VATTIKUTI TECHNOLOGIES

2025

CLINICAL EVIDENCE DOSSIER

Transforming Care Through Evidence and Insight

About this

MRgFUS Clinical Evidence Dossier

This compendium brings together global clinical evidence, insights, and real-world experience surrounding MR-guided Focused Ultrasound (MRgFUS) using the Insightec Exablate Neuro platform.
Developed as a comprehensive clinical reference, it is designed for neurologists, neurosurgeons, radiologists, and hospital administrators exploring how MRgFUS can enhance the management of movement disorders, and emerging neurological disorders indications.

Purpose

- To present peer-reviewed evidence on MRgFUS outcomes across neurological and functional disorders.
- To summarize regulatory approvals and guideline recommendations from leading authorities (FDA, CE, CDSCO).
- To highlight patient-centered advantages—non-invasive treatment, rapid recovery, and improved quality of life.
- To illustrate how MRgFUS serves as a complementary and future-ready modality alongside established therapies such as DBS and RF ablation.

Why MRgFUS, and Why Now?

- Expanding global footprint: 200+ active centers performing over 7,000 procedures annually.
- Proven technology: FDA and CE approvals for Essential Tremor and Parkinson's Disease, with ongoing studies in epilepsy, OCD, and depression.
- Growing patient demand: Non-incisional, radiation-free, and anesthesia-free neurosurgical alternative.
- Clinical transformation: Immediate, measurable symptom relief and reduced hospitalization, redefining patient recovery pathways.

Product Name	Company Name	Authorised Partner
Exablate Neuro	INSIGHTEC	VATTIKUTI TECHNOLOGIES

Table of Contents

How The Technology Works

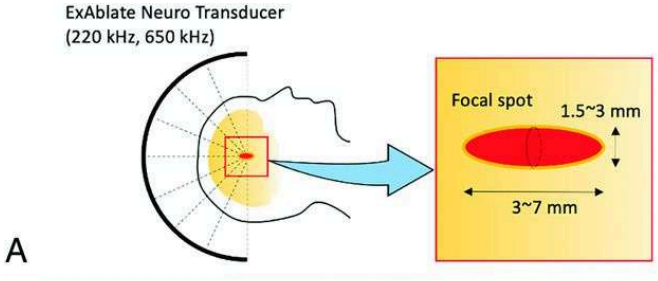
MR-Guided Focused Ultrasound

1. High-Frequency Sound Beams (>20 kHz):
Thousands of ultrasound waves are emitted from a hemispherical transducer. Each beam individually passes harmlessly through the skull but converges at a focal point deep inside the brain.

2. Water Bath – Cooling & Conduction:
The patient's head is submerged in a water-filled helmet. This serves two purposes —

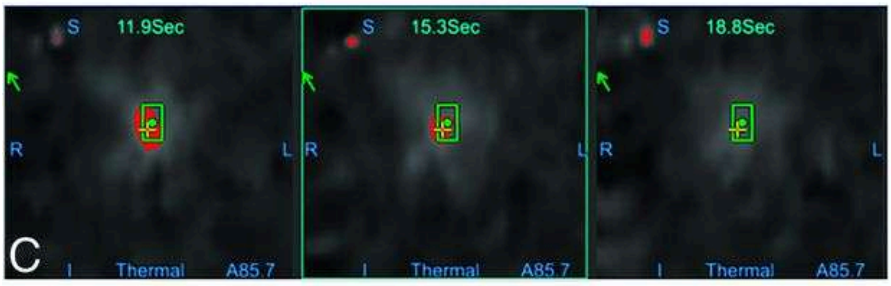
- Provides acoustic coupling for effective transmission of ultrasound waves.
- Keeps the scalp cool to prevent overheating.

3. 1024 Beams Focused at a Single Point:
The Exablate Neuro system uses 1024 phased array elements, focusing acoustic energy to a tiny spot — about 1.5 × 3 mm in size.
This focal precision allows creation of controlled lesions in deep brain targets like the Ventral Intermediate (Vim) nucleus for tremor.



A

4. Temperature Rise (>53°C):
At the focal point, temperature increases rapidly — causing thermal ablation of the targeted neurons while leaving surrounding tissue unharmed.

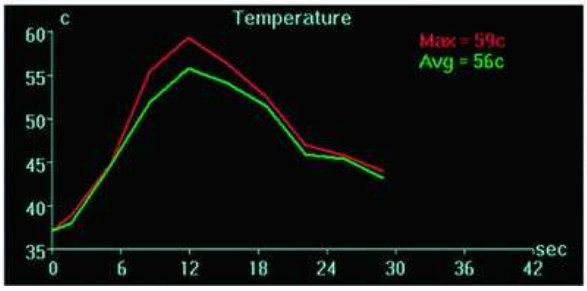


C

5. MRI Thermography – Real-Time Monitoring:
The MRI continuously monitors temperature and location (seen in images C & D).

