



Essential tremor (ET) is the most common movement disorder, impacting the lives of an estimated 10 million Americans and millions more worldwide. At this time, there is no cure for ET and only about 50% of patients receive a benefit from the current available medications. For patients with disabling tremor that interferes with daily activities and is not controlled by medications, surgical treatments may be an option. Advances in

the understanding of brain anatomy, more detailed imaging methods to view the brain, and improved surgical techniques allow for greater surgical accuracy and increased benefits with fewer complications. Surgical procedures for ET include thalamic deep brain stimulation (DBS), focused ultrasound thalamotomy, and radiosurgical thalamotomy.

A History of Surgical Treatment

Surgery for tremor disorders has been performed for almost 100 years. Initially, surgery involved destruction of large parts of the brain, which resulted in an improvement in tremor but significant side effects such as weakness and paralysis.

In 1947, stereotactic surgical techniques, which involve using electrodes to precisely locate a particular part of the brain without destroying surrounding brain areas, were first used in humans. These techniques allowed for improvement in tremor with fewer side effects.

In order to achieve optimal tremor control, it was necessary to determine the specific part of the brain to target for surgery. By the late 1950s, the ventralis intermedius (VIM) nucleus of the thalamus was found to be the most effective target for tremor. The thalamus is a group of cells deep in the brain involved in relaying motor and sensory signals from different portions of the brain. Creating a lesion or destroying a portion of the VIM nucleus of the thalamus is called thalamotomy.

The brain is divided into two halves, with each side controlling the opposite side of the body. For instance, thalamotomy on the left side of the brain (unilateral procedure) was found to be very effective in controlling the tremor of the right side of the body. However, thalamotomy on both sides of the brain (bilateral procedure) to improve

tremor on both sides often resulted in speech, balance, and memory problems.

In 1993, DBS of the thalamus was approved in Europe and in 1997 the United States Food and Drug Administration (FDA) also approved it as a treatment for ET. DBS was shown to have beneficial effects comparable to thalamotomy with fewer complications. In DBS, there is no destruction of the brain. Rather, a wire (electrode or lead) is placed in the VIM nucleus of the thalamus. The wire is connected under the skin to a pacemaker-like battery device typically in the chest that provides mild electrical currents to control symptoms. In ET, DBS of the VIM nucleus of the thalamus is the most commonly used surgical procedure to control tremor.

In 2011, the first focused ultrasound thalamotomy for the treatment of essential tremor was performed. This procedure involves focusing sound waves through the skull onto the thalamus, which destroys a portion of the VIM nucleus to reduce tremor. In 2012, a focused ultrasound system was approved in Europe for patients whose tremor did not respond to medication and was approved by the FDA in 2016 as a treatment for ET.

People who have disabling tremor which impacts their ability to perform daily activities are potential candidates for surgical procedures.

Patient selection

Persons with ET who do not have satisfactory tremor control with medications and have disabling tremor are potential candidates for surgical procedures. Disabling tremor is one that impacts people's ability to perform daily activities such as eating, writing, drinking, grooming, or enjoying hobbies and maintaining employment. Most physicians will try

medications such as propranolol and/or primidone to control tremor before recommending surgery. Patients who have significant memory problems and patients with unstable medical conditions which would increase surgical risk may not be good candidates for surgery.



Surgical Procedures Overview

Deep Brain Stimulation (DBS)

Currently, the most common surgical treatment for ET is deep brain stimulation (DBS). With DBS, electrical stimulation is delivered to the brain through an electrode implanted deep into the VIM nucleus of the thalamus. It is the most effective treatment for tremor, with the greatest effect on hand and arm tremor, but it may also be helpful in controlling head, voice, and leg tremor.

DBS can be done on either one (unilateral) or both sides (bilateral) of the brain; however, there is increased risk for speech and balance problems with bilateral procedures. So, if tremor significantly affects both hands, the dominant hand is typically targeted and in some cases, bilateral procedures may be considered. The implanted electrode(s) in the brain is connected to a neurostimulator (battery) which provides the appropriate amount of electrical stimulation to control tremor. Although, DBS can significantly reduce tremor, it is important to remember it is not a cure for ET.

