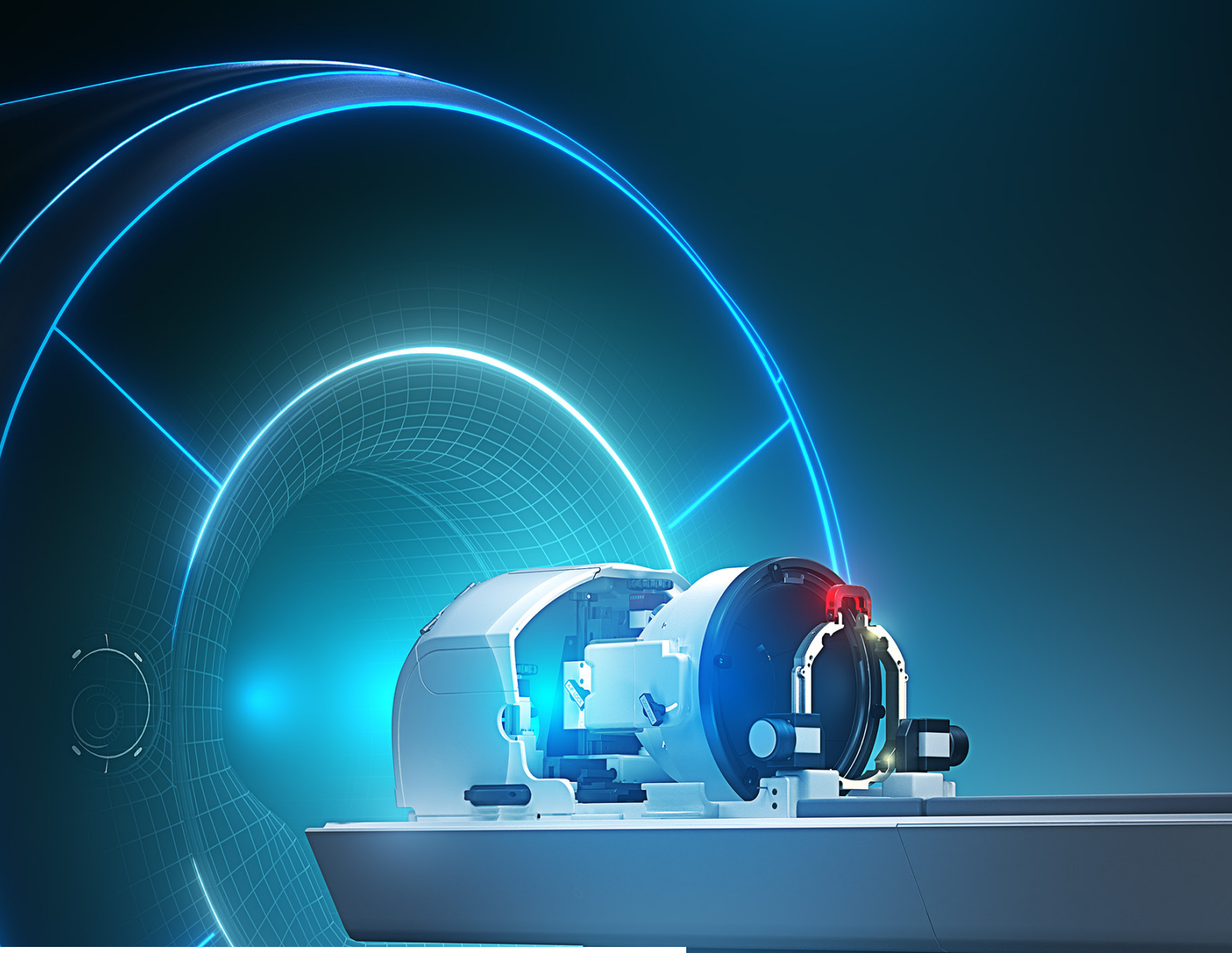

INSIGHTEC

CLINICAL STUDY **RESULTS**

Focused Ultrasound Thalamotomy for Essential Tremor

Background

Essential tremor impacts a person's ability to live an independent and active lifestyle by taking away their ability to perform certain daily activities. When an essential tremor patient does not get tremor relief from medications, invasive surgical interventions, may be considered. Focused ultrasound provides a new incisionless treatment option for essential tremor patients who do not respond to medications and do not want to have invasive surgery.

Insightec-sponsored clinical trials of focused ultrasound thalamotomy in patients with essential tremor have shown a durable reduction in hand tremor and improvement in quality of life.

Here we present an overview of the 2-and 3-year data from the long-term follow-up of the pivotal study of MRI-guided focused ultrasound thalamotomy for the treatment of medication-refractory essential tremor. For the up-to-date clinical results, please see Premarket Approval P150038:

www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P150038

Methods

Patients age 22 and older with moderate-to-severe essential tremor who did not show a response to at least two trials of medication were randomly assigned (3:1) to unilateral focused ultrasound thalamotomy or sham procedure. After 3 months, patients in the sham group could choose to cross over to active treatment. In the pivotal phase of this trial, patients were assessed with The Clinical Rating Scale for Tremor (CRST Parts A, B & C) and the Quality of Life in Essential Tremor Questionnaire (QUEST) at baseline,3 months, 6 months and 12 months.