- The red curve represents the peak temperature (~59°C),
- The green curve represents average temperature (~56°C).

This allows the surgeon to test dose, verify symptom improvement, and then apply full therapeutic energy confidently.



D

6. INCISIONLESS!!

- No burr hole, no implant, no anesthesia.
- The patient is awake and gives feedback during the procedure.
- Recovery is rapid, often discharged the same or next day.

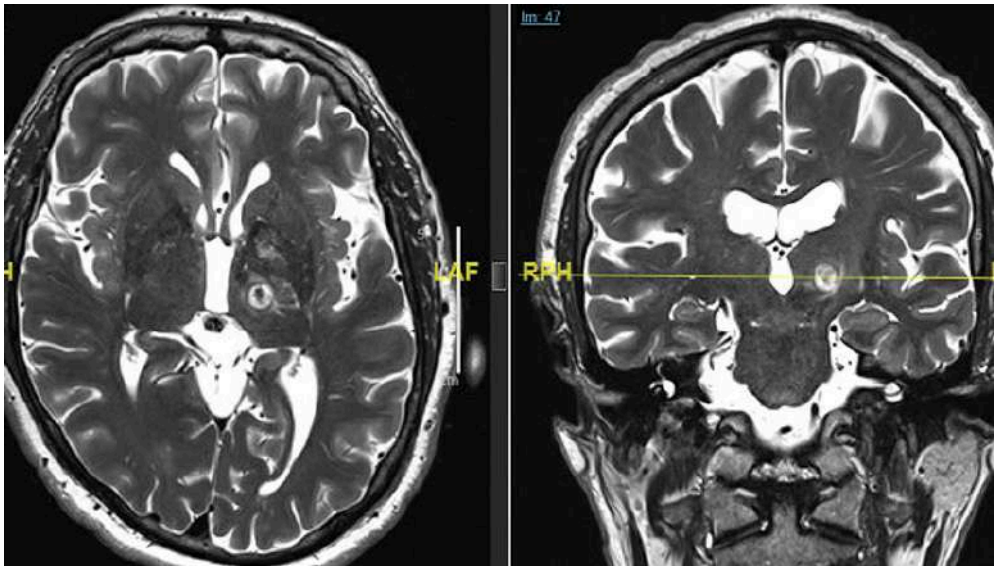
Reference:
Mattay RR, Kim K, Shah L, et al. **MR Thermometry during Transcranial MR Imaging–Guided Focused Ultrasound Procedures: A Review**. AJNR Am J Neuroradiol. 2023;45(1):1-8.

Lesion Biology and Thermal Zone

MR-Guided Focused Ultrasound

Mechanism of Action: Intense Thermal Heating at the Focus

- Focused ultrasound beams converge at a very small focal spot deep in the brain.
- This focused energy raises the temperature locally to >53°C, high enough to cause coagulative necrosis — i.e., cell death — only within that focal region.
- Because MRI thermometry continuously monitors the temperature, this process is precise and controlled.



1. **Zone 1 – Central Necrosis**
   - The core of the treated area (Zone 1) experiences the highest temperature and becomes irreversibly necrotic.
   - This zone represents the intended lesion—the therapeutic ablation of overactive or abnormal neurons responsible for tremor or other symptoms.
   - On MRI, this appears as a sharply defined non-enhancing core.
2. **Zone 2 – Cytotoxic Edema (Irreversible)**
   - Surrounding the necrotic core is a cytotoxic edema zone (Zone 2).
   - Here, cells are injured by heat stress and swelling occurs, but not all are necrotic immediately.
   - This area often evolves over a few days, contributing to some of the transient post-procedure effects like mild numbness or imbalance.
3. **Zone 3 – Vasogenic Edema (Reversible)**
   - The outermost region (Zone 3) shows vasogenic edema — leakage of plasma from small blood vessels due to increased permeability.
   - This zone is reversible, typically resolving within 1–2 weeks, and may appear as a faint hyperintensity on T2 MRI images.
   - This edema explains why some patients experience mild temporary side effects that subside with time.

Lak AM, Segar DJ, McDannold N, White PJ, Cosgrove GR. **Magnetic Resonance Image Guided Focused Ultrasound Thalamotomy. A Single Center Experience With 160 Procedures**. Front Neurol. 2022;13:743649.

