2023

State of the Field

Focused Ultrasound Foundation

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Focused Ultrasound Foundation

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FOCUSED ULTRASOUND FOUNDATION

Dear Friends,

As we look at advancements in the field of focused ultrasound in 2022, we continue to be in awe of a field that continues to grow. Last year, the steady drumbeat of growth across the depth and breadth of scientific discovery and translation to human treatments accelerated in earnest. With the dip in 2020 with Covid, we have seen a return to growth levels seen previously to the pandemic.

This year, we reorganized the report into distinct chapters.We hope that this change will allow readers to navigate quickly to the sections that most interest them. Additionally, this year we continue to fine-tune the mechanism of action data which underwent a major upgrade for the 2023 report. We have added a new graphic detailing the stage of research along with the various mechanisms of action associated with each of the indications; see Chapter II, page II.15. We are so proud to premiere this new graphic because we believe that, in the coming years, we will see a steady stream of regulatory approvals for ultrasound applications other than thermal ablation.

I encourage everyone to read this report and learn about what is new in focused ultrasound!

Until next year,

Emily White, MD
Editor in Chief
2023 State of the Field

FOCUSED ULTRASOUND FOUNDATION

Thank you

A special thank you to the hundreds of scientists, clinicians, and company representatives around the globe who contribute data to this report. The vast majority of this document is based on self-reported data, and this report would not be possible without their input.

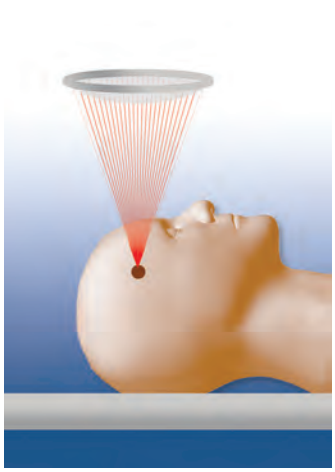
Also, thank you to the Board of Directors, Council members, and generous donors who support the Foundation, without whom we would not be able to produce this report.

Lastly, a special thank you to my State of the Field team. Sara, Mary Rose, and Mike—thank you for your incredible hard work and for always showing up to our weekly meetings with a can-do attitude, ready and willing to take on the next crazy idea. Your ability to keep hundreds of spreadsheets organized and verify millions of data points is a wonder and amazement to me. You are the heart of this report and your passion and dedication to it shine brilliantly each and every year.

Focused Ultrasound in Brief

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 broad range of indications. Focused ultrasound treats tissue with multiple intersecting beams of high-frequency sound, which can be focused accurately on targets deep in the body without damaging surrounding structures, much as 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.



Varying ultrasound power, utilizing continuous versus pulsing modes, and changing the total treatment time can all create different ultrasound applications. These applications can be categorized based on the type of energy they deliver—thermal or mechanical—and whether the effects of treatment are permanent or transient. When focused ultrasound produces a high-power, continuous pressure wave, thermal energy accumulates rapidly at the focal point. This technique, termed thermal ablation, is currently used most frequently in the clinic, and produces permanent effects. However, additional ultrasound treatment regimens are currently under investigation in preclinical experiments and clinical trials. One of the most promising ultrasound applications currently in clinical trials is a low-power, pulsed treatment that produces mild mechanical forces capable of enhancing drug delivery to the brain, by temporarily opening the blood-brain barrier. This effect is transient, and treated tissue reverts to normal function within a few hours.

The effects induced by focused ultrasound can vary greatly depending on the ultrasound application and the type of tissue being targeted. These biological effects are sometimes uniquely paired to a set of ultrasound parameters, as is the case with blood-brain barrier disruption, but others may be induced by multiple ultrasound applications. One active area of research is immunomodulation—altering the immune response in treated tissue. The altered immune response is dependent on the nature of the focused ultrasound treatment parameters, although most treatments do induce a response.

Focused Ultrasound Today

There are currently 166 clinical indications or disorders in various stages of development, and the number is increasing rapidly. Most are early stage. Worldwide, 32 indications have regulatory approval; in the US, 8 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 significant therapeutic and cost-effective value.

2023 Executive Summary

Focused Ultrasound Foundation

Advancements and Trends
2022 Data Analysis

New this year is an Executive Summary section where we highlight the major advancements in the field by topic area. If you are unable to review the entire document in detail, the next twenty or so pages should give you a good feel for what is going on at a high level. We are hopeful that these bite-sized nuggets of knowledge will spur your intellectual curiosity. When time is available, you will be able to do a deeper dive into the topics of particular interest to you.

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2022 Highlights

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I. 5 Research Sites
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Indication Development Pipeline

7

New indications

3

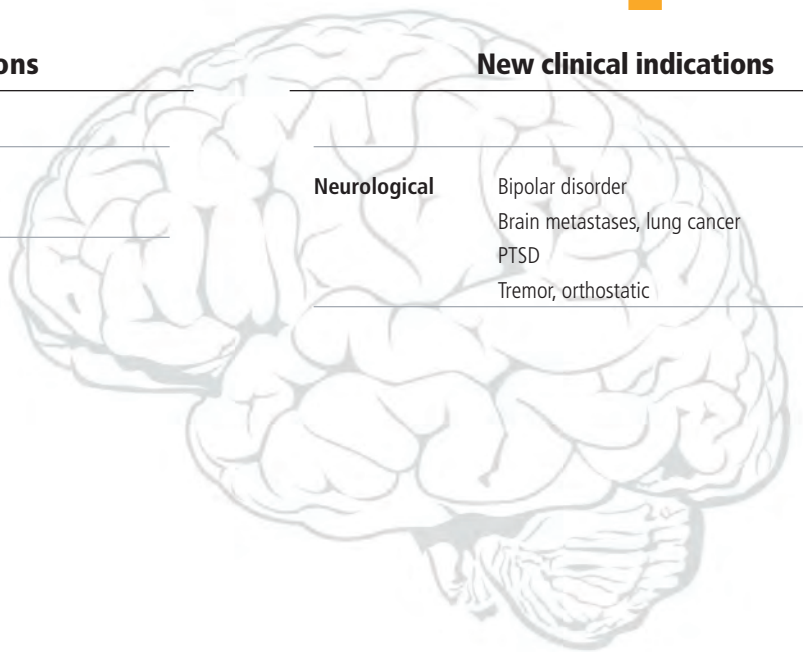
New preclinical indications

Gastrointestinal	Periodontal disease
Neurological	Autism Cerebral palsy

4

New clinical indications

Neurological	Bipolar disorder Brain metastases, lung cancer PTSD Tremor, orthostatic



2022 advancements

We saw seven new indications added to the focused ultrasound landscape in 2022. Four of these indications were identified when we learned of the first-in-human clinical trials for bipolar disorder, brain metastases for lung cancer, post traumatic stress disorder, and orthostatic tremor. It should be noted that six of the seven new indications are in the neurological space. New indications at the preclinical stage of development for 2022 include autism, cerebral palsy, and periodontal disease.

For further details
Chapter 2: Indication Development Pipeline

Clinical Trials with New MOAs

No.of Trials	Biological Effect	Indication	Clinical Trial ID
1	**Histotripsy**		
	Alteration of tissue mechanics	Heart valve calcifications	NCT05235568
1	**Hyperthermia**		
	Radiosensitization	Bone metastases	NCT05167669
18	**Nonthermal**		
	Liquid biopsy	Glioblastoma	NCT05383872
	Neuromodulation	Anxiety	NCT05228964
		Bipolar disorder	NCT05228964
		Dementia	NCT05417555
		Depression	NCT05228964, NCT05301036, NCT05697172
		Essential tremor	NCT05475340
		Neuropathic pain	NCT05145426, NCT05303415, NCT05624762
		Obsessive-compulsive disorder	NCT05467085
		Parkinson's disease, dyskinesia	NCT04593875
		Parkinson's disease, tremor	NCT05475340
		PTSD	NCT05228964
	Radiosensitization	Melanoma	NCT05620290
	Sonodynamic therapy	Glioblastoma	NCT05362409
		Pontine glioma	NCT05123534
2	**Nonthermal, BBB opening**		
	Drug delivery	Alzheimer's disease	NCT05469009
	Drug delivery, Immunotherapeutic	Brain metastases, lung cancer	NCT05317858

New ways to treat disease

As evidenced by the data in the referenced chapter, most research being conducted around other mechanisms of action is still early-stage, and the clinical trials underway are generally first-in-human safety and feasibility studies. Note that thermal ablation tissue destruction is the only mechanism of action that currently has regulatory approval and is commercially available for 32 indications.

New in 2022, we learned of a group using focused ultrasound to address the blood-nerve barrier to deliver drugs to the spinal cord and particular cells within the peripheral nerves that are notoriously difficult targets for drug delivery.

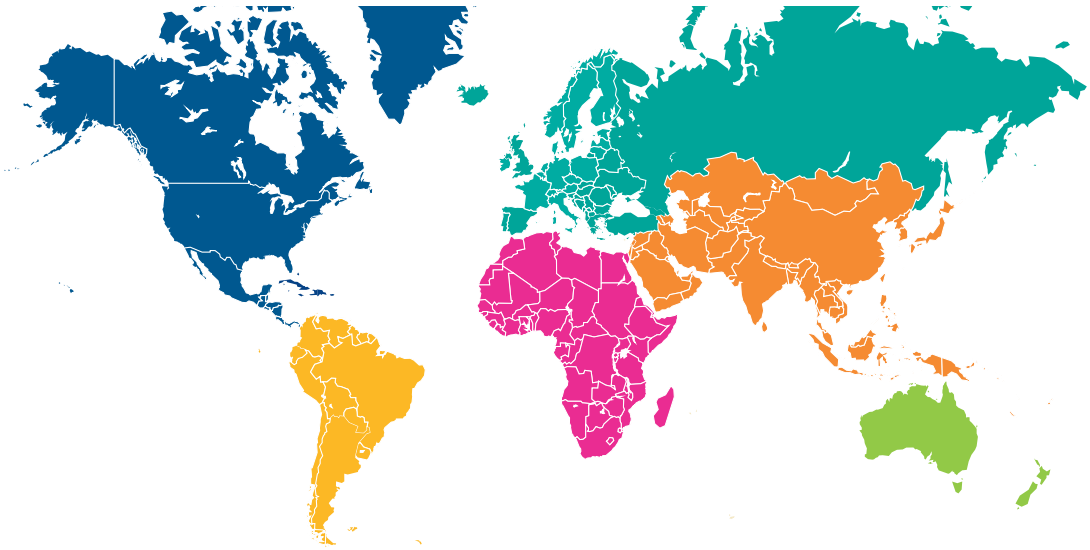
For further details
Chapter 3: Mechanisms of Action

Research Sites

21%

Increase over 2021 in clinical research sites

	Total	North America	Europe	Asia	South America	Oceania	Africa
Clinical research	**293**	85	104	99	–	5	–
Preclinical research	**152**	69	41	39	–	3	–
Mechanisms of action research	**180**	80	42	55	–	3	–
Technical research	**151**	61	49	39	–	2	–



Research and commercial sites expand globally

In 2022, the focused ultrasound field saw gains of 51 new clinical research sites worldwide. The greatest growth occurred in North America, with 25 additional new sites. The US became the top country in clinical research growth clocking in at 77 sites.

For further details
Chapter 4: Research Sites

Centers of Excellence

10

Centers of Excellence

2%

of the research sites worldwide are COEs

30%

of FUS publications came from COEs

Centers of Excellence

1 University of Virginia Health System
2 The Institute of Cancer Research and The Royal Marsden
3 Brigham and Women's Hospital
4 University of Maryland School of Medicine
5 Sunnybrook Health Sciences Centre
6 Stanford University School of Medicine
7 Inserm - LabTAU
8 Physics for Medicine Paris
9 Children's National Hospital
10 University Medical Center Utrecht

COEs lead the field

There are 10 Centers of Excellence (COEs) around the world. In 2022, the total number of publications by those 10 COEs was 202. Another way to say this is while only 2 percent of the focused ultrasound research sites are COEs, they contributed nearly a third of the scientific papers in 2022.

For further details
Chapter 5: Centers of Excellence

Awareness

677

FUS publications

Top three topics: radiology, engineering, and neurological science

FUS abstracts presented

72%

Increase at FUS meetings

108%

Increase at other symposia

518

Abstracts presented at FUS meetings

394

Abstracts presented at other symposia

Abstracts and publications gain a wider audience

In 2022 we began tracking an additional 12 symposia that are associations or societies of medical professionals, where focused ultrasound technology is consistently beginning to see wider exposure and rising levels of interest from practicing clinicians. We view this as an encouraging trend and hope it will lead to an increase in patient access to the technology in future years.

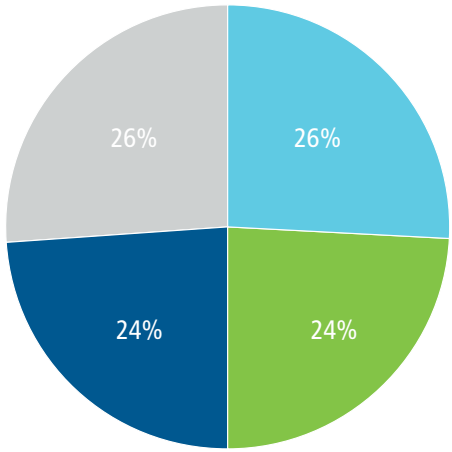
For further details
Chapter 6: Awareness

Patient Treatments

98,048

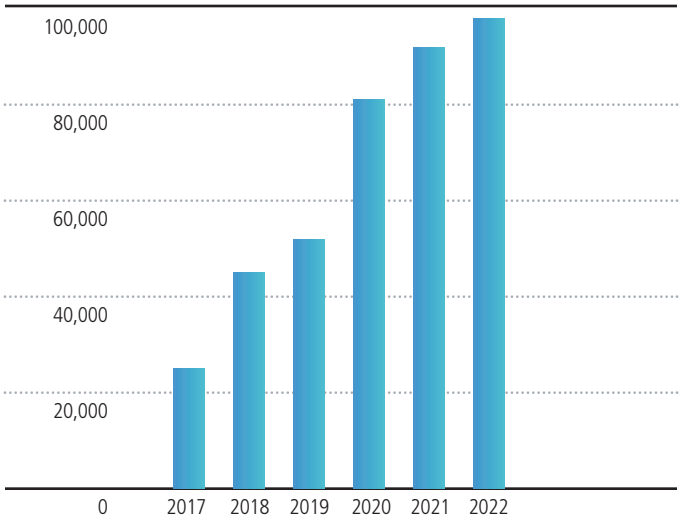
Treatments in 2022

565,210 cumulative treatments



2022 Indications treated

- Uterine fibroids
- Liver tumors
- Pancreatic tumors
- Other



Annual patient treatments

Commercial treatments center on cancer and women's health

Patient treatments increased in 2022 for both pancreatic and liver tumors. These two indications, combined with uterine fibroids, comprise nearly 75 percent of the total patient treatments last year.

For further details
Chapter 7: Patient Access

Commercial Treatment Sites

932

Sites

25%
North America
Annualized growth from 2013–2022
219 sites

4%
Europe
Annualized growth from 2013–2022
290 sites

12%
Asia
Annualized growth from 2013–2022
405 sites

4%
South America
Annualized growth from 2013–2022
7 sites

19%
Oceania
Annualized growth from 2013–2022
4 sites

15%
Africa
Annualized growth from 2013–2022
7 sites

Treatment sites grow with potential for further expansion

As of 2022 there are nearly 1,000 treatment sites worldwide, a mere 10 percent of the 10,000 potential treatment sites we estimate would exist if the global market were saturated.

For further details
Chapter 7: Patient Access

FUS Industry

104

Companies

17

Newly identified companies

- **10** Clinical device manufacturers
- **5** OEM
- **2** Microbubble

16

Companies with approved devices

- **3** North America
- **4** Europe
- **9** Asia

An expanding ecosystem

During 2022, 17 new focused ultrasound companies entered the ecosystem—ten manufacturers, five OEM, and two microbubble companies. We estimate the field employs approximately 3,000 individuals spread around the world. Just under half of the worldwide employee count is concentrated in the United States, Israel, and France. The median company size is 12 employees, and two thirds of the companies have 20 or fewer employees.

For further details
Chapter 8: FUS industry

Regulatory Approvals

13

New global regulatory approvals

China | NMPA

Benign prostatic hyperplasia

Macau | ISAF

Benign prostatic hyperplasia
Prostate tumors

United Arab Emirates | MOHAP

Essential tremor
Neuropathic pain
Parkinson's disease, tremor

Israel | AMAR

Prostate tumors

Taiwan | FDA

Parkinson's disease, tremor

United Kingdom | MHRA

Benign prostatic hyperplasia
Essential tremor
Neuropathic pain
Parkinson's disease, tremor
Prostate tumors

Previously approved indications spread to additional countries

Last year 13 new regulatory approvals were granted by six regulatory bodies. Two new countries, Macau and the United Arab Emirates, became part of the focused ultrasound treatment community.

For further details
Chapter 9: Regulatory Approvals

Approved Device Manufacturers

32
Unique approved Indications

39
Regulatory agencies

16
Companies with approved devices

337
Total approvals by agencies

Commercialization

We are seeing increasing evidence that the field is transitioning from primarily a science-based research environment to commercialization with patient treatment spaces focused on marketing and sales.

