



Advances in Treating Involuntary Tremors

MRI-guided Focused Ultrasound for Essential Tremor

Kara Beasley, DO

Boulder Neurosurgical & Spine Associates

303-536-3807



BOULDER
NEUROSURGICAL & SPINE
ASSOCIATES

Agenda

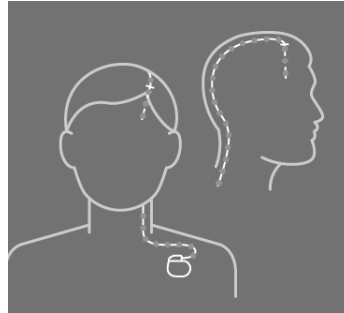
- Essential Tremor facts
- Essential Tremor treatment options
- What is Neuravive?
- How does it work?
- Who is a candidate for Neuravive?
- What can I expect from the Neuravive procedure?
- Clinical evidence
- Benefits of Neuravive
- In a patient's own words

Essential Tremor (ET) Facts

- The most common movement disorder affecting an estimated 10 million Americans.
- Usually affects the hands, but may also affect the voice, legs or torso.
- Daily activities such as eating and writing become difficult and may require care from family members.
- Exact cause unknown, but it runs in families about 50% of the time.
- The location in the brain that controls tremor is the Vim of the thalamus.



Essential Treatment Options



1ST LINE OF THERAPY

- Medications
- **Only 40-50%** of patients receive benefit from currently available medications such as Propranolol and Primidone

INVASIVE SURGERY

- Deep Brain Stimulation (DBS)
- Good tremor control, however requires 2 interventions with hardware implanted in brain and chest
- Risk of infection
- Lifetime of maintenance

INCISIONLESS MR-GUIDED FOCUSED ULTRASOUND SURGERY

- Immediate reduction of hand tremor
- Incisionless
- Low to no risk of infection
- Little to no hospitalization
- Fast recovery

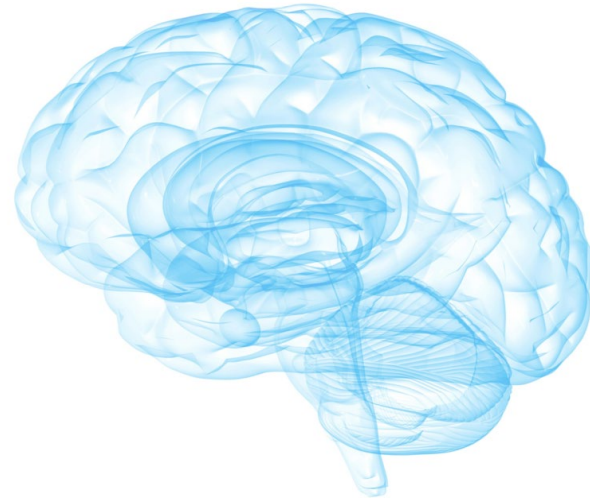
What is Neuravive MR-Guided Focused Ultrasound?

Focused Ultrasound

- More than 1,000 beams safely pass through the skull and brain
- Only where they meet, the temperature rises to create a tiny burn in the Vim

MR Imaging

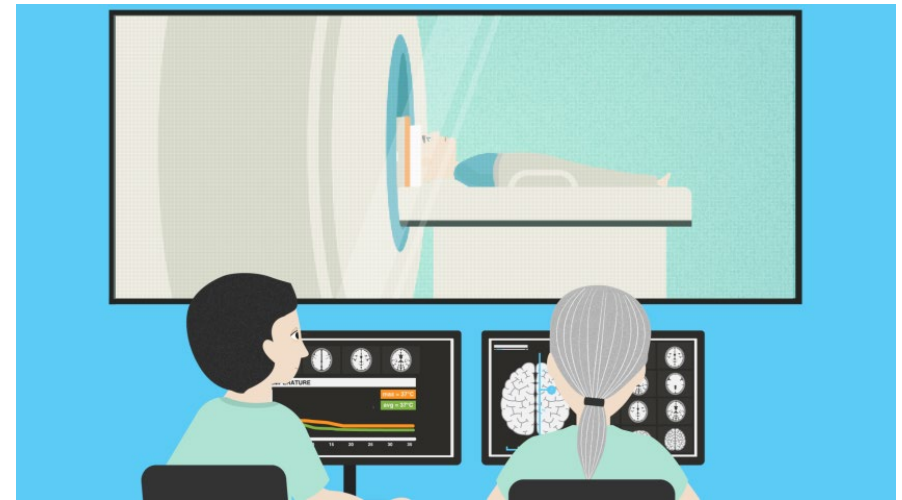
- Provides clear images of the treatment area for patient-specific planning
- Monitors temperatures in real-time for safety



The thalamus is about the size of a walnut.
The ablation is about 5mm in size. ●

Who is a candidate for Neuravive?

