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

Hemangioblastomas

IMPORTANT NOTE

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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 a Hemangioblastoma?

Hemangioblastomas are benign, highly vascular tumours that can occur in the brain and spine. Most hemangioblastomas occur as a single lesion. However, there are some patients who develop hemangioblastomas as part of a genetic syndrome called von Hippel Lindau disease (VHL).

Over their lifetimes, such patients develop multiple tumours within the brain and spinal cord. Nearly all brain lesions occur within the inferior back portion of the brain, known as the cerebellum. This part of the brain is especially important for balance and coordination.

Hemangioblastomas occur in two basic forms, solid and cystic. Solid tumours consist entirely of tumour cells. Cystic hemangioblastomas are composed of a generally small solid component, adjacent to an oftentimes much larger cystic portion of tumour.

With either form of hemangioblastoma, an enlarging tumour will press on the brain and can cause neurologic symptoms, such as headaches, weakness, sensory loss, balance and coordination problems, and/or hydrocephalus (a build up of spinal fluid). In rare cases, the tumour is discovered as an incidental finding during an evaluation for unrelated symptoms or another disorder.

How are hemangioblastomas diagnosed?

Hemangioblastomas can be diagnosed by either contrast CT or MRI scans of the brain or spine. On such studies, hemangioblastomas appear as bright white lesions within the brain or spine after intravenous contrast is administered. Hemangioblastomas can occasionally mimic other tumours, such as meningioma, brain metastases, or in some cases, an arteriovenous malformation.

Sometimes a cerebral angiogram aids in the diagnosis of hemangioblastoma, which have a characteristically profuse blood supply. In von Hippel Lindau disease, hemangioblastomas are inherited as a genetic disorder from either parent (dominant inheritance).

When a family history of von Hippel Lindau is present, there is a strong likelihood that other directly descended family members will be afflicted by this disorder.

What are treatment options for hemangioblastoma?

There are two basic treatment options for hemangioblastoma. Surgical resection involves operating on the brain or spine to physically remove a tumour. If a hemangioblastoma can be completely removed, and is not associated with von Hippel Lindau disease, then a patient is cured.

In the typical case of a cystic hemangioblastoma, only the solid portion of the tumour needs to be removed; the adjacent cyst that is drained during surgery will eventually disappear once the tumour nodule is removed.

If the entire hemangioblastoma cannot be resected, then there remains a high likelihood that either the tumour will re-grow or that additional cysts may form. Any operation on the brain or spine is invasive and can be associated with risks, such as stroke, infection, anaesthetic complication, or neurologic deficits. However, most hemangioblastomas can be safely removed with present day neurosurgical instrumentation.

As an alternative to an open operation, stereotactic radiosurgery can be used to target and destroy a hemangioblastoma (1).

A single radiosurgery session will result in the gradual death and eventual shrinkage of a treated lesion. In the case of cystic hemangioblastoma, only the solid portion of the tumour need be ablated with radiosurgery; cyst fluid gradually ceases to be produced and eventually the cyst decreases in size.

What are the advantages of treating hemangioblastomas with stereotactic radiosurgery?

The principle advantage of stereotactic radiosurgery relative to surgical resection of hemangioblastoma is that the former is noninvasive and does not carry the risks of conventional brain or spine surgery.

Furthermore, some hemangioblastomas are located in areas of the brain that are difficult to approach safely with conventional surgery. In such cases, radiosurgery may be a much safer option for the patient. Moreover, radiosurgery is an outpatient procedure, and does not require any recovery period before a patient can resume a normal lifestyle.

In patients with von Hippel Lindau disease, multiple hemangioblastomas tend to develop over time within both the brain and spine.

This situation very commonly necessitates that a patient undergo multiple operations over their lifetime. These operations even when successful, generally take their toll on the patient, often resulting in gradual disability. For these patients, stereotactic radiosurgery can be performed multiple times over the life of the patients to treat symptomatic hemangioblastomas when they occur, thereby preventing the need for numerous conventional operations.

What are the disadvantages of treating hemangioblastomas with radiosurgery?

There are two main disadvantages to ablating hemangioblastomas with radiosurgery. First, radiosurgery typically takes from six months to a year to destroy a hemangioblastoma.

Therefore, if a tumour is large and causing significant symptoms from pressure on the normal brain, standard surgical resection is usually necessary. Even after aggressive radiosurgery for cystic hemangioblastoma, fluid continues to be produced within the cyst for several months after treatment.

Also, if the cyst becomes large, it too can cause symptoms. Such large cystic tumours can be symptomatic and require surgical drainage, even though the tumour is dying from radiation. Secondly, radiation may cause injury to the normal brain immediately adjacent to the treated hemangioblastoma (see complications of radiosurgery below).

How is CyberKnife® radiosurgery different from other radiosurgical systems?

Most radiosurgery systems require the use of a metal frame for accurate targeting. This device attaches to the patient's head with four screws, each of which penetrates the scalp and anchors to the skull. Naturally, this technique results in pain for a patient.

In contrast, the CyberKnife® is "frameless", thereby avoiding any patient discomfort, yet still maintaining comparable, if not superior targeting accuracy. Furthermore, other radiosurgery systems limit treatment to hemangioblastoma of the brain.

Since CyberKnife® radiosurgery is frameless, hemangioblastomas located anywhere in the spinal cord can also be treated safely.

What to expect after radiosurgery for hemangioblastoma

Radiosurgery for tumours, such as hemangioblastomas, is typically performed on an outpatient basis. Generally, a patient feels nothing during treatment. After radiosurgery, patients are followed with periodic brain or spine scans. Most radiosurgery centres perform a follow-up MRI scan after six months to monitor tumour shrinkage and look for any radiation side-effects in the adjacent brain.

Once it can be demonstrated over a few years time that a tumour is not growing (or is actually shrinking), the lesion is thought to be destroyed and further MRI scans need only be performed on a more limited basis.

What are the possible complications of hemangioblastoma radiosurgery?

The main potential complication of radiosurgery is the chance that radiation may destroy the tumour but injure the adjacent normal brain. Such damage is called radiation oedema, or in severe cases, radiation necrosis. Particularly for small tumours, the likelihood of radiation injury to the brain is low.

The rate of complications is generally much lower than the risk of leaving the tumour untreated or undergoing an open surgical resection (2). The symptoms produced by radiation oedema will often improve significantly with oral steroids.

References

1. Chang SD, Main W, Martin DP, Gibbs IC, Heilbrun MP: An analysis of the CyberKnife: a robotic frameless stereotactic radiosurgical system. Neurosurgery. 2003 Jan: 52(1):140-7.

2. Maciunas RJ, Galloway RL Jr, Latimer JW: The application accuracy of stereotactic frames. Neurosurgery. 1994 Oct: 35(4): 682-94.

3. Chang SD, Adler JR Jr, Martin DP: LINAC radiosurgery for cavernous sinus meningiomas. Stereotactic and Functional Neurosurgery. 1998: 71(1):43-50.

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.