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., Pejman Ghanouni, M.D., Ph.D., Young G. Kim, M.D., Ph.D., Wonhee Lee, M.D., Ph.D., Michael Schwartz, M.D., Kullervo Hynynen, Ph.D., Andres M. Lozano, M.D., Binit B. Shah, M.D., Diane Huss, D.P.T., N.C.S., Robert F. Dallapiazza, M.D., Ph.D., Ryder Gwin, M.D., Jennifer Witt, M.D., Susie Ro, M.D., Howard M. Eisenberg, M.D., Ph.D., Paul S. Fishman, M.D., Ph.D., Dheeraj 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., Takaomi Taira, M.D., Ph.D., and Jin W. Chang, M.D., Ph.D.

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 enrolled 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 3:1 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).

RESULTS
Seventy-six patients were included in the analysis. Hand-tremor scores improved more after focused ultrasound thalamotomy (from 18.1 points at baseline to 9.6 at 3 months) than after the sham procedure (from 16.0 to 15.8 points); the between-group difference in the mean change was 8.3 points (95% confidence interval [CI], 5.9 to 10.7; P<0.001). The improvement in the thalamotomy group was maintained at 12 months (change from baseline, 7.2 points; 95% CI, 6.1 to 8.3). Secondary outcome measures assessing disability and quality of life also improved with active treatment (the blinded thalamotomy cohort) as compared with the sham procedure (P<0.001 for both comparisons). Adverse events in the thalamotomy group included gait disturbance in 36% of patients and paresthesias or numbness in 38%; these adverse events persisted at 12 months in 9% and 14% of patients, respectively.

CONCLUSIONS
MRI-guided focused ultrasound thalamotomy reduced hand tremor in patients with essential tremor. Side effects included sensory and gait disturbances. (Funded by InSightec and others; ClinicalTrials.gov number, NCT01827904.)
Essential tremor, the most common movement disorder,\(^1\) is characterized by a distinctive postural and intention tremor typically affecting the hands more than the legs, trunk, head, or voice.\(^2,3\) Essential tremor does not shorten life expectancy, but it can affect quality of life, functional activities, mood, and socialization.\(^4-6\)

Class I evidence exists for propranolol and primidone as first-line medications that reduce tremor by approximately 60% in 50% of patients.\(^7-11\) If resistance to medications develops or side effects are unacceptable, neurosurgical intervention is considered, primarily targeting the nucleus ventralis intermedius of the thalamus, a component of tremor circuitry that connects the cerebellum with cortical motor pathways. Two surgical therapies, radiofrequency thalamotomy and deep-brain stimulation, effectively suppress tremor,\(^2-16\) but relatively few patients choose surgery because of perceived invasiveness from the burr holes and intracerebral electrodes.

The use of ultrasound energy for the creation of discrete intracranial lesions (hereafter referred to as lesioning) has been of interest since the middle of the 20th century.\(^17\) Initial procedures required craniotomy to establish an acoustic window for the treatment of movement disorders and psychiatric conditions.\(^18,19\) The subsequent introduction of phased-array transducers\(^20\) eliminated the need for a craniotomy, and high-resolution imaging\(^21,22\) allows real-time, image-guided lesioning (see Fig. S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). Prospective pilot trials of focused ultrasound thalamotomy with magnetic resonance imaging (MRI) guidance in patients with essential tremor have shown reductions in hand tremor, improvements in quality of life, and minimal procedural morbidity.\(^23,25\) Here we describe the results of a prospective, sham-controlled trial of MRI-guided focused ultrasound thalamotomy for the treatment of medication-refractory essential tremor.

**METHODS**

**TRIAL DESIGN AND OVERSIGHT**

In this double-blind trial conducted at eight international centers, we randomly assigned patients in a 3:1 ratio to undergo focused ultrasound thalamotomy or a sham procedure in which no acoustic energy was delivered. The primary study end point was the change in tremor from baseline to 3 months, analyzed on the basis of videotaped assessments. After 3 months, patients in the sham-procedure group could cross over to active treatment (Fig. S2 in the Supplementary Appendix).

