosurgery was conceived in 1951 by Swedish neurosurgeon Lars Leksell as a non-invasive method for making precise lesions in the brain. The method he developed, Gamma Knife radiosurgery, used a metal frame that was screwed into the patient's skull to both immobilize (hold completely still) the head and accurately target radiation within the brain. Although this device was quite effective for brain radiosurgery, it was not practical to attach external frames to other parts of the body. As a result, until recently, radiosurgery has generally been restricted to treatment of intracranial (inside the skull) disorders. This shortcoming of first generation radiosurgical instrumentation is particularly unfortunate because many of the same lesions that have been so effectively treated with radiosurgery in the brain also occur throughout the spine.

The first device for performing spinal radiosurgery was developed at the University of Arizona and reported in 1995. This procedure used an external body frame that was surgically attached to the spine and pelvis under general anaesthesia. However, the invasiveness of this approach precluded widespread acceptance. It wasn't until the development of the CyberKnife® that a more elegant, i.e. less invasive, means of performing accurate spinal radiosurgery became available.

How does CyberKnife® spinal radiosurgery work?

The CyberKnife® enables the minimally invasive and extremely accurate delivery of aggressive doses of radiation to many spinal lesions. At the heart of this surgical instrument is a miniature linear accelerator, for producing high energy therapeutic x-rays, attached to a robotic arm. While the robot arm moves extensively around a patient, x-ray beams are precisely targeted to the tumour from hundreds of different directions. Perhaps of even greater significance, the CyberKnife® eliminates the need for a rigid external frame to be attached to the patient's skeleton. Instead, the CyberKnife® uses an x-ray (diagnostic energy as opposed to therapeutic radiation) image-guidance system that identifies the real-time position of the patient's bony anatomy and target throughout treatment delivery.

The CyberKnife® tracks the position of a spinal tumour with reference to either the skull anatomy (for tumours of the upper neck), or with reference to small stainless steel screws called fiducials. These metallic markers are anchored to the bones of either the lower neck, mid or lower back, the cervical, thoracic and lumbar spine, respectively, in a short outpatient procedure. Once in position, these fiducials can be automatically detected by the image-guidance system of the CyberKnife® and used to determine the exact position of the tumour. Throughout treatment, the system continually images and identifies these markers, communicating their updated position to the robotic arm so it can precisely re-adjust the aim of the radiation beam to compensate for any small movements made by a cooperative patient. This capacity to accurately target a spinal tumour without rigid external immobilization makes the CyberKnife® a unique solution for non-invasively treating many spinal lesions with radiosurgery.

Which spinal tumours are treatable with the CyberKnife®?

The CyberKnife® has the potential to treat most types of spinal tumours. However, if a lesion is to be considered for CyberKnife® radiosurgery, it must be reasonably discrete (distinct from the surrounding normal tissues) on CT or MRI images, and it cannot be too large in size--generally speaking, a volume of 150 cc is the upper limit of what is treatable. Both benign (non-cancerous) and malignant (cancerous or capable of spreading to other sites in the body) spinal tumours can be treated with the CyberKnife®. While some types of lesions develop within the substance of the spinal cord itself, these tumours more commonly develop in and around the vertebral column and disrupt neurologic function by compressing the spinal cord. The following lists detail the tumour pathologies that most commonly affect the spine and which can often be treated with the CyberKnife® depending on clinical circumstances:

Benign Lesions

- meningioma
- schwannoma
- neurofibroma
- hemangioblastoma
- arteriovenous malformations
- chondrosarcoma
- chordoma
- ependymoma
- other: giant cell tumour, aneurysmal bone cyst, epidermoid

Malignant Tumours

- spinal metastases from many sources
- myeloma
- lymphoma
- Ewing sarcoma

Spinal Metastases

Metastasis is a process whereby a malignant tumour originating from one part or organ of the body (a "primary" cancer) spreads to another location in the body, usually through the bloodstream. The spinal column (vertebral spine) is one of the most common sites for metastasis. The primary cancers that most frequently spread, or metastasise, to the spine include cancer of the breast, lung, kidney, prostate, and skin (malignant melanoma). Less common metastatic cancers of the spine include thyroid, cervical, and colorectal cancer as well as sarcoma and lymphoma.

Conventional radiation therapy is the standard treatment for painful metastases affecting the spinal column. However, conventional radiation therapy has several disadvantages, including more side effects within the surrounding normal tissue and a more prolonged course of treatment compared to CyberKnife® radiosurgery. Furthermore, some types of metastatic cancers, such as melanoma, sarcoma and renal cancer, respond very poorly to standard radiotherapy, yet are well controlled after more aggressive CyberKnife® treatment.

