Overview

Focused ultrasound is an early-stage, noninvasive, therapeutic technology with the potential to improve the quality of life and decrease the cost of care for patients with Parkinson’s disease. This novel technology precisely focuses beams of ultrasound energy on targets deep in the brain without damaging surrounding normal tissue. Where the beams converge, the ultrasound can produce a variety of therapeutic effects enabling the treatment of Parkinson’s disease without incisions or radiation.

Benefits

Currently, there is no cure for Parkinson’s disease. Treatment options include drug therapies and in select patients, surgeries such as deep brain stimulation or radiofrequency ablation.

Focused ultrasound has the ability to noninvasively treat some Parkinson’s disease patients through thermal ablation of the brain circuits that cause motor symptoms. Focused ultrasound can also open the blood-brain barrier (BBB), a naturally occurring barrier of tightly aligned cells along the blood vessels, allowing the diffusion of medications and antibodies into the brain that can potentially prevent progression and/or restore function.

Advantages:

- **Noninvasive** - no incisions, no risk of infection or bleeding, less pain, and rapid recovery
- **Image-guided** - precision targeting with minimal damage to surrounding tissue
- **Safe, temporary and repetitive opening of the blood brain barrier (BBB)** - enhancing the delivery of therapeutics and immune cells directly to the brain target site

State of the Field

In December 2018, the FDA approved the use of focused ultrasound to treat patients with tremor dominant Parkinson’s disease.

Clinical trials are now underway to evaluate if additional symptoms from Parkinson’s disease such as dyskinesia and involuntary movements can be treated with focused ultrasound ablation of targeted tissues at various anatomical sites. So far, one side of the brain has been safely treated, and projects will soon assess the ability to treat both sides of the brain with staged treatments.

An early pilot study is also evaluating the safety and feasibility of opening the BBB in patients with Parkinson’s dementia in hopes that if successful, disease modifying drugs can be delivered to the brain to help treat the dementia associated with Parkinson’s disease.

Recent preclinical laboratory studies demonstrate focused ultrasound’s ability to safely and temporarily open the BBB, improving the delivery of various neurotherapeutics, including:

- Genes, growth factors, stem cells, neuroprotective and/or neurorestorative drugs
- Anti-alpha synuclein antibodies

These various substances have the ability to slow the progression of the disease, halt the degeneration of nerves within the brain, and even promote healthy nerve tissue regeneration.

For more information visit [www.fusfoundation.org/diseases-and-conditions/neurological/parkinsons-disease](http://www.fusfoundation.org/diseases-and-conditions/neurological/parkinsons-disease)
Focused Ultrasound for Parkinson’s Disease

Mechanisms of Action

Focused ultrasound delivers a variety of effects on tissue, and the following mechanisms are currently in use or under investigation for the treatment of glioblastoma.

**TISSUE DESTRUCTION**
- Thermal Ablation: coagulative cell death

**DELIVERY OF THERAPEUTIC AGENTS**
- **BBB opening**: increased diffusion of therapeutics and immune cells to targeted brain tissue
- **Carrier mediated vehicle**: locally activate encapsulated therapies
- **Sonoporation**: temporarily create pores in the cell membrane, enhancing the delivery of therapeutics into cells

**IMMUNOMODULATION**
- Enhanced production and delivery of the body’s naturally produced antibodies

**NEUROMODULATION**
- Alteration of nerve activity through targeted delivery of a focused ultrasound stimulus

Clinical Trials

A Feasibility Trial Evaluating the Safety and Efficacy of ExAblate Transcranial Magnetic Resonance Guided Focused Ultrasound (MRgFUS) for Unilateral Pallidotomy for the Treatment of L-Dopa Induced Dyskinesia (LID) of Parkinson’s Disease (Sunnybrook Health Sciences Research Centre)

A Pivotal Clinical Trial of the Management of the Medically-Refractory Dyskinesia Symptoms or Motor Fluctuations of Advanced Idiopathic Parkinson’s Disease With Unilateral Lesioning of the Globus Pallidum Using the ExAblate Neuro System (Multi-center: Stanford University, University of Maryland, Brigham and Women’s Hospital, Ohio State University, University of Virginia, Mayo Clinic, University of Pennsylvania, Swedish Neuroscience Institute, Toronto Western Hospital, Rambam Medical Center, Severance Hospital, St. Mary’s Hospital)

A Study to Evaluate the Safety and Feasibility of Temporary Blood Brain Barrier Disruption (BBBD) Using ExAblate MR Guided Focused Ultrasound in Patients with Parkinson’s Disease Dementia (Centro Integral de Neurociencias HM Cinac)