Representatives of the manufacturer of the focused ultrasound system used in the study (InSightec) provided study oversight and technical support and obtained national regulatory permissions. Independent institutional approval of the study was obtained by the research team at each participating center, and all patients gave written informed consent. Clinical oversight of the trial was provided by the principal investigator and an independent data and safety monitoring board. The authors vouch for the veracity and completeness of the data and data analyses. The first author wrote the first draft of the manuscript, and all authors made the decision to submit the manuscript for publication. The study was conducted with fidelity to the study protocol, which is available at NEJM.org.

**PATIENTS**

Patients with essential tremor, diagnosed by a neurologist specializing in movement disorders, were enrolled on the basis of eligibility criteria that have been described previously.\(^24\) Briefly, patients were eligible if they had a postural or intention tremor of the hand that was moderate to severe (defined by a score of ≥2 on the Clinical Rating Scale for Tremor\(^20\) [CRST; scores range from 0 to 4 per component assessed and higher scores indicate more severe tremor]) and disabling (defined by a score of ≥2 on any of the eight items in the disability subsection of the CRST [scores range from 0 to 4 per item, and higher scores indicate greater disability]). Additional eligibility criteria were tremor that was refractory to at least two trials of medical therapy, including at least one first-line agent (propranolol or primidone). For patients receiving concurrent medical therapy, medication doses had to be stable for 30 days before randomization. Patients were excluded if they had a neurodegenerative condition, unstable cardiac disease, coagulopathy, risk factors for deep-vein thrombosis, severe depression (defined by a score ≥20 on Patient Health Questionnaire 9 [scores range from 0 to 27, with higher scores indicating more severe depression]), or cognitive impairment (defined by a score of <24 on the...
Focused Ultrasound Thalamotomy
The details of focused ultrasound thalamotomy have been described previously.23-25 Briefly, patients were placed in a stereotactic head frame that was coupled to an MRI-compatible ultrasound transducer. After stereotactic targeting with the use of MRI, acoustic energy was sequentially titrated to temperatures sufficient for tissue ablation (approximately 55 to 60°C). Each brief sonication was monitored with magnetic resonance thermometry, and the patient was clinically assessed for tremor reduction and adverse effects (for details, see the description in the Supplementary Appendix).

For patients randomly assigned to undergo a sham procedure, an identical procedure was performed with a randomized number of sonifications for which the acoustic power was disengaged so that no acoustic energy was delivered to the brain. Only the treatment team was aware of the group assignments; patients and assessors were unaware of the assignments.

Outcome Assessments
Tremor assessments, based on the CRST,26 were performed at each site by a movement-disorder specialist, and functional status was determined on the basis of the rating for the disability subsection (Part C) of the CRST, as well as the diseasespecific, self-reported Quality of Life in Essential Tremor Questionnaire (QUEST).27 Tremor evaluations were videotaped for primary analysis by an independent core group of neurologists (Tremor Research Group) at baseline and at 1, 3, 6, and 12 months after treatment.

The primary efficacy outcome measure was defined as the change from baseline to 3 months in the tremor score for the hand in the thalamotomy group as compared with the sham-procedure group. The tremor score (on a scale ranging from 0 to 32, with higher scores indicating more severe tremor) was derived from the CRST, Part A (three items: resting, postural, and action or intention components of hand tremor), and the CRST, Part B (five tasks involving handwriting, drawing, and pouring), in the hand contralateral to the thalamotomy.

The three prespecified secondary efficacy measures were functional limitations in daily activities, measured according to eight items in the disability subsection of the CRST (maximum overall score, 32; higher scores indicate greater disability); quality of life, assessed with the QUEST at 3 months; and the durability of the reduction in hand tremor at 12 months. We also performed a post hoc analysis of total tremor scores (maximum overall score for the most severe tremor, 152 points without supine assessments). Safety was assessed throughout the study on the basis of reported adverse events. MRI was performed immediately after the study procedure and at 12 months.

