FOCUSED ULTRASOUND FOUNDATION

Focused Ultrasound *Overview*

The Technology

Focused ultrasound is an early-stage, noninvasive therapeutic technology with the potential to improve the lives of millions of patients with a variety of serious medical disorders. It offers a disruptive, game changing alternative or complement to surgery, radiation therapy, drug delivery and cancer immunotherapy.

This revolutionary technology has the potential to increase the quality and longevity of life and decrease the cost of care by transforming the treatment of a range of indications including:

- **benign and malignant tumors of the brain, breast, prostate, liver and pancreas**
- **Parkinson's and Alzheimer's disease and epilepsy**
- **depression and obsessive compulsive disorder**
- **arthritis and hypertension**
- **uterine fibroids**

Focused ultrasound treats tissue with multiple intersecting beams of high-frequency sound focused accurately on targets deep in the body without damaging surrounding structures, much like beams of light can be focused on a point with a magnifying glass. At the focal point where the beams converge, the ultrasound energy can act in multiple ways to induce a variety of biological effects enabling the treatment of a wide variety of medical disorders. Currently there are 19 mechanisms of action under study including:

TISSUE DESTRUCTION

- **Thermal Ablation**: coagulative cell death
- **Histotripsy**: mechanical cell disruption
- **Microvascular disruption**: ischemic cell death
- **Sonodynamic therapy**: activation of cell toxic drugs
- **Gene therapy**: activation of apoptotic cell death

IMMUNOMODULATION

- **Tumor cell disruption**: increased immune cell trafficking; exposure of tumor antigens and release of cytokines
- **Augmentation of immunotherapy drugs**
- **Enhanced drug delivery**

DELIVERY OF THERAPEUTIC AGENTS

- **Drugs, genes, growth factors, and stem cells**
- **Increase vascular permeability and blood-brain barrier opening**
- **Increased cell membrane permeability**

RADIATION

- **Alternative to ionizing radiation**
- **Decreased radiation dose:** tumor preconditioning and sensitization

For a complete description of all 19 mechanisms of action, see the Foundation's website www.fusfoundation.org/the-technology/mechanisms-of-action.

There are currently more than 135 clinical indications or disorders in various stages of development, and the number is increasing rapidly. Most are early stage. Worldwide 33 indications have regulatory approval; in the US, six have been approved by the FDA. Focused ultrasound is not for every patient or every disorder. Much work remains to be done to determine where this technology provides unique cost-effective value. For a list of all clinical indications, see the Foundation's website www.fusfoundation.org/diseases-and-conditions-all/overview.

The Problem

It can take decades for a new therapeutic technology like focused ultrasound to become a mainstream standard of care. Every year that is subtracted from that process could reduce death, disability, and suffering for countless people.

Development Status

Development stage: Conceptual → Preclinical → Pilot Trials → Pivotal Trials → Outside US Approvals → FDA Approvals → US Reimbursement

Cardiovascular
- Hypertension
- Atrial fibrillation
- Peripheral artery disease
- Varicose veins
- Arteriovenous malformations
- Atherosclerosis
- Cardiac hypertrophy†
- Cardiac pacing
- Coarctation of the aorta†
- Congestive heart failure
- Deep vein thrombosis
- Fetal heart anomalies
- Heart valve calcifications
- Hematoma†
- Hemophilia B†
- Hypoplastic left heart syndrome
- Mitral regurgitation†
- Septal perforation
- Ventricular tachycardia†

Endocrine Disorders
- Thyroid nodules
- Graves' disease
- Hyperparathyroidism
- Thyroid cancer
- Diabetes

Gastrointestinal
- Liver metastases
- Liver tumors
- Pancreatic tumors
- Biliary tract cancer
- Colorectal tumors
- Malignant obstructive jaundice
- Esophageal tumors
- Liver fibrosis

Miscellaneous
- Dercum's disease†
- Head & neck tumors
- Hypersplenism
- Lipoma†
- Melanoma
- Multiple tumors[1]
- Obesity
- Root canal endodontia
- Ultrasound-induced local anesthesia
- Wound healing†