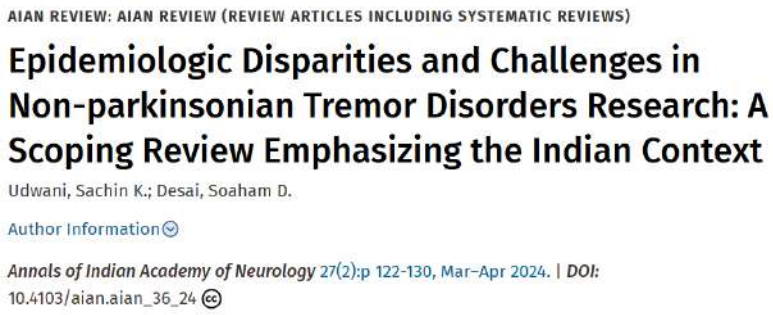
Focused Ultrasound for **Essential Tremors**

Essential tremor (ET) is the most common movement disorder, affecting an estimated 1.2% to 5.5% of the population in India[1]

ET is commonly viewed as a relatively benign disease.

However, the associated disabling aspects of ET, such as significant tremor of the hands, can impair patients' ability to eat, shave, write, perform household activities, and function in the workplace.

Reference 1


AIAN REVIEW: AIAN REVIEW (REVIEW ARTICLES INCLUDING SYSTEMATIC REVIEWS)

Epidemiologic Disparities and Challenges in Non-parkinsonian Tremor Disorders Research: A Scoping Review Emphasizing the Indian Context

Udwani, Sachin K.; Desai, Soaham D.

Author Information

Annals of Indian Academy of Neurology 27(2):p 122-130, Mar–Apr 2024. | DOI: 10.4103/aian.aian_36_24

The underlying etiology of ET is unclear, but cases often run in families (familial tremor). It has been estimated that approximately 50% of all cases are due to a genetic mutation, and the pattern of inheritance is most consistent with autosomal dominant transmission (i.e. dominant trait).

Focused Ultrasound Therapy

Focused ultrasound is a non-invasive, therapeutic technology with the potential to improve the quality of life and decrease the cost of care for patients with essential tremor. This novel technology focuses multiple beams of ultrasound energy precisely and accurately on targets deep in the brain without damaging surrounding normal tissue.

How it Works

Where the focused ultrasound beams converge, they produce precise ablation (thermal destruction of tissue), enabling ET to be treated noninvasively. The primary target is a region in the thalamus called the Ventral Intermediate Nucleus (Vim), but other adjacent targets and white matter pathways are also in use.

Advantages

- It is a non-invasive, single treatment that enables patients to recover rapidly and quickly return to activities of normal life (usually the next day).
- Compared to RF ablation or DBS, focused ultrasound offers a reduced risk of infection, of damage to the non-targeted area, and of blood clot formation.
- Focused ultrasound offers rapid resolution of symptoms.
- In contrast to lesioning performed with stereotactic radiosurgery, focused ultrasound does not use ionizing radiation, thus avoiding the side effects of exposure to radiation.
- Because it is non-invasive, focused ultrasound could be an option for medically refractory ET patients (those who do not respond well to medication) who do not want to undergo surgery.

Approvals for
Essential Tremors

FDA Approves First MRI-Guided Focused Ultrasound Device to Treat Essential Tremor
Date: July 2016

Focused Ultrasound for Essential Tremor: Five-Year Results
Date: August 2022

JNS JOURNAL OF NEUROSURGERY
OFFICIAL JOURNALS OF THE AANS SINCE 1944

CLINICAL ARTICLE
J Neurosurg 138:1028–1033, 2023

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

G. Rees Cosgrove, MD, Nir Lipsman, MD, PhD, et. al.
Publication Date: 05 Aug 2022
Page Range: 1028–1033
Volume/Issue: Volume 138: Issue 4
DOI link: https://doi.org/10.3171/2022.6.JNS212483

OBJECTIVE
The objective of this study was to evaluate, at 4 and 5 years posttreatment, the long-term safety and efficacy of unilateral MRI-guided focused ultrasound (MRgFUS) thalamotomy for medication-refractory essential tremor in a cohort of patients from a prospective, controlled, multi-center clinical trial.

METHODS
Outcomes per the Clinical Rating Scale for Tremor (CRST), including postural tremor scores (CRST Part A), combined hand tremor/motor scores (CRST Parts A and B), and functional disability scores (CRST Part C), were measured by a qualified neurologist. The Quality of Life in Essential Tremor Questionnaire (QUEST) was used to assess quality of life. CRST and QUEST scores at 48 and 60 months post-MRgFUS were compared to those at baseline to assess treatment efficacy and durability. All adverse events (AEs) were reported.

