INCISIONLESS MR-GUIDED FOCUSED ULTRASOUND FOR ESSENTIAL TREMOR: **CLINICAL STUDY OVERVIEW FOR PATIENTS**

Neuravive™

BACKGROUND

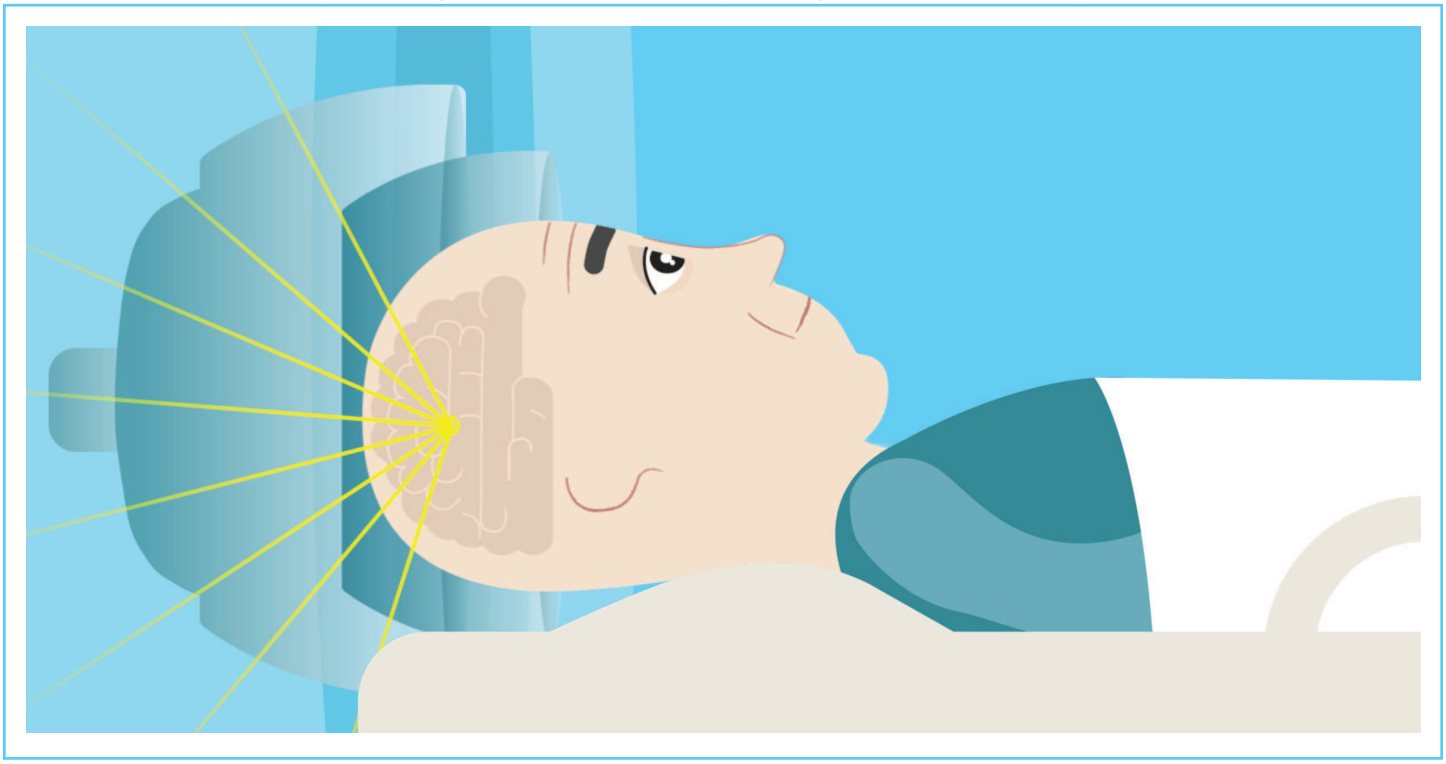
When a patient is diagnosed with essential tremor and is experiencing symptoms that are beginning to interfere with daily activities, their physician normally prescribes medication to help manage the tremor. While medication is the first line of treatment, it is estimated that 30-50% of essential tremor sufferers do not get much benefit or have unpleasant side effects.[1] If medication does not provide sufficient tremor relief, it may be time to speak with your physician about other treatment options.[2]

One option is deep brain stimulation, or DBS, which is a surgical intervention to implant permanent electrodes in the brain and a pulse generator in the chest. The treatment stimulates a portion of the brain, in the thalamus, which is involved in the tremor. It is generally quite effective in treating the tremor, but does carry the risks of any surgical procedure. In addition, DBS requires follow up throughout the patient's life for stimulation adjustments and battery replacement.