BLINDING
The study participants and the neurologist at each site were unaware of the treatment assignments throughout the first 3 months, and the primary assessors of the videotaped tremor evaluations were not involved in the study treatments and were unaware of the treatment assignments and the side that was treated (left vs. right). Since the patients’ heads were not covered, the assessors could see whether the videotapes showed preoperative or postoperative tremor evaluations; however, they could not determine whether the videotapes were taken 1, 3, 6, or 12 months after treatment.

STATISTICAL ANALYSIS
We calculated the sample size from pilot-study observations, accounting for a potential dropout rate of 20%. The null hypothesis was that thalamotomy would be either the same as or inferior to the sham procedure with respect to the per-
percentage improvement in the primary end point. The alternative hypothesis was that thalamotomy would be superior to the sham procedure. Given a sample of at least 60 patients, the study had almost 100% power to show the primary efficacy of thalamotomy, assuming, on the basis of historical results, average improvements of 78% and 4% in the thalamotomy and sham-procedure groups, respectively (standard deviation, 25%). Power calculations were performed with the use of an independent-groups t-test, with a randomization ratio of 3:1 for assignment to thalamotomy versus the sham procedure. The probability of detecting an adverse event rate of 1% was 0.45, and the probability of a 5% rate was 0.95. The statistical analysis was planned and conducted with the assistance of the biostatistics team at TechnoSTAT. The statistical analysis plan (see the study protocol) was approved by the Food and Drug Administration (FDA).

We used a hierarchical testing design to control for multiple comparisons across the one primary and three prespecified secondary end points. The primary efficacy analysis was confirmed at an alpha level of 0.05, and then each of the three secondary efficacy end points was tested at an alpha level of 0.05. No confirmatory statements were made about other end points. Thus, type 1 error was controlled across all end points tested in this study.

A sensitivity analysis with multiple imputation was planned, but in the primary analysis, only two patients had missing data. Since worst-case and best-case scenarios yielded such similar results, additional imputation was not carried out. A second sensitivity analysis, performed because five patients were found to meet exclusion criteria after randomization, confirmed that their exclusion had no effect on the results of the primary outcome analysis (see the Supplementary Appendix). The data reported here were locked on September 17, 2015, and the report was finalized on October 14, 2015.

**RESULTS**

**STUDY PARTICIPANTS**

The 76 patients had a mean (±SD) age of 71.0±8.3 years (range, 47 to 89) and a mean disease duration of 16.8±12.3 years. Most of the patients were men (68%), right-handed (83%), and white (75%), and most had a family history of tremor (72%).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>FUS Thalamotomy (N = 56)</th>
<th>Sham Procedure (N = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age — yr</td>
<td>70.8±8.7</td>
<td>71.4±7.3</td>
</tr>
<tr>
<td>BMI†</td>
<td>26.9</td>
<td>27.9</td>
</tr>
<tr>
<td>Male sex — no. (%)</td>
<td>37 (66)</td>
<td>15 (75)</td>
</tr>
<tr>
<td>Race or ethnic group — no. (%)‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>41 (73)</td>
<td>16 (80)</td>
</tr>
<tr>
<td>Black</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Asian</td>
<td>14 (25)</td>
<td>4 (20)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>1 (2)</td>
<td>0</td>
</tr>
<tr>
<td>Disease duration — yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>From initial symptoms</td>
<td>28.3±16.4</td>
<td>27.9±14.9</td>
</tr>
<tr>
<td>From initial diagnosis</td>
<td>16.4±13.1</td>
<td>17.8±10.2</td>
</tr>
<tr>
<td>From start of medical therapy</td>
<td>13.9±10.7</td>
<td>14.7±10.5</td>
</tr>
<tr>
<td>Tremor score§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand</td>
<td>18.1±4.8</td>
<td>16.0±4.4</td>
</tr>
<tr>
<td>Overall</td>
<td>50.1±14.0</td>
<td>44.1±12.7</td>
</tr>
</tbody>
</table>

* Plus–minus values are means ±SD. There were no significant differences in baseline characteristics between the two study groups. FUS denotes focused ultrasound.
† The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters.
‡ Race or ethnic group was determined by the investigator.
§ The tremor score was derived from the Clinical Rating Scale for Tremor, which ranges from 0 to 32 for tremor in the hand and from 0 to 152 overall. In this study, the hand tremor was measured in the hand contralateral to the thalamotomy.