Musculoskeletal
- Bone metastases
- Arthritis - facetogenic
- Bone cancer
- Bone tumors, benign
- Epicondylitis
- Multiple myeloma[2]
- Osteoid osteoma
- Plantar fasciitis
- Soft tissue cancer
- Soft tissue injury
- Soft tissue tumor, benign
- Arthritis
- Arthritis - ankle†
- Arthritis - hand
- Arthritis - hip
- Arthritis - knee
- Arthritis - sacroiliac
- Desmoid tumors
- Disc degeneration
- Sacral chordoma
- Muscle atrophy
- Osteomyelitis†
- Rotator cuff injury

Neurological
- Essential tremor
- Parkinson's disease, tremor dominant
- Depression
- Neuropathic pain
- Obsessive-compulsive disorder
- Parkinson's disease, dyskinesia
- Alzheimer's disease
- Amyotrophic lateral sclerosis
- Astrocytoma (SEGA)
- Brain metastases
- Cancer pain
- Dementia
- Dystonia
- Epilepsy
- Glioblastoma
- Holmes tremor
- Huntington's disease
- Neuroblastoma, pediatric
- Painful amputation neuromas
- Pontine glioma
- Traumatic brain injury
- Addiction
- Cavernomas
- Hydrocephalus
- Intracerebral hemorrhage
- Migraine†
- Multiple sclerosis
- Spinal cord injury
- Thromboembolic stroke
- Trigeminal neuralgia
- Anorexia

Ophthalmological
- Glaucoma
- Keratoplasty
- Macular degeneration

Pulmonary
- Lung cancer
- Lung metastases
- Rhinitis

Urological
- Benign prostatic hyperplasia[3]
- Prostate cancer[3]
- Kidney tumors
- Kidney stones
- Acute kidney injury
- Acute tubular necrosis
- Bladder tumors
- Ureterocele
- Urinary tract infection

Women's Health
- Uterine fibroids
- Breast cancer
- Breast fibroadenoma
- Cervicitis
- Uterine adenomyosis
- Cervical tumors
- Ectopic pregnancy
- Endometrial tumors
- Endometriosis
- Endometriosis, colorectal
- Ovarian tumors
- Retained placenta
- Vaginal tumors
- Vulvar dystrophy
- Fetal bladder obstruction
- Polycystic ovary syndrome
- Twin-twin transfusion syndrome

Development Status

Development stage: Conceptual → Preclinical → Pilot Trials → Pivotal Trials → Outside US Approvals → FDA Approvals → US Reimbursement

Oncological

- Bone metastases
- Prostate cancer[3]
- Bone cancer
- Breast cancer
- Kidney tumors
- Liver metastases
- Liver tumors
- Multiple myeloma[2]
- Pancreatic tumors
- Soft tissue cancer
- Biliary tract cancer
- Brain metastases
- Cancer pain
- Cervical tumors
- Colorectal tumors
- Endometrial tumors
- Glioblastoma
- Head & neck tumors
- Lung cancer
- Lung metastases
- Malignant obstructive jaundice
- Melanoma
- Multiple tumors[1]
- Neuroblastoma, pediatric
- Ovarian tumors
- Pontine glioma
- Sacral chordoma
- Thyriod cancer
- Vaginal tumors
- Bladder tumors
- Esophageal tumors

Pain

- Bone metastases
- Arthritis - facetogenic
- Bone cancer
- Bone tumors, benign
- Multiple myeloma[2]
- Neuropathic pain
- Osteoid osteoma
- Pancreatic tumors
- Soft tissue injury
- Arthritis
- Arthritis - ankle†
- Arthritis - hand
- Arthritis - hip
- Arthritis - knee
- Arthritis - sacroiliac
- Cancer pain
- Dercum's disease†
- Desmoid tumors
- Painful amputation neuromas
- Migraine†
- Osteomyelitis†
- Rotator cuff injury
- Trigeminal neuralgia

