

FOCUSED ULTRASOUND (FUS) **PATIENT EDUCATION** **SERIES**

**INCISIONLESS.
OUTPATIENT.
LIFE-CHANGING.**

SPEAKER DETAILS

Presenter:

Dr. Michael Horowitz

HCA Florida Orange Park

- Dr. Michael Horowitz is Board Certified in Neurological Surgery, Fellowship Trained in Endovascular Neurointerventional Surgery, and CAST Certified in Endovascular Neurosurgery
- He graduated with a Highest Honors BA from Williams College in Williamstown, MA
- He was granted his Medical Degree from the University of Rochester in Rochester, NY.
- After completing a Neurological Surgery Residency at the University of Pittsburgh, he completed a Fellowship in Vascular/Neuroendovascular Surgery at the University of Texas Southwestern Medical Center in Dallas.



DISCLOSURES OF FACULTY

NONE

TODAY'S AGENDA

- **Essential Tremor Facts**
- **What's the Fuss with FUS?**
- **Who is Suitable for Treatment?**
- **Five-year Clinical Results**
- **Treatment Day**
- **Insurance Coverage**
- **Second Side**
- **Q&A**

Essential Tremor Facts

ESSENTIAL TREMOR

The facts.

- Also referred to as familial, idiopathic or benign tremor.
- Essential means that there is no known cause of the medical condition.
- In up to 50% of the cases, it is hereditary.¹
- Can progress to the point that daily activities are difficult and may require assistance.



¹ <https://www.webmd.com/brain/essential-tremor-basics>

ESSENTIAL TREMOR

The impact.

- Affects an estimated 10 million Americans.²
- People often live with the debilitating tremor and do not seek treatment.
- For those that do, up to 50% do not get satisfactory relief from medications or have intolerable side effects.³



2. [International Essential Tremor Foundation](#)

3. Zesiewicz, T.A. et al. Neurology November 8, 2011 vol. 77 no. 19 1752-1755

MOVEMENT DISORDERS TOTAL ADDRESSABLE MARKET (U.S.)

ET population



Diagnosed



Drug Refractory



50% of Diagnosed Patient are reported to be drug refractory

97%

*Don't seek treatment beyond medication

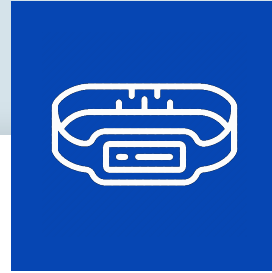
1. U.S., which represents ~1/3 of worldwide opportunity
2. Requires a second procedure - FDA approved 12/2022
3. Actual for 2022-Treatment volumes from CMS and Private Payor Data from Carevoyance

SPECTRUM OF THERAPY FOR ESSENTIAL TREMOR



PHARMACOTHERAPY

Beta-blockers (propranolol ie Inderal),
Anti-seizure medications (primidone),
Anti-anxiety medications



WEARABLE DEVICES

Wearable neurostimulators
Weighted gloves
Assistive devices



PROCEDURAL INTERVENTION

Focused Ultrasound (FUS)
Injectable Neurotoxin
Deep Brain Stimulation (DBS)
RF Thalamotomy
Stereotactic Radiosurgery/Gamma Knife

What's the Fuss with FUS?

20+ Years of Firsts in MRgFUS

Key

Milestones

1999

INSIGHTEC
founded

2005

First brain
treatment with
intact skull

2016

FDA Approval
for First Side ET

2018

Nationwide
Medicare
Coverage

2018

FDA Approval
for TDPD (Vim)

2022

FDA Approval
for PD (GPi)
(not covered by
Insurance currently)