For many years, a treatment called thalamotomy was performed by neurosurgeons to treat essential tremor. Like DBS, it treats the thalamus, but instead of stimulating, it creates a lesion (destroys a small portion of the thalamus). It required making an incision in the scalp, drilling a small hole in the skull and inserting a radiofrequency probe to heat and create the lesion (thalamotomy).

Today, there is a new generation incisionless thalamotomy, called Neuravive. It uses focused ultrasound guided by MR imaging and has been shown to be effective in tremor control.

During treatment, ultrasound waves are focused through a helmet-like device to meet at a point deep in the patient's brain. This target, the thalamus, is heated to cause a tiny ablation, or burn. The result for many patients is improvement in hand tremor immediately following the treatment and they often go home the same day.



PATIENT PROFILE

Patients for the Neuravive treatment must have a confirmed diagnosis of essential tremor that does not respond to medication, be at least 22 years and be able to tolerate the procedure with or without some form of sedation (e.g., conscious sedation).

*This information is not intended to be medical advice. Please consult with a qualified physician for medical advice.

CLINICAL STUDY[3]

A clinical trial was designed to evaluate the safety and effectiveness of using MR-guided focused ultrasound to perform an incisionless thalamotomy. Patients were enrolled at 8 international medical centers. All patients had moderate-to-severe essential tremor and had taken at least two rounds of medication without improvement.
Patients were randomly assigned to two groups:

- The treatment group which received unilateral focused ultrasound thalamotomy (Neuravive).
- The sham group, which received no ultrasound treatment. In clinical trials, sham surgery controls for potential placebo effect.

After 3 months, patients in the sham group were given the opportunity to receive the same focused ultrasound treatment as the treatment group.
The treatment was performed on one side (unilateral), even if the patient suffered from tremor on both sides. Two tools were used to evaluate the patients before treatment (referred to as baseline), immediately after the treatment and at 1, 3, 6, 12 and 24 months:

- A rating system for tremors called Clinical Rating Scale for Tremor (CRST), which has three parts: Part A rates tremor; Part B rates tasks and Part C rates disability.
- A questionnaire with 30 essential tremor specific questions called Quality of Life in Essential Tremor Questionnaire (QUEST).

In addition, the tremor assessments were videotaped and rated by an independent group of neurologists who did not know if the patient was part of the treatment or sham group.

THE RESULTS

There were 76 participants enrolled in the study, of which 75% had a family history of tremor. The average age of the patients was 71 years.

HAND TREMOR. At 3 months, the patients that received the focused ultrasound treatment showed an improvement of 47% in their hand tremor (CRST Part A & B). The patients in the sham group showed an improvement of less than 1%. At 12 months, the treatment group maintained a 40% improvement, which was not statistically different from the 3-month score.

FUNCTIONAL DISABILITY AND QUALITY OF LIFE. At 3 months, patients that received the focused ultrasound treatment showed a 63% reduction in total disability score (CRST Part C). The patients in the sham group showed a 2% reduction. The improvement for the treatment group was sustained at 12 months. Patient-reported quality of life (QUEST) scores also improved significantly (43% reduction) in the treatment group as compared to sham (5% reduction).

SAFETY. In clinical trials, safety is assessed by the occurrence of adverse events. Adverse events are unfavorable and unintended symptoms or medical occurrences temporally associated with the use of a medical product.

In this clinical trial, the majority of events were transient (gone by 6 months) and all but one of the reported adverse events related to the treatment were mild or moderate. The one serious event was a persistent tingling in the thumb that was bothersome to the patient. Overall, the study showed a very favorable safety profile. The most common persistent adverse events were numbness/tingling (12%), imbalance (5%), unsteadiness (2%), and gait disturbance (problems with walking) (2%).