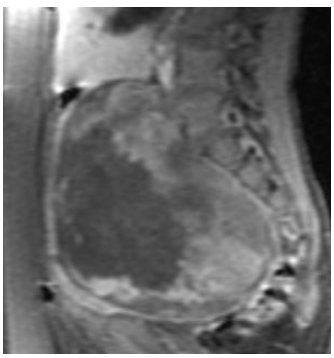
Pediatrics

- Bone metastases
- Osteoid osteoma
- Soft tissue cancer
- Soft tissue tumor, benign
- Astrocytoma (SEGA)
- Desmoid tumors
- Epilepsy
- Multiple tumors[1]
- Neuroblastoma, pediatric
- Sacral chordoma
- Arteriovenous malformations
- Coarctation of the aorta†
- Hydrocephalus
- Hypoplastic left heart syndrome
- Septal perforation

Desmoid tumor


Uterine fibroid


Pelvic tumor

Pancreatic cancer


The Focused Ultrasound Foundation

SAVING TIME = SAVING LIVES

The Foundation is a unique medical research, education, and advocacy organization created as the catalyst to accelerate the development and adoption of focused ultrasound and thereby reduce death, disability, and suffering for countless patients. To achieve its goals, the Foundation utilizes an approach that is entrepreneurial, high-impact, high performance, market-driven and results oriented.

By identifying opportunities and overcoming barriers, the Foundation is shortening the time from laboratory research to widespread treatment. Major initiatives include:

- Influencing the direction of the field, setting research priorities, and creating an urgent, patient centric culture
- Providing resources, both human and financial capital
- Fostering collaboration and stimulating innovation
- Creating, aggregating and sharing knowledge
- Cultivating the next generation of clinicians and scholars
- Increasing awareness

The Foundation has a robust research program and organizes, conducts, and supports clinical trials and pre-clinical laboratory studies with an emphasis on brain disorders, cancer, and immunotherapy. It is the largest non-governmental source of focused ultrasound research funding.

Board of Directors

Neal F. Kassell, MD
Chairman, Focused Ultrasound Foundation
Former Co-chair of Neurosurgery, University of Virginia

Scott Beardsley, PhD
Dean, University of Virginia Darden School of Business

Eugene V. Fife
Founding Principal, Vawter Capital, LLC
Former Chairman, Goldman Sachs International

John R. Grisham
Author

William A. Hawkins III
Senior Advisor, EW Healthcare Partners
Retired Chairman & CEO, Medtronic

Daniel P. Jordan, PhD
President Emeritus, Thomas Jefferson Foundation

Syaru Shirley Lin, PhD
Adjunct Faculty, Chinese University of Hong Kong
Director, Goldman Sachs Asia Bank

Michael R. Lincoln
Global Business Department Chair, Cooley LLP

Michael Milken
Chairman, Milken Institute

Edward D. Miller, MD
Former CEO, Johns Hopkins Medicine

Frederic H. Moll, MD
Chief Development Officer, J&J Medical Devices
Co-founder, Auris Health & Intuitive Surgical

Charles "Wick" Moorman IV
Former Chairman & CEO, Norfolk Southern
Former CEO, Amtrak

Steve H. Rusckowski
Chairman, President and CEO, Quest Diagnostics Inc.
Former CEO, Philips Healthcare

Gary Shapiro
President & CEO, Consumer Technology Association (CTA)®

Carl P. Zeithaml, PhD
Former Dean and F. S. Cornell Professor of Free Enterprise, McIntire School of Commerce, University of Virginia

Council

Co-chairs
Jane P. Batten
Charles H. Seilheimer, Jr.

.....

John B. Adams, Jr.
Dorothy N. Batten
Ellen Block
Amanda Brown
Deborah Caldwell
Jessica Che-yi Chao
Nancy J. & Thomas N. Chewning
Marguerite & Norwood Davis
Peter Gabriel
David Goode
Rick Hamilton
Diane Heller
Cecelia S. & William J. Howell
Kat Imhoff
Dean L. Kamen
Ann Kingston
Harry Lester
Jonna Mendez
Paula F. Newcomb
Wyndham G. Robertson
Mary Lou Seilheimer
Alice H. Siegel
Allan C. Stam, PhD
Aaron Stern, MD, PhD
Fredi & Howard Stevenson
Bernice Szeto
Andrew C. von Eschenbach, MD

Focused Ultrasound Foundation

For more information, visit **www.fusfoundation.org** or email FUND@fusfoundation.org
1230 Cedars Court , Suite 206 | Charlottesville, VA 22903 | 434.220.4993