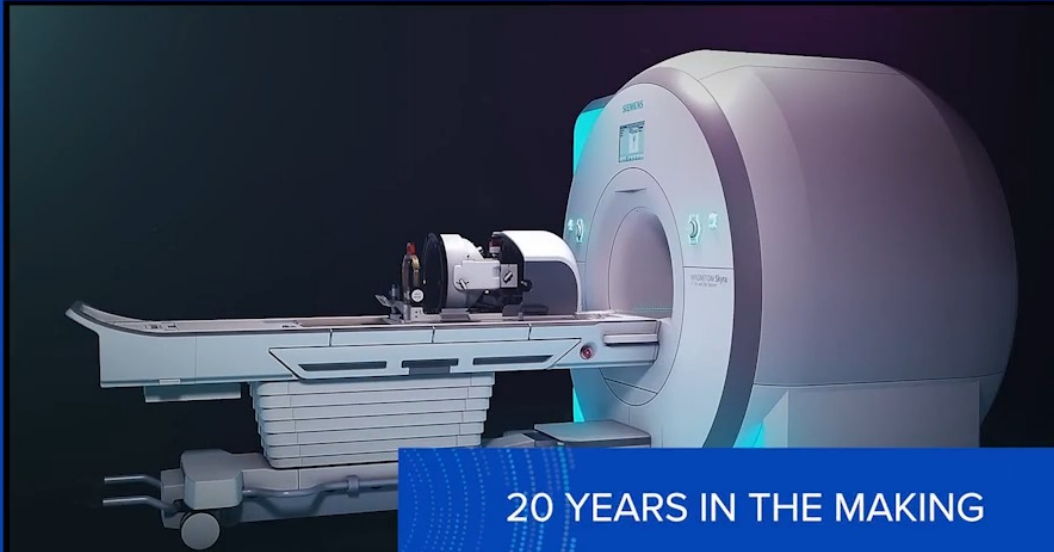
2022

FDA Approval
for Second
Side ET
(9 month between first
and second side)