- A confirmed diagnosis of medication-refractory essential tremor.
- Men and women age 22 years or older.
- Patient is able to tolerate the procedure with or without some form of sedation (e.g., conscious sedation), communicate sensations during the procedure, fit in the MRI scanner and activate the Stop Sonication button.



What to expect during the Neuravive Treatment



Patient Prep

The patient's head is shaved so nothing interferes with the ultrasound beams. After local numbing medication is applied, a frame is secured to their head.



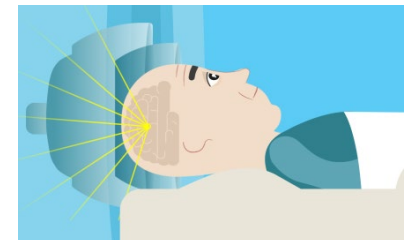
Planning

During the treatment, the patient is awake and lies inside the MRI scanner. MR images are taken to plan the treatment.



Target Verification

Light doses of energy are applied to accurately pinpoint the target and assess tremor improvement and identify any potential side effects.

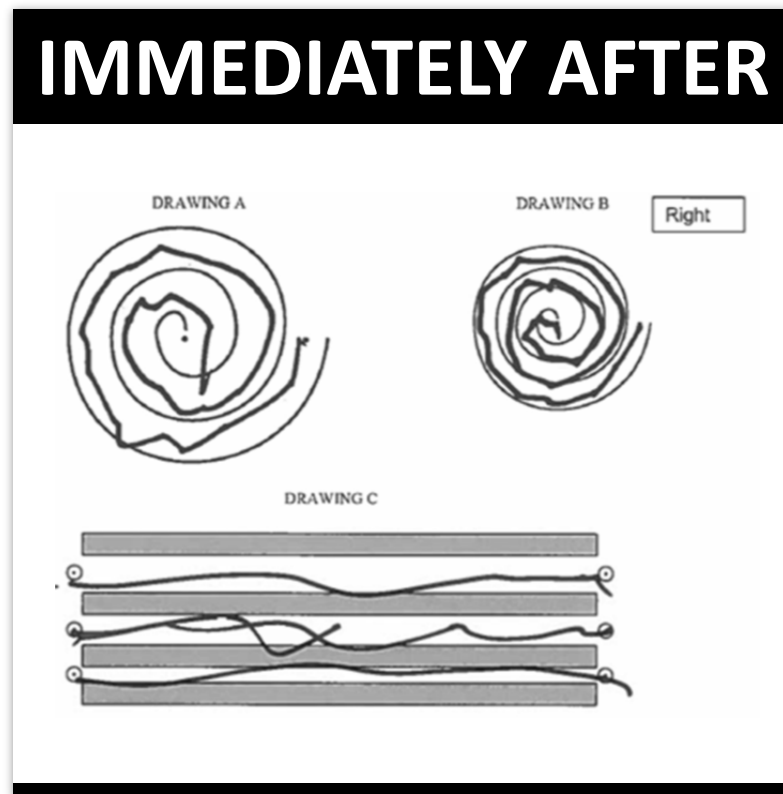
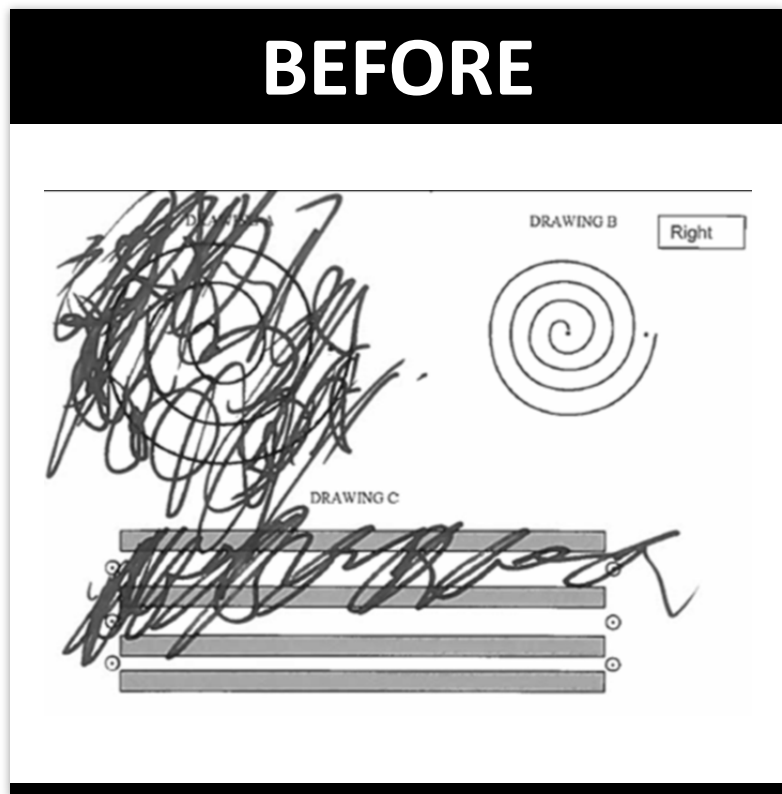


