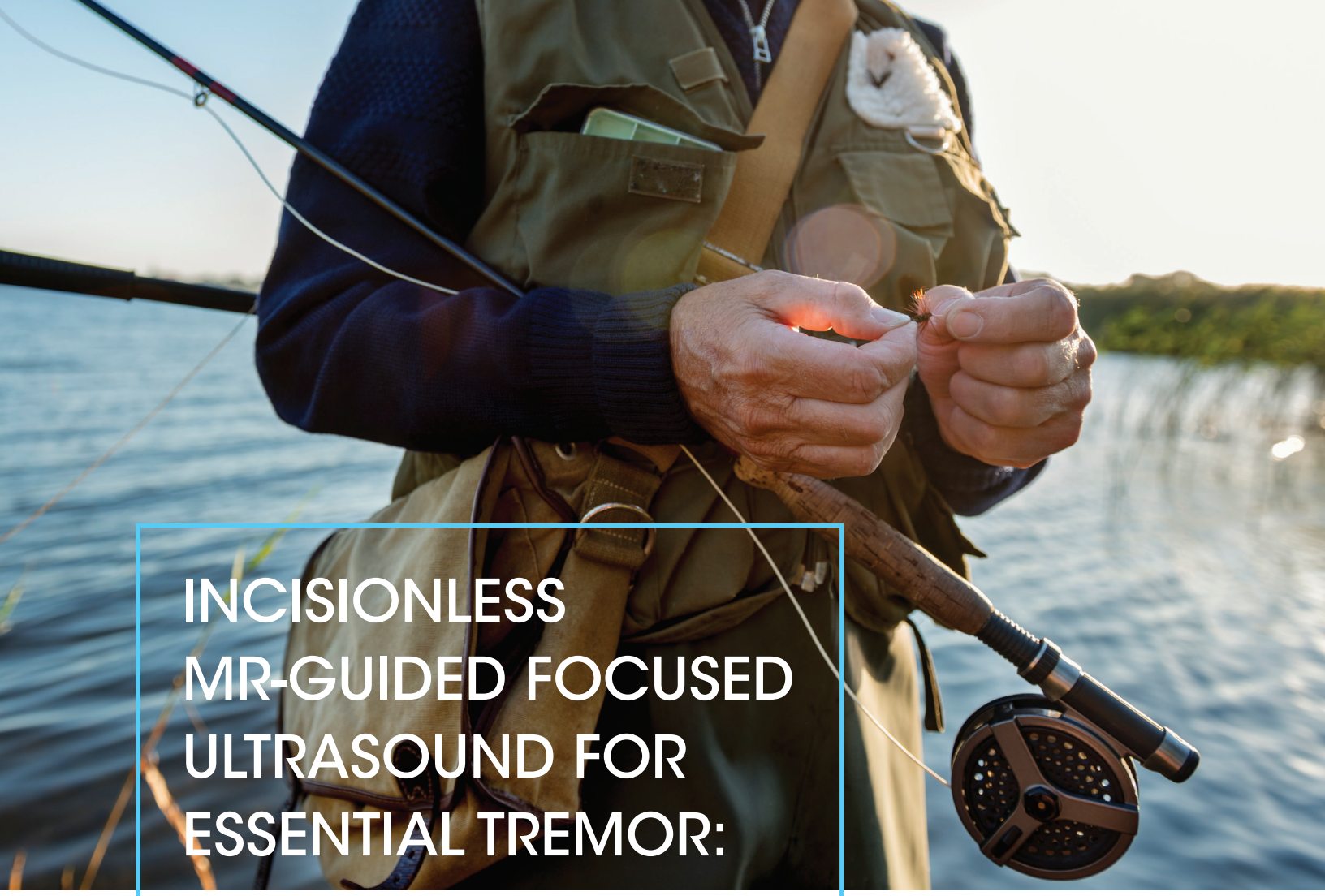


INCISIONLESS MR-GUIDED FOCUSED ULTRASOUND FOR ESSENTIAL TREMOR:

CLINICAL STUDY OVERVIEW FOR PATIENTS

INSIGHTEC®

BACKGROUND

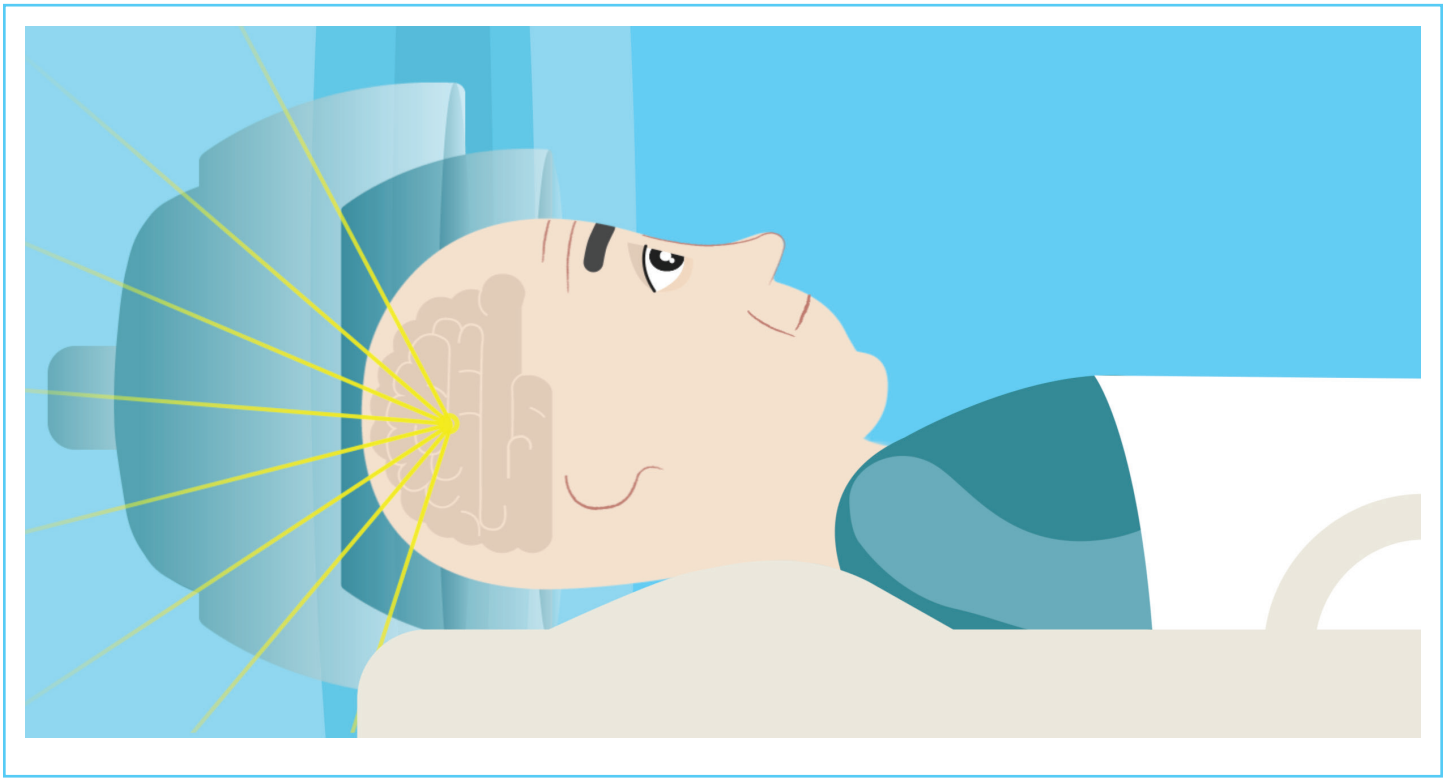
When a patient is diagnosed with essential tremor and is experiencing symptoms that are beginning to interfere with daily activities, the physician normally prescribes medication to help manage the hand tremor. While medication is the first line of treatment, it is estimated that 30-50% of essential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

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.[2]

For many years, a treatment called thalamotomy was performed by neurosurgeons to treat essential tremor. Like DBS, it treats a specific location in the thalamus, called the Vim, 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.