RESULTS
Forty-five and 40 patients completed the 4- and 5-year follow-ups, respectively. CRST scores for postural tremor (Part A) for the treated hand remained significantly improved by 73.3% and 73.1% from baseline at both 48 and 60 months posttreatment, respectively (both $p < 0.0001$). Combined hand tremor/motor scores (Parts A and B) also improved by 49.5% and 40.4% ($p < 0.0001$) at each respective time point. Functional disability scores (Part C) increased slightly over time but remained significantly improved through the 5 years ($p < 0.0001$). Similarly, QUEST scores remained significantly improved from baseline at year 4 ($p < 0.0001$) and year 5 ($p < 0.0003$). All previously reported AEs remained mild or moderate, and no new AEs were reported.

CONCLUSIONS
Unilateral MRgFUS thalamotomy demonstrates sustained and significant tremor improvement at 5 years with an overall improvement in quality-of-life measures and without any progressive or delayed complications.

Approvals for
Essential Tremors

Focused Ultrasound Now FDA Approved to Treat Essential Tremor Patients' Second Side
Date: January 2023

Journal of Neurology, Neurosurgery & Psychiatry

J Neurol Neurosurg Psychiatry
2021 Sep;92(9):927-931.
doi: 10.1136/jnnp-2020-325278. Epub 2021 Apr 27.

Bilateral staged magnetic resonance-guided focused ultrasound thalamotomy for the treatment of essential tremor: a case series study

Raúl Martínez-Fernández, Sujitha Mahendran, et. al
.Movement Disorder: Short Report

Background:
Unilateral magnetic resonance-guided focused ultrasound (FUS) thalamotomy is efficacious for the treatment of medically refractory essential tremor (ET). Viability of bilateral FUS ablation is unexplored.

Methods:
Patients diagnosed with medically refractory ET and previously treated with unilateral FUS thalamotomy at least 5 months before underwent bilateral treatment. The timepoints were baseline (before first thalamotomy) and FUS1 and FUS2 (4 weeks before and 6 months after second thalamotomy, respectively). The primary endpoint was safety. Efficacy was assessed through the Clinical Rating Scale for Tremor (CRST), which includes subscales for tremor examination (part A), task performance (part B) and tremor-related disability (part C).

Results:
Nine patients were treated. No permanent adverse events were registered. Six patients presented mild gait instability and one dysarthria, all resolving within the first few weeks. Three patients reported perioral hypoesthesia, resolving in one case. Total CRST score improved by 71% from baseline to FUS2 (from 52.3±12 to 15.5±9.4, $p<0.001$), conveying a 67% reduction in bilateral upper limb A+B (from 32.3±7.8 to 10.8±7.3, $p=0.001$). Part C decreased by 81% (from 16.4±3.6 to 3.1±2.9, $p<0.001$). Reduction in head and voice tremor was 66% (from 1.2±0.44 to 0.4±0.54, $p=0.01$) and 45% (from 1.8±1.1 to 1±0.8, $p=0.02$), respectively.

Conclusion:
Bilateral staged FUS thalamotomy for ET is feasible and might be safe and effective. Voice and head tremor might also improve. A controlled study is warranted.

Treatment Continues to Improve for **Essential Tremors**

Key Points

- On the nine-year anniversary of its first regulatory approval, researchers continue to advance focused ultrasound to treat essential tremor.
- Six new publications show the future of this life-changing technology.

Nine years in, research is revealing methods to improve targeting and assess outcome measurements.

Targeting

The team at the University of Maryland is continuing to explore how focused ultrasound lesioning works in the brain. They conducted a retrospective study to analyze functional connectivity in tremor-related regions and correlated those imaging findings with clinical outcomes. The associations that they found suggested that the functional connectivity abnormalities could be the best target for alleviating symptoms in patients with essential tremor. See "MR-Guided Focused Ultrasound Thalamotomy Modulates Cerebello-Thalamo-Cortical Tremor Network in Essential Tremor Patients," by Li Jiang et al., published in Frontiers in Neurology in April 2025.