For further details
Chapter 10: Commercial FUS Manufacturers

✪ Location of device manufacturers with regulatory approval

Investments

$3.14B

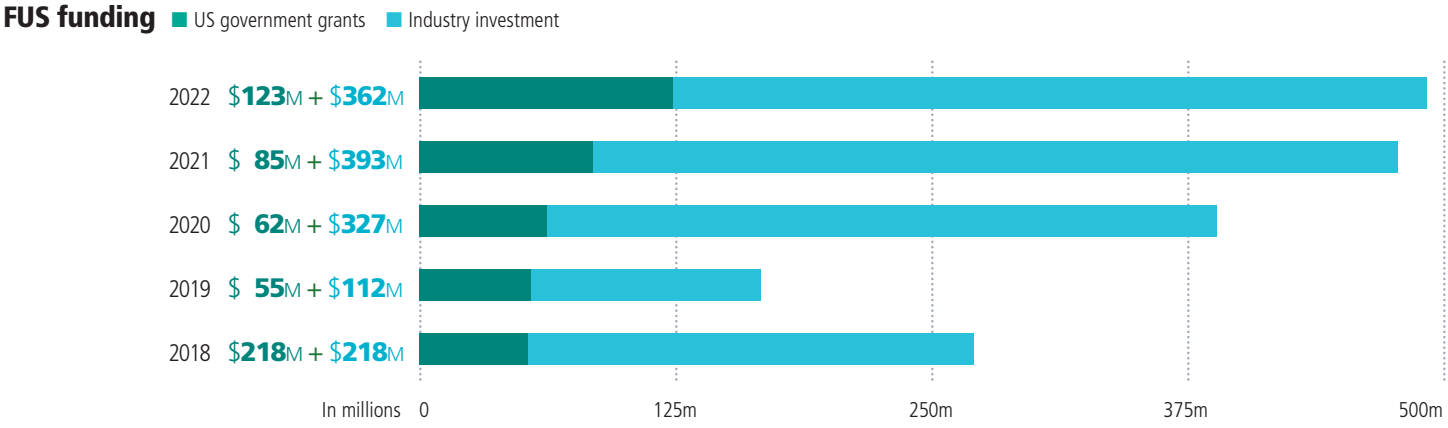
Industry investments
Cumulative

$362.3M

Industry investments
in 2022

$122M

US government investments
in 2022



By the numbers

For the third year in a row more than 300 million dollars was invested in focused ultrasound industry companies bringing the total for those three years to more than one billion dollars. Additionally, 2022 was the first year that the US government invested more than one hundred million dollars in research funding.

Last year we saw the first investment in focused ultrasound from a pharmaceutical company. We also saw existing investors in the ecosystem diversify with investments in additional companies—noteworthy investors include Johnson and Johnson Innovations, OrbiMed Advisors, and the Yongjin Group.

For further details
Chapter 11: Financial Landscape

Reimbursement

32

Indications with regulatory approvals
Worldwide

8

Indications with US FDA approvals

44%

have reimbursement
with varying levels in at least one country

63%

have reimbursement
5 indications are insured in some US states

Breaking a barrier to treatment

Since very few patients can pay out-of-pocket for their medical care, reimbursement of medical procedures is a critical element of the healthcare ecosystem. Despite its importance, the process of medical reimbursement is not straightforward. As patients and physicians alike experience, reimbursement is a complicated system that involves a labyrinth of policies. What works in one country, or even region within a country, does not in others. In the coming years, the issue of reimbursement will become more important as the field collectively moves the technology through clinical trials and regulatory approvals.

Reimbursement is critical to patient access and to driving further investment in the field as early-stage investors need to know there is a profitable road map.

For further details
Chapter 12: Reimbursement

Veterinary Program

67%

Sites growth rate

from 2021 to 2022

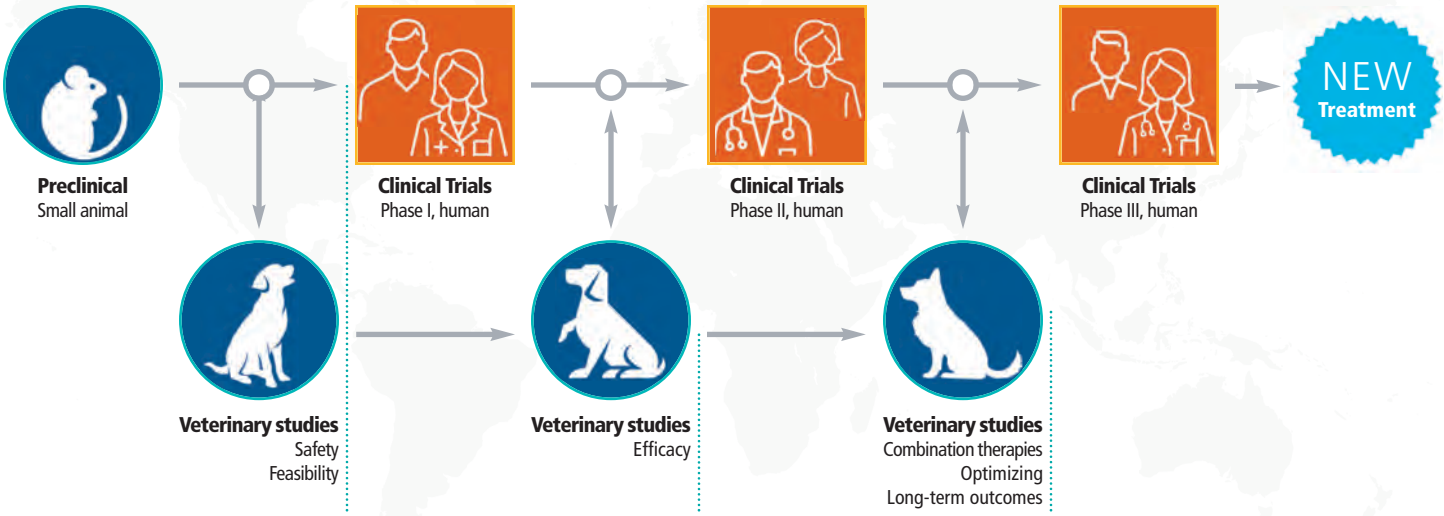
14

Indications studied in clinical trials

Active or completed trials

Comparative medicine

Integrated and comparative device development plan



Research and growth in treating companion animals

Veterinary medicine offers researchers a unique opportunity to expand their research and introduce commercial focused ultrasound applications into a market with reduced regulatory burdens, while also collecting data in naturally occurring disease models to support human clinical trials.

For further details
Chapter 13: Veterinary Medicine

2023 Indication Development Pipeline

Focused Ultrasound Foundation

Overview

Chapter 2 includes a high-level overview of the indication pipeline and a deep dive for each indication on the various mechanisms of action and their stage of development. In the State of Research and Regulatory Approvals (nicknamed "the rainbow chart") we list the most advanced stage of research/regulation/reimbursement regardless of geographic location. Further detail on indication status by geographic location can be found later in the report.

New this year we saw the addition of three preclinical indications—periodontal disease, autism, and cerebral palsy. Four indications advanced to first-in-human trials, all of which were neurological—bipolar disorder, lung cancer brain metastases, post traumatic stress disorder, and orthostatic tremor.

II. Indication Development Pipeline

II. 2 Overview
II. 3 Development State Advancements and New Indications

State of Research and Regulatory Approvals

II. 4 By Body System
II. 8 Neurological Indications
II. 9 Indications with Anecdotal Case Reports
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Mechanisms of Action

II.14 About MOAs
II.15 By Body System
- II.15 Cardiovascular
- II.17 Endocrine disorders
- II.18 Gastrointestinal
- II.20 Miscellaneous
- II.22 Musculoskeletal
- II.24 Neurological
- II.33 Ophthalmological
- II.34 Pulmonary
- II.35 Urological
- II.37 Women's health

Development Stage Advancements and New Indications

2022

7

New indications

Gastrointestinal	Periodontal disease
Neurological	Bipolar disorder
	Brain metastases, lung cancer
	PTSD
	Tremor, orthostatic
	Autism
	Cerebral palsy

Development stage

Preclinical Clinical trials

2022

4

Indications advanced to first-in-human clinical trials

Neurological	Bipolar disorder†
	Brain metastases, lung cancer†
	PTSD†
	Tremor, orthostatic†

† New Indication for 2021

State of Research and Regulatory Approvals by Body System

Cardiovascular

Cardiac

- Atrial fibrillation
- Heart valve calcifications
- Cardiac hypertrophy
- Cardiac pacing
- Coarctation of the aorta
- Congestive heart failure
- Fetal heart anomalies
- Hypoplastic left heart syndrome
- Mitral regurgitation
- Septal perforation
- Ventricular tachycardia

Peripheral

- Varicose veins
- Hypertension
- Peripheral artery disease
- Twin-twin transfusion syndrome
- Arteriovenous malformations
- Atherosclerosis
- Deep vein thrombosis
- Hematoma
- Hemophilia

Endocrine disorders

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

Gastrointestinal

- Pancreatic tumors, malignant
- Liver metastases
- Liver tumors
- Biliary tract cancer
- Colorectal tumors
- Dental infections[1]
- Esophageal tumors
- Gastric tumors
- Malignant obstructive jaundice
- Nonalcoholic steatohepatitis (NASH)
- Pancreatic tumors, benign
- Inflammatory bowel disease
- Irritable bowel syndrome
- Liver fibrosis
- Periodontal disease†

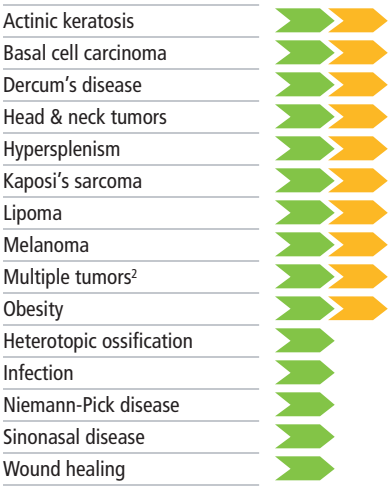
There are 166 distinct indications for 2022.

1 Indication was listed as root canal endodontia in last year's State of the Field Report.

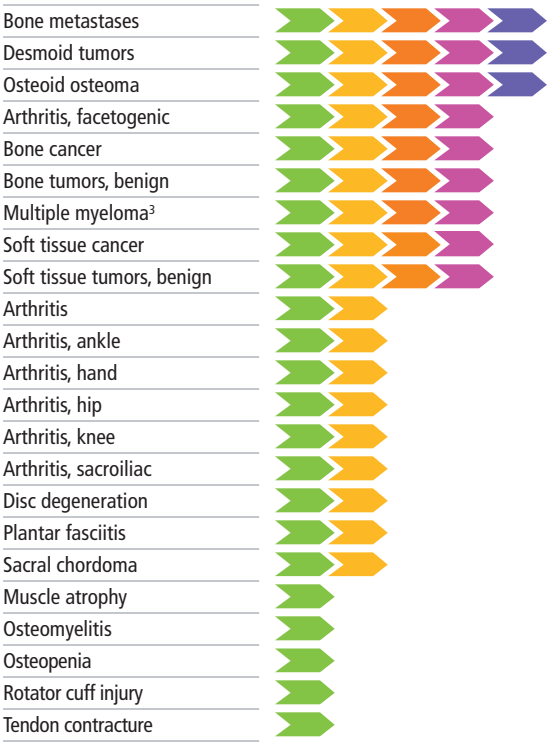
† New in 2022

State of Research and Regulatory Approvals by Body System continued

Miscellaneous



Musculoskeletal



There are 166 distinct indications for 2022.

2 Protocols inclusive of more than one indication

3 Multiple myeloma approval is based on bone metastases.

State of Research and Regulatory Approvals by Body System continued

Development stage: Preclinical → Pilot trials → Pivotal trials → Approvals → Reimbursement

Neurological

Movement disorder
- Essential tremor
- Parkinson's disease, tremor
- Parkinson's disease, dyskinesia
- Dystonia
- Dystonia, hand
- Epilepsy
- Holmes tremor
- Tremor, orthostatic†
- Cerebral palsy†

Neurodegenerative
- Alzheimer's disease
- Amyotrophic lateral sclerosis
- Dementia
- Huntington's disease
- Multiple sclerosis
- Parkinson's disease, other[4]
- Rett syndrome

Other
- Hydrocephalus
- Neuromyelitis optica

Pain
- Neuropathic pain
- Cancer pain
- Headache
- Neuropathy
- Painful amputation neuromas
- Trigeminal neuralgia

Psychiatric
- Depression
- Obsessive-compulsive disorder
- Anxiety
- ADHD
- Bipolar disorder†
- Mood disorder
- Opioid and other addictions
- PTSD†
- Schizophrenia
- Autism†

Neurological continued

Trauma
- Traumatic brain injury
- Spinal cord injury

Tumor
- Brain tumors, general
- Glioblastoma
- Astrocytoma
- Brain metastases, breast cancer
- Brain metastases, lung cancer†
- Neuroblastoma
- Neurofibromatosis
- Pontine glioma
- Brain metastases, melanoma

Vascular
- Stroke, intracerebral hemorrhage
- Stroke, thromboembolic
- Cavernomas

There are 166 distinct indications for 2022.

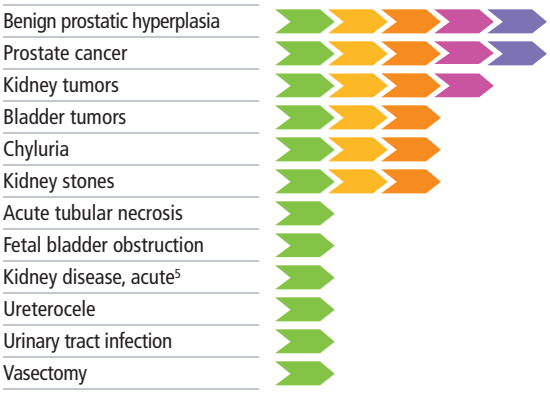
4 Treatment of the underlying cause of the disease
† New in 2022

State of Research and Regulatory Approvals by Body System continued

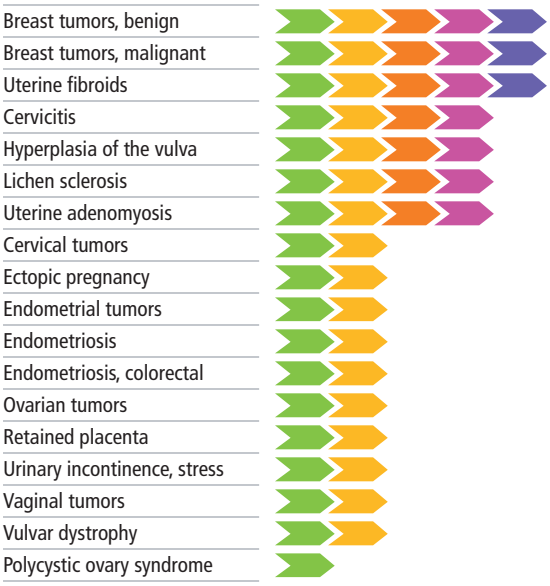
Ophthalmological

Pulmonary

Urological



Women's health



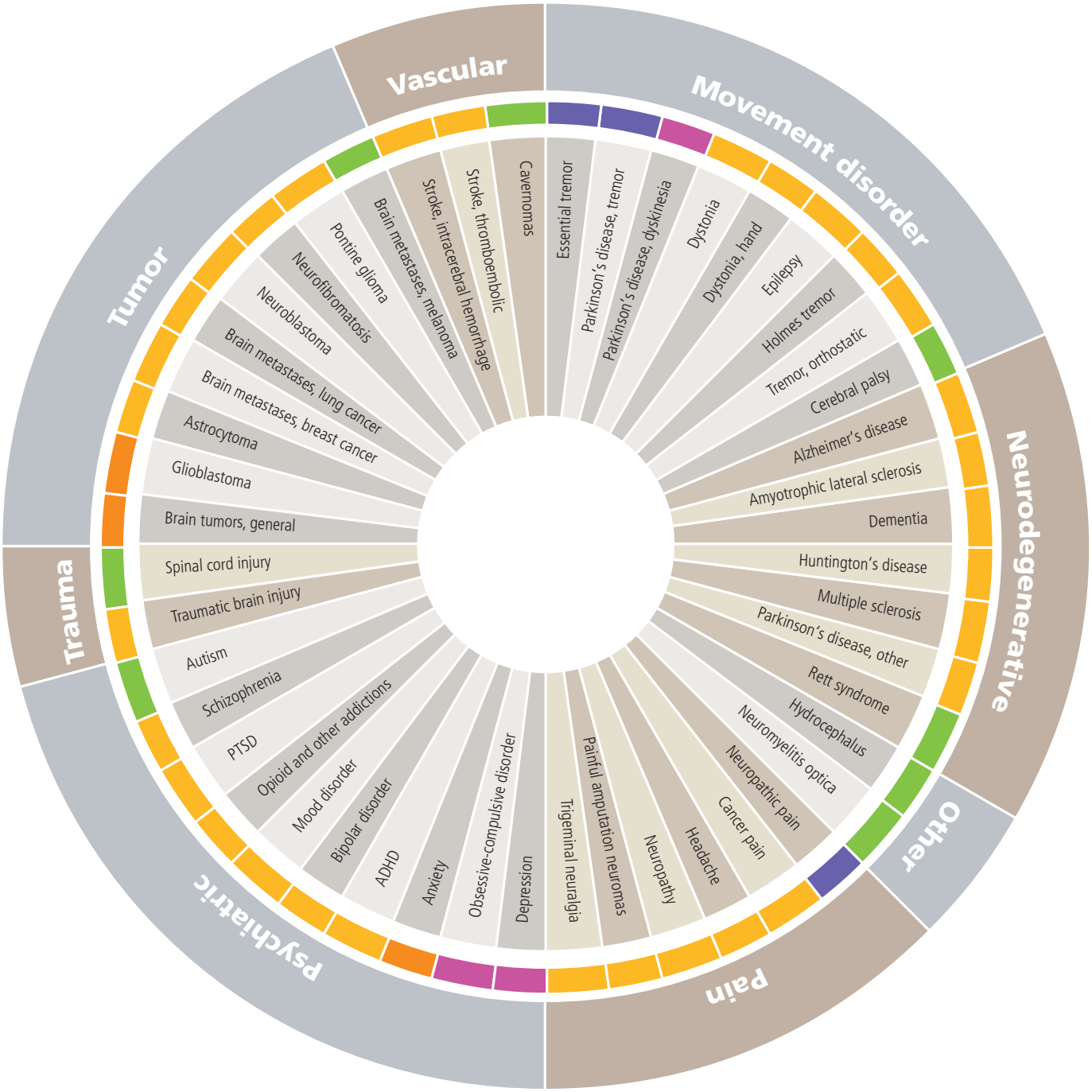
There are 166 distinct indications for 2022.