There are two DBS systems approved by the FDA for the treatment of ET, both of which have been shown to significantly reduce tremor. In general, the systems are similar, but they each have specific features that make them unique. If you choose to receive DBS, you should discuss with your neurologist and neurosurgeon which device would be best for you.

Pre-Op

A specially trained neurosurgeon uses state-of-the-art equipment to take several images of the brain, in order to pinpoint the correct location for electrode placement. In one surgical approach, a stereotactic frame is attached to the individual's head to hold it still during surgery. The frame is attached with four small screws. Local anesthesia is used to numb the area where the screws are placed. Alternatively, some surgical centers use a frameless (mini-frame) procedure which does not require the use of the head frame. Instead, small fixation screws are placed on the head and are used to assist in determining the exact area to target for surgery.

After the frame or frameless markers are attached, the patient undergoes a brain scan such as a CT or MRI which provides detailed pictures of the brain. The neurosurgeon uses these images to help determine the exact location of the VIM nucleus, the target location within the thalamus. Then a small area on the top of the head is cleaned and shaved. After local anesthesia, a small hole, called a burr hole, about the size of a nickel is made in the skull.

Once the neurosurgeon is satisfied with the placement of the lead wire, the pacemaker-like battery is placed in the individual's chest and connected to the lead wire by an extension wire.

Procedure

Most patients go through lead placement while fully awake. The brain itself does not contain nerve endings, so there is no pain. Actually, you don't feel anything at all. And although it is not required you be awake for this surgery, it is helpful if you are so the surgical team is able to see the effects of the stimulation on your tremor, as well as any side effects that may occur. They will often have the individual do a task, such as draw a spiral or hold a cup against gravity, to measure the effectiveness of the placement. They know when they find the correct spot because the tremor will be suddenly and significantly reduced. This also allows them to observe any side effects of the stimulation so they can be resolved during surgery.

Once the neurosurgeon is satisfied with the placement of the electrode, the implantation is complete. Either on the same day or about a week later, the neurostimulator (battery) is placed, typically in the individual's chest, and connected to the electrode by an extension wire, tunneled from the chest to the brain through the side of the neck. Neither the wires nor the battery are visible.

The complete procedure usually takes three to four hours to complete.



Post-Op

Although it can vary at different centers, a few weeks or a month after the surgery is completed, the physician or nurse programmer will turn the device on and program the settings to optimally control tremor. Most people don't feel the stimulation, although some may feel a brief tingling when the stimulation is first turned on. Getting the initial settings right may take several programming sessions.

DBS is surgery and there is downtime immediately after the procedure. Patients will usually stay overnight after surgery and are asked to take it easy when they are released from the hospital the next day. But within a few weeks after the procedure, you can go back to your normal daily activities. Always follow your doctor's instructions, but usually you can gradually try activities that had become difficult for you because of your ET.

Considerations

DBS involves physically going into the brain and implanting foreign objects, increasing the risk of infection and other complications. The most serious risks include infection, bleeding inside the brain, and seizures, but these occur in less than five percent of people. Some of these complications can be serious and, although rare, may be fatal.

Although it is fairly uncommon, once implanted, the system may become infected, parts may wear through the skin, or the device may malfunction. Any of these situations may require additional surgery or cause your ET symptoms to return. When implanted on both sides of the brain, DBS may also cause speech and language impairments. In addition, the system's battery will need to be replaced every 3-7 years depending on the stimulation settings used. Battery replacement is an outpatient procedure. There are also rechargeable systems available.

Patients with DBS should avoid receiving diathermy, which is the use of electric currents to generate heat in tissue. It is often used during various surgeries, physical therapy for pain, and dentistry. The heat

from the diathermy can be transferred to the brain through the DBS electrode resulting in brain damage and rarely death. In addition, if it is necessary to

receive an MRI after the DBS system is implanted, it is important to contact the surgical center. MRIs can lead to heating of the DBS system which can cause damage to the brain. They can generally be performed without any problems as long as the proper safety measures are followed.

Finally, if the device is not effective or if a new treatment option becomes available, the device can be removed without any destruction of brain tissue.

