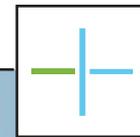


# Exablate Neuro

INCISIONLESS  
MR-GUIDED FOCUSED  
ULTRASOUND FOR  
ESSENTIAL TREMOR &  
TREMOR-DOMINANT  
PARKINSON'S DISEASE



Tremor can take away a person's independence, self-esteem and the freedom to live an active life by impacting the person's ability to function in the workplace and perform daily activities. Exablate Neuro™ is FDA-approved to treat medication-refractory essential tremor and tremor-dominant Parkinson's disease.

## FOCUSED ULTRASOUND THALAMOTOMY

### by Exablate Neuro

MR-guided focused ultrasound is a next generation incisionless thalamotomy for patients who don't get acceptable tremor relief from medication. With no incisions or implants, the risk of infection is minimized or eliminated, hospitalization is minimized or avoided altogether, and patients can return quickly to their lives.

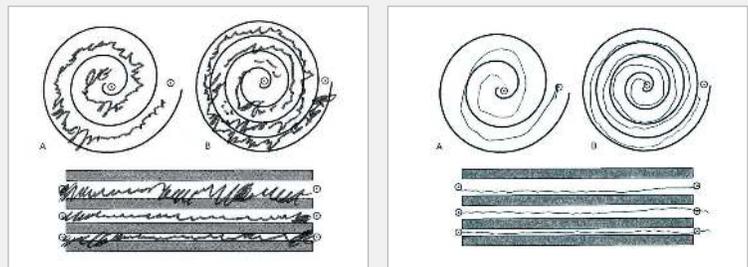
Thermal ablation of the ventral intermediate nucleus (Vim) of the thalamus is done under MR imaging for visualization of patient anatomy, real-time thermometry as well as immediate confirmation of treatment outcome.

During the procedure, patients are awake and responsive to evaluate treatment response including tremor improvement and potential side effects. Many patients report immediate and lasting improvement of the tremor in their treated hand.

### WHY REFER PATIENTS?

- Tremor improvement immediately post-procedure.<sup>1</sup>
- No craniotomy with low to no risk of infection or bleeding.
- No implanted hardware or multiple follow up visits.
- Minimal hospitalization.
- Majority of adverse events were minor or moderate, and were transient.<sup>1</sup>

Example of essential tremor patient writing tasks before and after the Exablate Neuro treatment.



Before

After

### PATIENT SELECTION

- A confirmed diagnosis of medication-refractory tremor from essential tremor or tremor-dominant Parkinson's disease.
- Men and women age 22 years or older for ET and 30 years or older for TDPD.
- 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.

### ET 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.

### TREMOR-DOMINANT PD INDICATIONS FOR USE

The Exablate Model 4000 ("Neuro") is intended for use in the unilateral Thalamotomy (ventralis intermedius) treatment of Tremor-dominant Parkinson's Disease with medication-refractory tremor. Patients must be at least age 30.

### Medication-refractory essential tremor

A randomized, blinded sham pivotal study was performed to assess the safety and efficacy of unilateral focused ultrasound thalamotomy for patients with essential tremor. Of the total 75 subjects treated, 57 are included in the 2-year and 54 in the 3-year analysis of the long-term study results.<sup>2</sup>

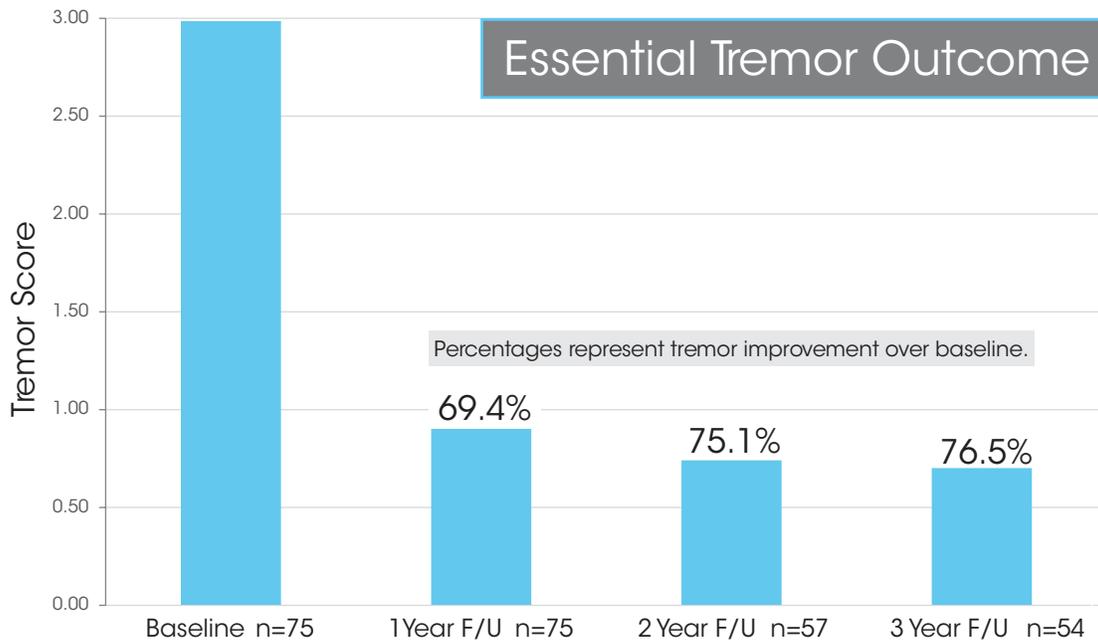
Tremor improvement was shown under the study to be durable.<sup>1</sup>

- The tremor severity score (CRST Part A posture score) improved 75.1% and 76.5% over baseline at 2- and 3-year follow-up, respectively, for combined (Exablate Neuro and crossover) subjects.
- Improvement in tremor/motor function (CRST Part A & B) was 53.1% at 3-years.