5 Indication was listed as acute kidney injury in last year's State of the Field Report.

Neurological Indications

Out of the 48 neurological indications, only 6 have regulatory approval.

Development stage: Preclinical Pilot trials Pivotal trials Outside US approvals Reimbursement



Indications with Anecdotal Case Reports

Indications	Date	Mechanism of action	Reference
Endocrine disorders			
Insulinoma	2010	Thermal ablation, Tissue destruction	https://doi.org/10.1007/s00270-010-9884-0
Gastrointestinal			
Liver alveococcosis	2015	Thermal ablation, Tissue destruction	https://doi.org/10.1007/s10396-018-0914-x
Miscellaneous			
Warts	2021	Thermal ablation, Tissue destruction	https://doi.org/10.1159/000515075
Neurological			
Ataxia	2022	Thermal ablation, Tissue destruction	https://doi.org/10.1002/mds.28918
Women's health			
Gestational trophoblastic disease	2022	Thermal ablation, Tissue destruction	https://doi.org/10.1186/s12905-022-02114-0

What are anecdotal case reports?

Anecdotal case reports are publications that describe instances wherein a clinician used focused ultrasound technology to treat a patient, or a very small number of patients, outside of a clinical trial. Many of these indications are extremely rare, making it difficult to recruit enough patients for a clinical trial, or are too early stage for clinical trial. However, we believe it is worth including these anecdotal cases to show the many ways in which clinicians are using focused ultrasound around the world to help patients in need.

Areas of Interest

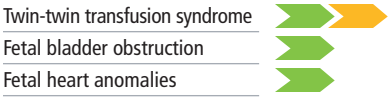
A note on multiple listings

In the so-called rainbow chart—see pages II.4–II.7—the categories are body systems, comprising a group of tissues structured to perform specific functions. All indications in development for focused ultrasound treatment appear on this chart, in the body system category to which they belong. Thus, bone metastases is in the Musculoskeletal category, but nowhere else.

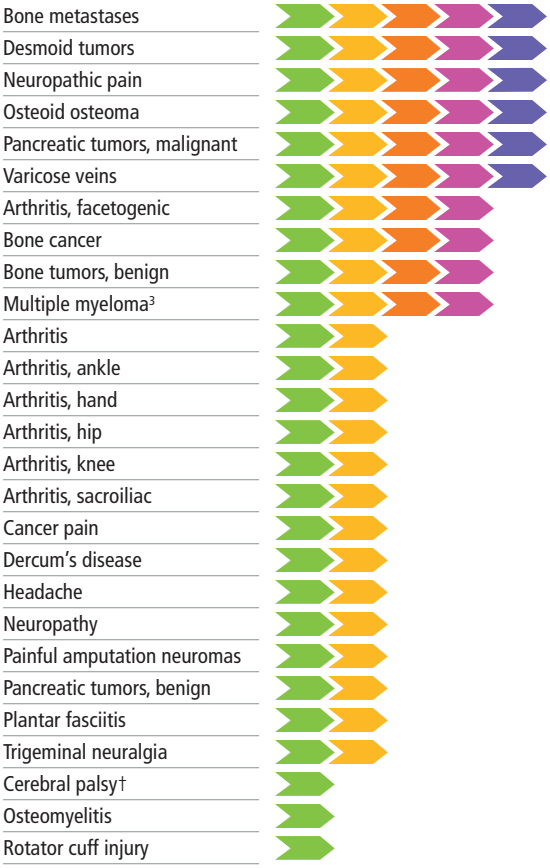
In an effort to see the data through a different lens, four "Areas of Interest"—Fetal, Oncology, Pain, and Pediatrics—have been identified and comprise the categories in the chart on pages II.11–II.12. Indications that do not match with any of the Areas of Interest will not appear in this chart, but those that do may appear in multiple categories; bone metastases, for example, appears in Oncology, Pain, and Pediatrics. Looking at the indications by "Area of Interest" reveals patterns and trends over time that might otherwise be difficult to discern.

State of Research and Regulatory Approvals by Area of Interest

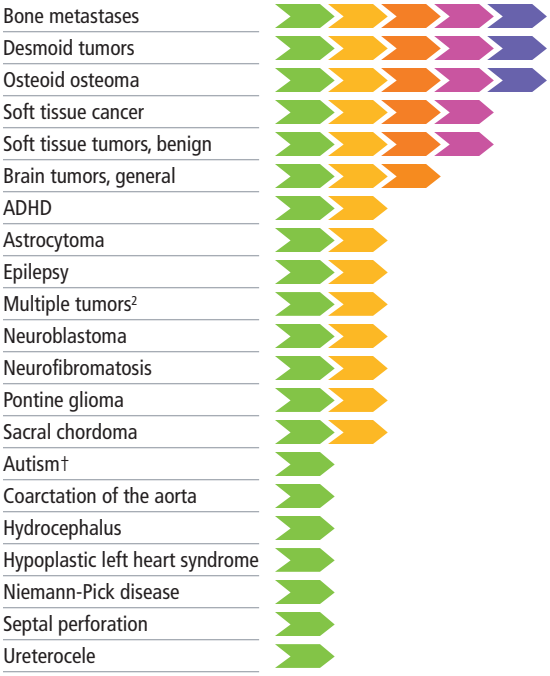
Fetal



Pain

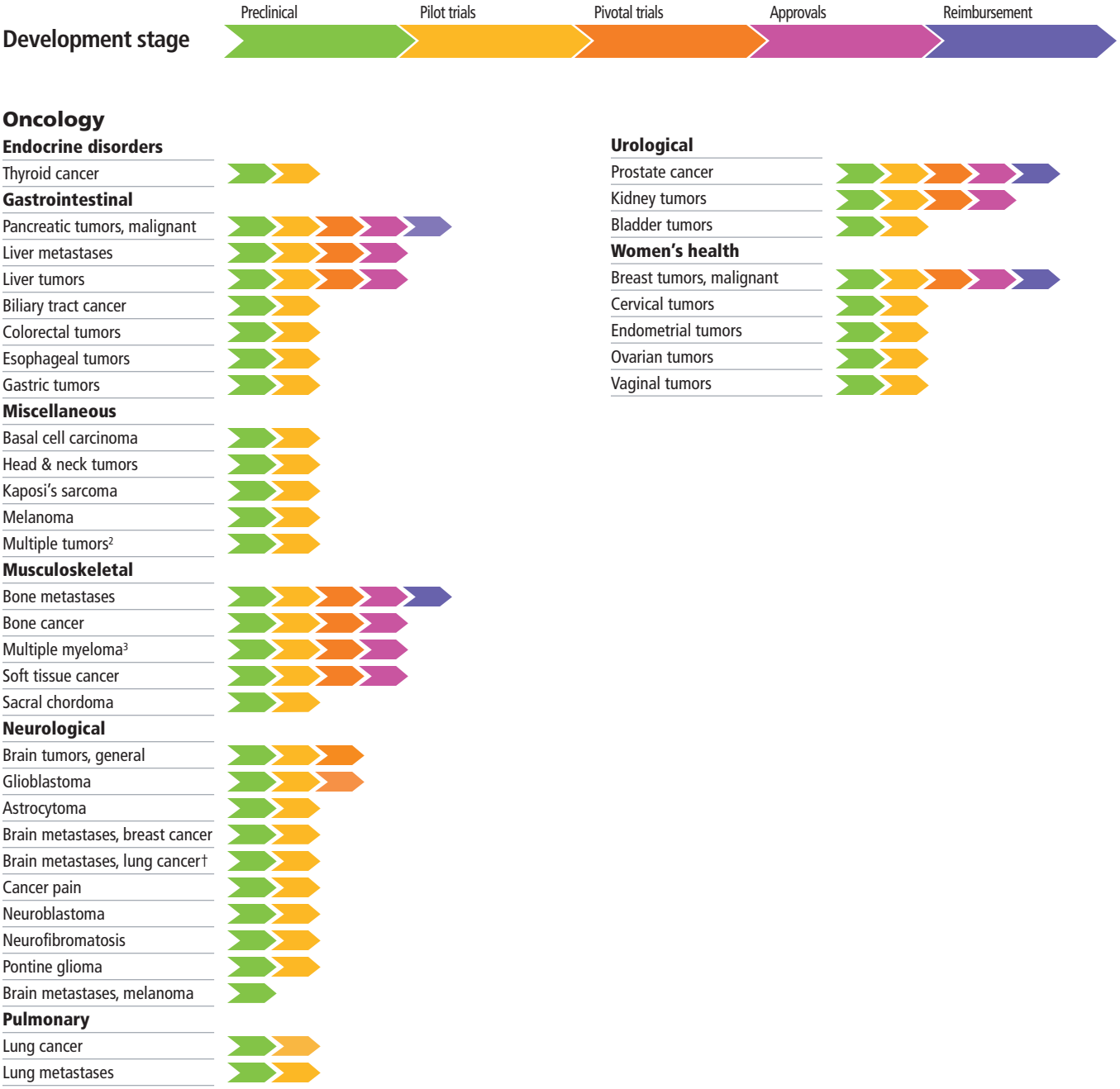


Pediatrics



2 Protocols inclusive of more than one indication
3 Multiple myeloma approval is based on bone metastases.
† New in 2022

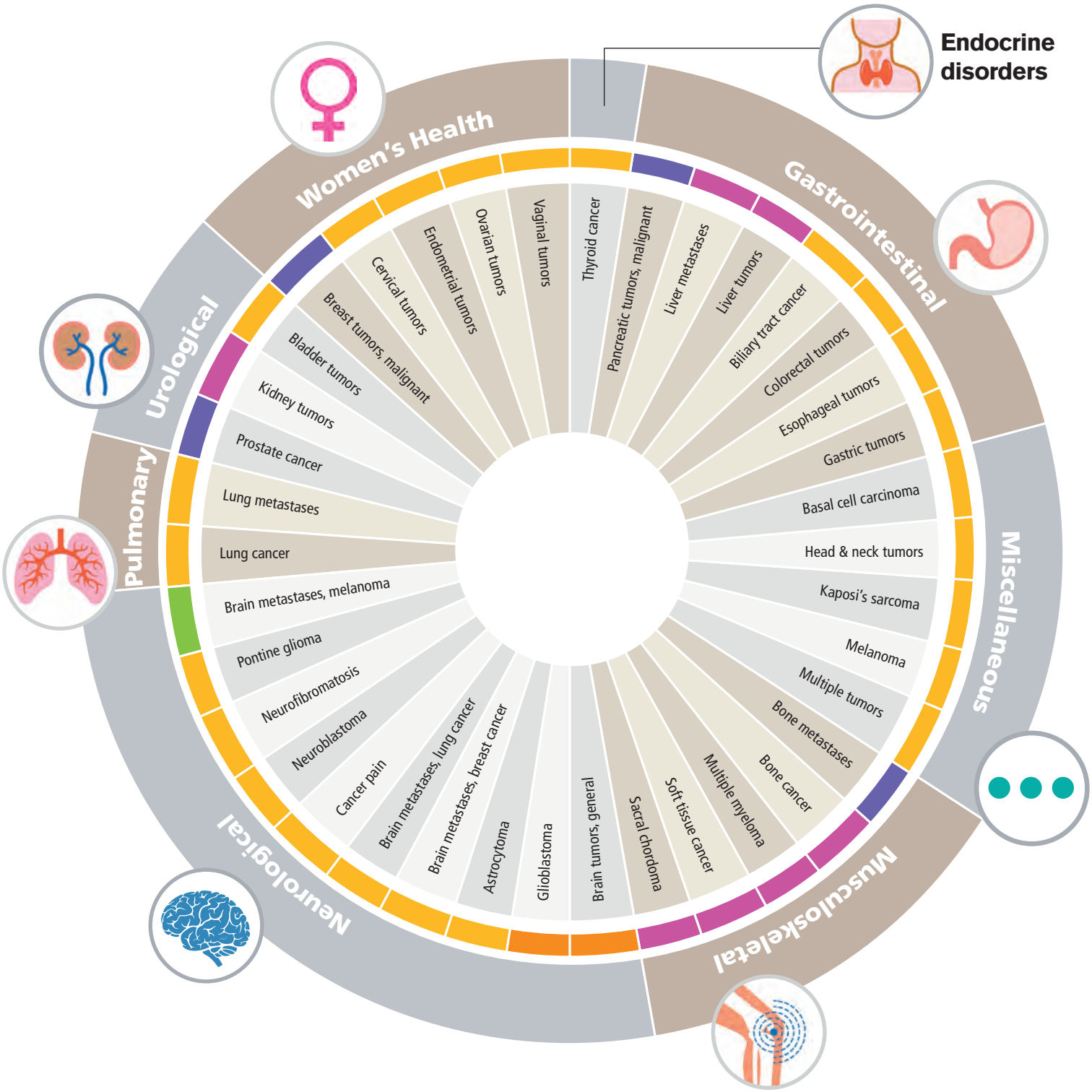
State of Research and Regulatory Approvals by Area of Interest continued



2 Protocols inclusive of more than one indication
3 Multiple myeloma approval is based on bone metastases.
† New in 2022

Oncology Indications

Development stage: Preclinical Clinical trials Pilot trials Outside US approvals Reimbursement



Mechanisms of Action

Ultrasound applications and biological effects

In its most simple form, a Mechanism of Action (MOA) occurs when an ultrasound application produces a biological effect. Please see Chapter Three for a comprehensive overview of the ultrasound applications and biological effects currently under investigation. The following table is the state of development of all the indications by biological effect. This information was presented for the first-time last year, but in a slightly different form. As you review this table notice that the diseases with increased numbers of MOA under investigation trend towards the diseases where the current standard of care is lacking and where the medical community wants new treatment options. Pay particular attention to both pancreatic cancer and glioblastoma both in the number of MOA's, and, as is evidenced in Chapter 3, the number of research sites performing this type of research.