2023

FDA Approval
of 5-year data

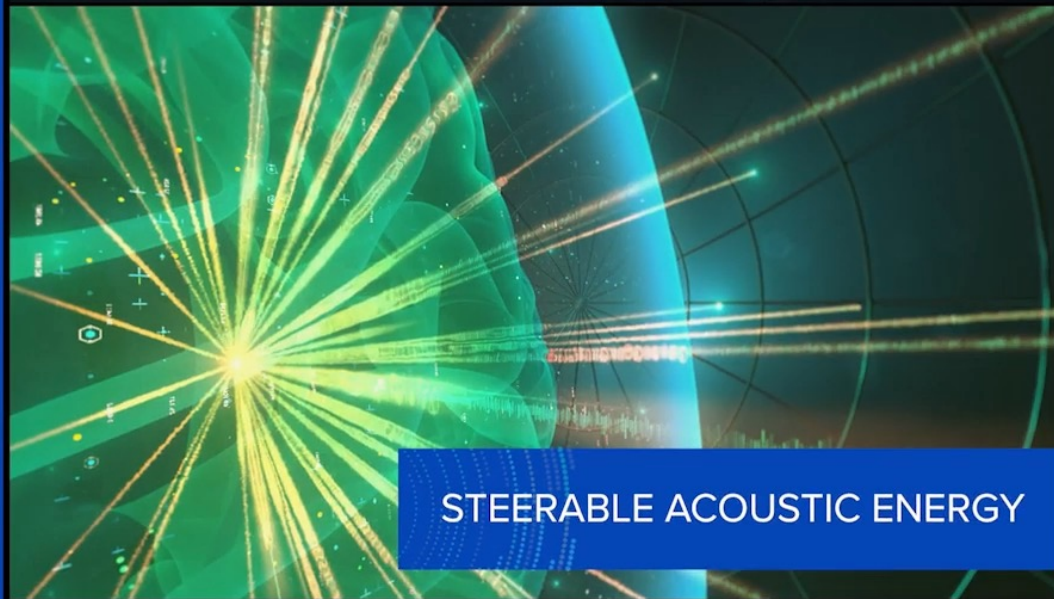
HOW IT WORKS



20 YEARS IN THE MAKING



CLOSED LOOP SYSTEM WITH REAL TIME IMAGING AND THERMOMETRY



STEERABLE ACOUSTIC ENERGY



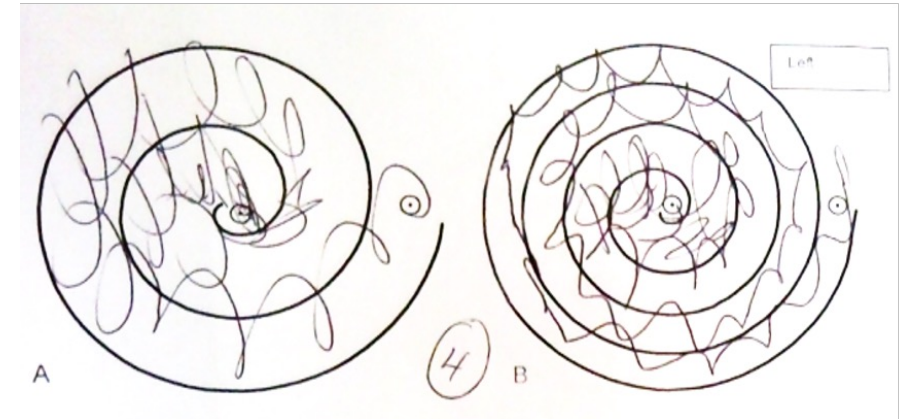
NON-IONIZING RADIATION

WHAT'S THE FUSS WITH FUS?

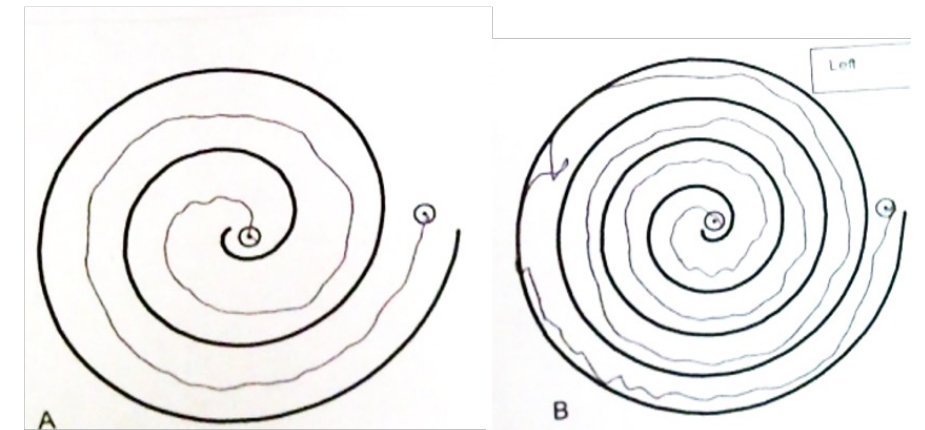
The therapeutic power of focused ultrasound

- Sound waves are directed from a helmet-shaped device with no incisions
- Where the sound waves meet, a lesion about the size of a pea is made to disrupt the abnormal circuit
- The target is the Vim of the thalamus, same as used for deep brain stimulation (DBS) and surgical thalamotomy
- Many patients experience immediate tremor improvement with minimal complications¹

BEFORE TREATMENT



IMMEDIATELY AFTER TREATMENT



Who's Suitable for Treatment

WHO IS SUITABLE FOR TREATMENT?

- Confirmed diagnosis of medication-refractory essential tremor or tremor-dominant PD
- 22 years or older for ET, 30 years or older for tremor-dominant PD
- Can tolerate the procedure
- Able to communicate sensations during procedure
- Can fit in the MRI scanner and activate Stop Sonication button
- Contraindications:
 - Standard contraindications for MRI including non-MRI compatible implants
 - Patients with skull density ratio (cortical:cancellous) of 0.45 (\pm 0.05) or less as calculated from a screening CT
 - See IFP for complete list

4. [Pre-Market Approval \(PMA\) P150038](#)



MEET MITCHELL

Essential Tremor (ET)