Functional connectivity was also used in another study. In research partly funded by the Focused Ultrasound Foundation, a collaborative group of neurologists, neurosurgeons, radiologists, and data scientists from Brigham and Women's Hospital, Harvard Medical School, Sunnybrook Research Centre, and the University of Toronto sought to determine the optimal lesion location when using focused ultrasound to treat essential tremor. After analyzing 351 cases from three international hospitals, the team found a specific subregion within the ventral intermediate nucleus of the cerebellothalamic tract that needed to be included in order to obtain optimal tremor improvement. Conversely, other locations and tracts were found to be associated with specific side effects. See "Optimal Focused Ultrasound Lesion Location in Essential Tremor," by Melissa M. J. Chua, et al., published in Science Advances in May 2025.

Mass General Brigham's press release about this study garnered media interest from Physician's Weekly and Medscape.

Continuing on the theme of targeting, neurosurgeons at Mass General Brigham have used a new, advanced MR imaging technique for direct anatomical targeting of the ventral intermediate nucleus. This new MRI sequence, called "white matter null magnetization prepared rapid gradient echo," (or WMnMPRAGE) can be integrated with focused ultrasound lesioning strategies to create a more effective and conformal thalamotomy lesion. Next, the team will conduct further studies to confirm safety and correlate the image data with clinical outcomes.

Treatment Continues to Improve for **Essential Tremors**

See "New Technique for Direct Targeting of the Ventral Intermediate Nucleus Using Magnetic Resonance-Guided Focused Ultrasound," by Juan Ángel Aibar-Duran et al., published as a methods article in Frontiers in Radiology in May 2025.

This article is also part of the Precision Neuroimaging for MRgFUS in Neurological Disorders collection.

Outcome Assessment

To determine whether a quantitative method could be used to measure essential tremor treatment effect (in place of clinical examination), a collaborative team of researchers in Paris led by Jean-François Aubry, PhD, tested accelerometry as a potential technique. Patients undergoing focused ultrasound were tested before, during (inside the MRI bore), and after the treatment. The accelerometer measurements successfully provided real-time, rater-independent feedback on tremor reduction, leading the team to suggest that using them could shorten procedure time and reduce the number of sonications needed to achieve the desire treatment effect. See "Quantitative Tremor Monitoring Before, During and After MR-Guided Focused Ultrasound Thalamotomy for Essential Tremor with MR Compatible Accelerometers," by Thomas Bancel et al., published in the International Journal of Hyperthermia in April 2025.

Also with quantitative measurements in mind, researchers in Bonn, Germany, are investigating new ways to evaluate tremors before and after focused ultrasound thalamotomy. This team tested the use of a wearable triaxial accelerometer before and then 1, 6, and 12 months after treatment. The team concluded that accelerometric recordings provided a fast and investigator-independent method to both characterize and quantify tremors before and after an intervention. See "Quantitative and Qualitative Tremor Evaluation After MR-Guided Focused Ultrasound Thalamotomy," by Veronika Purrer et al., published in Frontiers in Neurology in May 2025.

Because there is a risk for cognitive decline after a second side thalamotomy, researchers at Sunnybrook Health Sciences Centre and the University of Toronto tested patients who underwent staged focused ultrasound treatment of essential tremor. The cognitive tests were administered before and four months after undergoing second-sided focused ultrasound thalamotomy. They found a minimal risk at both the group and individual levels. See "Cognitive Outcomes Following Second-Sided Focused Ultrasound Thalamotomy for Tremor," by Silina Z. Boshmaf et al., published in Movement Disorders Clinical Practice in April 2025.

Notable Papers for
Essential Tremors

The NEW ENGLAND JOURNAL of MEDICINE

Published August 25, 2016
N Engl J Med 2016;375:730-739 DOI: 10.1056/NEJMoa1600159
VOL. 375 NO. 8 Copyright © 2016

A Randomized Trial of Focused Ultrasound Thalamotomy for Essential Tremor

Authors: 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., +20 , 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.)

Focused Ultrasound for **Parkinson's Disease**

Focused Ultrasound Now FDA Approved to Treat Tremor Dominant Parkinson's Disease (TDPD)
Date: December 2018

FDA expanded approval to cover other Parkinson's symptoms, including bradykinesia, rigidity, and dyskinesia
Date: November 2021

FDA has approved the use of its Exablate Neuro platform for staged bilateral Pallidothalamic Tractotomy treatment in patients living with advanced Parkinson's disease (PD).
Date: July 2025

Focused ultrasound has the potential to achieve symptomatic relief by making thermal lesions deep in the brain to interrupt circuits involved with tremor and dyskinesia. Symptoms and targets being assessed for treatment using focused ultrasound include:

- Parkinsonian tremor – target in the thalamus (thalamotomy)
- Parkinsonian dyskinesia – target in the globus pallidus (pallidotomy) or subthalamic nucleus
- Parkinsonian tremor, akinesia or dyskinesia – target in the pallidothalamic tract

