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

Acoustic Neuroma

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

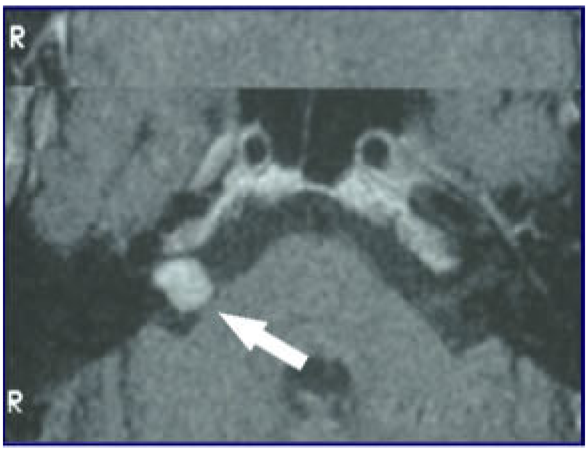
CyberKnife® treats a range of cancers and other medical conditions and there are now many CyberKnife® centres around the world, but not all countries yet have one and some centres specialise more in certain areas than in others or only accept international patients for specific types of treatment. CyberKnife®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

Acoustic neuromas (AN) are benign, generally slow growing tumours that intimately involve the seventh and eighth cranial nerve (CN VII and VIII) in a portion of the brain commonly referred to as the cerebellar-pontine angle (CPA). CN VIII has two distinct parts; the cochlear (hearing) nerve that transmits sound-induced nerve impulses between the inner ear and the brainstem, and the vestibular nerve that transmits balance information along similar pathways.

Meanwhile, CN VII, or the facial nerve, is responsible for the movement of half the face on the same side as the nerve. All these cranial nerves travel through a narrow bony opening termed the internal auditory canal. Acoustic neuromas most commonly arise from schwann cells, which make insulation (myelin) for the vestibular nerve. As a consequence these tumours are often appropriately referred to as vestibular schwannomas.



What is Neurofibromatosis Type II?

There are two types of acoustic neuromas: 1) Sporadic and 2) Neurofibromatosis Type II (NF-II), which is often aptly termed bilateral (affecting both sides) acoustic neuroma disease. The sporadic form of AN is responsible for

95% of cases, while NF-II causes the remainder. The bilateral nature of the disease in NF-II poses special challenges in terms of treatment.
NF-II is a rare, dominantly inherited genetic condition with a prevalence of 1 in 100,000 people. Virtually all patients with NF-II eventually manifest bilateral acoustic neuromas. Compared to sporadic AN, those associated with NF-II tend to grow faster, present at a younger age (oftentimes by the teenage years), and respond more poorly to virtually all forms of treatment. The implication of the latter is a greater likelihood of tumour recurrence and an increased risk of cranial nerve complications. Eventual complete (bilateral) deafness is not uncommon among patients with NF-2. By contrast, the sporadic form of AN presents in middle age, and patients have better outcomes with all types of surgical intervention.

What are the presenting symptoms for an acoustic neuroma?

Acoustic neuromas most commonly present with hearing loss. However a disturbance in balance, ringing in the ear (tinnitus), facial weakness, pain or even facial numbness, alone or in any combination, are other potential presenting symptoms. The fifth cranial (CN V), or trigeminal nerve, which is involved in transmitting facial sensation is often situated immediately adjacent to a moderately sized AN. As a consequence, pressure from an enlarging tumour can often cause facial numbness or pain.

In summary, the symptoms produced by acoustic neuromas include:

- Hearing loss
- Ringing in the ear (tinnitus)
- Imbalance
- Dizziness (vertigo)
- Facial weakness
- Facial numbness or pain
- Discomfort (feeling of fullness/pressure) in or around the ear

Hearing loss

The vast majority of patients with acoustic neuromas suffer some hearing loss as a result of injury to the cochlear division of CN VIII. This damage results from either direct infiltration or compression of the nerve by the tumour, or alternatively, interference with the normal blood supply. The hearing loss experienced by patients with AN is typically subtle, disproportionately affects the high frequency hearing range, and gradually progresses over years as the tumour increases in size. The damage to the hearing is such that it becomes ever more difficult for a patient to distinguish the texture of different sounds, thereby making it harder to identify discrete words when spoken at usual volumes. This capability is referred to as the speech reception threshold (SRT), and is a standard measured value in most hearing tests.

Loss of hearing is sufficiently slow in onset and painless, so as to go unnoticed by many AN patients, who might for example, unconsciously stop using the phone with their affected ear. The time period over which hearing worsens is highly variable and most likely correlates with the rate of tumour growth. However, sudden hearing loss is also a well-recognized phenomenon with these tumours. Furthermore, ringing in the ear (tinnitus) frequently accompanies loss of hearing, and for many patients can be very bothersome. Rarely, tinnitus occurs in the absence of hearing loss, and when this occurs in a single ear, it is sufficient justification for a patient to undergo an evaluation for acoustic neuroma.

Imbalance and vertigo

Because AN most commonly arise from the vestibular or balance nerve, it should not be surprising that affected patients frequently suffer from some dysequilibrium (loss of balance). When the visual and other sensory systems are working normally, patients can usually compensate for the faulty input that comes from the affected balance nerve. However, patients have a greater tendency to lose their balance than normal individuals especially when walking and turning quickly.

Vertigo is much less frequently associated with acoustic neuromas than lesser disturbances of the balance apparatus. However, when this symptom occurs, it can be extremely disabling. The vertiginous patient experiences profound dizziness, even when at rest, which can be severe enough to mimic seasickness. Interestingly, vertigo tends to occur most often with smaller acoustic neuromas.

Facial weakness

As acoustic neuromas enlarge, they eventually injure the CN VII, or the facial nerve, which controls facial movement on one side of the face. Facial nerve palsies range from hardly noticeable to profoundly disfiguring.

The most troubling problems for patients with facial nerve palsies are an inability to completely close the eye as well as difficulty keeping liquids from running out the corner of their mouth when drinking or eating. Typically, however, the facial nerve is able to adjust to even very large acoustic neuromas without causing noticeable facial weakness. When facial weakness accompanies smaller CPA tumours, it raises the suspicion that the tumour is arising from the facial nerve, and is a facial nerve schwannoma, instead of the much more common vestibular schwannoma.

Facial numbness

The largest acoustic neuromas produce facial numbness or ironically severe pain (trigeminal neuralgia) in some patients. Pain or numbness can involve any portion of the face or inside the mouth from the jaw up to the scalp on the affected side. The characteristic pain consists of brief lightening-like jabs that is characteristic of trigeminal neuralgia. The combination of facial weakness and numbness can be very disabling if it involves the region around the eye. Patients with this combination of problems have difficulty protecting the cornea (outer surface of the eye) from abrasion.

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.