PROCEDURES

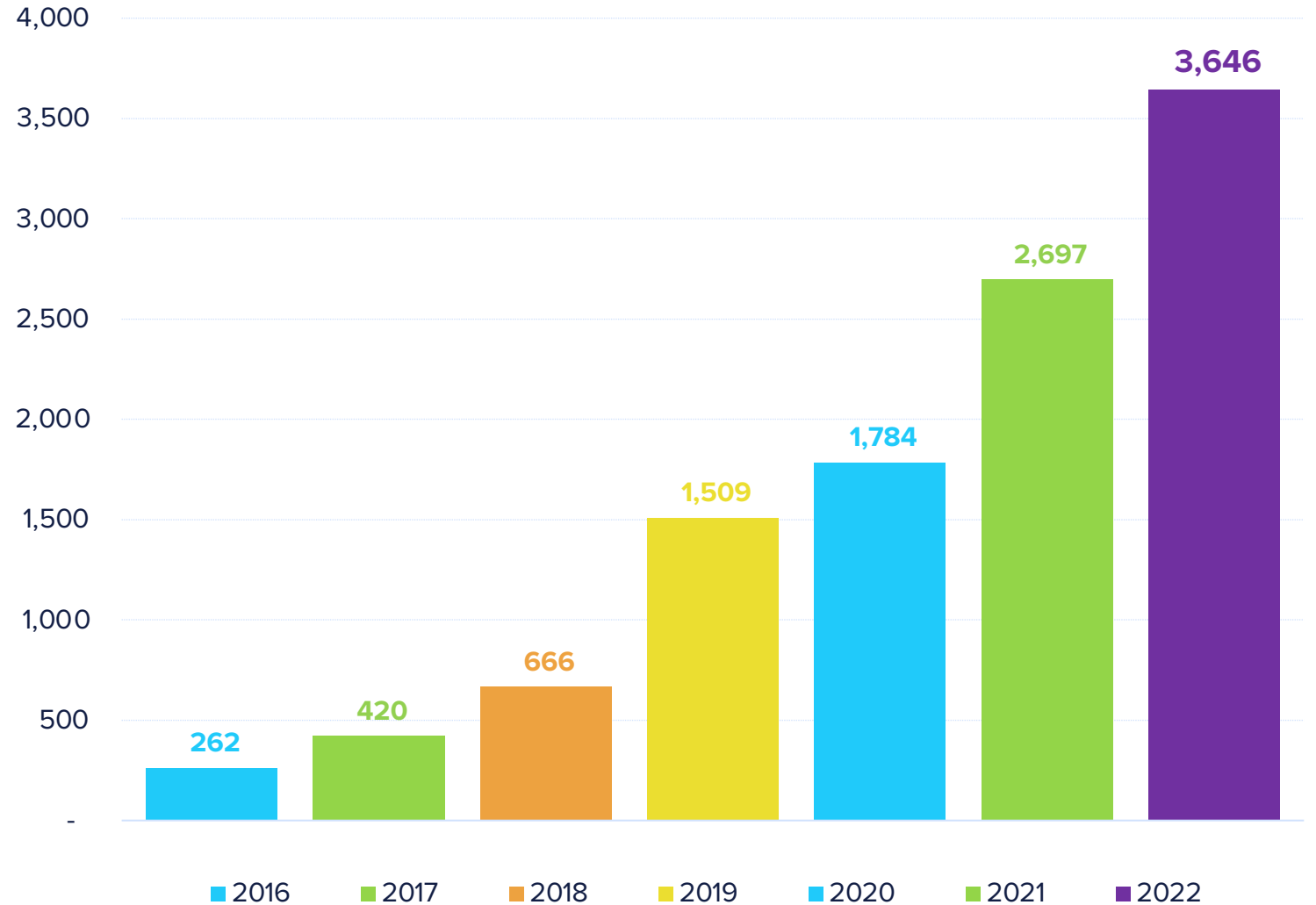
10,000+

Essential Tremor and Tremor-dominant PD patients treated (including research)¹¹

- In 2021, FUS surpassed DBS as the most common interventional procedure for ET
- Your patients are asking! In 2022 there were >66,000 inquiries from Insightec digital campaigns

EXABLATE NEURO

Total Number of Global FUS Thalamotomies



5-year Clinical Results

MULTI-YEAR DATA AND SOCIETY SUPPORT



The NEW ENGLAND
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.,
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 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.,
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.,
Keiichi Abe, M.D., Takaomi Taira, M.D., Ph.D., and Jin W. Chang, M.D., Ph.D.