MRgFUS Targets:

Feature	VIM	GPi	PTT
Patient Selection	Tremor-dominant PD	Dyskinesia, rigidity, bradykinesia	Mixed phenotypes (tremor + akinetic-rigid)
Laterality	Bilateral Staged	Mostly unilateral	Bilateral Staged
Durability	Durable tremor control >5 years	Unknown, modest results	Durable > 1 year (still under study)

Most adverse effects are mild and transient, typically resolving within days to weeks as per multiple long-term studies.

frontiers in Neurology

Front. Surg., 14 January 2020
Sec. Neurosurgery

MRgFUS Pallidothalamic Tractotomy for Chronic Therapy-Resistant Parkinson's Disease in 51 Consecutive Patients: Single Center Experience

Gallay MN, Moser D, Rossi F, et al. Front Surg. 2020;6:76.
Volume 6 - 2019 | https://doi.org/10.3389/fsurg.2019.00076

Background: There is a long history, beginning in the 1940s, of ablative neurosurgery on the pallidal efferent fibers to treat patients suffering from Parkinson's disease (PD). Since the early 1990s, we undertook a re-actualization of the approach to the subthalamic region, and proposed, on a histological basis, to target specifically the pallidothalamic tract at the level of Forel's field H1. This intervention, the pallidothalamic tractotomy (PTT), has been performed since 2011 using the MR-guided focused ultrasound (MRgFUS) technique. A reappraisal of the histology of the pallidothalamic tract was combined recently with an optimization of our lesioning strategy using thermal dose control.

Objective: This study was aimed at demonstrating the efficacy and risk profile of MRgFUS PTT against chronic therapy-resistant PD.

Methods: This consecutive case series reflects our current treatment routine and was collected between 2017 and 2018. Fifty-two interventions in 47 patients were included. Fifteen patients received bilateral PTT. The median follow-up was 12 months.

Results: The Unified Parkinson's Disease Rating Scale (UPDRS) off-medication postoperative score was compared to the baseline on-medication score and revealed percentage reductions of the mean of 84% for tremor, 70% for rigidity, and 73% for distal hypobradykinesia, all values given for the treated side. Axial items (for voice, trunk and gait) were not significantly improved. PTT achieved 100% suppression of on-medication dyskinesias as well as reduction in pain ($p < 0.001$), dystonia ($p < 0.001$) and REM sleep disorders ($p < 0.01$). Reduction of the mean L-Dopa intake was 55%. Patients reported an 88% mean tremor relief and 82% mean global symptom relief on the operated side and 69% mean global symptom improvement for the whole body. There was no significant change of cognitive functions. The small group of bilateral PTTs at 1 year follow-up shows similar results as compared to unilateral PTTs but does not allow to draw firm conclusions at this point.

Conclusion: MRgFUS PTT was shown to be a safe and effective intervention for PD patients, addressing all symptoms, with varying effectiveness. We discuss the need to integrate the preoperative state of the thalamocortical network as well as the psycho-emotional dimension.

Notable Papers for **Parkinson's Disease**

Current applications for magnetic resonance-guided focused ultrasound in the treatment of Parkinson's disease

Lu, Haoxuan1; Wang, Xiaoyu1,2; Lou, Xin1

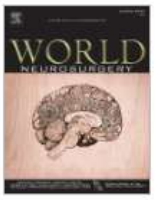
Chinese Medical Journal 136(7):p 780-787, April 5, 2023. | DOI: 10.1097/CM9.0000000000002319

Authors, years	Authors, years	Conclusions
Magara et al, 2014 (Click)	Unilateral PTT-MRgFUS in 13 patients (3 months follow-up)	60.9% improvement in UPDRS 56.7% improvement in GSR (9 patients) No serious clinical side effects
Gallay et al, 2021 (Click)	Bilateral PTT-MRgFUS in 10 patients (12 months follow-up)	52% improvement in off-medication UPDRS Adverse effect including speech difficulties
Jung et al, 2018 (Click)	Unilateral GPi-MRgFUS in 10 patients (12 months follow-up)	39.1% improvement in off-medication UPDRS part III 42.7% improvement in off-medication UdysRS No serious clinical side effects
Eisenberg et al, 2020 (Click)	Unilateral GPi-MRgFUS in 20 patients (12 months follow-up)	43% improvement in off-medication UdysRS 45.2% improvement in off-medication MDS-UPDRS part III No serious clinical side effects
Martínez-Fernández et al, 2018 (Click)	Unilateral STN-MRgFUS in 10 patients (6 months follow-up)	53% improvement in off-medication MDS-UPDRS part III 47% improvement in on-medication MDS-UPDRS part III Adverse effects: gait ataxia, pin-site head pain, and high blood pressure
Martínez-Fernández et al, 2020 (Click)	Unilateral STN-MRgFUS in 27 patients (12 months follow-up)	50.3% improvement in MDS-UPDRS part III in thalamotomy group at 4 months 8.5% improvement in MDS-UPDRS part III in sham group at 4 months Adverse effects including dyskinesia, motor weakness, and gait and speech disturbances