* A Feasibility Clinical Trial of the Management of the Medically-Refractory Dyskinesia Symptoms of Advanced Idiopathic Parkinson’s Disease With Unilateral Lesioning of the Globus Pallidum Using the ExAblate Transcranial System (Multi-center: Stanford University, University of Maryland, Brigham and Women’s Hospital, Ohio State University, University of Virginia)

* The Focused Ultrasound Foundation is fully or partially funding these research projects.
**Clinical Trials (Cont.)**

- A Feasibility Study to Evaluate the Initial Effectiveness of ExAblate Transcranial MRgFUS for Unilateral Thalamotomy in the Treatment of Medication Refractory Tremor Dominant Idiopathic Parkinson's Disease (Multi-center: Provincial Peoples Hospital China, Shonan Fujisawa Tokushukai Hospital, Japan).

- A Feasibility Study to Evaluate Safety and Initial Effectiveness of ExAblate Transcranial MR Guided Focused Ultrasound for Unilateral Pallidotomy in the Treatment of Dyskinesia of Parkinson’s Disease (Yonsei University Health System)

- ExAblate Transcranial MR Guided Focused Ultrasound for the Treatment of Parkinson’s Disease
  Exablate Transcranial MRgFUS targeting the Pallidothalamic Tracts for PD- a Staged Bilateral Approach (Tokyo Women’s Hospital)

- * A Prospective, Randomized, Sham Controlled Study to Evaluate the Safety and Efficacy of ExAblate Subthalamotomy for the Treatment of Parkinson’s Disease Motor Features (Centro Integral de Neurociencias HM Cinac)

- A Pilot Clinical Trial of the Feasibility, Safety, and Efficacy of Subthalamotomy using ExABlate Transcranial System to Treat Cardinal Motor Features of Parkinson’s Disease (Centro Integral de Neurociencias HM Cinac)

- A Feasibility Study on the Safety and Preliminary Efficacy of Bilateral Subthalamotomy Using ExAblate Transcranial System to Treat the Cardinal Motor Features of Parkinson’s Disease (Centro Integral de Neurociencias HM Cinac)

- *Functional Neuroimaging Feedback for Focused Ultrasound Thalamotomy for Tremor Surgery (Ohio State University)

- The Effect of Lesion Characteristics in Magnetic Resonance Guided Focused Ultrasound Surgery (MRgFUS) on Tremor in Essential Tremor and Parkinson's Disease (Rambam Medical Center)

- A Feasibility Study to Evaluate Safety and Initial Effectiveness of ExAblate Transcranial MRgFUS for Unilateral Thalamotomy in the Treatment of Medication Refractory Tremor Dominant Idiopathic Parkinson’s Disease (Multi-center: University of Virginia, Swedish Medical Center)

- A Feasibility Clinical Trial of the Magnetic Resonance Guided Focused Ultrasound (MRgFUS) for the Management of Treatment-Refractory Movement Disorders (Multi-center: Sunnybrook Health Sciences Centre, Toronto Western)

- Global Registry: ExAblate 4000 Transcranial MR Guided Focused Ultrasound (TcMRgFUS) of Neurological Disorders (Multi-center: Rambam Medical Center, Sheba Medical Center, Sunnybrook Health Sciences Centre, Swedish Medical Center, University of Virginia, Pennsylvania Hospital, University of Maryland)

* The Focused Ultrasound Foundation is fully or partially funding these research projects.
## Research Project Inventory

### Preclinical Studies

* MRgFUS Blood-Brain Barrier Drug Delivery with AAV2 Gene Therapy Microbubble Drug Conjugates (Artenga, Inc)

* Antibody Delivery Through the BBB Opening in an Alpha-Synuclein Model (Columbia University)

* Focused Ultrasound for Increased Delivery of Intranasal DNA Nanoparticles to Rat Brain (Northeastern University)

* Functional Neuroimaging Feedback for Focused Ultrasound Thalamotomy for Tremor Surgery (Ohio State University)

* MRgFUS Gene Delivery for Neuroprotection in Parkinson’s Disease (Weill Cornell Medical Center)

* The Focused Ultrasound Foundation is fully or partially funding these research projects.
Research Sites