The mean total CRST score for tremor severity was 49.5 (highest possible score, 152). Baseline tremor and demographic characteristics did not differ significantly between the randomized groups (Table 1).

**TREMOR**

The mean score for hand tremor (highest possible score, 32) improved by 47% at 3 months (from 18.1±4.8 to 9.6±5.1) in the thalamotomy group and by 0.1% in the sham-procedure group (from 16.0±4.4 to 15.8±4.9). The between-group difference in the mean change at 3 months, the primary efficacy end point, was 8.3 points (95% confidence interval [CI], 5.9 to 10.7; P<0.001), indicating that there was greater improvement after focused ultrasound thalamotomy than after the sham procedure. The improvement in hand-tremor scores in the patients who underwent fo-
Cocused ultrasound thalamotomy persisted throughout the 12-month study period (change in the tremor score from baseline to 12 months, 7.2 points; 95% CI, 6.1 to 8.3; P<0.001), representing a 40% improvement (from a mean score of 18.1±4.8 to 11.6±5.5 at 3 months, P=0.50).

A total of 21 participants (19 assigned to the sham procedure group who crossed over to thalamotomy and 2 assigned to thalamotomy in whom the procedure was incomplete) were treated after the 3-month blinded assessment period. In this unblinded cohort, the mean score for tremor in the hand contralateral to the thalamotomy, assessed according to the same videotape procedures used for the 3-month assessment period, improved by 55% at 3 months (from 16.5±4.2 to 7.4±3.9, P<0.001) and by 52% at 6 months (from 16.5±4.2 to 8.0±3.9, P<0.001) (Table S1 and Fig. S3 in the Supplementary Appendix).

Even with this unilateral procedure, mean total tremor scores on the CRST improved by 41% at 3 months (from 50.1±14.0 at baseline to 29.6±13.0) and by 35% at 12 months (from 50.1±14.0 to 32.4±14.5). This improvement was not observed with the sham procedure; the mean total tremor score for patients who underwent the sham procedure was 44.1±12.7 at baseline and 43.1±13.1 at 3 months, representing a 2% change (P<0.001 for the between-group comparison of the change from baseline to 3 months). The improvement in total tremor scores in the cohort treated after the 3-month blinded phase was similar to the improvement in the patients who underwent thalamotomy during the blinded phase (Table S2 in the Supplementary Appendix).

Functional Improvement and Quality of Life
Focused ultrasound thalamotomy significantly improved the total disability score from Part C of the CRST at 3 months, as compared with the sham procedure (a 62% reduction in the score from baseline to 3 months [from 16.5±4.6 to 6.2±5.6] vs. a 3% reduction [from 16.0±4.3 to 15.6±4.6], P<0.001), and the improvement was sustained at 12 months (6.3±6.2). The mean disability scores at baseline were highest for drinking and writing. At 12 months, the score for every activity had improved, with a reduction to a score of 0 (normal) or 1 (mild disability) for each item except writing (1.2±1.1) (Fig. 2A and 2B, and Table S3 in the Supplementary Appendix).

Patients’ ratings of their quality of life, assessed on the basis of the QUEST score, also improved significantly at 3 months after focused ultrasound thalamotomy as compared with the sham procedure (a 46% reduction in the score from baseline to 3 months [from 42.6±18.3 to 23.1±16.9] vs. a 3% reduction [from 42.8±19.5 to 41.4±19.4],...
Focused Ultrasound Thalamotomy for Essential Tremor

P<0.001) (Fig. 2C and 2D, and Table S4 in the Supplementary Appendix). The largest improvement was in the psychosocial domain.