As a general rule, it is safest and easiest to treat tumours with radiosurgery that have not been previously treated with conventional fractionated radiation therapy. However, CyberKnife® technology makes it possible to safely contour the dose of therapeutic x-ray away from the spinal cord and other critical radiosensitive structures. As a result, when using the CyberKnife®, it is still possible to get good results, even if a spinal tumour has been previously irradiated. In patients with severe spinal cord compression, or impending vertebral (bony) collapse, standard open surgical decompression followed by internal hardware fixation and fusion is generally indicated.

The primary rationale for treating spinal metastases is the relief of pain and prevention of neurologic deterioration. Prospective and retrospective clinical studies conducted at multiple institutions have now demonstrated that CyberKnife® treatment of spinal metastases is quite effective in achieving these two objectives. Meanwhile, patients with metastatic cancer who develop neurologic deficits, such as sensory change, bladder dysfunction or weakness, and/or localized back pain, will experience a substantial improvement if treated within a relatively short time of symptom onset. Pain relief and improvement in neurologic function after radiosurgery generally translates into an improved quality of life. Not surprisingly, the response of a spinal metastasis to CyberKnife® radiosurgery will vary depending on the type of primary cancer, the duration of neurologic symptoms, tumour location, and size of the tumour.

Benign Tumours

Meningioma and nerve sheath tumours, such as neurofibroma and schwannoma, are relatively resistant to conventional fractionated radiotherapy. Because of the limited radiation tolerance of the spinal cord and other adjacent normal tissues, the dose of conventional radiation therapy required to control these tumours is often prohibitive. As a result, conventional radiation is used only in patients where surgery is not feasible. Fortunately, spinal radiosurgery appears to offer an important new alternative to surgery and conventional radiation for selected patients with benign lesions.

Unlike metastatic tumours that primarily affect the bones of the spine, meningioma and nerve sheath tumours originate from both the soft tissue coverings of the spinal cord and the attached nerves. Consequently, these tumours are often in intimate contact with the spinal cord. As these lesions slowly enlarge, the spinal cord becomes compressed and its normal function is disrupted. In severe cases, patients will become gradually paraplegic or quadriplegic depending on the exact location of the lesion.

When treating benign spinal tumours with radiosurgery, the primary intermediate objective is to stop all tumour growth. Over the longer term, which oftentimes means many years, these tumours will gradually shrink in size. Preliminary results with CyberKnife® radiosurgery for meningioma and schwannoma show excellent control of tumour growth. However, experience with biologically identical tumours that occur in the brain, suggests that neurofibromas which occur in the setting of genetic disorders, like neurofibromatosis, may be more difficult to control with radiosurgery, or for that matter, any other form of current treatment. Importantly, in those patients with benign tumours where significant spinal cord compression on imaging studies is accompanied by severe neurologic dysfunction, CyberKnife® radiosurgery is usually NOT a good option. In such cases, any clinical benefit from tumour shrinkage takes too long to be recognized.

Other Tumours and Lesions

Primary malignant tumours affecting the spine, such as myeloma, lymphoma, osteosarcoma, and Ewing sarcoma, are generally treated by a combination of chemotherapy and conventional radiation therapy. When there are isolated tumours or tumours that recur (re-grow) after conventional treatment, radiosurgery can be considered and is generally quite effective.

Low-grade, i.e. less malignant, tumours of the bony spine and spinal cord, such as chondrosarcoma, hemangioblastoma and ependymoma, are typically managed by open surgical resection. However, for selected patients with these lesions, CyberKnife® radiosurgical ablation represents a very effective treatment option. In particular, patients with the genetic condition von Hippel Lindau's disease, who have a proclivity to develop multiple spinal tumours over their lifetime, can be well-managed with CyberKnife® spinal radiosurgery if the tumour is caught sufficiently early in its course. Other miscellaneous and even rarer spinal tumours can sometimes be treated with the CyberKnife® radiosurgery depending on clinical circumstances.

What is the CyberKnife® patient treatment process?

CyberKnife® spinal radiosurgery treatment consists of three distinct components:

1. CT image acquisition based upon skull bony landmarks or implanted bone fiducials.

2. Treatment planning.

3. Treatment delivery.

Patient set-up

For lesions located in the neck or cervical spine, patients are first fitted with a non-invasive moulded facemask that stabilizes the head and neck on a radiographically transparent headrest. For lesions of the thoracic or lumbar spine or sacrum, patients must first undergo the placement of tiny markers into their spine that will allow the radiation beam to be focused directly at the lesion. This technique involves a surgical procedure that is usually performed in the operating room. Either general or local anaesthesia will be used. The surgeon will place the tiny markers around the lesion through small punctures in the skin. Usually, between four and six markers are used. The procedure is usually performed as an outpatient with minimal pain associated with it.