Annals of
NEUROLOGY

A Prospective Trial of Magnetic Resonance–Guided Focused Ultrasound Thalamotomy for Essential Tremor: Results at the 2-Year Follow-up

Jin Woo Chang, MD, PhD,^{1*} Chang Kyu Park, MD,^{1*} Nir Lipsman, MD, PhD,²
Michael L. Schwartz, MD,² Pejman Ghanouni, MD, PhD,³
Jaimie M. Henderson, MD,⁴ Ryder Gwinn, MD,⁵ Jennifer Witt, MD,⁶
Travis S. Tierney, MD, PhD,⁷ G. Rees Cosgrove, MD,⁸ Binit B. Shah, MD,⁹
Keiichi Abe, MD,¹⁰ Takaomi Taira, MD, PhD,¹⁰ Andres M. Lozano, MD,¹¹
Howard M. Eisenberg, MD,¹² Paul S. Fishman, MD, PhD,¹³ and
W. Jeffrey Elias, MD¹⁴

JNS JOURNAL OF
NEUROSURGERY
OFFICIAL JOURNALS OF THE AANS SINCE 1944

Magnetic resonance imaging–guided focused ultrasound thalamotomy for essential tremor: 5-year follow-up results

G. Rees Cosgrove, MD,¹ Nir Lipsman, MD, PhD,² Andres M. Lozano, MD, PhD,³
Jin Woo Chang, MD, PhD,⁴ Casey Halpern, MD,⁵ Pejman Ghanouni, MD, PhD,⁶
Howard Eisenberg, MD,⁷ Paul Fishman, MD, PhD,⁸ Takaomi Taira, MD, PhD,⁹
Michael L. Schwartz, MD, MSc,² Nathan McDannold, PhD,¹⁰ Michael Hayes, MD,¹¹
Susie Ro, MD,¹² Binit Shah, MD,¹³ Ryder Gwinn, MD,¹⁴ Veronica E. Santini, MD, MA,¹⁵
Kullervo Hynynen, PhD,¹⁶ and W. Jeff Elias, MD¹⁷

Neurology®

Three-year follow-up of prospective trial of focused ultrasound thalamotomy for essential tremor

Casey H. Halpern, MD, Veronica Santini, MD, Nir Lipsman, MD, PhD, Andres M. Lozano, MD, PhD,
Michael L. Schwartz, MD, Binit B. Shah, MD, W. Jeff Elias, MD, Garth R. Cosgrove, MD, Michael T. Hayes, MD,
Nathan McDannold, PhD, Christina Aldrich, RN, MSN, Howard M. Eisenberg, MD, Dheeraj Gandhi, MD,
Takaomi Taira, MD, PhD, Ryder Gwinn, MD, Susie Ro, MD, Jennifer Witt, MD, Na Young Jung, MD,
Jin Woo Chang, MD, Jarrett Rosenberg, PhD, and Pejman Ghanouni, MD, PhD

Neurology® 2019;93:e1-e10. doi:10.1212/WNL.00000000000008561

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ASSFN Position Statement on

MR-guided Focused Ultrasound for
the Management of Essential Tremor

FIRST SIDE – 5 YEAR CLINICAL RESULTS

73.1%

Improvement in tremor
at five-year follow-up¹

What else does the data tell us?

No serious adverse events recorded

No new or worsening adverse events

Significant ADL and QoL improvement

44.5% functional disability

improvement remained at 5 years

(CRST Part C: Activities of Daily

Living / Quality of Life functional)

1. [Pre-Market Approval \(PMA\) P150038](#)

After treatment, the most common adverse events (AEs) included:

imbalance/gait disturbance (26% of study subjects)

numbness/tingling (33% of study subjects)

headache/head pain (51% of study subjects)

Of all AEs, 48% resolved within 30 days. Additional infrequent events include dizziness, taste disturbance, slurred speech, fatigue and vomiting

At five years, persistent AEs were reported to remain moderate or mild and NO NEW AEs were reported.