Clinical Trials
Brigham and Women’s Hospital (United States)
Catholic University of Korea (Korea)
Centro Integral de Neuociencias HM Cinac (Spain)
Henan Provincial Peoples Hospital (China)
Mayo Clinic (United States)
Ohio State University (United States)
Rambam Medical Center (Israel)
Severance Hospital (South Korea)
St. Mary’s Hospital (United Kingdom)
Stanford University School of Medicine (United States)
Sunnybrook Health Sciences Centre (Canada)
Swedish Neuroscience Institute (Seattle, WA, United States)
Tokyo Women’s Hospital (Japan)
Toronto Western Hospital (Canada)
Universitats-Kinderspital Zurich FUS-Center (Switzerland)
University of Maryland School of Medicine (United States)
University of Pennsylvania (United States)
University of Toronto (Canada)
University of Virginia (United States)
Yonsei University Health System, Severance Hospital (Korea)
Weill Cornell Medical Center (United States)

Preclinical laboratories
Columbia University (United States)
Johns Hopkins University (United States)
Northeastern University (United States)
Sunnybrook Health Sciences Centre (Canada)
University of Virginia (United States)
Weill Cornell Medical Center (United States)
Focused Ultrasound for Parkinson’s Disease

Commercial Treatment Sites

- Brigham and Women’s Hospital (United States)
- Centre Medic Diagostic Alomar, ResoFus Alomar (Spain)
- Centro Integral de Neurociencias HM Cinac (Spain)
- Kantonsspital St. Gallen (Switzerland)
- Mayo Clinic (United States)
- Ohio State University (United States)
- Rambam Medical Center (Israel)
- Sonimodul, AG (Switzerland)
- St. Mary’s Hospital (United Kingdom)
- Stanford University (United States)
- Sunnybrook Health Sciences Research Centre (Canada)
- Swedish Medical Center (United States)
- Universita degli Studi di Palermo (Italy)
- Universitats-Kinderspital Zurich FUS-Center (Switzerland)
- University of Maryland (United States)
- University of Pennsylvania (United States)
- University Sperling Medical Group (United States)
- University of Utah (United States)
- University of Virginia (United States)
- Weill Cornell Medical Center (United States)

Manufacturers

- **Artenga** | Ottawa, ON, Canada | www.artenga.com
- **BrainSonix Corp.** | Sherman Oaks, CA | www.brainsonix.com
- **CarThera** | Paris, France | www.carthera.eu
- **INSIGHTEC LTD** | Tirat Carmel, Israel | www.insightec.com
- **MBInsight Systems** | Miaoli County, Taiwan
- **NaviFUS** | New Taipei City, Taiwan | www.navi-fus.com
- **TheraWave, LLC** | New York, NY
Focused Ultrasound for Parkinson’s Disease

Media

**Ultrasound Treatment Might Ease Parkinson’s Tremors**
WebMD – November 27, 2019

“The clinical application of this technique for neurological diseases is an absolute novelty. Few patients know of this treatment option so far, and there are not many specialized centers equipped with the required technology.” - Dr. Federico Bruno, University of L’Aquila in Italy.

**Focused Ultrasound Treats Tremors from Parkinson’s Disease**
Philadelphia Tribune – July 22, 2019

“After three hours, Collier came out of the MRI. The procedure targeted the part of his brain giving him a tremor in his right hand. That hand was now still, unlike his trembling left hand.”

**How Ultrasound Could Help Curb Parkinson’s**
Medical News Today – June 10, 2019

“We were able to curb the rapid progression of neurodegeneration while improving the neuronal function. We expect our study will open new therapeutic avenues for the early treatment of central nervous system diseases.” – Dr. Elisa Konofagou, Colombia University

**Parkinson’s Tremors Vanish with Incisionless Surgery**
HealthLeaders Media – April 30, 2019

“We’re still in the early stages of this technology, and I think there’s going to be a lot of development in terms of what can be done with it.” – Dr. Gordon H. Baltuch, University of Pennsylvania Perelman School of Medicine.

**Roanoke native gains FDA approval to treat Parkinson’s tremors with focused sound waves**
Roanoke Times – December 21, 2018

Elias said the procedure will give Parkinson’s patients whose tremors are no longer controlled by medication the option of trying a less invasive procedure than deep brain stimulation.

**UVa study: Focused ultrasound’s benefits extend to quality of life, mood**
The Daily Progress – November 11, 2018

Participants also reported improved emotional well-being and ability to perform simple tasks and lower incidence of depression and anxiety, [Dr. Jeff Elias] said.
Focused Ultrasound for Parkinson’s Disease

Videos

Kimberly Spletter, Parkinson’s patient, University of Maryland:

Ron Nickelson, Parkinson’s patient, The Ohio State University Wexner Medical Center:

To view these and other videos about focused ultrasound technology and patients, visit
https://www.fusfoundation.org/the-foundation/news-media/multimedia
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Key Publications


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