Focused Ultrasound - Dual Lesion

Parkinson's Disease

World Neurosurgery
Volume 171, March 2023, Pages e464-e470



Stepwise Dual-Target Magnetic Resonance-Guided Focused Ultrasound in Tremor-Dominant Parkinson Disease: A Feasibility Study.

Chen JC, Lu MK, Chen CM, Tsai CH.
World Neurosurg. 2023;171:e464-e470.

Background
Magnetic resonance–guided focused ultrasound (MRgFUS) has been applied successfully in treating refractory tremors in Parkinson disease (PD). It generates a precise thermal ablation in a specific nucleus or tract, such as ventral intermediate nucleus (VIM) or pallidothalamic tract (PTT). Despite a single lesion improving parts of the PD symptoms, the feasibility and efficacy of a stepwise dual-lesion in VIM and PTT are yet to be explored.

Methods
Three patients with tremor-dominant PD (aged 60.7 ± 6.0 years) received dual-target MRgFUS treatment with a series of primary and secondary outcome measures. The VIM and PTT were navigated based on individual magnetic resonance imaging planning of the brain. The primary outcome measures were the off-status Clinical Rating Scale for Tremor and Unified Parkinson's Disease Rating Scale part III (UPDRS-III). The secondary outcome measures included UPDRS I, II, IV, Hohen and Yahr score, Neuropsychiatry Inventory, Quality of life in PD Rating Scale, Non-Motor Symptoms Scale, and Clinical Global Impression. The baseline data were compared with those acquired 1 day and 1 month following the treatment.

Results
The severity of tremor and motor deficits represented by Clinical Rating Scale for Tremor–part B and UPDRS III were significantly improved ($P < 0.05$ by nonparametric Mann–Whitney U tests) after dual-target ablations. The nonmotor symptoms investigated by UPDRS II and Non-Motor Symptoms Scale also showed significant improvement at the 1-day and 1-month follow-up. There was no adverse effect except temporary procedure-related headache and dizziness during the treatment.

Conclusions
Stepwise dual-lesion targeting VIM and PTT is a safe and effective MRgFUS therapeutic strategy for patients with PD.

MRgFUS Subthalamotomy for **Parkinson's Disease**

Movement Disorders
Official Journal of the International Parkinson and Movement Disorder Society

Unilateral Magnetic Resonance–Guided Focused Ultrasound Lesion of the Subthalamic Nucleus in Parkinson's Disease: A Prospective Study

Armengou-Garcia L, Sanchez-Catasus CA, Aviles-Olmos I, et al.

Mov Disord. 2024;39(12):2230-2241.

Background
Unilateral subthalamic nucleus (STN) ablation using magnetic resonance–guided focused ultrasound (MRgFUS) is being explored as a new treatment for asymmetric Parkinson's disease (PD).

Objectives
The aims were to study the efficacy and safety of this treatment in asymmetric PD patients and to characterize the lesions.

Methods
This prospective, single-center, open-label study evaluated asymmetric PD patients at 6 (n = 20) and 12 months (n = 12) after MRgFUS lesion of the STN. The primary outcome was the change in the Movement Disorders Society-Unified Parkinson's Disease Rating Scale, Part III (MDS-UPDRS III), score in off medication on the treated side and the adverse events (AEs) at 6-month follow-up. We also evaluated cognitive–neuropsychological changes, self-assessment of clinical improvement, and the correlation of the lesion volume with the motor outcomes.

Results
On the treated side, the MDS-UPDRS III score (mean difference = 13.8) and the scores in rigidity, bradykinesia, and tremor improved ($P < 0.001$) throughout the follow-up compared to baseline (at 6 months: rigidity mean difference = 2.8, improvement: 83.5%; bradykinesia mean difference = 6.0, improvement: 69.4%; tremor mean difference = 4.7, improvement: 91.5%). One patient had severe weakness in the treated hemibody, 1 had moderate dyskinesia, and 1 was in moderate confusional state that became mild (weakness) or completely resolved (dyskinesia and confusional state) at 6 months. The rest of the AEs were mild. We observed no clinically relevant changes in cognitive–neuropsychological tests. The percentage of ablation of the STN correlated with the improvement in the total MDS-UPDRS III and contralateral tremor scores ($P < 0.05$).