Histotripsy
- Alteration of tissue mechanics
- Immunomodulation
- Liquid biopsy
- Tissue destruction

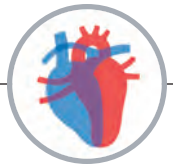
Hyperthermia
- Chemosensitization
- Drug delivery
- Drug delivery, immunotherapeutic
- Immune cell trafficking
- Immunomodulation
- Radiosensitization
- Tissue destruction
- Vasodilation

Nonthermal
- Alteration of tissue mechanics
- Amplification of cancer biomarkers
- Angiogenesis
- Cardiac pacing
- Clot lysis
- Drug delivery
- Drug delivery, immunotherapeutic
- Drug delivery, vehicle
- Gene delivery
- Immune cell trafficking
- Immunomodulation
- Increased vascular permeability
- Kidney stone fragmentation
- Kidney stone propulsion
- Liquid biopsy
- Neuromodulation
- Radiosensitization
- Sonodynamic therapy
- Sonoporation
- Stem cell delivery
- Tissue destruction
- Vascular occlusion
- Vasodilation

Nonthermal - BBB opening
- BBB opening
- Drug delivery
- Drug delivery, immunotherapeutic
- Drug delivery, vehicle
- Gene delivery
- Stem cell delivery

Thermal ablation
- Alteration of tissue mechanics
- Chemosensitization
- Hemostasis
- Immunomodulation
- Liquid biopsy
- Neuromodulation
- Tissue destruction

Mechanisms of Action and Indications—Body Systems



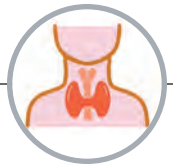
Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Cardiovascular				
Cardiac				
Atrial fibrillation	Thermal ablation Tissue destruction			
Cardiac hypertrophy	Nonthermal Drug delivery, vehicle			
Cardiac pacing	Nonthermal Cardiac pacing			
Fetal heart anomalies	Histotripsy Tissue destruction			
Heart valve calcifications		Histotripsy Alteration of tissue mechanics		
Mitral regurgitation	Histotripsy Tissue destruction			
Ventricular tachycardia	Thermal ablation Tissue destruction			
Peripheral				
Arteriovenous malformations	Nonthermal Tissue destruction	Nonthermal Vascular occlusion	Thermal ablation Tissue destruction[6]	
Atherosclerosis	Nonthermal Drug delivery Sonodynamic therapy Sonoporation Stem cell delivery			

6 Off-label treatment

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Cardiovascular continued				
Peripheral continued				
Deep vein thrombosis	Histotripsy Alteration of tissue mechanics Tissue destruction Nonthermal Clot lysis Drug delivery, vehicle Increased vascular permeability Sonodynamic therapy			
Hematoma	Histotripsy Tissue destruction Thermal ablation Hemostasis			
Hemophilia	Nonthermal Drug delivery			
Hypertension		Thermal ablation Tissue destruction		
Peripheral artery disease	Nonthermal Drug delivery, vehicle	Thermal ablation Tissue destruction		
Twin-twin transfusion syndrome	Nonthermal Vascular occlusion Thermal ablation Tissue destruction	Thermal ablation Hemostasis		
Varicose veins		Nonthermal Vascular occlusion		Thermal ablation Tissue destruction

Mechanisms of Action and Indications—Body Systems continued



Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Endocr ine disorders				
Diabetes	Nonthermal Neuromodulation			
Thyroid cancer	Histotripsy Tissue destruction			
Thyroid nodules				Thermal ablation Tissue destruction

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Gastrointestinal				
Colorectal tumors	Nonthermal Drug delivery, vehicle	Nonthermal Drug delivery Thermal ablation Tissue destruction		
Dental infections[1]		Histotripsy Tissue destruction		
Esophageal tumors		Thermal ablation Immunomodulation		
Gastric tumors		Thermal ablation Immunomodulation	Thermal ablation Tissue destruction[6]	
Inflammatory bowel disease	Nonthermal Drug delivery			
Liver metastases	Histotripsy Tissue destruction Nonthermal Tissue destruction	Nonthermal Drug delivery Sonoporation		Thermal ablation Tissue destruction
Liver tumors	Histotripsy Alteration of tissue mechanics Immunomodulation Hyperthermia Immunomodulation Radiosensitization Tissue destruction Nonthermal Tissue destruction	Histotripsy Tissue destruction Nonthermal Drug delivery, vehicle Sonoporation		Thermal ablation Tissue destruction

1 Indication was listed as root canal endodontia in 2022 State of the Field Report.

6 Off-label treatment

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Gastrointestinal continued				
Pancreatic tumors	Nonthermal Drug delivery, vehicle			Thermal ablation Tissue destruction
Pancreatic tumors, benign			Thermal ablation Tissue destruction	
Pancreatic tumors, malignant	Histotripsy Immunomodulation Hyperthermia Drug delivery, immunotherapeutic Immunomodulation Nonthermal Drug delivery, immunotherapeutic Drug delivery, vehicle Immunomodulation Sonodynamic therapy Tissue destruction Thermal ablation Immunomodulation	Histotripsy Tissue destruction Hyperthermia Chemosensitization Drug delivery Nonthermal Drug delivery Immunomodulation Sonoporation	Thermal ablation Tissue destruction	
Periodontal disease	Histotripsy Tissue destruction Nonthermal Drug delivery, vehicle			

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Miscellaneous				
Actinic keratosis		Thermal ablation Tissue destruction		
Basal cell carcinoma		Thermal ablation Tissue destruction		
Dercum's disease		Thermal ablation Tissue destruction		
Head & neck tumors	Hyperthermia Drug delivery Nonthermal Sonoporation Tissue destruction	Hyperthermia Radiosensitization Nonthermal Radiosensitization Thermal ablation Tissue destruction		
Heterotopic ossification	Histotripsy Tissue destruction			
Hypersplenism		Thermal ablation Tissue destruction		
Infection	Histotripsy Tissue destruction Nonthermal - BBB Opening Drug delivery Thermal ablation Tissue destruction			
Kaposi's sarcoma		Thermal ablation Tissue destruction		
Lipoma		Thermal ablation Tissue destruction		

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Stages: Clinical	Stages: Commercial treatment	Stages: Approvals
Miscellaneous continued				
Melanoma	Histotripsy Immunomodulation	Nonthermal Radiosensitization Thermal ablation Immunomodulation		
Multiple tumors[2]	Histotripsy Tissue destruction Nonthermal Drug delivery, immunotherapeutic Thermal ablation Tissue destruction	Hyperthermia Chemosensitization Drug delivery Thermal ablation Immunomodulation		
Niemann-Pick disease	Nonthermal - BBB Opening Gene delivery			
Sinonasal disease	Thermal ablation Tissue destruction			
Wound healing	Histotripsy Alteration of tissue mechanics Hyperthermia Drug delivery Nonthermal Alteration of tissue mechanics Drug delivery			

2 Protocols inclusive of more than one indication

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Musculoskeletal				
Arthritis, facetogenic	Nonthermal Tissue destruction			Thermal ablation Tissue destruction
Arthritis, knee		Thermal ablation Tissue destruction		
Arthritis, sacroiliac		Thermal ablation Tissue destruction		
Bone cancer				Thermal ablation Tissue destruction
Bone metastases		Histotripsy Tissue destruction Hyperthermia Radiosensitization Thermal ablation Chemosensitization		Thermal ablation Tissue destruction
Bone tumors, benign				Thermal ablation Tissue destruction
Desmoid tumors				Thermal ablation Tissue destruction
Multiple myeloma[3]				Thermal ablation Tissue destruction
Muscle atrophy	Nonthermal Angiogenesis Gene delivery Stem cell delivery			
Osteoid osteoma				Thermal ablation Tissue destruction

3 Multiple myeloma approval is based on bone metastases.

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Musculoskeletal continued				
Osteopenia	Hyperthermia Drug delivery Nonthermal Alteration of tissue mechanics			
Plantar fasciitis		Thermal ablation Tissue destruction		
Rotator cuff injury	Histotripsy Tissue destruction			
Sacral chordoma		Thermal ablation Tissue destruction		
Soft tissue cancer	Histotripsy Immunomodulation Tissue destruction Hyperthermia Drug delivery Drug delivery, immunotherapeutic Nonthermal Tissue destruction	Thermal ablation Immunomodulation		Thermal ablation Tissue destruction
Soft tissue tumors, benign				Thermal ablation Tissue destruction
Tendon contracture	Histotripsy Tissue destruction Thermal ablation Tissue destruction			

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Neurological				
Movement disorder				
Dystonia		Nonthermal Neuromodulation	Thermal ablation Tissue destruction[6]	
Dystonia, hand			Thermal ablation Tissue destruction[6]	
Epilepsy	Histotripsy Tissue destruction Nonthermal Gene delivery Immunomodulation Nonthermal - BBB Opening BBB opening Drug delivery Gene delivery Thermal ablation Neuromodulation	Nonthermal Neuromodulation	Thermal ablation Tissue destruction[6]	
Essential tremor		Nonthermal Neuromodulation		Thermal ablation Tissue destruction
Parkinson's disease, dyskinesia	Nonthermal - BBB Opening Gene delivery			Thermal ablation Tissue destruction

6 Off-label treatment

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Neurological continued				
Movement disorder continued				
Parkinson's disease, tremor	Nonthermal - BBB Opening Drug delivery	Nonthermal Neuromodulation		Thermal ablation Tissue destruction
Tremor, orthostatic		Nonthermal Neuromodulation Thermal ablation Tissue destruction		
Neurodegenerative				
Alzheimer's disease	Nonthermal Alteration of tissue mechanics Drug delivery Nonthermal - BBB Opening Drug delivery, immunotherapeutic Gene delivery Stem cell delivery	Nonthermal Increased vascular permeability Nonthermal - BBB Opening BBB opening Drug delivery	Nonthermal Neuromodulation[6]	
Amyotrophic lateral sclerosis	Nonthermal - BBB Opening BBB opening	Nonthermal - BBB Opening Drug delivery		
Dementia	Nonthermal - BBB Opening BBB opening			
Huntington's disease	Nonthermal - BBB Opening Gene delivery			

6 Off-label treatment

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Neurological continued				
Neurodegenerative continued				
Multiple sclerosis		Thermal ablation Tissue destruction		
Parkinson's disease, underlying cause	Nonthermal Drug delivery, vehicle Gene delivery Neuromodulation Nonthermal - BBB Opening Drug delivery Gene delivery Thermal ablation Tissue destruction	Nonthermal Liquid biopsy		
Rett syndrome	Nonthermal - BBB Opening Gene delivery			
Other				
Hydrocephalus	Nonthermal Clot lysis			
Neuromyelitis optica	Nonthermal - BBB Opening Drug delivery			
Pain				
Cancer pain	Nonthermal Neuromodulation	Thermal ablation Tissue destruction		
Headache	Nonthermal Neuromodulation			

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Neurological continued				
Pain continued				
Neuropathic pain	Nonthermal Alteration of tissue mechanics Drug delivery, vehicle	Nonthermal Neuromodulation		Thermal ablation Tissue destruction
Neuropathy	Nonthermal Vasodilation	Nonthermal Neuromodulation	Thermal ablation Tissue destruction[6]	
Painful amputation neuromas		Thermal ablation Tissue destruction		
Trigeminal neuralgia			Thermal ablation Tissue destruction[6]	
Psychiatric				
ADHD		Nonthermal Neuromodulation		
Anxiety	Nonthermal - BBB Opening Drug delivery	Nonthermal Neuromodulation		
Autism	Nonthermal - BBB Opening Drug delivery			
Bipolar disorder		Nonthermal Neuromodulation		

6 Off-label treatment

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Neurological continued				
Psychiatric continued				
Depression		Nonthermal Neuromodulation		Thermal ablation Tissue destruction
Mood disorder		Nonthermal Neuromodulation		
Obsessive-compulsive disorder		Nonthermal Neuromodulation		Thermal ablation Tissue destruction
Opioid and other addictions		Nonthermal Neuromodulation		
PTSD		Nonthermal Neuromodulation		
Schizophrenia		Nonthermal Neuromodulation		
Trauma				
Spinal cord injury	Nonthermal - BBB Opening Drug delivery			
Traumatic brain injury	Nonthermal - BBB Opening Drug delivery	Nonthermal Neuromodulation		

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Neurological continued				
Tumor				
Astrocytoma	Nonthermal - BBB Opening Drug delivery	Thermal ablation Tissue destruction		
Brain metastases, breast cancer	Histotripsy Tissue destruction Nonthermal Immunomodulation Nonthermal - BBB Opening BBB opening Drug delivery, immunotherapeutic	Nonthermal - BBB Opening Drug delivery		
Brain metastases, lung cancer		Nonthermal - BBB Opening Drug delivery, immunotherapeutic		
Brain metastases, melanoma	Nonthermal Immunomodulation Sonodynamic therapy Nonthermal - BBB Opening Drug delivery, immunotherapeutic	Nonthermal - BBB Opening Drug delivery		

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Stages: Clinical	Stages: Commercial treatment	Stages: Approvals
Neurological continued				
Tumor continued				
Brain tumors, general	Histotripsy Immunomodulation Hyperthermia Immune cell trafficking Radiosensitization Tissue destruction Nonthermal Amplification of cancer biomarkers Drug delivery Gene delivery Immunomodulation Neuromodulation Radiosensitization Sonodynamic therapy Tissue destruction Vascular occlusion Nonthermal - BBB Opening Drug delivery, immunotherapeutic Drug delivery, vehicle Gene delivery	Nonthermal Liquid biopsy Nonthermal - BBB Opening BBB opening Drug delivery Thermal ablation Liquid biopsy Tissue destruction		

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Neurological continued				
Tumor continued				
Glioblastoma	Histotripsy Immunomodulation Tissue destruction Hyperthermia Drug delivery Drug delivery, immunotherapeutic Immunomodulation Nonthermal Drug delivery, vehicle Immune cell trafficking Immunomodulation Tissue destruction Vascular occlusion Nonthermal - BBB Opening Drug delivery, immunotherapeutic Drug delivery, vehicle Gene delivery	Nonthermal Amplification of cancer biomarkers Liquid biopsy Radiosensitization Sonodynamic therapy Nonthermal - BBB Opening BBB opening Drug delivery Thermal ablation Tissue destruction		
Neuroblastoma		Thermal ablation Tissue destruction		
Neurofibromatosis	Nonthermal - BBB Opening Drug delivery	Thermal ablation Tissue destruction		

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Neurological continued				
Tumor continued				
Pontine glioma	Histotripsy Liquid biopsy Nonthermal Drug delivery	Nonthermal Sonodynamic therapy Nonthermal - BBB Opening Drug delivery Drug delivery, immunotherapeutic		
Vascular				
Cavernomas	Nonthermal Sonodynamic therapy			
Stroke, intracerebral hemorrhage	Histotripsy Tissue destruction Nonthermal Drug delivery Drug delivery, vehicle Nonthermal - BBB Opening Drug delivery	Nonthermal Neuromodulation		
Stroke, thromboembolic	Nonthermal Drug delivery Drug delivery, vehicle Sonoporation Vasodilation Nonthermal - BBB Opening Drug delivery	Nonthermal Angiogenesis Neuromodulation		

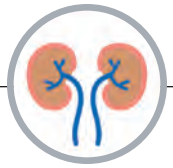
Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Ophthalmological				
Glaucoma		Nonthermal Immunomodulation		Thermal ablation Tissue destruction
Macular degeneration	Nonthermal Vascular occlusion			
Presbyopia	Nonthermal Tissue destruction Thermal ablation Tissue destruction			
Retinal injury	Nonthermal Gene delivery			

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Pulmonary				
Lung cancer	Histotripsy Tissue destruction Hyperthermia Tissue destruction Thermal ablation Tissue destruction	Thermal ablation Immunomodulation		
Rhinitis				Thermal ablation Tissue destruction
Tuberculosis	Thermal ablation Tissue destruction			

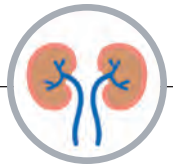
Mechanisms of Action and Indications—Body Systems continued



Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Urological				
Acute tubular necrosis	Nonthermal Stem cell delivery			
Benign prostatic hyperplasia	Histotripsy Tissue destruction Nonthermal Tissue destruction			Thermal ablation Tissue destruction
Bladder tumors	Nonthermal Drug delivery			
Chyluria		Thermal ablation Tissue destruction		
Fetal bladder obstruction	Thermal ablation Tissue destruction			
Kidney disease, acute[5]	Nonthermal Stem cell delivery			
Kidney stones		Nonthermal Kidney stone fragmentation Kidney stone propulsion		
Kidney tumors	Histotripsy Tissue destruction Nonthermal Drug delivery, vehicle			Thermal ablation Tissue destruction

5 Indication was listed as acute kidney injury in 2022 State of the Field Report.

Mechanisms of Action and Indications—Body Systems continued



Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Urological continued				
Prostate cancer	Histotripsy Tissue destruction Hyperthermia Immunomodulation Radiosensitization Nonthermal Drug delivery, vehicle Tissue destruction	Hyperthermia Tissue destruction Nonthermal Immunomodulation		Thermal ablation Tissue destruction
Urinary tract infection	Nonthermal Drug delivery, vehicle			

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Women's health				
Breast tumors, benign		Hyperthermia Tissue destruction		Thermal ablation Tissue destruction
Breast tumors, malignant	Hyperthermia Drug delivery, immunotherapeutic Immunomodulation Vasodilation Nonthermal Drug delivery Drug delivery, vehicle Gene delivery Increased vascular permeability Tissue destruction Nonthermal - BBB Opening BBB opening	Hyperthermia Drug delivery Radiosensitization Nonthermal Immunomodulation Radiosensitization Thermal ablation Immunomodulation		Thermal ablation Tissue destruction
Cervical tumors		Thermal ablation Immunomodulation Tissue destruction		
Cervicitis				Thermal ablation Tissue destruction
Ectopic pregnancy		Thermal ablation Tissue destruction		
Endometrial tumors			Thermal ablation Tissue destruction[6]	

6 Off-label treatment

Mechanisms of Action and Indications—Body Systems continued

Indications by body systems	Stages: Preclinical	Clinical	Commercial treatment	Approvals
Women's health continued				
Endometriosis		Hyperthermia Tissue destruction	Thermal ablation Tissue destruction[6]	
Hyperplasia of the vulva				Thermal ablation Tissue destruction
Lichen sclerosis				Thermal ablation Tissue destruction
Ovarian tumors		Thermal ablation Immunomodulation Tissue destruction		
Retained placenta		Thermal ablation Tissue destruction		
Urinary incontinence, stress			Thermal ablation Alteration of tissue mechanics[6]	
Uterine adenomyosis		Hyperthermia Tissue destruction		Thermal ablation Tissue destruction
Uterine fibroids	Histotripsy Tissue destruction Nonthermal Tissue destruction			Thermal ablation Tissue destruction
Vaginal tumors		Thermal ablation Tissue destruction		

6 Off-label treatment

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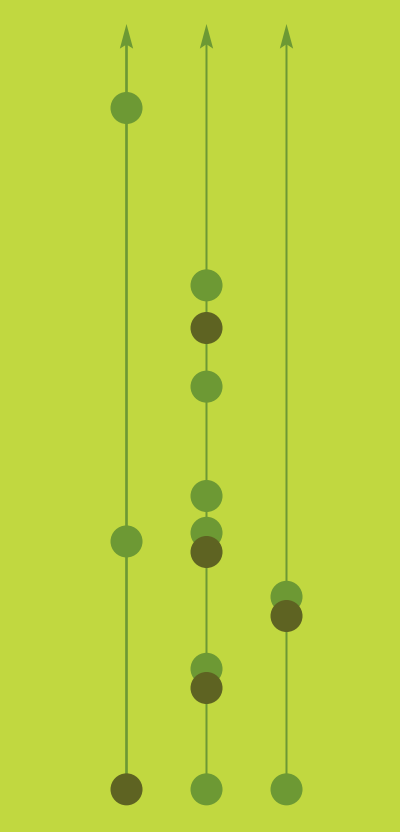
2023 Mechanisms of Action

Focused Ultrasound Foundation



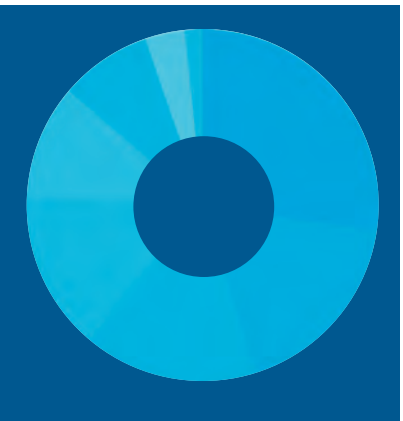
Mechanisms of Action
Ultrasound Applications and Biological Effects

A mechanism of action occurs when an ultrasound application produces a biological effect.