ADVERSE EVENTS

Adverse events associated with focused ultrasound thalamotomy included gait disturbance in 36% of patients and paresthesias or numbness in 38%; these adverse events persisted at 12 months in 9% and 14% of patients, respectively (Table 2). The sensory side effects of numbness or paresthesia involved the face (in 8 patients), hand (in 6), or both (in 6), presumably from involvement of the adjacent ventral posterolateral (sensory) nucleus. One patient had dense and permanent hypesthesia of the dominant thumb and index finger, categorized as a serious adverse event. Gait disturbances also occurred, with ataxia noted on postoperative neurologic examination (in 11 patients [20%]) and at 12 months (in 2 patients [4%]). Subjective unsteadiness was reported by 9 patients (16%), which persisted at 12 months in 3 patients (5%). Weakness contralateral to the thalamotomy, probably resulting from internal-capsule involvement, occurred in 2 patients, persisting for 6 months in 1 and 12 months in the other. Intracerebral hemorrhage was noted by 2 patients (4%) at 3 months and at 12 months.

Figure 2. Functional Activities of Daily Living and Quality of Life.

Panel A shows total disability scores, which were significantly improved at 3 months (P<0.001 for the between-group difference in the change from baseline) with unilateral FUS thalamotomy but not with the sham procedure. Panel B shows the percent improvement at 3 months after thalamotomy in individual activities typically affected by essential tremor. These eight items represent the disability subsection, or Part C, of the CRST. Panel C shows scores for patient-reported quality of life on the Quality of Life in Essential Tremor Questionnaire (QUEST). Scores were significantly improved at 3 months in the thalamotomy group as compared with the sham-procedure group (P<0.001 for the between-group difference in the change from baseline). Panel D shows the percent improvement at 3 months after thalamotomy in individual domains of the QUEST. The largest improvement in quality of life reported by patients was in the psychosocial domain.
procedural sensations resolved within seconds after the delivery of acoustic energy (Table 2). A similar profile of side effects was observed in the unblinded cohort of patients undergoing focused ultrasound thalamotomy (Table S5 in the Supplementary Appendix). One patient had a transient ischemic attack 6 weeks after undergoing thalamotomy (Table S6 in the Supplementary Appendix).
SONICATIONS
For the 56 patients undergoing focused ultrasound thalamotomy, a mean of 18.5±5.2 sonication were administered. The highest-energy sonication for tissue ablation delivered a mean acoustic energy of 14,497.0±6695.7 J (range, 3500 to 34,860), which resulted in a mean peak voxel temperature of 55.6±3.3°C (range, 50.0 to 60.7). The sham-procedure cohort received an average of 15.3±2.3 sonications, with no energy or heating delivered. In 39 active treatments, intraoperative clinical or imaging feedback led to a mean adjustment in the stereotactic target location by 1.6±1.1 mm (range, 1.1 to 5.5). In 5 patients, the full therapeutic temperature could not be achieved, despite their receiving similar doses of acoustic energy.

SURVEY OF PATIENTS AND ASSESSORS ABOUT RANDOMIZED ASSIGNMENTS
Special procedures were implemented to ensure blinding of the treatment assignments. Even so, 95% of patients who underwent active treatment and 80% of those who underwent the sham procedure correctly guessed their assignment immediately after the procedure. At the end of the 3-month blinded phase, the correct guesses were 86% and 95%, respectively, with patients accrediting their opinion to the clinical effect of the treatment or lack thereof. Assessors who reviewed the videotaped examinations at 3 months correctly identified the treatment assignment for 70% of the patients in the active-treatment group and 75% of those in the sham-procedure group, most likely on the basis of the presence or absence of a clinical effect.

DISCUSSION
In this randomized, controlled trial involving 76 patients with medication-refractory essential tremor, transcranial focused ultrasound thalamotomy significantly reduced hand tremor at 3 months, and the effect persisted during the 12-month study period. This unilateral procedure reduced disability and improved quality of life as measured by a patient questionnaire that is specific for essential tremor.

The trial was controlled with a sham procedure, and the results show that tremor reduction was related to treatment, not a placebo effect. In addition, the Tremor Research Group, a group of experts who were not involved in the treatments, was recruited to objectively evaluate the clinical outcomes from videotape analysis. There was high accountability in this trial, with 97% of patients completing study visits throughout the 3-month primary assessment period, and 91% of the thalamotomy group assessed through 12 months (Fig. S2 in the Supplementary Appendix).