Treatment

High energy is applied to create a small ablation, or burn and provide a therapeutic effect, reducing the hand tremor.

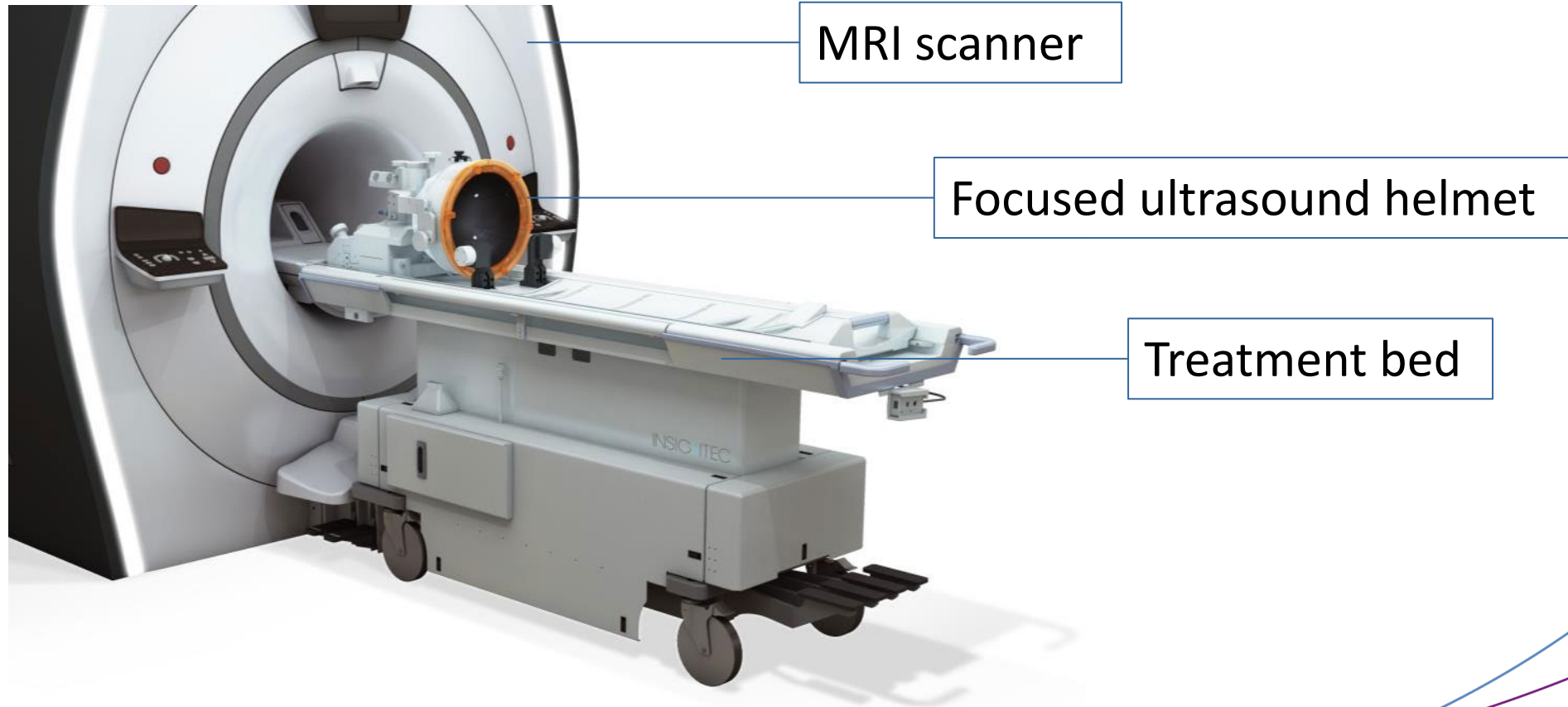
What results can be expected?

