FOCUSED **ULTRASOUND**

An incisionless treatment for **essential tremor** with instant, durable tremor improvement

INSIGHTEC

For use outside the US only

What is Essential Tremor?

Essential tremor (ET) is a neurological condition that causes shaking of the hands, head and voice, but it can also cause legs and trunk to shake. Some people even have a feeling of internal tremor. ET is often confused with Parkinson's disease although it's eight times more common, affecting an estimated **over 60 million people worldwide.**[1] Unlike Parkinson's disease, ET is not a resting tremor but is caracterized by intentional or action tremor.

+60 Million people worldwide

are affected by Essential Tremor.[1]

Symptoms

The primary symptoms associated with essential tremor include:

- Uncontrollable shaking that occurs for brief periods of time during action
- Begins gradually, usually on one side of the body
- Occurs in the hands first, affecting one hand or both
- Can include a shaking voice or tremor of the head
- Nodding head
- Worsening during periods of emotional stress and purposeful movement

What is Focused Ultrasound?

Focused Ultrasound is an incisionless unilateral treatment (i.e., treatment of one side, usually the dominant hand), for essential tremor patients who have not responded to medication. It uses sound waves guided by MRI to treat deep in the brain with no incisions or permanent implants.

The ultrasound waves are focused on a small spot in the brain, the Vim of the thalamus, considered to be responsible for tremor. The temperature at the target rises high enough to create a small ablation or burn, providing a therapeutic effect. The MRI is the eyes of the treatment, enabling the physician to plan, guide and target the area for treatment. It also acts like a thermometer, providing continuous temperature monitoring in the focus and surrounding area to avoid unintended heating of the surrounding tissue. With focused ultrasound you treat only one side of the body at the time (the treated target in the brain is on the opposite side of the impacted limb).

For intended use in each country, please see insightec.com/regulatory-approvals/

The woman in this image is not an ET patient.

“Don’t let essential tremor take away the simple things in life.”

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Benefits of Focused Ultrasound

5-year persistent effect was reported[3]

In an Insightec-sponsored clinical study, patients reported an immediate tremor improvement maintained at 73% at the 5 year follow up.[2]

Significant life quality improvement

The same study[3] showed significant improvement in terms of physical activity and psychological effect sustained 5 years after the treatment.

Incisionless

Insightec's device uses focused ultrasound waves that can pass safely through the skull into the brain, with no incision.

Quick Recovery

With no surgical cuts, there is minimal to no risk of infection. You can expect to resume normal activities within days.

Specific benefits and potential risks might be related to your personal health condition, therefore it is important to discuss therapeutic options with your physician.

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I always loved baking, so I decided to open my own a bakery. One day, my right hand started to shake. Gradually I couldn't do daily activities like drink or eat, not to mention baking or serving coffee to my customers. I became completely dependent on my staff.

At first, the doctors prescribed medications, but they didn't work for me. Then they suggested the MRI-guided focused ultrasound treatment. I knew I would have to shave my head, but I just wanted to live my dream - to serve my customers again.

After a couple of hours or so, on the MRI bed, my hand didn't shake anymore.

Haya Mendlebaum, Focused Ultrasound Patient

Results may not be representative of all treatment outcomes.

Is the treatment an option for me?

It is important to consult with your physician or a Focused Ultrasound Treatment Center to determine if the Focused Ultrasound treatment is right for you.

As part of the evaluation process, the severity of your tremor and your overall health will be evaluated.

Patients will need to undergo a CT scan in order to determine if they are candidates for the Focused Ultrasound treatment.

If you have metallic implants such as pacemakers, neuro-stimulators, spine or bone fixation devices, total joints, metal clips, screws, etc, you will need to consult with a physician to determine if Focused Ultrasound is an option for you. Any metallic implants must be MRI-compatible to prevent injury to the patient from the MRI's strong magnetic field.

Also, if you are not generally healthy enough to withstand the treatment and lie still in the same position for on average 2.5 hours, you may not be a good candidate for this treatment. There are additional limitations and a physician will do an assessment to verify if you are a candidate for the treatment.

For safety information, please visit:
https://insightec.com/safety-information

What happens before, during, and after the treatment?

Preparation

The Focused Ultrasound treatment requires that a patient have a cleanly shaven head. The Ultrasound waves will be transmitted into the brain from a helmet-like transducer. This is in order to ensure no interference of the sound waves. A local numbing medication will be applied and a head frame will be secured to your head so that your head does not move during treatment.

Your heart rate, blood pressure and blood oxygen levels will be monitored throughout the treatment. You will be awake, communicating with the treatment team throughout the treatment. You may be given additional medication to keep you comfortable.

Cool water will circulate in the helmet around the top of your head and you will be kept warm in case you get chilled. You will also be given a “stop sonication” button to indicate to the physician that you want to stop the treatment for any reason.