Focused ultrasound is a medical technology that provides a uniquely flexible treatment platform, making it applicable to a wide range of diseases and conditions. It can produce treatments across the spectrum of thermal to mechanical effects, and these various treatments elicit a multitude of responses in biological tissues.

Varying ultrasound power, utilizing continuous versus pulsing modes, and changing the total treatment time create different ultrasound applications. These applications can be categorized based on the type of energy they deliver, thermal or mechanical, and whether the effects of treatment are permanent or transient. When focused ultrasound produces a high-power, continuous pressure wave, thermal energy accumulates rapidly at the focal point. This technique, termed thermal ablation, is currently used most frequently in the clinic, and produces permanent effects, but additional ultrasound treatment regimens are under investigation in preclinical experiments and clinical trials. One of the most promising ultrasound applications being assessed in clinical trials is a low-power, pulsed treatment that produces mild mechanical forces capable of enhancing drug delivery to the brain. This effect is transient, and treated tissue reverts to normal function within a few hours.

The effects induced by focused ultrasound can vary greatly depending on the ultrasound application and the type of tissue targeted. These biological effects are sometimes uniquely paired



III. Mechanisms of Action

III. 2 Mechanisms of Action
Ultrasound Applications and Biological Effects

Research

III. 4 Ultrasound Applications and Biological Effects
Table
III. 5 Ultrasound Applications and Biological Effects
Graphic
III. 6 Research Sites by Region
III. 8 Clinical Trials for Indications with New MOAs

Number of Sites for Biological Effects by Indications

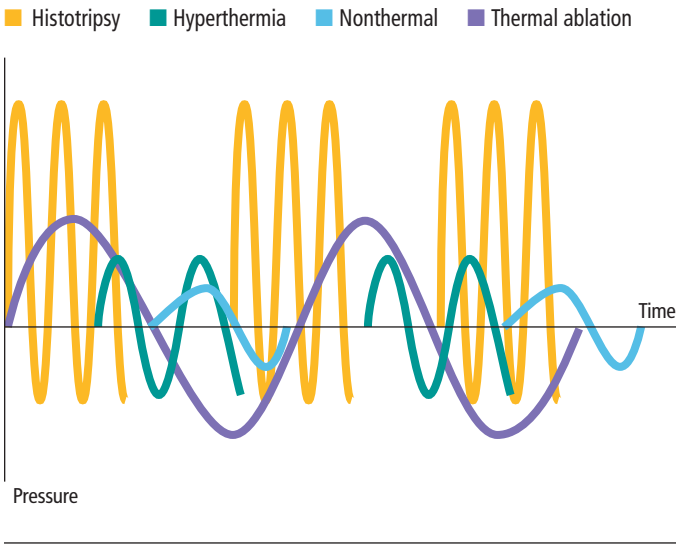
III. 9 Histotripsy
III.12 Hyperthermia
III.16 Nonthermal
III.24 Nonthermal - BBB opening
III.28 Thermal ablation

to a set of ultrasound parameters, as is the case with blood-brain barrier (BBB) disruption, but others may be induced by multiple ultrasound applications. One active area of research is immunomodulation—altering the immune response to treated tissue. The immune response to focused ultrasound is dependent on the nature of the treatment parameters, although most treatments do induce a response.

In this section, we describe several ultrasound applications and the various biological effects they are known to produce. Researchers are working actively on many of these combinations of ultrasound application and biological effects, and more are discovered each year.

The following pages include a detailed breakdown of each ultrasound application and the resulting biological effects under investigation. As will become very apparent, most of this work is early stage. Thermal ablation is the only mechanism of action that currently has regulatory approval and is commercially available for 32 indications

What do sound waves look like?



Ultrasound Applications and Biological Effects*

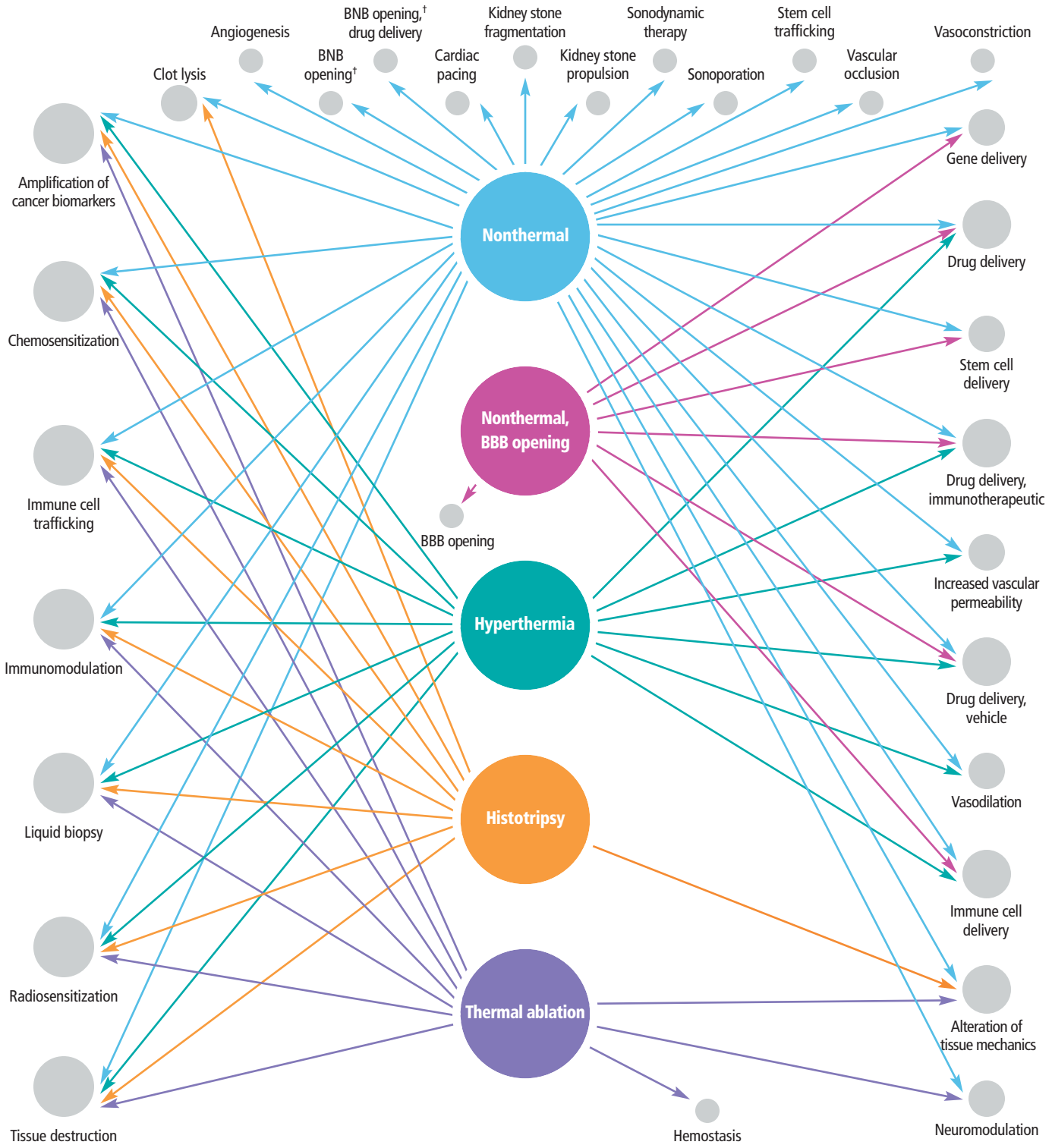
Table

HISTOTRIPSY	HYPERTHERMIA	NONTHERMAL	NONTHERMAL, BBB OPENING	THERMAL ABLATION
9 biological effects	**13** biological effects	**29** biological effects	**7** biological effects	**10** biological effects
Alteration of tissue mechanics	Amplification of cancer biomarkers	Alteration of tissue mechanics	BBB opening	Alteration of tissue mechanics
Amplification of cancer biomarkers	Chemosensitization	Amplification of cancer biomarkers	Drug delivery	Amplification of cancer biomarkers
Chemosensitization	Drug delivery	Angiogenesis	Drug delivery, immunotherapeutic	Chemosensitization
Clot lysis	Drug delivery, immunotherapeutic	BNB opening†	Drug delivery, vehicle	Hemostasis
Immune cell trafficking	Drug delivery, vehicle	BNB opening†, drug delivery	Gene delivery	Immune cell trafficking
Immunomodulation	Immune cell delivery	Cardiac pacing	Immune cell delivery	Immunomodulation
Liquid biopsy	Immune cell trafficking	Chemosensitization	Stem cell delivery	Liquid biopsy
Radiosensitization	Immunomodulation	Clot lysis		Neuromodulation
Tissue destruction	Increased vascular permeability	Drug delivery		Radiosensitization
	Liquid biopsy	Drug delivery, immunotherapeutic		Tissue destruction
	Radiosensitization	Drug delivery, vehicle		
	Tissue destruction	Gene delivery		
	Vasodilation	Immune cell delivery		
		Immune cell trafficking		
		Immunomodulation		
		Increased vascular permeability		
		Kidney stone fragmentation		
		Kidney stone propulsion		
		Liquid biopsy		
		Neuromodulation		
		Radiosensitization		
		Sonodynamic therapy		
		Sonoporation		
		Stem cell delivery		
		Stem cell trafficking		
		Tissue destruction		
		Vascular occlusion		
		Vasoconstriction		
		Vasodilation		

* This table lists all mechanisms of action utilized across all treatments and research types. Not all of these are being investigated specifically in mechanisms of action research projects and may not appear in other tables in this section. All other tables reflect self-reported data by research and treatment sites.

† BNB opening stands for blood-nerve barrier opening.

Ultrasound Applications and Biological Effects
Graphic



Mechanisms of Action Research Sites by Region

	Regions				Total
	N. America	Europe	Asia	Oceania	
Histotripsy | 56 sites					
Alteration of tissue mechanics	1	1	–	1	**3**
Amplification of cancer biomarkers	3	–	–	–	**3**
Chemosensitization	2	–	–	–	**2**
Immune cell trafficking	2	–	–	–	**2**
Immunomodulation	8	3	–	–	**11**
Liquid biopsy	3	–	–	–	**3**
Radiosensitization	–	1	–	–	**1**
Tissue destruction	22	6	2	1	**31**
Hyperthermia | 54 sites					
Chemosensitization	1	–	–	–	**1**
Drug delivery	12	7	3	1	**23**
Drug delivery, immunotherapeutic	1	1	–	–	**2**
Drug delivery, vehicle	1	2	–	–	**3**
Immune cell trafficking	1	–	–	–	**1**
Immunomodulation	1	1	–	–	**2**
Increased vascular permeability	1	–	–	–	**1**
Radiosensitization	4	4	1	–	**9**
Tissue destruction	6	2	4	–	**12**
Nonthermal | 338 sites					
Alteration of Tissue Mechanics	–	1	–	–	**1**
Amplification of cancer biomarkers	6	–	1	–	**7**
Angiogenesis	3	1	2	–	**6**
BNB opening, drug delivery	1	–	–	–	**1**
Cardiac pacing	–	–	1	–	**1**
Chemosensitization	5	2	–	–	**7**
Clot lysis	13	2	2	–	**17**
Drug delivery	14	7	3	1	**25**
Drug delivery, immunotherapeutic	8	2	–	1	**11**
Drug delivery, vehicle	29	9	20	–	**58**
Gene delivery	4	–	–	–	**4**
Immune cell delivery	2	–	–	–	**2**

For more information about specific mechanisms of action research sites, please visit: www.fusfoundation.org/the-technology/research-sites.
Use the "search by biological effects research" dropdown menu.

Mechanisms of Action Research Sites by Region continued

	Regions				Total
	N. America	Europe	Asia	Oceania	
Nonthermal continued					
Immune cell trafficking	3	–	–	–	**3**
Immunomodulation	14	4	3	–	**21**
Increased vascular permeability	1	–	–	–	**1**
Kidney stone fragmentation	2	–	–	–	**2**
Liquid biopsy	5	2	1	–	**8**
Neuromodulation	30	10	16	1	**57**
Radiosensitization	6	–	–	–	**6**
Sonodynamic therapy	6	4	7	1	**18**
Sonoporation	8	2	2	–	**12**
Stem cell delivery	6	–	1	–	**7**
Stem cell trafficking	3	–	–	–	**3**
Tissue destruction	20	12	12	1	**45**
Vascular occlusion	9	2	4	–	**15**
Nonthermal, BBB opening | 113 sites					
Blood-brain barrier opening	21	11	4	–	**36**
Drug delivery	34	18	23	2	**77**
Thermal ablation | 93 sites					
Amplification of cancer biomarkers	3	1	–	–	**4**
Chemosensitization	2	1	–	–	**3**
Hemostasis	2	–	–	–	**2**
Immune cell trafficking	2	1	–	–	**3**
Immunomodulation	7	4	2	–	**13**
Neuromodulation	1	–	–	–	**1**
Radiosensitization	1	–	1	–	**2**
Tissue destruction	32	18	14	1	**65**

Drug delivery spans three different ultrasound applications—hyperthermia, nonthermal, and nonthermal BBB opening—for a total of 180 sites worldwide working on focused ultrasound-related drug delivery.

For more information about specific mechanisms of action research sites, please visit: www.fusfoundation.org/the-technology/research-sites.
Use the "search by biological effects research" dropdown menu.

Clinical Trials for Indications with New MOAs

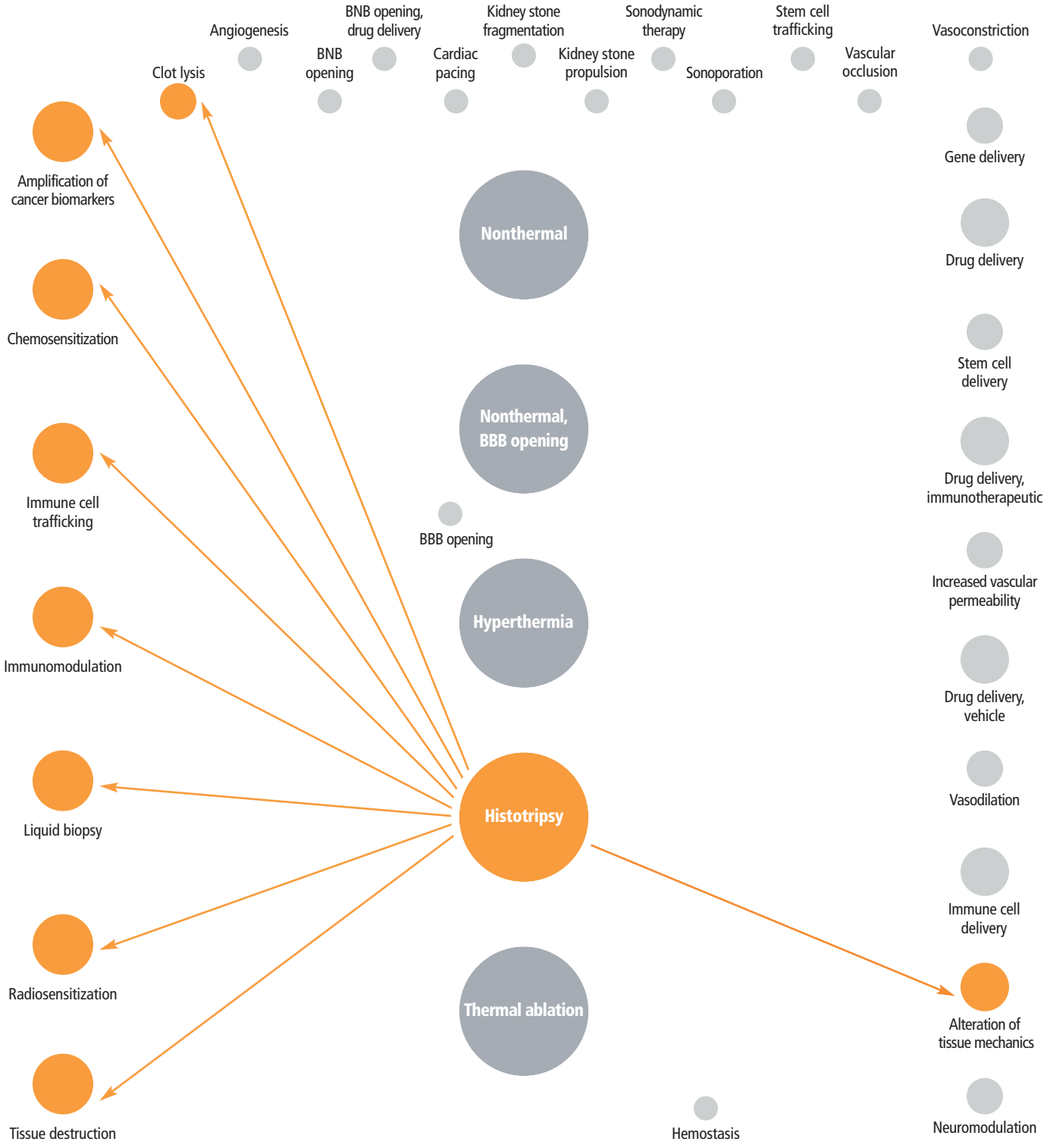
2022

Indication	Mechanism of Action	Clinical Trial ID
Alzheimer's disease	Nonthermal, BBB opening - Drug delivery	NCT05469009
Anxiety	Nonthermal - Neuromodulation	NCT05228964
Bipolar disorder	Nonthermal - Neuromodulation	NCT05228964
Bone metastases	Hyperthermia - Radiosensitization	NCT05167669
Brain metastases, lung cancer	Nonthermal, BBB opening - Drug delivery, Immunotherapeutic	NCT05317858
Dementia	Nonthermal - Neuromodulation	NCT05417555
Depression	Nonthermal - Neuromodulation	NCT05228964, NCT05301036, NCT05697172
Essential tremor	Nonthermal - Neuromodulation	NCT05475340
Glioblastoma	Nonthermal - Liquid biopsy	NCT05383872
Glioblastoma	Nonthermal - Sonodynamic therapy	NCT05362409
Heart valve calcifications	Histotripsy - Alteration of tissue mechanics	NCT05235568
Melanoma	Nonthermal - Radiosensitization	NCT05620290
Neuropathic pain	Nonthermal - Neuromodulation	NCT05145426, NCT05303415, NCT05624762
Obsessive-compulsive disorder	Nonthermal - Neuromodulation	NCT05467085
Parkinson's disease, dyskinesia	Nonthermal - Neuromodulation	NCT04593875
Parkinson's disease, tremor	Nonthermal - Neuromodulation	NCT05475340
Pontine glioma	Nonthermal - Sonodynamic therapy	NCT05123534
PTSD	Nonthermal - Neuromodulation	NCT05228964

The 22 clinical trials listed above all began in 2022. While there were many additional trials begun last year, these 22 were first-in-human studies where a new mechanism of action was being utilized to treat a particular disease. As mentioned previously, thermal ablation is the only mechanism of action that has regulatory approval to date. This table is one just one indicator that the field as a whole, and how we use ultrasound technology to treat diseases, is changing rapidly.