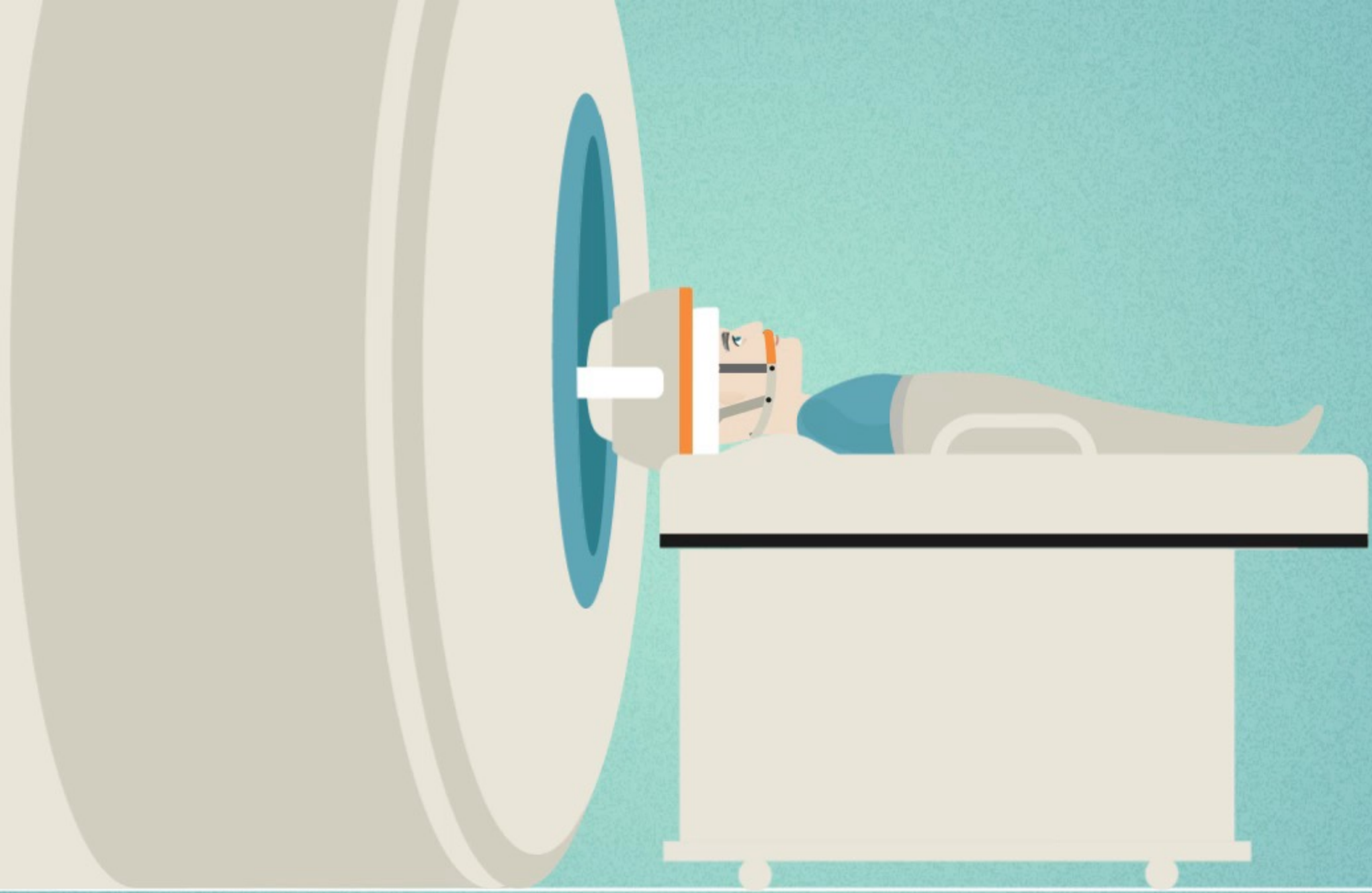
The most common adverse event was:

paresthesia (20% of study subjects)

Additional infrequent events include unsteadiness, limb weakness, gait disturbance, dysmetria, and dysgeusia.

