www.mediluxprofessional.net **Patients: www.cyberknifeuk.net** **E-mail: enquiries@cyberknifeuk.net**

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

Trigeminal Neuralgia

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 Trigeminal Neuralgia?

Trigeminal Neuralgia (TN), often referred to as Tic Douloureux, is a disorder characterized by repeated episodes of severe facial pain. The pain can be localized over either side of the face and affects one or more of the divisions of the trigeminal nerve. This nerve, which gives rise to sensation within the face, originates in the brainstem and reaches the cavernous sinus through a structure called Meckel's cave. In the cavernous sinus, the trigeminal nerve divides into three branches, termed the 1st, 2nd and 3rd branches, or ophthalmic, maxillary and mandibular nerves, respectively.

These nerve branches leave the intracranial (brain) cavity through separate exits, the superior orbital fissure and the foramen ovale and rotundum, and travel to innervate and give sensation to different areas of the face. TN usually affects one or two branches of the trigeminal nerve and is characterized by sudden, sharp paroxysms of "lancinating" pain.

This intense pain is described as a superficial electrical sensation and can be triggered by touching specific skin areas (trigger points) with cold air or activities like chewing, talking, swallowing, etc. Because chewing precipitates attacks, it is not uncommon for TN patients to lose weight.

What is typical and atypical Trigeminal Neuralgia?

TN is usually related to the chronic compression of the trigeminal nerve by a blood vessel (usually an artery, occasionally a vein). Arterial rhythmic pulsations are a normal effect of the pressure wave produced by the heart.

This pressure wave from the heart is propagated throughout the vascular system when blood is pumped into the aorta, and from there, into all the arteries of the body. In some people, if a brain artery is very close to a nerve, its rhythmic pulsation can irritate the nerve and produce abnormal nerve signals.

Since the trigeminal nerve is anatomically close to the superior cerebellar artery, contact between the two structures sometimes permits arterial beating to short circuit nerve impulses and thereby result in trigeminal neuralgia.

The primary support for this theory is provided by the fact that moving the artery away from the nerve through an operation called Microvascular Decompression (MVD) produces immediate pain relief in up to 80% of the patients.

In typical TN, patients suffer from unpredictable electric-like lancinating pains that are episodic and felt in a constant facial location. Affected patients can consistently reproduce an attack by touching a skin "trigger point" on the skin or performing a specific activity like chewing or talking.

In cases of atypical TN, the pain is characterized by a persistent dull aching or burning sensation localized to a more diffuse region of the face. Paroxysms of pain can complicate atypical TN resulting in some measure of baseline discomfort. There is usually not a specific trigger point with atypical TN.

TN is more common in women and is much more typically seen during the middle or later years of life. The unpredictable nature of such severe lancinating pain makes it emotionally incapacitating and produces a disruptive effect on a patient's quality of life.

What is the natural history of Trigeminal Neuralgia?

Typical TN has a sudden onset and can last several years and even decades. The number of attacks can be seasonal and vary from many per day to a few per year. Spontaneous resolution is rare. Atypical TN is characterized by a slow and gradual worsening of facial pain.

What are the treatment options for Trigeminal Neuralgia?

Over the years, numerous medical and surgical treatments have been offered to TN patients with varying degrees of success. Medications, such as dilantin, tegretol and neurontin, have the ability to stabilize nerve cell membranes and relieve pain in most patients. However, these medications are not always effective, and can produce fatigue or other significant side-effects in some patients. Nevertheless, such medications are generally the first line of treatment.

Patients that fail multiple medical trials are offered surgical treatment ranging from peripheral ablative (destructive) procedures to an open "craniotomy" for microvascular decompression (MVD). In the youngest patients, the most invasive operation, an MVD, is often preferred because it holds the potential of long-term cure without causing significant facial numbness.

Meanwhile, radiofrequency (thermal) rhizotomy, glycerol rhizotomy or nerve balloon compression are all ablative procedures that attempt to destroy, in a minimally invasive fashion, the trigeminal pain fibres that cause pain. However, these operations have variable degrees of success, and relief oftentimes does not last more than a few years (1-5 yrs). Therefore, treatment is typically repeated several times over a patient's lifetime.

Furthermore, all such operations are invasive and carry with them the inherent risks of infection, arterial or cranial nerve injury, or even stroke. Certain patients have medical contraindications that preclude any invasive operation, while still others may choose for personal reasons to avoid invasive surgery.

CyberKnife® radiosurgery for Trigeminal Neuralgia

Radiosurgery is the newest treatment for TN. This non-invasive procedure is based on the concept that very many focused beams of radiation can be precisely targeted onto the trigeminal nerve and used to administer an ablative dose of energy.

In effect, one can "cut" pain fibres with radiosurgery. Initially, such treatment was administered only with frame-based radiosurgical technologies, such as the Gamma Knife and Linac-based systems. These procedures all require that a metal "stereotactic" ring be attached to the patient's skull under local anaesthesia. However, the CyberKnife® has recently emerged as an effective and safe radiosurgical alternative for TN patients. In contrast to other forms of radiosurgery, the CyberKnife® does not require a painful stereotactic frame to be attached to a patient's skull.

There is actually no pain whatsoever with CyberKnife® radiosurgery. CyberKnife® radiosurgical treatment has been demonstrated to be as accurate and precise as frame-based systems with the added benefit of enhanced patient convenience and comfort.

How does the CyberKnife® work?

The process of treating TN with the CyberKnife® begins with a very high resolution CT scan of the brain, and in particular, the immediate vicinity of the trigeminal nerve. To optimally visualize the trigeminal nerve, a radio-opaque iodinated dye (or contrast) agent called metrizamide is often injected into the spinal fluid through a spinal tap.

Such metrizamide-enhanced CT scan imaging shows the trigeminal nerve in great detail. Alternatively, the treating neurosurgeon can visualize the trigeminal nerve with an MRI scan, and then use a computer to merge (fuse) the MRI and CT scans with one another. Regardless, the purpose of imaging is to visualize the trigeminal nerve in as much detail as possible so that an extremely accurate customized treatment plan can be created.

During the actual CyberKnife® treatment, a focused high intensity beam of radiation is precisely targeted along a segment of the trigeminal nerve, beginning from a point 2-3 mm from its brainstem origin to the entry into Meckel's cave.

Throughout treatment, a patient's smallest head movements are detected and accurately compensated for by the controlling computer. A single CyberKnife® treatment session for TN is completed in slightly over 1 hour.

How successful is CyberKnife® radiosurgery for Trigeminal Neuralgia?

Up to 80% of TN patients treated with the CyberKnife® will experience substantial and long lasting pain relief. The most common side-effect is an area of numbness over the face that probably correlates with the degree of pain relief.

The onset of pain relief after the CyberKnife® may be substantially faster than with other forms of radiosurgery. This effect may be due to the increased accuracy of this procedure. Longer follow-up will be needed before it will be possible to estimate the duration of pain relief.

Nevertheless, it is clear that the painless CyberKnife® procedure is a safe and effective treatment option for many patients with TN.

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.