Ultrasound Applications and Biological Effects

Graphic—Histotripsy



Histotripsy—Number of Sites for Biological Effects by Indications

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Histotripsy | Alteration of tissue mechanics				
Deep vein thrombosis	1	–	–	**1**
Heart valve calcifications	1	9	–	**10**
Liver tumors	1	–	–	**1**
Wound healing	1	–	–	**1**
Histotripsy | Immunomodulation				
Brain tumors, general	1	–	–	**1**
Glioblastoma	1	–	–	**1**
Liver tumors	2	–	–	**2**
Melanoma	3	–	–	**3**
Pancreatic tumors, malignant	4	–	–	**4**
Soft tissue cancer	2	–	–	**2**
Histotripsy | Liquid biopsy				
Pontine glioma	1	–	–	**1**
Histotripsy | Tissue destruction				
Benign prostatic hyperplasia	1	–	–	**1**
Bone metastases	–	1	–	**1**
Brain metastases, breast cancer	1	–	–	**1**
Deep vein thrombosis	4	–	–	**4**
Dental infections	–	1	–	**1**
Epilepsy	1	–	–	**1**
Fetal heart anomalies	1	–	–	**1**
Glioblastoma	3	–	–	**3**
Hematoma	1	–	–	**1**
Heterotopic ossification	1	–	–	**1**
Infection	1	–	–	**1**
Kidney tumors	2	–	–	**2**
Liver metastases	1	–	–	**1**
Liver tumors	3	14	–	**17**
Lung cancer	1	–	–	**1**

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.

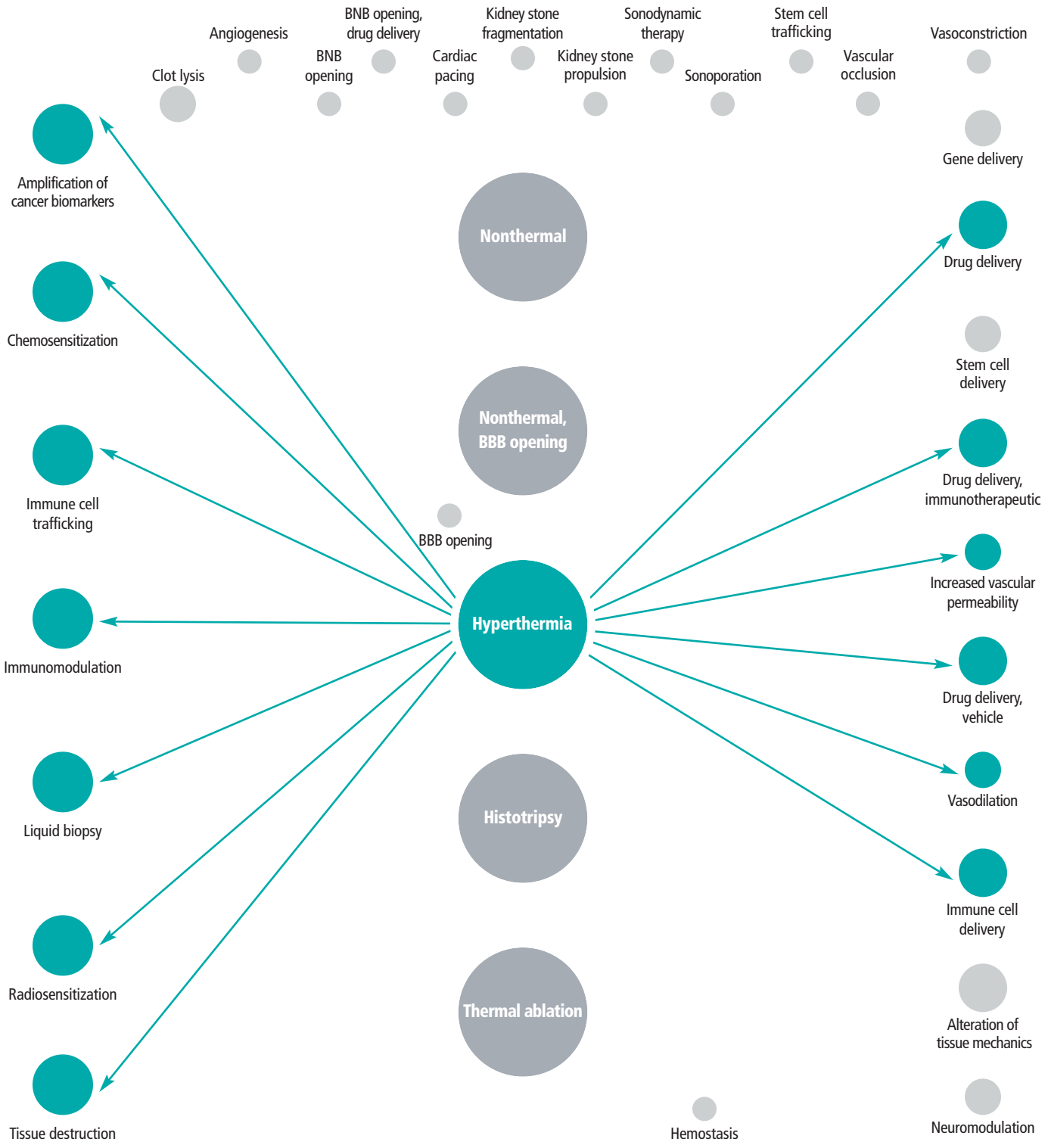
Histotripsy—Number of Sites for Biological Effects by Indications continued

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Histotripsy | Tissue destruction continued				
Mitral regurgitation	1	–	–	**1**
Multiple tumors[2]	1	–	–	**1**
Pancreatic tumors, malignant	3	1	–	**4**
Periodontal disease	1	–	–	**1**
Prostate cancer	1	–	–	**1**
Rotator cuff injury	1	–	–	**1**
Soft tissue cancer	2	–	–	**2**
Stroke, intracerebral hemorrhage	1	–	–	**1**
Tendon contracture	1	–	–	**1**
Thyroid cancer	1	–	–	**1**
Uterine fibroids	1	–	–	**1**

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.
2 Protocols inclusive of more than one indication

Ultrasound Applications and Biological Effects

Graphic—Hyperthermia



Hyperthermia—Number of Sites for Biological Effects by Indications

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Hyperthermia | Chemosensitization				
Multiple tumors[2]	–	1	–	**1**
Pancreatic tumors, malignant	–	1	–	**1**
Hyperthermia | Drug delivery				
Breast tumors, malignant	–	1	–	**1**
Glioblastoma	1	–	–	**1**
Head & neck tumors	1	–	–	**1**
Multiple tumors[2]	2	1	–	**3**
Osteopenia	1	–	–	**1**
Pancreatic tumors, malignant	1	2	–	**3**
Soft tissue cancer	1	–	–	**1**
Wound healing	2	–	–	**2**
Hyperthermia | Drug delivery, immunotherapeutic				
Breast tumors, malignant	1	–	–	**1**
Glioblastoma	1	–	–	**1**
Pancreatic tumors, malignant	1	–	–	**1**
Soft tissue cancer	1	–	–	**1**
Hyperthermia | Immune cell trafficking				
Brain tumors, general	1	–	–	**1**
Hyperthermia | Immunomodulation				
Breast tumors, malignant	1	–	–	**1**
Glioblastoma	1	–	–	**1**
Liver tumors	1	–	–	**1**
Pancreatic tumors, malignant	1	–	–	**1**
Prostate cancer	1	–	–	**1**

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.
2 Protocols inclusive of more than one indication

Hyperthermia—Number of Sites for Biological Effects by Indications continued

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Hyperthermia | Radiosensitization				
Bone metastases	–	1	–	**1**
Brain tumors, general	1	–	–	**1**
Breast tumors, malignant	–	1	–	**1**
Head & neck tumors	1	1	–	**2**
Liver tumors	1	–	–	**1**
Prostate cancer	1	–	–	**1**
Hyperthermia | Tissue destruction				
Brain tumors, general	1	–	–	**1**
Breast tumors, benign	–	1	–	**1**
Endometriosis	–	1	–	**1**
Liver tumors	1	–	–	**1**
Lung cancer	1	–	–	**1**
Prostate cancer	1	2	–	**3**
Uterine adenomyosis	–	1	–	**1**
Hyperthermia | Vasodilation				
Breast tumors, malignant	1	–	–	**1**

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.

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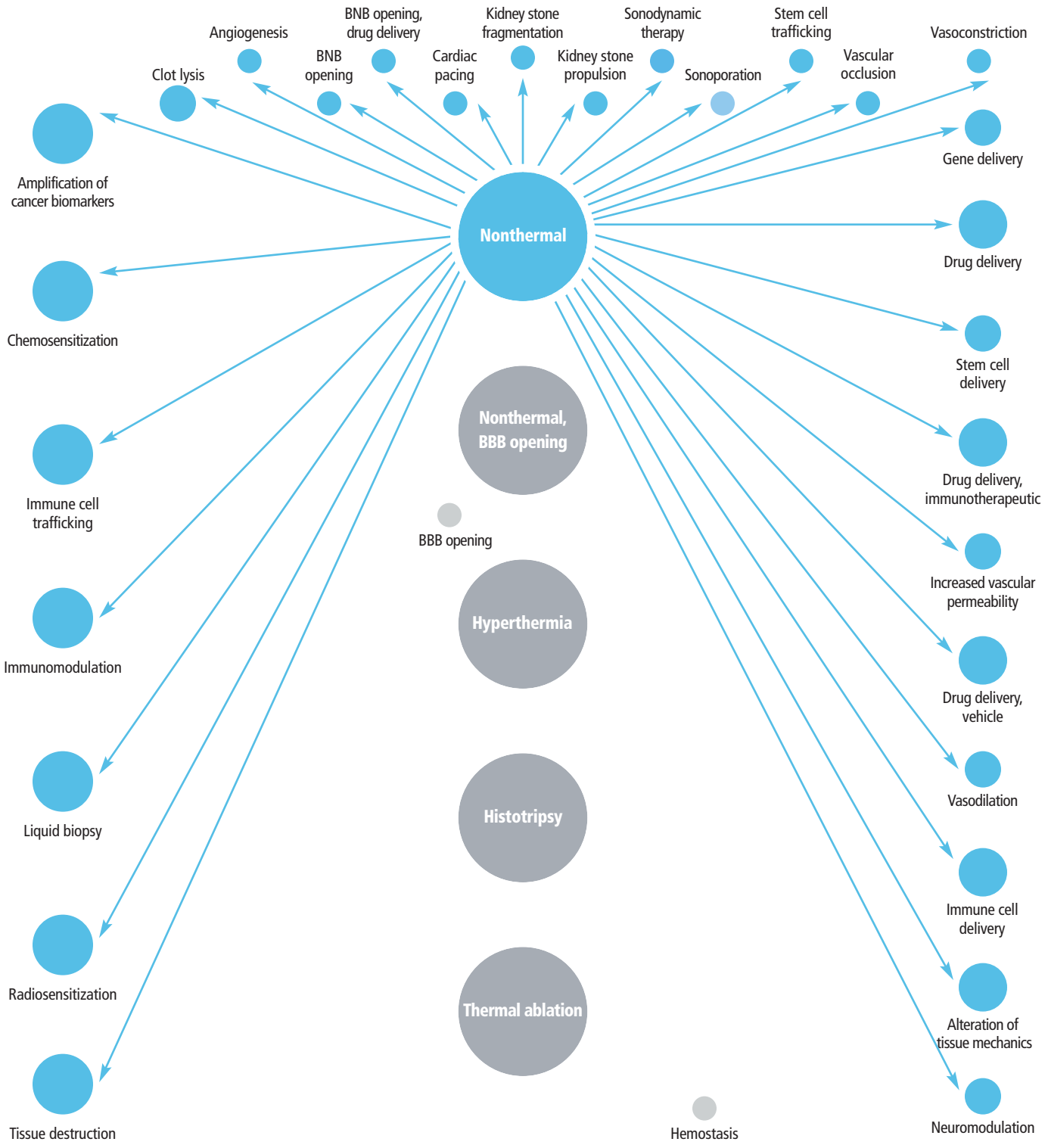
Ultrasound Applications and Biological Effects

Graphic—Nonthermal



Nonthermal—Number of Sites for Biological Effects by Indications

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Nonthermal | Alteration of tissue mechanics				
Alzheimer's disease	2	–	–	**2**
Neuropathic pain	1	–	–	**1**
Osteopenia	1	–	–	**1**
Wound healing	1	–	–	**1**
Nonthermal | Amplification of cancer biomarkers				
Brain tumors, general	1	–	–	**1**
Glioblastoma	–	1	–	**1**
Nonthermal | Angiogenesis				
Muscle atrophy	1	–	–	**1**
Stroke, thromboembolic	–	1	–	**1**
Nonthermal | Cardiac pacing				
Cardiac pacing	1	–	–	**1**
Nonthermal | Clot lysis				
Deep vein thrombosis	1	–	–	**1**
Hydrocephalus	1	–	–	**1**
Nonthermal | Drug delivery				
Alzheimer's disease	1	–	–	**1**
Atherosclerosis	3	–	–	**3**
Bladder tumors	1	–	–	**1**
Brain tumors, general	1	–	–	**1**
Breast tumors, malignant	1	–	–	**1**
Colorectal tumors	–	1	–	**1**
Hemophilia	1	–	–	**1**
Inflammatory bowel disease	1	–	–	**1**
Liver metastases	–	3	–	**3**

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.
2 Protocols inclusive of more than one indication

Nonthermal—Number of Sites for Biological Effects by Indications continued

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Nonthermal | Drug delivery continued				
Pancreatic tumors, malignant	1	3	–	**4**
Pontine glioma	1	–	–	**1**
Stroke, intracerebral hemorrhage	1	–	–	**1**
Stroke, thromboembolic	2	–	–	**2**
Wound healing				
Nonthermal | Drug delivery, immunotherapeutic				
Multiple tumors[2]	1	–	–	**1**
Pancreatic tumors, malignant	1	–	–	**1**
Nonthermal | Drug delivery, vehicle				
Breast tumors, malignant	3	–	–	**3**
Cardiac hypertrophy	1	–	–	**1**
Colorectal tumors	1	–	–	**1**
Deep vein thrombosis	1	–	–	**1**
Glioblastoma	2	–	–	**2**
Kidney tumors	1	–	–	**1**
Liver tumors	–	1	–	**1**
Neuropathic pain	1	–	–	**1**
Pancreatic tumors	1	–	–	**1**
Pancreatic tumors, malignant	4	–	–	**4**
Parkinson's disease, underlying cause	1	–	–	**1**
Periodontal disease	1	–	–	**1**
Peripheral artery disease	1	–	–	**1**
Prostate cancer	1	–	–	**1**
Stroke, intracerebral hemorrhage	2	–	–	**2**
Stroke, thromboembolic	1	–	–	**1**
Urinary tract infection	1	–	–	**1**

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.
2 Protocols inclusive of more than one indication

Nonthermal—Number of Sites for Biological Effects by Indications continued

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Nonthermal | Gene delivery				
Brain tumors, general	1	–	–	**1**
Breast tumors, malignant	1	–	–	**1**
Epilepsy	1	–	–	**1**
Muscle atrophy	1	–	–	**1**
Parkinson's disease, underlying cause	1	–	–	**1**
Retinal injury	1	–	–	**1**
Nonthermal | Immune cell trafficking				
Glioblastoma	1	–	–	**1**
Nonthermal | Immunomodulation				
Brain metastases, breast cancer	1	–	–	**1**
Brain metastases, melanoma	1	–	–	**1**
Brain tumors, general	1	–	–	**1**
Breast tumors, malignant	2	1	–	**3**
Epilepsy	1	–	–	**1**
Glaucoma	–	1	–	**1**
Glioblastoma	2	–	–	**2**
Pancreatic tumors, malignant	2	1	–	**3**
Prostate cancer	2	1	–	**3**
Nonthermal | Increased vascular permeability				
Alzheimer's disease	–	1	–	**1**
Breast tumors, malignant	1	–	–	**1**
Deep vein thrombosis	1	–	–	**1**
Nonthermal | Kidney stone fragmentation				
Kidney stones	2	1	–	**3**
Nonthermal | Kidney stone propulsion				
Kidney stones	1	1	–	**2**

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.