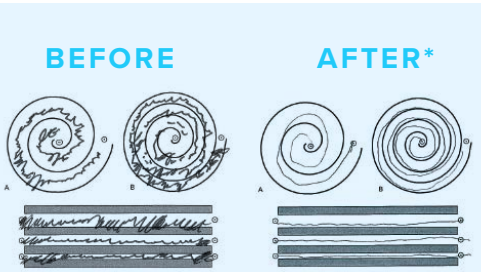
Planning

A series of MRI images will be taken for planning the treatment according to your specific anatomy. The treating physician will first apply light doses of ultrasound energy. This helps to identify the precise spot in the brain for treatment by assessing temporary tremor improvement and any potential side effects.

After each application of energy, called a sonication, you will be asked to perform specific tasks to evaluate your tremor improvement. Tasks may include touching your nose with your finger and/or drawing spirals.

Treatment

The treating physician will then gradually increase the energy to create a small lesion, usually resulting in a therapeutic effect, improvement of hand tremor in the treated side. Although individual results may vary, you should notice improvement during the treatment itself. The treatment lasts on average 2.5 hours.



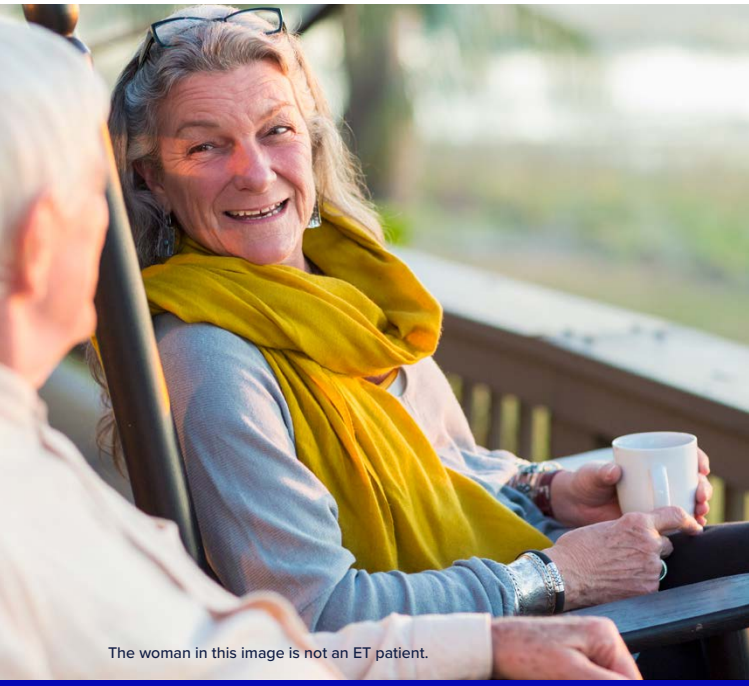
After Treatment

After treatment, the the transducer and head frame will be removed. will be removed and you will go to the recovery room. The physician will let you know when you can go home and when you may need to return for a follow-up visit. Within days you should be able to return to normal activities. The treatment team will provide you with instructions related to your post-treatment recovery.

*Results may not be representative of all treatment outcomes.

What results can I expect?

The outcomes of the Insightec sponsored clinical trial demonstrated 73% sustained tremor improvement at 5-years.[3]



The woman in this image is not an ET patient.

> “That peace I felt was unbelievable.”

Marie Baker, Focused Ultrasound Patient

Results may not be representative of all treatment outcomes.

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.

An Insightec sponsored clinical study in 76 patients[2] have shown that the most common adverse events after treatment are:

- Imbalance/gait disturbance (26% of study patients)
- Numbness/tingling (33%)
- 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. Additional infrequent events include dizziness, taste disturbance, slurred speech, fatigue and vomiting.

Adverse events recorded at 5-year follow up in 40 patients:[3]

- No new AEs recorded at 5 year follow up
- No new or worsening of AEs recorded 1 year after treatment or at 5 year follow up

1 Welton, T., Cardoso, F., Carr, J.A. et al. Essential tremor. Nat Rev Dis Primers 7, 83 (2021). https://www.nature.com/articles/s41572-021-00314-w

2. Pre-Market Approval (PMA) P150038: https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150038B.pdf

3. Cosgrove GR, Lipsman N, Lozano AM, et al. Magnetic resonance imaging-guided focused ultrasound thalamotomy for essential tremor: 5-year follow-up results.

J Neurosurg. 2022;1-6. doi:10.3171/2022.6.JNS212483.

Based on an Insightec sponsored clinical trial.

Drs Cosgrove, Lipsman and Lozano received clinical or research support from Insightec for the study described; further these doctors are or have been paid consultants by Insightec.

INSIGHTEC

Device name: Exablate Neuro

Visit our website for more information about the focused ultrasound treatment for essential tremor:

www.insightec.com/essential-tremor-treatment/

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