Functional disability (CRST Part C) showed a 64.0% improvement at one year with some decline to 56.9% improvement over baseline at three years under the study.

Long-term follow-up under the study continues to support a favorable safety profile:

- No new device or procedure adverse events were reported
- Long-term safety profile confirms that 74% of AEs were mild and the rest were moderate. Of the total AEs, 48% resolved within 30 days of the procedure.
- Persistent adverse events (AEs) at 3 years were mild or moderate and included gait disturbance (2%), imbalance (4%), musculoskeletal weakness (2%), unsteadiness (4%) and numbness (9%). The number in parenthesis is the percentage of active subjects experiencing these adverse events.



### Medication-refractory tremor-dominant Parkinson’s disease

A randomized, double-blinded sham pilot study<sup>3</sup> was performed to assess the safety and efficacy of unilateral focused ultrasound thalamotomy for patients with disabling tremor-dominant PD.

The study showed significant improvement in tremor that was maintained through 12-month follow up.

- Change in the tremor-motor sub-score (CRST Part A & B) for the focused ultrasound treated group (n=20) was 51.9% compared to 12.7% for the sham group (n=7) at 3 month follow-up.
- The improvement for the focused ultrasound group was also shown in functional outcome (CRST Part C) and Quality of Life (QUEST) measures.

The study showed a favorable safety profile for unilateral focused ultrasound thalamotomy:

- 95% of AEs were reported as mild or moderate. Most were transient.
- The most common treatment-related complications included numbness/tingling (7%), imbalance (4%), gait disturbance (2%) and unsteadiness (1%). The number in parenthesis is the percentage of active subjects experiencing these adverse events.
- Two treatment-related severe AEs were reported: one subject experienced ataxia/hemiparesis which resolved in 30 days and one subject experienced severe hemiparesis.

# Exablate Neuro



## CONTRAINDICATIONS

- Patients with standard contraindications for MR imaging such as non-MRI compatible implanted metallic devices including cardiac pacemakers, size limitations, allergies to MR contrast agent etc.
- Patients who have an overall Skull Density Ratio of 0.45 ( $\pm 0.05$ ) or less as calculated from the screening CT.
- Patients with a history of abnormal bleeding, hemorrhage, and/or coagulopathy.
- Patients receiving anticoagulant or drugs known to increase risk of hemorrhage within one month of focused ultrasound procedure.
- Patients with advanced kidney disease or on dialysis, unstable cardiac status, severe hypertension, cerebrovascular disease or brain tumors.
- Patients exhibiting any behavior(s) consistent with ethanol or substance abuse.
- Patients who are not able or unwilling to tolerate the required prolonged stationary position during treatment (approximately 2 hours).
- Pregnant women.

## SAFETY INFORMATION

Infrequent complications that have been reported following the Neuravive treatment are described below.

### SHORT TERM RISKS: DAY OF TREATMENT UP TO 3-MONTHS POST-TREATMENT

The most common potential risks associated with the Exablate Neuro device and thalamotomy procedure are transient numbness and tingling. These sensations are typically mild to moderate in intensity and can last as briefly as the length of the sonication or up to several days. Headaches or head pain and nausea/vomiting may occur during sonication. Imbalance, unsteadiness, and bruising in the area of the IV catheter are also potential risks, but usually end within a week after treatment.

### LONG TERM RISKS: LONGER THAN 3-MONTHS POST-TREATMENT

Overall, Exablate MRgFUS has a very favorable safety profile in treating Tremor-Dominant Parkinson's Disease. Infrequent complications that have been reported following Exablate treatment include long-term numbness and tingling. If you experience a blood clot or deep vein thrombosis after the procedure that is not treated urgently, you may experience long term complications, including muscle, heart, brain or lung damage.

Note: The system may only be operated by licensed Neurosurgeons that have successfully completed the INSIGHTEC Exablate training program.

<sup>1</sup>Information for Prescribers. <https://www.insightec.com/media/31393/exablateneuroinformationforprescribers0usa.pdf>

<sup>2</sup> Chang, JW, Park, CK, Lipsman, N, Schwartz, ML, Ghanouni, P, Henderson, JM, Gwinn, R, Witt, J, Tierney, TS, Cosgrove, GR, Shah, BB, Abe, K, Taira, T, Lozano, AM, Eisenberg, HM, Fishman, PS, Elias, WJ. A Prospective Trial of Magnetic Resonance-Guided Focused Ultrasound Thalamotomy for Essential Tremor: Results at the 2-Year Follow-up. ANNALS of Neurology. 2018;83:107-114

<sup>3</sup> Bond, AE, Shah, BB, Huss, DS, Dallapiazza, RF, Warren, A, Harrison, MB, Sperling, SA, Xin-QunWang, Gwinn, R, Witt, J, Ro, S, Elias, WJ. HYPERLINK "<https://archneur.jamanetwork.com/article.aspx?doi=10.1001/jamaneurol.2017.3098>" Safety and Efficacy of Focused Ultrasound Thalamotomy for Patients With Medication-Refractory, Tremor-Dominant Parkinson Disease. JAMA Neurology 2017.