Nonthermal—Number of Sites for Biological Effects by Indications continued

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Nonthermal | Liquid biopsy				
Brain tumors, general	1	1	–	**2**
Glioblastoma	–	6	–	**6**
Parkinson's disease, underlying cause	1	1	–	**2**
Nonthermal | Neuromodulation				
ADHD	–	1	–	**1**
Alzheimer's disease	2	4	***1****	**7**
Anxiety	2	4	–	**6**
Bipolar disorder	1	–	–	**1**
Brain tumor, general	–	1	–	**1**
Cancer pain	1	–	–	**1**
Depression	5	9	–	**14**
Diabetes	2	–	–	**2**
Dystonia	–	1	–	**1**
Epilepsy	9	4	–	**13**
Essential tremor	–	1	–	**1**
Headache	1	–	–	**1**
Mood disorder	–	2	–	**2**
Neuropathic pain	3	4	–	**7**
Neuropathy	–	2	–	**2**
Obsessive-compulsive disorder	–	2	–	**2**
Opioid and other addictions	4	1	–	**5**
Parkinson's disease, tremor	1	2	–	**3**
Parkinson's disease, underlying cause	2	–	–	**2**
PTSD	–	1	–	**1**
Schizophrenia	–	1	–	**1**
Stroke, intracerebral hemorrhage	1	1	–	**2**
Stroke, thromboembolic	–	3	–	**3**
Traumatic brain injury	–	3	–	**3**
Tremor, orthostatic	–	1	–	**1**

* Indications being performed off label in a region are shown in bold italic. A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary at the top.

For more information about specific commercial treatment sites and indications, please visit: www.fusfoundation.org/the-technology/treatment-sites. Use the "search by disease" dropdown menu and/or location.

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.

Nonthermal—Number of Sites for Biological Effects by Indications continued

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Nonthermal | Radiosensitization				
Brain tumors, general	2	–	–	**2**
Breast tumors, malignant	–	1	–	**1**
Glioblastoma	2	1	–	**3**
Head & neck tumors	–	1	–	**1**
Melanoma	–	1	–	**1**
Nonthermal | Sonodynamic therapy				
Atherosclerosis	1	–	–	**1**
Biliary tract cancer	–	1	–	**1**
Brain metastases, melanoma	1	–	–	**1**
Brain tumors, general	4	–	–	**4**
Cavernomas	1	–	–	**1**
Deep vein thrombosis	1	–	–	**1**
Glioblastoma	2	6	–	**8**
Pancreatic tumors, malignant	2	–	–	**2**
Pontine glioma	1	3	–	**4**
Nonthermal | Sonoporation				
Atherosclerosis	1	–	–	**1**
Head & neck tumors	1	–	–	**1**
Liver metastases	–	1	–	**1**
Liver tumors	–	1	–	**1**
Pancreatic tumors, malignant	1	1	–	**2**
Stroke, thromboembolic	1	–	–	**1**
Nonthermal | Stem cell delivery				
Acute tubular necrosis	1	–	–	**1**
Atherosclerosis	1	–	–	**1**
Kidney disease, acute	1	–	–	**1**
Muscle atrophy	1	–	–	**1**

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.

Nonthermal—Number of Sites for Biological Effects by Indications continued

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Nonthermal | Tissue destruction				
Arteriovenous malformations	1	–	–	**1**
Arthritis, facetogenic	1	–	–	**1**
Benign prostatic hyperplasia	1	–	–	**1**
Brain tumors, general	1	–	–	**1**
Breast tumors, malignant	2	–	–	**2**
Glioblastoma	1	–	–	**1**
Head & neck tumors	1	–	–	**1**
Liver metastases	1	–	–	**1**
Liver tumors	2	–	–	**2**
Pancreatic tumors, malignant	3	–	–	**3**
Presbyopia	1	–	–	**1**
Prostate cancer	2	–	–	**2**
Soft tissue cancer	1	–	–	**1**
Uterine fibroids	1	–	–	**1**
Nonthermal | Vascular occlusion				
Arteriovenous malformations	–	1	–	**1**
Brain tumors, general	1	–	–	**1**
Glioblastoma	1	–	–	**1**
Macular degeneration	1	–	–	**1**
Twin-twin transfusion syndrome	4	–	–	**4**
Varicose veins	–	1	–	**1**
Nonthermal | Vasodilation				
Neuropathy	1	–	–	**1**
Stroke, thromboembolic	1	–	–	**1**

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.

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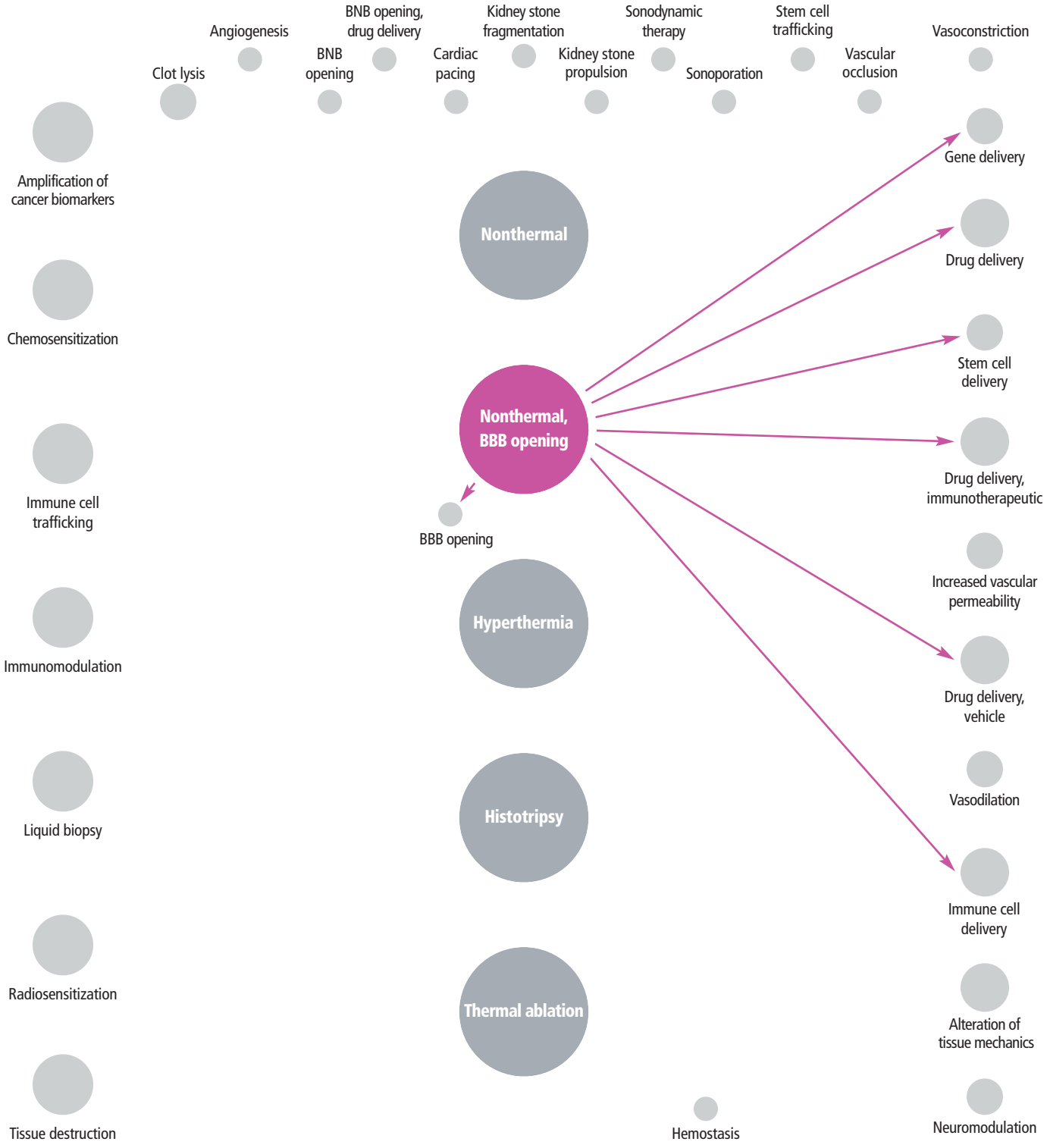
Ultrasound Applications and Biological Effects

Graphic—Nonthermal, BBB opening



Nonthermal, BBB opening—
Number of Sites for Biological Effects by Indications

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Nonthermal, BBB opening | BBB opening				
Alzheimer's disease	8	12	–	**20**
Amyotrophic lateral sclerosis	1	–	–	**1**
Brain metastases, breast cancer	1	–	–	**1**
Brain tumors, general	4	1	–	**5**
Breast tumors, malignant	1	–	–	**1**
Dementia	1	–	–	**1**
Epilepsy	1	–	–	**1**
Glioblastoma	1	4	–	**5**
Nonthermal, BBB opening | Drug delivery				
Alzheimer's disease	7	3	–	**10**
Amyotrophic lateral sclerosis	1	1	–	**2**
Anxiety	1	–	–	**1**
Astrocytoma	1	–	–	**1**
Autism	1	–	–	**1**
Brain metastases, breast cancer	1	1	–	**2**
Brain metastases, melanoma	–	1	–	**1**
Brain tumors, general	4	2	–	**6**
Epilepsy	3	–	–	**3**
Glioblastoma	15	16	–	**31**
Infection	1	–	–	**1**
Neurofibromatosis	1	–	–	**1**
Neuromyelitis optica	1	–	–	**1**
Parkinson's disease, tremor	1	–	–	**1**
Parkinson's disease, underlying cause	3	–	–	**3**
Pontine glioma	2	1	–	**3**
Spinal cord injury	2	–	–	**2**
Stroke, intracerebral hemorrhage	1	–	–	**1**
Stroke, thromboembolic	1	–	–	**1**
Traumatic brain injury	1	–	–	**1**

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.

Nonthermal, BBB opening—
Number of Sites for Biological Effects by Indications continued

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Nonthermal, BBB opening | Drug delivery, immunotherapeutic				
Alzheimer's disease	2	–	–	**2**
Brain metastases, breast cancer	2	–	–	**2**
Brain metastases, lung cancer	–	4	–	**4**
Brain metastases, melanoma	1	–	–	**1**
Brain tumors, general	1	–	–	**1**
Glioblastoma	1	–	–	**1**
Pontine glioma	–	1	–	**1**
Nonthermal, BBB opening | Drug delivery, vehicle				
Brain tumors, general	1	–	–	**1**
Glioblastoma	2	–	–	**2**
Nonthermal, BBB opening | Gene delivery				
Alzheimer's disease	1	–	–	**1**
Brain tumors, general	2	–	–	**2**
Epilepsy	1	–	–	**1**
Glioblastoma	1	–	–	**1**
Huntington's disease	1	–	–	**1**
Niemann-Pick disease	1	–	–	**1**
Parkinson's disease, dyskinesia	1	–	–	**1**
Parkinson's disease, underlying cause	7	–	–	**7**
Rett syndrome	1	–	–	**1**
Nonthermal, BBB opening | Stem cell delivery				
Alzheimer's disease	1	–	–	**1**

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.

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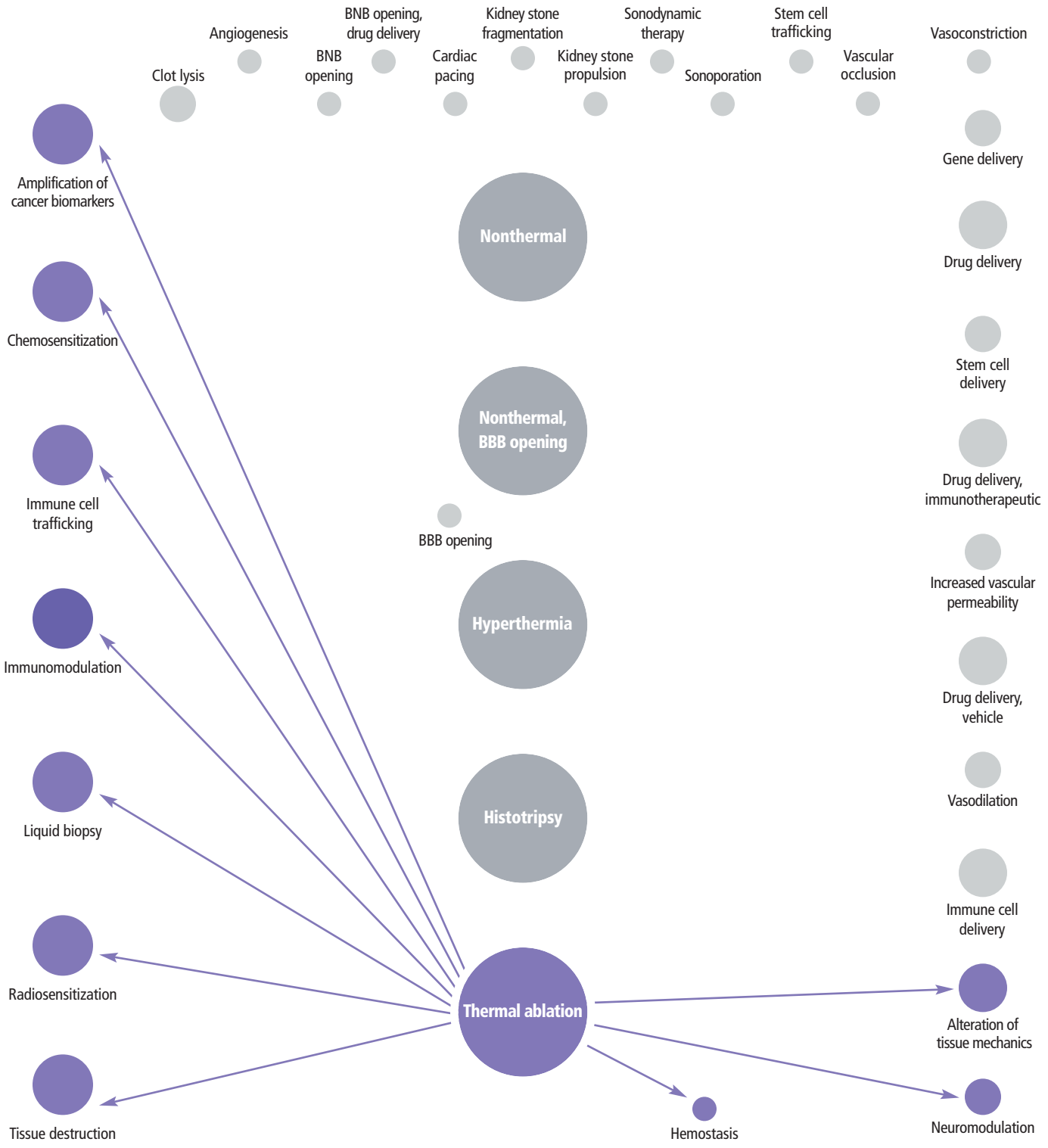
Ultrasound Applications and Biological Effects

Graphic—Thermal ablation



Thermal ablation—Number of Sites for Biological Effects by Indications

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Thermal ablation | Alteration of tissue mechanics				
Urinary incontinence, stress	–	–	***1****	**1**
Thermal ablation | Chemosensitization				
Bone metastases	–	1	–	**1**
Thermal ablation | Hemostasis				
Hematoma	1	–	–	**1**
Twin-twin transfusion syndrome	–	1	–	**1**
Thermal ablation | Immunomodulation				
Breast tumors, malignant	5	1	–	**6**
Cervical tumors	–	1	–	**1**
Esophageal tumors	–	1	–	**1**
Gastric tumors	–	1	–	**1**
Lung cancer	–	1	–	**1**
Melanoma	2	1	–	**3**
Multiple tumors[2]	1	2	–	**3**
Ovarian tumors	1	1	–	**2**
Pancreatic tumors, malignant	4	–	–	**4**
Soft tissue cancer	1	1	–	**2**
Thermal ablation | Liquid biopsy				
Brain tumors, general	–	1	–	**1**
Thermal ablation | Neuromodulation				
Epilepsy	1	–	–	**1**

* Indications being performed off label in a region are shown in bold italic. A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary at the top.