As part of the long term follow-up of this study, all participating subjects continued to be followed for general health, efficacy measurements and device/procedure related adverse events (AEs) at 2 and 3 years. The long-term safety was assessed by evaluating any new adverse events that occurred during the follow-up period as well as events that were ongoing as of the 12-month follow-up visit.

Efficacy was assessed by the change from baseline in tremor motor function score using the Clinical Rating Scale for Tremors (CRST Part A + B combined), upper extremity posture score (CRST Part A), functional disability (CRST Part C) and Quality of Life using the Questionnaire for Essential Tremor (QUEST).

Clinical 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 57 subjects are included in the 2-year and 54 in the 3-year analysis of the long-term study results.

Safety

The most common adverse events experienced after treatment included:

- 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. 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%)
- Musculoskeletal weakness (2%)

Additional infrequent events include dizziness, taste disturbance, slurred speech, fatigue and vomiting.

Efficacy

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. The percentage of tremor improvement over baseline is shown in the graph below.

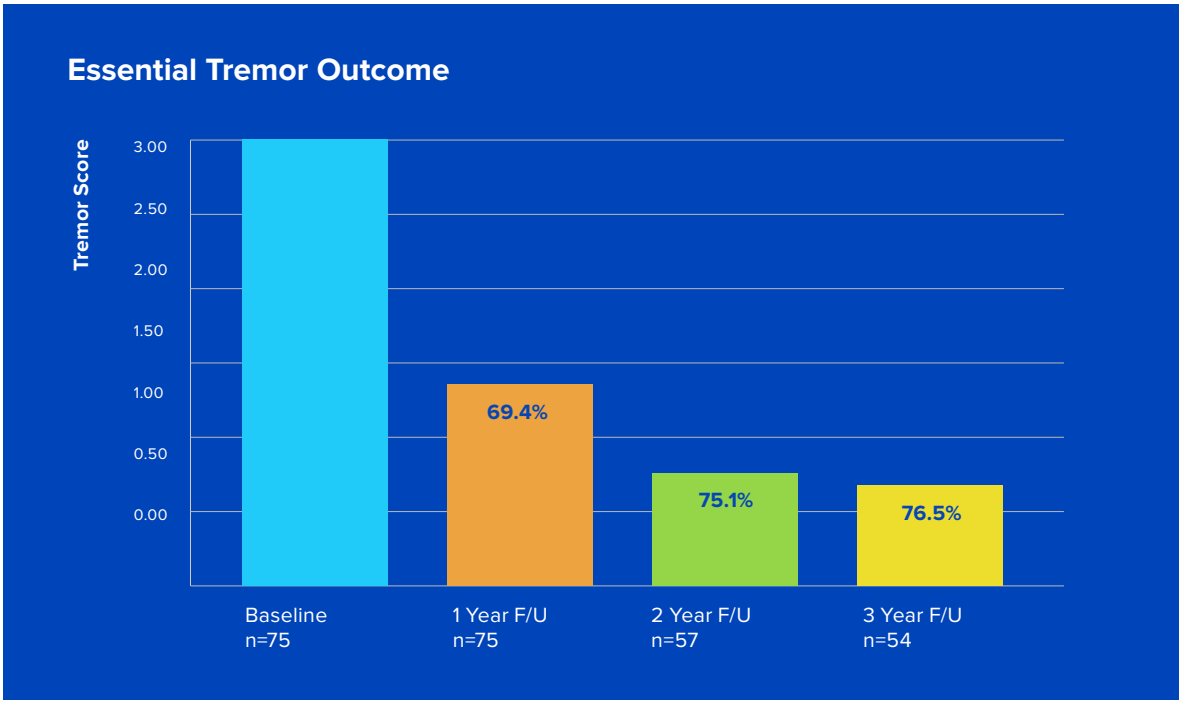

Figure 1: Percentage of tremor improvement over baseline.
Premarket Approval P150038
www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P150038

Additionally, improvement in tremor/motor function (CRST Part A & B) was 39.6% at one year and 53.1% at three 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.

About Exablate Neuro

Exablate Neuro is a first-to-market Focused Ultrasound platform that delivers precise and controlled thermal ablation to a target deep in the brain in a single outpatient procedure. To perform a focused ultrasound thalamotomy, energy is delivered to the target in the Vim nucleus of the thalamus to cause a therapeutic effect.

First, low energy is applied to evaluate patient response including tremor improvement as well as potential side effects. This allows the treating physician to fine tune the target in sub-millimeter adjustments before making the permanent lesion. High energy is then applied to heat and ablate the target tissue. The treatment is guided by MR imaging for patient-specific planning, continuous real-time temperature monitoring as well as immediate confirmation of treatment outcome. Many patients demonstrate immediate improvement in their hand tremor as well as improved quality of life with minimal complications.

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Device name: Exablate Neuro