Many patients show immediate tremor improvement in their dominant hand.



This may not be representative of all treatment outcomes.

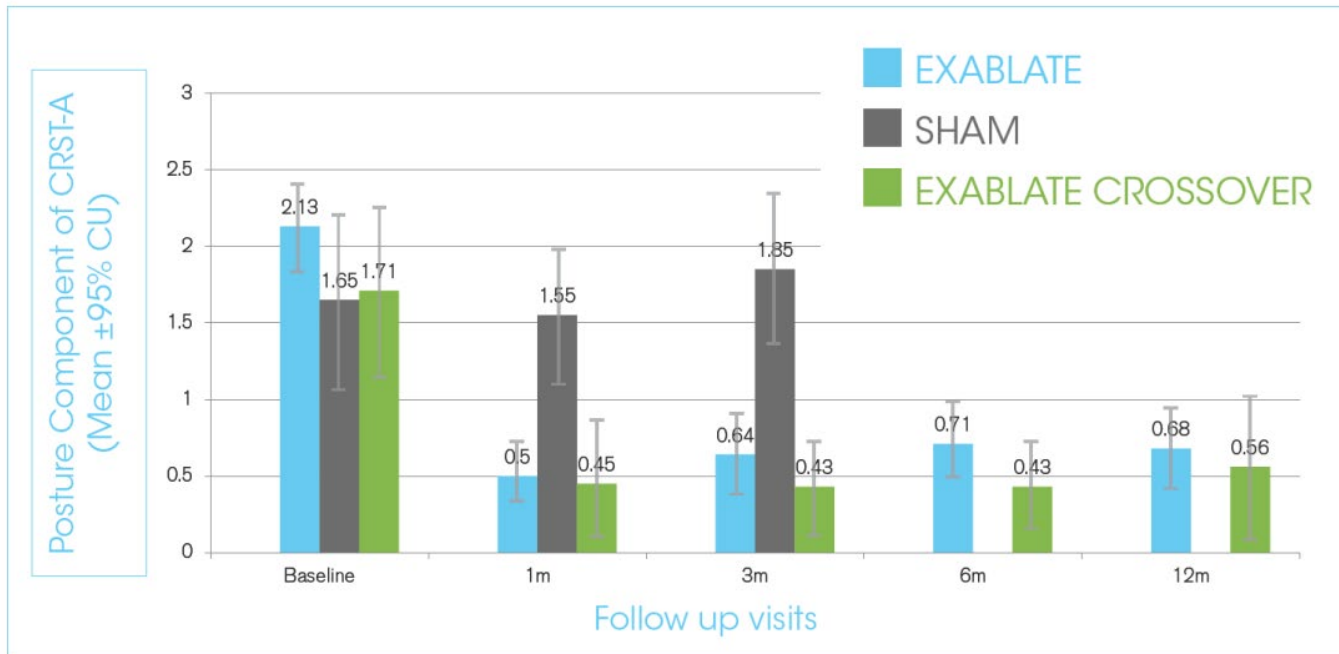
The Exablate Neuro System



Clinical Evidence: Reduction in Tremor

In a multicenter clinical trial, results showed a **69.5% reduction in tremor amplitude** at 3 months, which was maintained at 24 months.