Today, there is a an incisionless treatment option, which uses focused ultrasound guided by MR imaging without surgical incisions or probes.

During treatment, ultrasound waves are focused through a helmet-like device to meet at a point deep in the patient's brain. Applying the ultrasound energy is called a sonication and the small target is heated to cause a tiny ablation, or burn. This incisionless treatment has been shown to result in immediate tremor improvement with minimal hospitalization.[3]



[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
3 Pre-Market Approval (PMA) P150038

CLINICAL STUDY

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.
- 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. A rating system for tremors called Clinical Rating Scale for Tremor (CRST) was used to evaluate patients. Part A rates tremor; Part B rates tasks and Part C rates disability. Patients were evaluated before treatment (referred to as baseline), immediately after the treatment and at 1, 3, 6, 12 and 24 months. As part of the long term follow-up from this study, all subjects continued to be evaluated for general health, efficacy measurements and device/procedure related adverse events at 2 and 3 years.

STUDY RESULTS

During the clinical trial, 56 subjects received focused ultrasound treatment and 19 received the sham procedure and then crossed over. Of these 75 subjects, a total of 54 are included in the 3-year analysis of the long-term study results.

HAND TREMOR. The tremor severity score (CRST Part A) improved 76.5% over baseline at 3-year follow-up for combined (focused ultrasound and crossover) subjects.

FUNCTIONAL DISABILITY AND QUALITY OF LIFE. Improvement in tremor/motor function (CRST Part A & B) was 53% at three years. Functional disability (CRST Part C) showed a 56.9% improvement from baseline at three years.

SAFETY. In clinical trials, safety is assessed by the occurrence of adverse events. Adverse events are unfavorable and unintended symptoms or medical occurrences temporarily associated with the use of a medical product.
In discussion of adverse events below, the number in parenthesis is the percentage of active subjects experiencing these adverse events.

SAFETY INFORMATION

Overall, the focused ultrasound treatment has been shown to be safe for treating essential tremor with minimal risk, but as with any medical procedure, there are risks. You should have a detailed conversation with your physician regarding complications, also known as adverse events, that you may experience. Insightec-sponsored clinical studies have shown that the most common adverse events associated with this treatment are 1) imbalance/gait disturbance (26% of study patients), 2) numbness/tingling (33%), and 3) headache/head pain (51%). Most of these events were classified as mild or moderate, and 48% of all adverse events resolved on their own within 30 days.