Data is from Insightec-sponsored clinical subjects of 40 subjects at 5-year time point.

Treatment Day



DAY OF THE PROCEDURE



PATIENT PREP

The patient's head is shaved so nothing interferes with the ultrasound waves. After local numbing medication is applied, a frame is secured to their head to prevent it from moving during treatment.



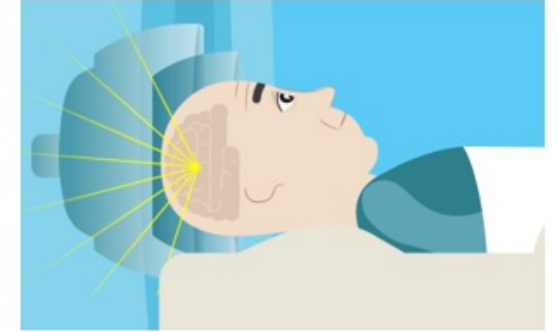
PLANNING

During the treatment, the patient is awake and lies on the MRI table which moves in and out of the MRI scanner. MRI images are taken to plan the treatment according to the patient's anatomy.



TARGET & TEST

Light doses of energy are applied to accurately pinpoint the target and assess the temporary tremor improvement and identify any potential side effects. Sub-millimeter target adjustments can be made.



TREATMENT

High energy is applied to create a small ablation and provide a therapeutic effect, improvement of the hand tremor.

WHAT TO EXPECT

Benefits for patients.

- Immediate and durable tremor improvement⁴
- Significant improvement in Quality of Life⁴
- Outpatient, home the same day
- Little to no risk of infection
- No implants, probes or ionizing radiation
- No anesthesia
- Minimal complications⁴

4. [Pre-Market Approval \(PMA\) P150038](#)