CRST PART A POSTURE SCORE



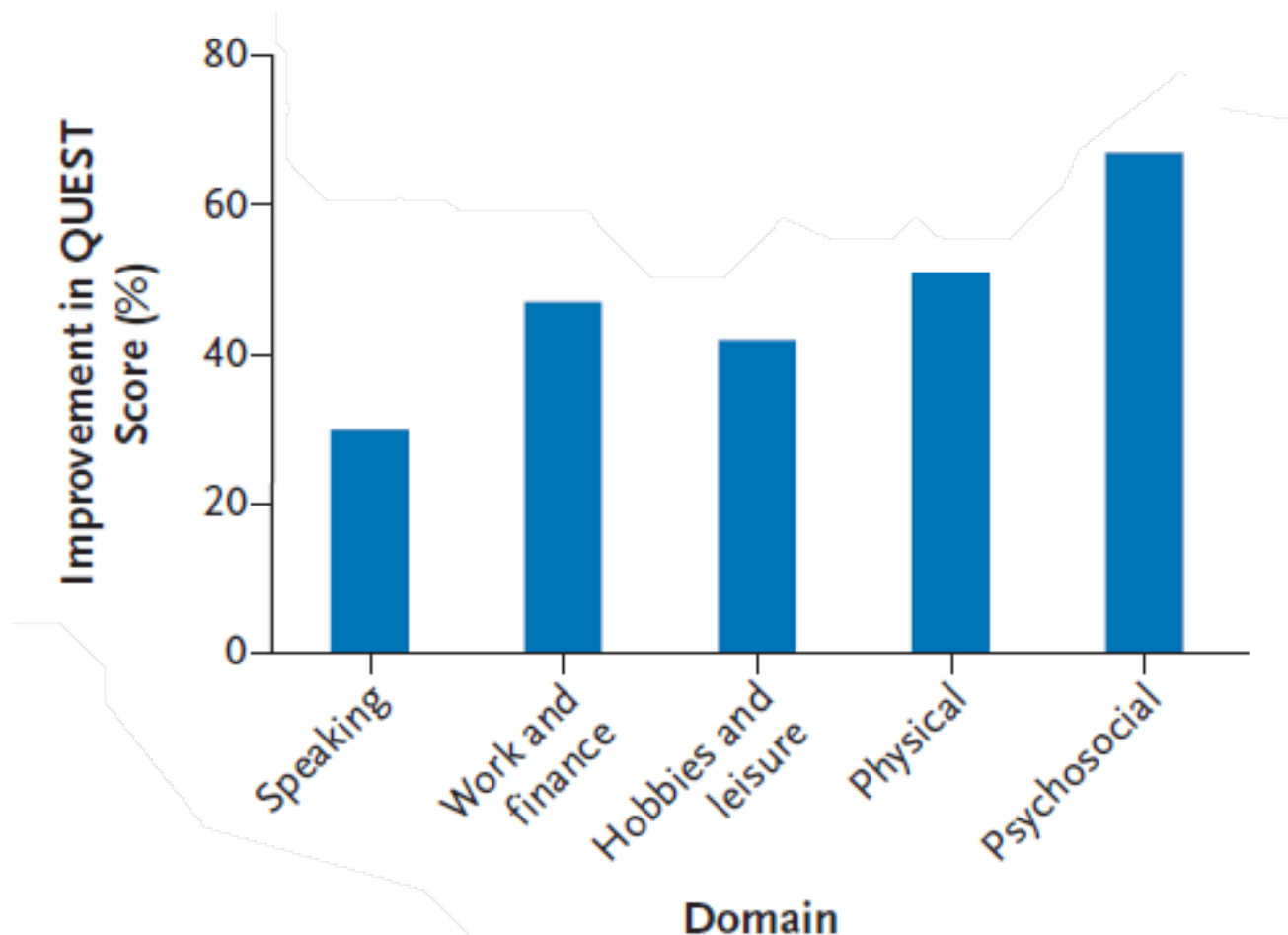
The NEW ENGLAND JOURNAL of MEDICINE



Elias WJ, Lipsman N, Ondo WG, Ghanouni P, Kim YG, Lee W, Schwartz M, Hynynen K, Lozano AM, Shah B, Huss D, Dallapiazza RF, Gwinn R, Witt J, Ro S, Eisenberg HM, Fishman PS, Gandhi D, Halpern CH, Chuang R, Butts Pauly K, Tierney TS, Hayes MT, Cosgrove GR, Yamaguchi T, Abe K, Taira T, Chang JW. An International, Randomized, Controlled Trial of Focused Ultrasound Thalamotomy for Essential Tremor. The New England Journal of Medicine, Aug 2016.