Outcomes

Several reports have demonstrated DBS has a comparable improvement in tremor to thalamotomy, but with fewer complications. The majority of studies have reported improvements in tremor in 90% of patients. Long-term studies have shown the improvement in tremor is maintained in the majority of patients up to at least 7-10 years after the surgery; however, the magnitude of the benefit may reduce over time. Multiple studies have demonstrated the immediate and long-term benefits of DBS in controlling tremor with improvements in hand tremor of approximately 90%, and improvements in functional ability and performance of activities of daily living of approximately 85%. Although all of the large studies have targeted patients with disabling hand tremor, in these studies head and voice tremor have had some improvement. The greatest improvements in head and voice tremor were seen with bilateral procedures.

Other Uses

DBS is used to treat a number of neurological conditions, such as Parkinson's disease, dystonia, and obsessive compulsive disorder. It is also being studied as a treatment option for severe depression, epilepsy, Tourette's syndrome, stroke, addiction, and dementia.

Focused Ultrasound Thalamotomy

The FDA approved a new treatment for ET in 2016 – it's called focused ultrasound. Now this surgical option is available in the U.S., Canada, and many other parts of the world. Although similar to radiosurgical thalamotomy, focused ultrasound utilizes sound waves rather than radiation to destroy



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Surgical Options (cont.)

brain tissue within the VIM nucleus, thus stopping tremor.

Most people are familiar with ultrasound being used to “see” unborn babies inside the womb. These same sound waves are applied in focused ultrasound, but in a very different way. This technology uses multiple beams of sound focused in on one spot deep within the brain. The point of intersection of these sound waves generates heat, much like how a magnifying glass focuses beams of sunlight to burn a hole in a leaf.

Pre-Op

The patient has their head shaved and wears a stereotactic frame similar to the one described in the DBS section. Transducers in the frame deliver the ultrasound waves to the brain. The individual sound waves safely travel through the skin, skull, and brain until they converge at the target tissue. The destruction of the target tissue interrupts circuits of the brain responsible for tremor.

Procedure

With the frame in place, patients are moved into an MRI (magnetic resonance imaging) machine, where they remain for the entire procedure. MRI allows the surgeon to see the brain in real-time, validate they are targeting the correct region, and monitor the exact amount of heat being applied (approximately 55- 60°C/131-140°F).

Patients are fully awake during the procedure, interacting with the medical team as they assess progress in reducing tremor throughout the process. And although the process takes several hours, the benefits can be felt immediately.

There is virtually no down-time and patients are usually able to go home the same day. Most return to activities of normal life within 24 hours.

Considerations

Even though the procedure is transcranial and involves no incision or drilling, it does create a thalamic lesion, which destroys a part of the brain and can result in permanent neurologic deficits. Initial study results indicated that of the 76 ET patients who received the treatment, 74 neurologic adverse events were reported in 56 of the people

treated. The most common side effect was an alteration in sensation, which was reported by 38% of the patients and persisted at 12 months in 14%. Gait disturbance occurred in 36% of patients and persisted at 12 months in 9%. The incidence of cerebellar deficits such as dysmetria (coordination issue where movements undershoot or overshoot intended position), ataxia (loss of full control of bodily movements, often affecting walking and balance), and unsteadiness of gait approached 5% each at 12 months.

As this is a new procedure, there are no statistics on the long-term effectiveness (beyond 12 months) of this treatment. Patients who participated in this original study, however, will continue to be followed by researchers for five years.

Outcomes

Focused ultrasound has been reported to have a 47% improvement in targeted hand tremor after three months and a 40% improvement one year after surgery. It offers a reduced risk of infection and blood clot formation, and there is no exposure to radiation. It also offers tremor relief without the need for periodic equipment adjustments. However, treatment is currently considered safe to treat just one side of the brain, usually the dominant side.

Focused ultrasound is currently available to treat ET at several academic medical centers in North America, Europe, and Asia.

Other Uses

Research is ongoing to expand the use of this technology to treat patients with other neurological disorders, including Parkinson’s disease, epilepsy, brain tumors, obsessive-compulsive disorder, depression, dystonia, and Alzheimer’s disease.