The patient will then return for imaging. Computed tomographic (CT) images are acquired using a standard CT scanner. Sometimes, an IV is started to inject contrast for the physicians to better see the lesion in question. For patients with allergies to IV contrast who cannot be given IV contrast or for other reasons, non-enhanced CT imaging is performed. The CT scan is usually performed in a normal supine (lying on one's back) position. For cervical lesions, the facemask is placed to immobilize the head and neck.

Treatment Planning

After the CT scan is performed, a team comprised of a surgeon, a radiation oncologist, and a radiation physicist outlines the lesion in question. Normal structures, such as the spinal cord or kidneys, are also identified. The team creates a treatment plan that will allow the delivery of a large amount of radiation to the lesion in question, while limiting the amount of radiation delivered to normal, healthy structures.

Treatment Delivery

The patient will then return for the treatment itself. Treatments usually last between one to two hours. They are performed in an outpatient setting without any form of sedation. Patients who normally have pain while lying on their back will be asked to take their pain medicines prior to the procedure. The patient lies on a comfortable table known as a "couch." For cervical lesions, the facemask is placed to immobilize the head. For other lesions, because the fiducials or markers are already inside the body, no such immobilization is necessary.

The patient is observed throughout the treatment by closed circuit television. The patient may wave their hand or speak if they would like to temporarily halt the treatment. The patient has the opportunity to pause the treatment at any time if they so desire. There are no direct side effects of the treatment itself. Occasionally, patients receiving treatment to lower back lesions may experience mild, transient nausea. This is because the radiation passes through the intestines and might irritate the intestines. In these cases, patients might be given anti-nausea medicine prior to the treatment.

After the treatment, the patient is able to go home immediately. There is no recovery time. Occasionally, treatments are fractionated (staged radiosurgery) meaning that they are separated over several days to allow a larger dose of radiation to be given. The decision to fractionate a treatment is determined by the CyberKnife® Team on a case-by-case basis.

What are the differences between the common radiosurgery technologies?

Several SRS systems are available for the treatment of patients. The most widely used SRS devices include: cobalt-sourced systems (Gamma Knife), modified linear accelerators, and the CyberKnife®. All of these devices, if properly operated, are capable of delivering the desired radiation dose to a designated target. However, for certain clinical situations, there can be important differences between these devices, which for some patients may have a significant impact on clinical outcome. CyberKnife® System

CyberKnife® System

The CyberKnife® System is an SRS system utilizing contemporary technology that is designed to be the most accurate and flexible tool available for aggressive therapeutic irradiation. The CyberKnife® was designed to address the limitations of frame-based SRS systems and expands the application of radiosurgery to sites outside of the head. It is the only system to incorporate a miniature linear accelerator mounted on a flexible, robotic arm. An image-guidance system that can track target location during treatment also enables the CyberKnife® to offer superior targeting accuracy without the need for the invasive head frame. While Gamma Knife and linac-based systems can perform radiosurgery in the brain, true radiosurgery for areas outside of the brain is difficult if not impossible to perform with these systems.

Advantages of the CyberKnife® include:

- No invasive head frame or other rigid immobilization device is required

The ability to perform radiosurgery (1-5 fractions) on targets throughout the body, not just the brain and spine

- Precise targeting (within 1 mm) of selected lesions in the brain and body

- A unique ability to provide real time monitoring of the treated target throughout treatment using an advanced image-guidance system

- A unique ability to correct during treatment for limited target motion (e.g. due to small patient movements) - - The capacity to easily perform staged radiosurgery

- Because the CyberKnife® system is so accurate as well as versatile and painless, it is often the radiosurgical procedure of choice from a patient's perspective.

Disadvantages of the CyberKnife® include:

- The need for placement of very small markers (fiducials) via a needle for the treatment of targets outside of the head

[Note: by using additional medical software the European CyberKnife® Centre is also able to treat targets in the spine without fiducials]

- Compared to other radiosurgical devices, treatment takes longer when multiple tumours are ablated during the same treatment session.