Clinical Evidence: Improvement in QOL

QUEST Scores representing Quality of Life (QoL) significantly improved **47.4%** at 12 months



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JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Randomized Trial of Focused Ultrasound Thalamotomy for Essential Tremor

W. Jeffrey Elias, M.D., Nir Lipsman, M.D., Ph.D., William G. Ondo, M.D.,
Feyzi Ghanouni, M.D., Ph.D., Young G. Kim, M.D., Ph.D., Worhlee Lee, M.D., Ph.D.,
Michael Schwartz, M.D., Kallevo Hynnen, Ph.D., Andres M. Lozano, M.D.,
Binli B. Shah, M.D., Diane Huss, D.P.T., N.C.S., Robert F. Dallapiazza, M.D., Ph.D.,
Byder Gwinn, M.D., Jennifer Witt, M.D., Susie Ro, M.D.,
Howard M. Eisenberg, M.D., Ph.D., Paul S. Fishman, M.D., Ph.D.,
Dhara Gandhi, M.D., M.B., B.S., Casey H. Halpern, M.D.,
Rosalind Chuang, M.D., Kim Butts Pauly, Ph.D., Travis S. Tierney, M.D., Ph.D.,
Michael T. Hayes, M.D., G. Rees Cosgrove, M.D., Toshio Yamaguchi, M.D., Ph.D.,
Keichi Abe, M.D., Takaoi Taira, M.D., Ph.D., and Jin W. Chang, M.D., Ph.D.

ABSTRACT

BACKGROUND
Uncontrolled pilot studies have suggested the efficacy of focused ultrasound thalamotomy with magnetic resonance imaging (MRI) guidance for the treatment of essential tremor.

METHODS
We studied patients with moderate-to-severe essential tremor that had not responded to at least two trials of medical therapy and randomly assigned them in a 1:1 ratio to undergo unilateral focused ultrasound thalamotomy or a sham procedure. The Clinical Rating Scale for Tremor and the Quality of Life in Essential Tremor Questionnaire were administered at baseline and at 1, 3, 6, and 12 months. Tremor assessments were videotaped and rated by an independent group of neurologists who were unaware of the treatment assignments. The primary outcome was the between-group difference in the change from baseline to 3 months in hand tremor, rated on a 32-point scale (with higher scores indicating more severe tremor). After 3 months, patients in the sham-procedure group could cross over to active treatment (the open-label extension cohort).

Elias WJ, Lipsman N, Ondo WG, Ghanouni P, Kim YG, Lee W, Schwartz M, Hynnen K, Lozano AM, Shah B, Huss D, Dallapiazza RF, Gwinn R, Witt J, Ro S, Eisenberg HM, Fishman PS, Gandhi D, Halpern CH, Chuang R, Butts Pauly K, Tierney TS, Hayes MT, Cosgrove GR, Yamaguchi T, Abe K, Taira T, Chang JW. An International, Randomized, Controlled Trial of Focused Ultrasound Thalamotomy for Essential Tremor. The New England Journal of Medicine, Aug 2016.

Clinical Evidence: Temporary Side Effects During Treatment

Adverse Events	Number n=56	%
Heat or pressure discomfort	17	30%
Vertigo	12	21%
Nausea	11	20%
Vomiting	2	4%
Scalp tingling	4	7%
Back pain	5	9%
Anxiety	3	5%
Pain, edema, bruising due to frame	17	30%

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Clinical Evidence: Side Effects at 12 months

Adverse Events	Number n=56	%
Paresthesias (tingling or numbness)	8	14%
Taste Disturbance	2	4%
Ataxia (objective) (lack of coordination when walking)	2	4%
Unsteadiness (subjective)	3	5%
Dysmetria (difficulty judging distance)	2	4%
Weakness	1	2%
Vertigo	1	2%

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Neuravive Treatment for Essential Tremor

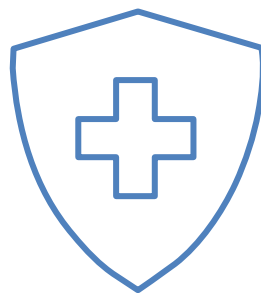
Benefits

- The first & only focused ultrasound treatment for ET approved by FDA
- Results immediately following treatment



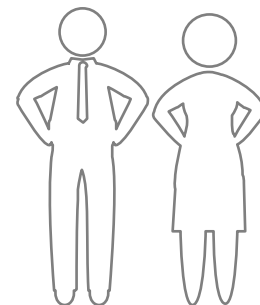
Safety Benefits

- Incisionless
- No implants
- No radiation
- Low risk of infection



Patient Benefits

- Outpatient/short hospitalization
- Short recovery
- Return to normal life within days





Thank You!

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