Conclusion
Unilateral MRgFUS lesion of the STN resulted in a significant motor improvement. We observed no persistent severe AEs, although mild, mostly transient AEs were frequent. © 2024 The Author(s). Movement Disorders published by Wiley Periodicals LLC on behalf of International Parkinson and Movement Disorder Society.

Emerging Indications
MR guided Focused Ultrasound

Emerging Indications

- **Obsessive Compulsive Disorder (OCD)** – *Ventral anterior capsulotomy*

MRgFUS offers precise, incisionless modulation of fronto-striatal pathways. Long-term studies report sustained symptom reduction and improved quality of life.

- **Major Depressive Disorder (MDD)** – *Ventral anterior capsulotomy*

Early clinical experience shows significant mood improvement in treatment-resistant depression. Outcomes remain promising with ongoing trials for durability.

- **Chronic Pain** – *Cingulotomy, thalamotomy, mesencephalotomy*

Focused ablation of pain pathways has shown meaningful relief in refractory pain syndromes. Preliminary data supports safety with encouraging functional outcomes.

- **Epilepsy** – *Target: Hypothalamic hamartoma / focal lesions*

MRgFUS enables precise, incisionless ablation of epileptogenic zones. Studies in hypothalamic hamartoma report high seizure freedom rates and low complication risk.

Ongoing Clinical Trials

Condition / Indication	Trial ID (NCT)	Target / Approach	Notes
Drug-Resistant Epilepsy (DRE)	NCT02804230	MRgFUS ablation of epileptic foci	Direct lesioning of seizure focus
	NCT03417297	MRgFUS targeting anterior nucleus of thalamus	Neuromodulation approach
	NCT05032105	MRgFUS thalamic target (with comorbid anxiety)	Exploring psychiatric overlap
Essential Tremor	NCT04815508	MRgFUS thalamotomy (VIM nucleus)	Refining targeting, long-term outcomes
Parkinson's Disease	NCT05161988	MRgFUS pallidotomy / subthalamotomy	Expanding beyond tremor to motor symptoms

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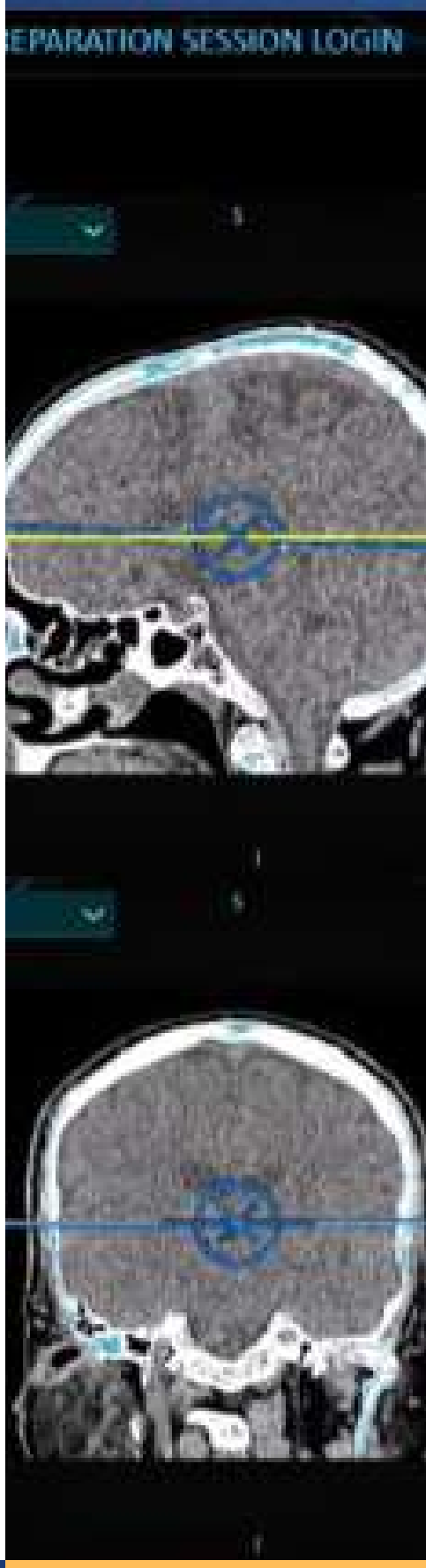

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