Radiosurgical (Gamma Knife®) Thalamotomy

Despite its name, Gamma Knife® isn’t a special, hi-tech, laser-beam surgical knife; it’s a complex machine that delivers finely focused beams of radiation to a single point deep within the brain. Like focused ultrasound, each beam has very little effect on the tissue it passes through. However, a strong



dose of radiation is delivered when the individual beams are focused to a single point, destroying the target tissue. The destruction of the target interrupts the signal the brain is sending out telling the muscles to move. Radiosurgical thalamotomy acts as a signal roadblock.

Pre-Op

The technique that allows radiosurgery to precisely target the correct area within the brain is called stereotaxy. Several imaging techniques are used together with special computers and instruments, to provide 3-D views of the target area and surrounding brain tissue. Like in DBS, computerized tomography (CT) scanning takes X-ray images from different angles, to produce cross-section images of the brain. This allows the neurosurgeon to see inside the patient's brain without ever picking up a scalpel.

Magnetic resonance imaging (MRI) uses a powerful magnetic field and radio frequency pulses to produce detailed pictures of organs, soft tissues, bone and virtually all other internal body structures. Angiography (x-ray of blood vessels) is also used to ensure the neurosurgeon can even see inside blood vessels and other vital organs. By studying all these images together, a team of specialists can accurately locate the VIM nucleus within the brain, and focus the radiation beams on just that area.

The procedure is not painful. There are no cuts into the scalp or through the skull. However, the neurosurgeon will use local anesthesia to numb four spots on your scalp and forehead before attaching a stereotactic frame. This frame is similar to the one used in DBS and focused ultrasound, and is meant to keep the head immobile and in the correct position during the procedure.

Procedure

Two hundred-one highly focused beams of ionizing radiation are generated by activated cobalt. The cobalt beams are directed to converge at the targeted location in the thalamus. The spot where the beams converge is where the tissue destruction occurs. Radiosurgical thalamotomy, similar to focused ultrasound, does not involve putting any foreign objects into the brain. It uses neuroimaging, such as MRI scanning to determine the target location.

This procedure takes approximately one hour.

Post-Op

Radiosurgical thalamotomy is an outpatient procedure, so after the procedure the frame will be removed and you will generally be allowed to go home.

Considerations

There are early complications or side effects with this procedure, but they are usually temporary. Tiredness and fatigue may occur for the first few weeks. Swelling in the brain at or near the treatment site can cause symptoms such as headache, nausea and vomiting. The patient's scalp may be red, irritated, or sensitive at sites where the halo- device was attached to the head during the treatment. Some people also temporarily lose a small amount of hair.

People may also experience late side effects, such as other brain or neurological problems, months after the procedure. In addition, the full benefits of this procedure are often not fully realized until several months post-op.

Outcomes

Radiosurgical thalamotomy is rarely used as a treatment for ET; however, it may be an option in patients that cannot undergo DBS. Significant improvement in tremor has been reported; however, over time, improvement may diminish and additional complications may emerge. Occasionally, patients may require additional surgery if the initial benefits are lost.

Other Uses

Radiosurgery is most commonly used to treat brain tumors, arteriovenous malformations (AVM), and trigeminal neuralgia.



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Surgical Options

(cont.)

If you are considering surgery:

- Be proactive in asking questions to ensure you know what to expect.
- Involve your family members and invite them to be there with you as you are going through the process. Well informed patients and families make better decisions about their medical treatment.
- False expectations and inaccurate information are avoided when the appropriate research has been done in advance. Make sure your expectations are reasonable, and you understand both the benefits and risks of undergoing a surgical treatment for ET.

This information was reviewed by Kelly E. Lyons, PhD. Dr. Lyons is the President of the IETF Board of Directors and is a Research Professor of Neurology & Director of Research and Education of the Parkinson's Disease and Movement Disorder Center at the University of Kansas Medical Center in Kansas City, KS.

This information is not intended as medical advice or to replace your current medical therapy. Discuss your difficulties with your physician or other healthcare professional in order to help develop a well-rounded treatment plan that is right for you.

The IETF does not make medical recommendations.



The mission of the International Essential Tremor Foundation is to provide hope to the essential tremor (ET) community worldwide, through awareness, education, support and research.