Even though the procedure is transcranial and involves no incision or craniotomy, it does create a thalamic lesion, which can result in permanent neurologic deficits. There were 74 neurologic adverse events reported in the 56 patients who underwent active treatment. The most common side effect was an alteration in sensation, which was reported by 38% of the patients and persisted at 12 months in 14%. Gait disturbance occurred in 36% of patients and persisted at 12 months in 9%. The incidence of cerebellar deficits such as dysmetria, ataxia, and subjective unsteadiness of gait approached 5% each at 12 months. There were no infectious or hemorrhagic events, but contralateral weakness occurred twice. Qualitatively, the intensity of side effects seemed to peak at approximately 1 week, corresponding to the maximal size of the lesion with perilesional edema.

Although randomized, controlled studies of medical therapies have shown tremor reductions in roughly 50% of study participants, these studies were performed at the early stages of the disease. The current trial shows that focused ultrasound thalamotomy can further control tremor when it has become advanced and resistant to medication.

Deep-brain stimulation is currently the surgical standard for medication-refractory essential tremor. Since FDA approval of the procedure in 1997, numerous studies have confirmed that it is highly effective for tremor suppression, but guidelines have classified the findings as level C evidence in the absence of placebo-controlled trials. Deep-brain stimulation has been safely administered for bilateral and axial symptoms. The procedure requires surgical placement of a neurostimulator that can be reversed and adjusted to minimize side effects. Focused ultrasound thalamotomy is also an invasive intervention, which can result in permanent side effects as a consequence of tissue ablation. A control group of patients undergoing deep-brain stimulation was not included in this trial; the two technologies were not compared.
Stereotactic radiofrequency thalamotomy for tremor has been available since the 1950s, with numerous retrospective studies documenting efficacy similar to that of thalamic stimulation. Recently, a prospective, uncontrolled trial of stereotactic radiosurgery showed improvements in tremor from blinded, videotaped ratings at 1 year. Radiosurgical thalamotomy has not been embraced because intraoperative validation is not possible, the effects are delayed, and there are theoretical concerns about radiation side effects, secondary neoplasia, and a less-sharp dose gradient.

Our study has several limitations. First, the procedures were all performed unilaterally. Although unilateral focused ultrasound thalamotomy improved total tremor scores by 47% in the study cohort, there was no reduction of ipsilateral tremor and only minimal improvement in axial tremors of the head, neck, and voice. Second, some patients may be reluctant or unwilling to undergo MRI studies or it may be unsafe for them to do so. Third, lesioning procedures require a balance between the size of the lesion and the risk of adverse effects, since larger lesions are expected to have more enduring efficacy but a greater incidence of side effects. Finally, transcranial delivery of focused ultrasound was difficult to achieve in five of the study patients, probably because of the frequency and other properties of the acoustic wave, as well as individual cranial characteristics. Additional research is needed to address this issue.

In conclusion, our study showed that MRI-guided focused ultrasound thalamotomy reduced hand tremor and improved the quality of life in patients with essential tremor. Side effects included sensory and gait disturbances. The benefits and risks of focused ultrasound thalamotomy performed in a carefully controlled clinical trial may differ from the benefits and risks with routine practice in diverse clinical settings.

Supported by InSightec, the Focused Ultrasound Foundation, and the Binational Industrial Research and Development (BIRD) Foundation.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank Rodger Elble, M.D., Ludy Shih, M.D., Peter Lewitt, M.D., Raj Pahwa, M.D., Dan Tarsy, M.D., and Theresa Zesiewicz, M.D., of the Tremor Research Group for performing videotape tremor ratings, and Vera Hashem, Ph.D., for coordinating the core laboratory.

REFERENCES

1. Louis ED, Ferreira JJ. How common is the most common adult movement disorder? Update on the worldwide prevalence of essential tremor. Mov Disord 2010;25: 534-41.
17. Fry WJ, Mosberg WH Jr, Barnard JW,
Focused Ultrasound Thalamotomy for Essential Tremor


Copyright © 2016 Massachusetts Medical Society.