Cobalt-Sourced Systems (Gamma Knife)

The first radiosurgical device was conceived and developed in the 1950s by Professor Lars Leksell at the Karolinska Institute in Stockholm, Sweden. His work culminated in the development of the Gamma Knife (Elekta Inc), which was used to treat patients beginning in 1968. This device is capable of precisely irradiating small intracranial [glossary term] (inside the skull) target with gamma ray photons. The treated lesion is targeted and the patient's head immobilized (held completely still) through the use of an external metal frame attached to the skull by four screws. A large helmet-shaped device with 201 separate, fixed "holes" or ports allows the radiation emitted by discrete (separate) radioactive cobalt-60 sources to enter the patient's head in small beams that converge on the designated target. The Gamma Knife is designed to treat intracranial targets only.

Advantages of the Gamma Knife include:

Over 30 years of clinical use with a large number of studies published in the medical literature

Targeting precision within 2 mm

Multiple targets in the brain are easily treated during a single treatment session

Disadvantages of the Gamma Knife include:

The basic design limits use to the brain only

The procedure for radiation targeting requires the placement of a somewhat painful stereotactic head frame

It can be difficult to treat patients with lesions located in certain areas (e.g. the periphery) of the brain

It cannot be used for staged radiosurgery (delivering the radiation dose in more than one fraction or treatment session); staged radiosurgery can be particularly beneficial for larger tumours or lesions located near nerves and other sensitive structures

Modified Linear Accelerator Systems

An alternative to the Gamma Knife was developed in the mid 1980s and utilized the conventional linear accelerators (linac) that are commonplace in most large hospitals. By combining a series of small modifications to the radiation delivery mechanism of the linac with specialized planning software, it is possible to do many types of brain radiosurgery. There are both dedicated and non-dedicated linac-based radiosurgery devices. Dedicated linac systems are used solely for radiosurgery treatment. In contrast, non-dedicated systems are the daily workhorses for conventional radiation therapy departments which can also be temporarily modified to perform radiosurgery. Compared to the latter multi-purpose linacs, dedicated systems tend to be more carefully calibrated for spatial accuracy and optimised for radiosurgical efficiency. Unlike the radioactive cobalt-based Gamma Knife, linac-based systems use X-ray beams generated from a linear accelerator. As a result, these devices do not require or generate any radioactive material. When treating brain tumours with linac radiosurgery, a metal head frame is attached to the patient's skull and used to precisely target the radiation beam. Common brand names for modified linacs include X-Knife (Radionics Inc).

Advantages of Multi-Purpose Linac Radiosurgical Systems include:

- More commonplace technology in hospitals

Disadvantages of Multi-Purpose Linac Radiosurgical Systems include:

- Less accurate
- Less efficient than dedicated systems, which results in longer treatment time
- Frame-based targeting only works for brain lesions

Shaped Beam Systems

The recent development of IMRT or Intensity Modulated Radiation Therapy has added another dimension to multi-fraction radiation therapy. These linac-based technologies use computer-controlled "beam-shaping" to do a better job of conforming the radiation dose to the shape of the tumour or other lesion. This form of advanced radiation therapy can be utilized at virtually any location in the body. IMRT technology enables a mechanical device (called a multi-leaf collimator) that is typically attached to most modern medical linear accelerators, to dynamically reshape the outlines and intensity of the radiation field during cancer treatment. When combined with sophisticated planning software, IMRT fits the dose of radiation to a target much better than conventional radiation therapy, and thereby minimizes the volume of surrounding normal tissue that is injured by treatment. While it appears that IMRT may produce fewer side-effects than conventional radiation therapy, IMRT is not as spatially precise as radiosurgery. Because of this imprecision, a full course of IMRT treatment is typically administered over multiple treatment sessions (typically 20-30+). Common brand names include X-Knife (Radionics) and Novalis (Brain Lab).

Advantages of Shaped-Beam systems include:

- The capacity to treat most regions of the body with IMRT

- When coupled to an invasive stereotactic frame, precision targeting for brain tumours that approaches, but does not equal, that of the Gamma Knife or CyberKnife®

- The capacity to more accurately target extracranial (non-brain) tumours than standard radiation therapy

An ability to deliver fractionated intracranial or extracranial treatment

Disadvantages of the Shaped Beam systems include:

- The need for an invasive head frame (similar to the Gamma Knife) to assure treatment accuracy when used for brain radiosurgery (single fraction)

- Less treatment accuracy when multiple fractions are used to treat areas of the brain where the use of an invasive head frame is impractical

- A significantly lesser degree of targeting accuracy when treating extracranial tumours compared to brain radiosurgery Treatment accuracy is degraded further when the target moves during radiation delivery from either natural breathing or patient movement.