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1. Zesiewicz,T.A. et al. Evidence-based guideline update: Treatment of essential tremor. Neurology November 8, 2011 vol. 77 no. 19 1752-1755.
2. http://www.aans.org/Patients/Neurosurgical-Conditions-and-Treatments/Deep-Brain-Stimulation
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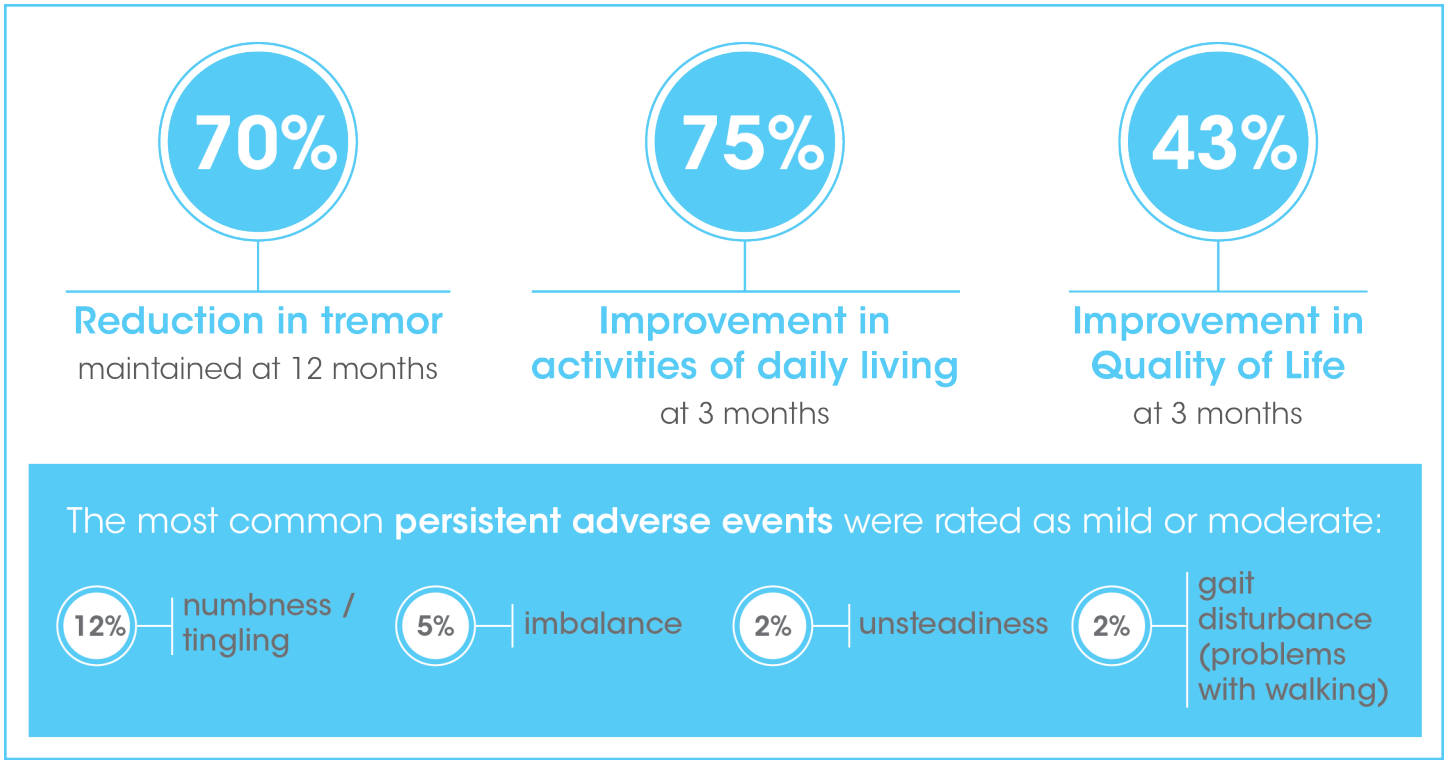

FOR MORE INFORMATION, PLEASE REFER TO:
http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm510521.htm

INTENDED USE / INDICATIONS FOR USE

The Exablate Neuro is intended for use in the unilateral thalamotomy treatment of idiopathic essential tremor patients with medication-refractory tremor. Patients must be at least age 22. The designated area in the brain responsible for the movement disorder symptoms (ventralis intermedius) must be identified and accessible for targeted thermal ablation by the Exablate device.

RISKS

Risks associated with any thalamotomy include transient and/or permanent sensory paresthesias, numbness, imbalance, and/or gait disturbance. These events are generally transient and mild or moderate in severity. Risks and adverse events also associated with the Exablate Neuro treatment include brief sonication-related pain, brief sonication-related dizziness and nausea or potential for deep vein thrombosis associated with lengthy time on the treatment bed.

Visit our website for more information about the Focused Ultrasound treatment for Essential Tremor:

www.essential-tremor.com

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Information for Prescribers. http://www.accessdata.fda.gov/cdrh_docs/pdf15/P150038C.pdf

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Device name: Exablate Neuro