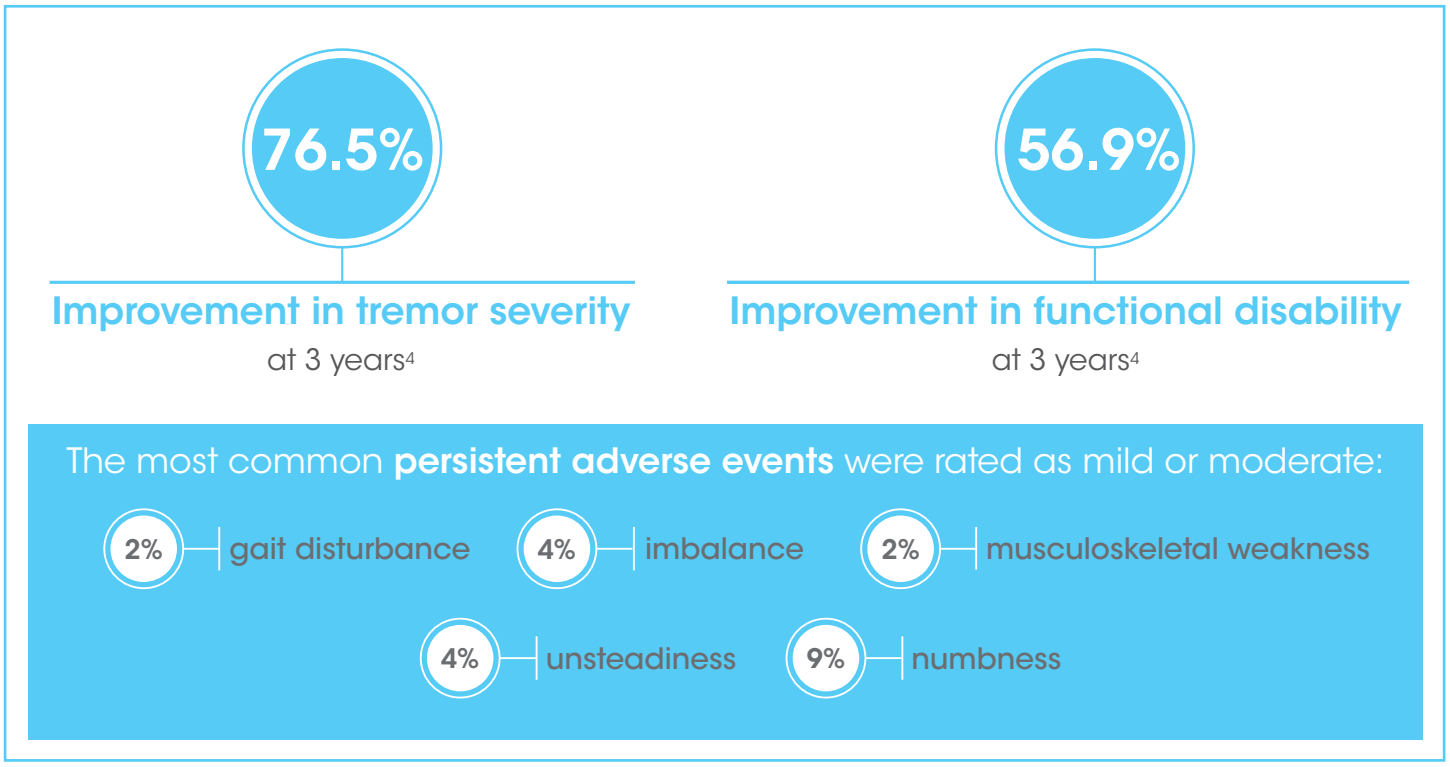
Adverse events that persisted at 3 years were all mild or moderate and included: numbness/tingling (9% of study patients), imbalance (4%), unsteadiness (4%), gait disturbance (2%), and musculoskeletal weakness (2%). Additional infrequent events include dizziness, taste disturbance, slurred speech, fatigue and vomiting.

For additional safety information, please refer to: Pre-Market Approval (PMA) P150038. Again, you should discuss in detail the risks, benefits and treatment options with your physician prior to treatment.

SAFETY INFORMATION (CON'T.)

Infrequent complications that have been reported include long-term (more than 3 months following treatment numbness/tingling, imbalance, unsteadiness, gait disturbance, and muscle weakness. If a blood clot or deep vein thrombosis (DVT) occurs after the procedure and is not treated urgently it could lead to long term muscle, heart, brain, or lung damage. There is a possibility that your tremor may return months or years after treatment. This procedure does not treat the underlying disease nor prevent its progression.

For more information on the focused ultrasound treatment, including warnings, precautions, potential side effects and contraindications, please see the Safety Information page https://usa.essential-tremor.com/safety-information/.



4 Pre-Market Approval (PMA) P150038

Of the total 54 subjects included in the analysis, percentages represent those experiencing these events at 3 years.

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.

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

www.essential-tremor.com

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PUB41003695-NA Rev. 3
Device name: Exablate Neuro