PATIENT TRANSFORMATION

Before & after focused ultrasound treatment

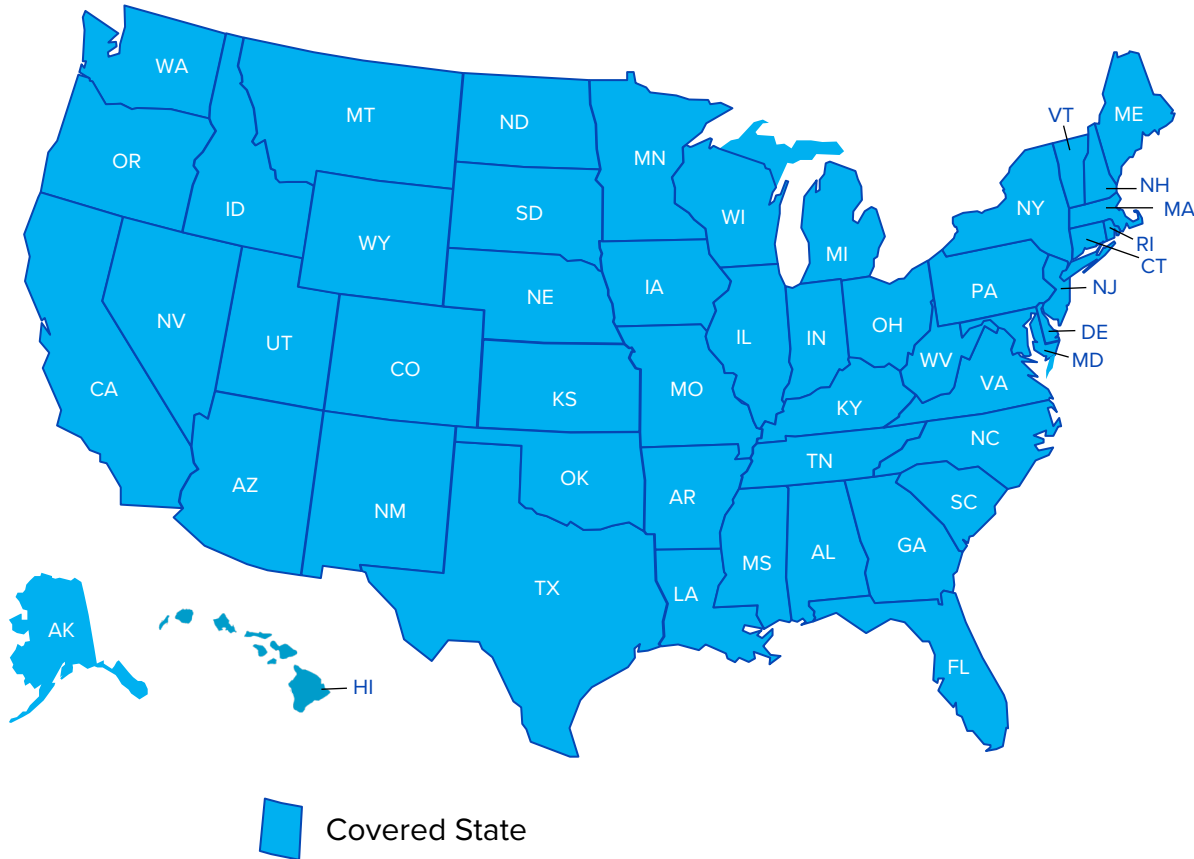


Results may not be representative of all treatment outcomes.

Insurance Coverage

NATIONWIDE COVERAGE

Full coverage for Medicare, CIGNA, Aetna, Anthem and BCBS Federal Employee Plans



- Medicare coverage in all 50 states for essential tremor, through Local Medicare Administrative Contractor Coverage Determinations
- 43 Independent BSBS plans in 44 states cover treatment of first side essential tremor, including BCBS Federal Employee Plan (Nationally)
- Second Side coverage is determined on a case-by-case basis
- Patient should contact their health plan's Member Service department by calling the phone number listed on the back of their insurance ID card to confirm that MR-guided Focused Ultrasound for treating essential tremor (CPT code 0398T) is a covered benefit in the outpatient setting based on their independent plan benefits.

SECOND SIDE

Clinical Trial Info and Results

WHO IS SUITABLE FOR 2nd SIDE TREATMENT?

- Essential Tremor patients with medication-refractory tremor
- Treatment of the contralateral side (that was not previously treated) must be staged by at least 9 months after the first thalamotomy
- Patients must be at least age 22
- Designated area in the brain responsible for movement disorder symptoms (Ventralis Intermedius) must be identified and accessible for targeted thermal ablation by the Exablate device

SECOND SIDE – FDA TRIAL CLINICAL RESULTS

80.2%

Improvement of tremor
at 6-month follow-up.¹

Tremor/ Motor Function – 64.3% improvement

Effective improvement immediately following treatment, with results sustained through at least six months. Consistent with treatment of the first side.

Functional Disability – 74.3% improvement

This significant and sustained improvement in functional disability is clinically meaningful and suggests that subjects have enhanced independence in activities of daily living.

1. [Pre-Market Approval \(PMA\) P150038 - S022](#)

Data is from Insightec-sponsored clinical studies of 51 subjects at 6-month time point.

After treatment, the most common adverse events (AEs) included:

- Numbness / Tingling (31% of study subjects)
- Dysarthria – (29% of study subjects)
- Ataxia – (23% of subjects)

Majority of events were mild or moderate

No device related adverse events.

Only one related serious event occurred (urinary tract infection following use of catheter during procedure).

Additional infrequent (< 2%) adverse events include weakness, decrease in synchronicity, dizziness, dry mouth, hypoesthesia, intermittent diplopia, sialorrhea, and voice change.

Question & Answer

Next Steps

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