For more information about specific commercial treatment sites and indications, please visit: www.fusfoundation.org/the-technology/treatment-sites. Use the "search by disease" dropdown menu and/or location.

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.

2 Protocols inclusive of more than one indication

Thermal ablation—Number of Sites for Biological Effects by Indications continued

Thermal ablation is the most mature of the focused ultrasound effects. This is evidenced by how few bench research sites there are working in this area, or, conversely, how many sites are clinical and commercial stage.

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Thermal ablation | Tissue destruction				
Cardiovascular				
Arteriovenous malformations	–	–	***2****	**2**
Atrial fibrillation	2	–	–	**2**
Hypertension	–	3	–	**3**
Peripheral artery disease	–	1	–	**1**
Twin-twin transfusion syndrome	1	–	–	**1**
Varicose veins	–	5	9	**14**
Ventricular tachycardia	2	–	–	**2**
Endocrine disorders				
Graves' disease	–	1	–	**1**
Thyroid nodules	–	9	19	**28**
Gastrointestinal				
Colorectal tumors	1	4	–	**5**
Gastric tumors	1	–	1	**2**
Liver metastases	3	–	3	**6**
Liver tumors	14	20	137	**171**
Pancreatic tumors	2	4	41	**47**
Pancreatic tumors, benign	–	1	1	**2**
Pancreatic tumors, malignant	6	10	9	**25**

* Indications being performed off label in a region are shown in bold italic. A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary at the top.

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Thermal ablation—Number of Sites for Biological Effects by Indications continued

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Thermal ablation | Tissue destruction continued				
Miscellaneous				
Actinic keratosis	–	2	–	**2**
Basal cell carcinoma	–	3	–	**3**
Dercum's disease	–	1	–	**1**
Head & neck tumors	–	1	–	**1**
Hypersplenism	–	1	–	**1**
Infection	1	–	–	**1**
Kaposi's sarcoma	–	1	–	**1**
Lipoma	–	1	–	**1**
Multiple tumors[2]	1	–	–	**1**
Sinonasal disease	1	–	–	**1**
Musculoskeletal				
Arthritis, facetogenic	2	15	4	**21**
Arthritis, knee	–	1	–	**1**
Arthritis, sacroiliac	–	3	–	**3**
Bone cancer	–	6	8	**14**
Bone metastases	5	24	27	**56**
Bone tumors, benign	1	3	1	**5**
Desmoid tumors	–	8	11	**19**
Osteoid osteoma	4	23	103	**130**
Plantar fasciitis	–	1	–	**1**
Sacral chordoma	–	1	–	**1**
Soft tissue cancer	2	5	2	**9**
Soft tissue tumors, benign	3	21	92	**116**
Tendon contracture	1	–	–	**1**

1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.
2 Protocols inclusive of more than one indication

Thermal ablation—Number of Sites for Biological Effects by Indications continued

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Thermal ablation | Tissue destruction continued				
Neurological				
Astrocytoma	–	3	–	**3**
Brain tumors, general	1	1	–	**2**
Cancer pain	1	1	–	**2**
Depression	1	2	***1****	**4**
Dystonia	–	3	***1****	**4**
Dystonia, hand	–	1	1	**2**
Epilepsy	2	6	***2****	**10**
Essential tremor	1	17	102	**120**
Glioblastoma	1	3	–	**4**
Multiple sclerosis	–	1	–	**1**
Neuroblastoma	–	1	–	**1**
Neurofibromatosis	–	3	–	**3**
Neuropathic pain	1	2	3	**6**
Neuropathy	–	–	***2****	**2**
Obsessive-compulsive disorder	–	2	2	**4**
Painful amputation neuromas	–	1	–	**1**
Parkinson's disease, dyskinesia	–	14	6	**20**
Parkinson's disease, tremor	–	12	57	**69**
Parkinson's disease, underlying cause	1	–	–	**1**
Tremor, orthostatic	–	1	–	**1**
Trigeminal neuralgia	–	1	***1****	**2**
Ophthalmological				
Glaucoma	3	6	14	**23**
Presbyopia	1	–	–	**1**

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1 A site may use the same mechanism of action to treat or research the same indication across multiple stages. Because of this, the totals may not equal the sum of the three preceding columns.

Thermal ablation—Number of Sites for Biological Effects by Indications continued

Ultrasound application | Biological effects	Stages: Preclinical	Stages: Clinical	Stages: Commercial	Total[1]
Thermal ablation | Tissue destruction continued				
Pulmonary				
Lung cancer	3	–	–	**3**
Rhinitis	–	1	–	**1**
Tuberculosis	1	–	–	**1**
Urological				
Benign prostatic hyperplasia	–	2	45	**47**
Chyluria	–	1	–	**1**
Fetal bladder obstruction	1	–	–	**1**
Kidney tumors	2	15	91	**108**
Prostate cancer	7	64	432	**503**
Women's health				
Breast tumors, benign	2	8	12	**22**
Breast tumors, malignant	9	22	96	**127**
Cervical tumors	1	3	–	**4**
Cervicitis	–	–	1	**1**
Ectopic pregnancy	–	1	–	**1**
Endometrial tumors	2	1	***1****	**4**
Endometriosis	1	1	***2****	**4**
Lichen sclerosis	–	1	1	**2**
Ovarian tumors	2	1	–	**3**
Retained placenta	–	1	–	**1**
Uterine adenomyosis	2	26	115	**143**
Uterine fibroids	10	64	319	**393**
Vaginal tumors	–	2	–	**2**

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2023 Research Sites

Focused Ultrasound Foundation

State of Research

Like previous reports, we report on clinical, preclinical, mechanisms of action, and technical research in this section.

In 2022 the field saw gains of 51 new clinical research sites worldwide. The greatest growth was in North America with 25 additional new sites. The United States superseded China as the top country with clinical research growth. There are 77 clinical research sites in the United States compared to 57 in China. In third place, France had 33 clinical trial sites, up significantly from 13 sites the previous year.

IV. Research Sites

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IV. 3 Summary of Types of Research and Treatment Site by Region

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- IV. 8 Miscellaneous
- IV. 9 Musculoskeletal
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Summary of Types of Research Sites by Region

Number of sites

	Total	North America	Europe	Asia	South America	Oceania	Africa
Clinical research	**293**	85	104	99	–	5	–
Preclinical research	**152**	69	41	39	–	3	–
Mechanisms of action research	**180**	80	42	55	–	3	–
Technical research	**151**	61	49	39	–	2	–

Clinical Research Sites

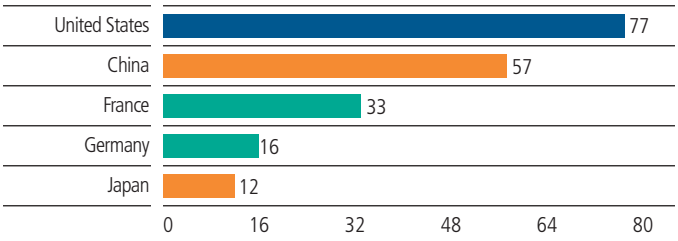
293 Clinical research sites worldwide*

North America	Europe	Asia	South America	Oceania	Africa
85	104	99	–	5	–

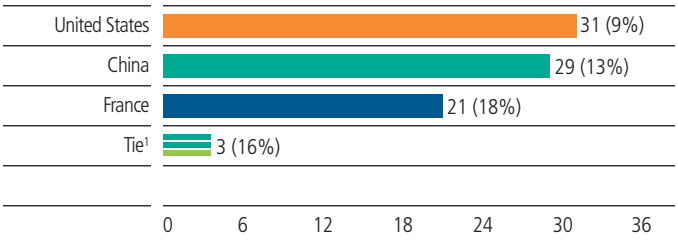
Annual growth by region from 2013–2022

North America	Europe	Asia	South America	Oceania	Africa
6%	8%	11%	–	12%	–

Top Countries for Clinical Research
Number of sites



Top Countries with Clinical Research Growth
Sites added, cumulative 2017 to 2022



Clinical research additional content

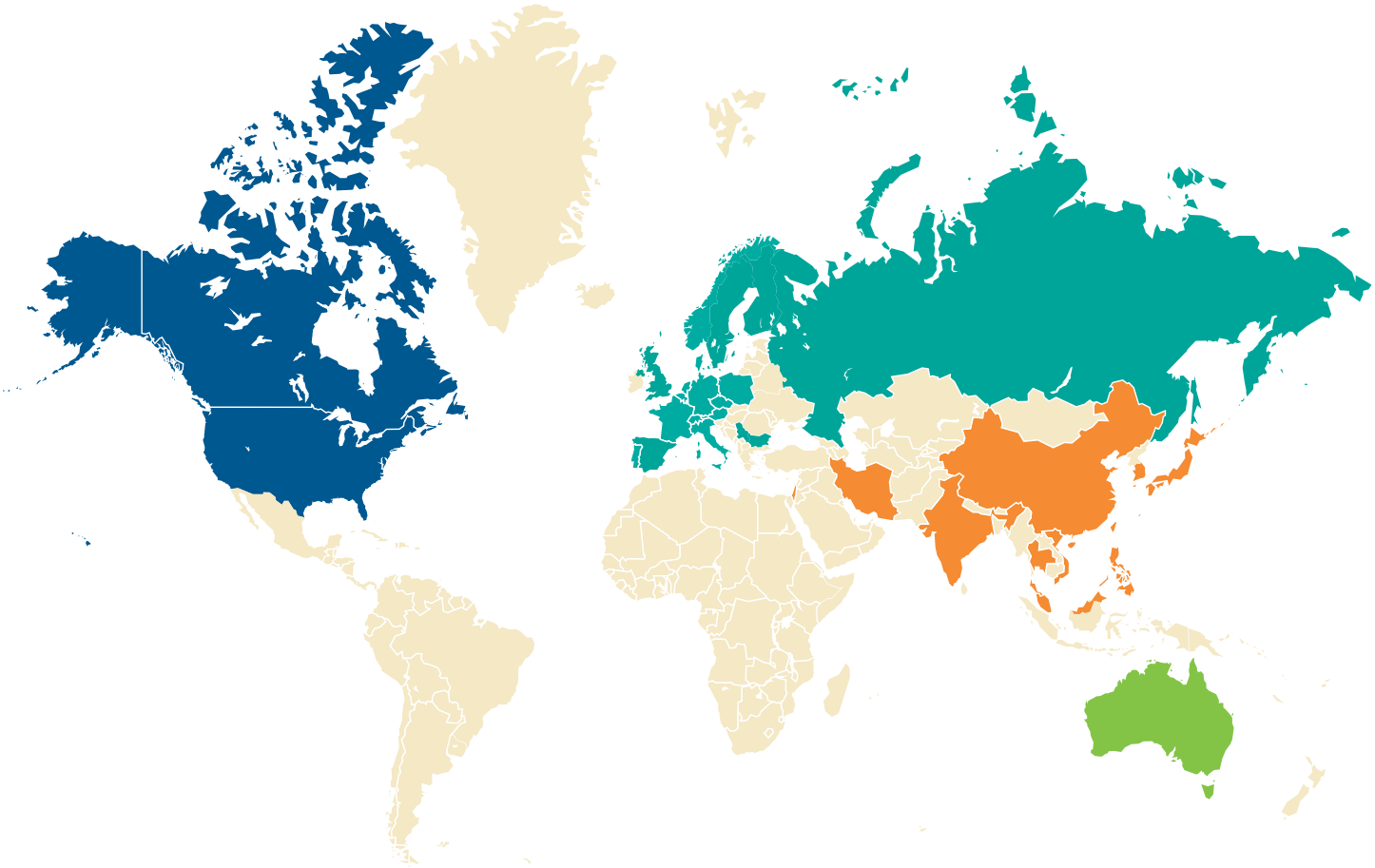
For more information about specific clinical research sites and indications, please visit:
www.fusfoundation.org/the-technology/research-sites

Use the "search by disease research" and/or "search by research stage" dropdown menu.

* Clinical research sites treat patients as part of a clinical study.

1 Three-way tie: Australia, The Netherlands, and Norway

Clinical Research Sites by Country



North America

8 Canada
77 United States

Europe

1 Austria
2 Belgium
1 Bulgaria
1 Czech Republic
2 Denmark
1 Finland
33 France
16 Germany
11 Italy
5 The Netherlands
5 Norway
1 Poland
1 Portugal
5 Russian Federation
1 Serbia
4 Spain
1 Sweden
4 Switzerland
9 United Kingdom

Asia

57 China
2 India
1 Iran
3 Israel
12 Japan
1 Malaysia
1 Philippines
1 Singapore
11 South Korea
8 Taiwan
1 Thailand
1 Vietnam

Oceania

5 Australia

Clinical Research Sites by Indication and Body System*

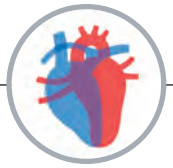
97 indications are being researched at clinical sites worldwide.

21 Cardiovascular sites 6 indications	**10** Endocrine disorders sites 2 indications	**56** Gastrointestinal sites 10 indications	**11** Miscellaneous sites 9 indications
63 Musculoskeletal sites 12 indications	**96** Neurological sites 37 indications	**7** Ophthalmological sites 1 indication	**2** Pulmonary sites 2 indications
83 Urological sites 6 indications	**82** Women's health sites 12 indications		

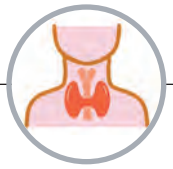
* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary above.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites. Use the "search by disease research" and/or "search by research stage" dropdown menu.

Clinical Research Sites by Indication and Region*



Indications	Regions: N. America	Regions: Europe	Regions: Asia	Regions: Oceania	Totals
Cardiovascular					
Cardiac					
Heart valve calcifications	–	9	–	–	**9**
Peripheral					
Arteriovenous malformations	–	1	–	–	**1**
Hypertension	–	–	3	–	**3**
Peripheral artery disease	–	1	–	–	**1**
Twin-twin transfusion syndrome	–	1	–	–	**1**
Varicose veins	1	3	2	–	**6**



Indications	Regions: N. America	Regions: Europe	Regions: Asia	Regions: Oceania	Totals
Endocrine disorders					
Graves' disease	–	–	1	–	**1**
Thyroid nodules	–	–	9	–	**9**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites. Use the "search by disease research" and/or "search by research stage" dropdown menu.

Clinical Research Sites by Indication and Region* continued

Indications	Regions: N. America	Europe	Asia	Oceania	Totals
Gastrointestinal					
Biliary tract cancer	–	–	1	–	**1**
Colorectal tumors	–	3	2	–	**5**
Dental infections	1	–	–	–	**1**
Esophageal tumors	2	–	–	–	**2**
Gastric tumors	1	–	–	–	**1**
Liver metastases	–	4	–	–	**4**
Liver tumors	9	14	13	–	**36**
Pancreatic tumors	–	–	4	–	**4**
Pancreatic tumors, benign	–	–	1	–	**1**
Pancreatic tumors, malignant	3	14	6	–	**23**

Indications	Regions: N. America	Europe	Asia	Oceania	Totals
Miscellaneous					
Actinic keratosis	–	2	–	–	**2**
Basal cell carcinoma	–	3	–	–	**3**
Dercum's disease	–	–	1	–	**1**
Head & neck tumors	3	–	–	–	**3**
Hypersplenism	–	–	1	–	**1**
Kaposi's sarcoma	–	1	–	–	**1**
Lipoma	–	–	1	–	**1**
Melanoma	2	–	–	–	**2**
Multiple tumors[1]	3	–	2	–	**5**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites. Use the "search by disease research" and/or "search by research stage" dropdown menu.

1 Protocols inclusive of more than one indication.

Clinical Research Sites by Indication and Region* continued

Indications	Regions: N. America	Europe	Asia	Oceania	Totals
Musculoskeletal					
Arthritis, facetogenic	7	5	3	–	**15**
Arthritis, knee	–	–	1	–	**1**
Arthritis, sacroiliac	1	1	1	–	**3**
Bone cancer	4	2	1	–	**7**
Bone metastases	6	12	9	–	**27**
Bone tumors, benign	–	3	–	–	**3**
Desmoid tumors	2	5	1	–	**8**
Osteoid osteoma	3	8	12	–	**23**
Plantar fasciitis	–	1	–	–	**1**
Sacral chordoma	–	1	–	–	**1**
Soft tissue cancer	4	3	–	–	**7**
Soft tissue tumors, benign	2	5	13	1	**21**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

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Use the "search by disease research" and/or "search by research stage" dropdown menu.

Clinical Research Sites by Indication and Region* continued

Indications	Regions: N. America	Europe	Asia	Oceania	Totals
Neurological					
Movement disorder					
Dystonia	–	1	3	–	**4**
Dystonia, hand	–	–	1	–	**1**
Epilepsy	8	–	2	1	**11**
Essential tremor	6	6	6	–	**18**
Parkinson's disease, dyskinesia	9	3	4	–	**16**
Parkinson's disease, tremor	6	6	2	–	**14**
Tremor, orthostatic	2	–	–	–	**2**
Neurodegenerative					
Alzheimer's disease	13	–	3	4	**20**
Amyotrophic lateral sclerosis	1	–	–	–	**1**
Multiple sclerosis	1	–	–	–	**1**
Parkinson's disease, underlying cause	1	–	–	–	**1**
Pain					
Cancer pain	1	–	–	–	**1**
Neuropathic pain	4	1	2	–	**7**
Neuropathy	2	–	–	–	**2**
Painful amputation neuromas	–	–	1	–	**1**
Trigeminal neuralgia	1	–	–	–	**1**

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Clinical Research Sites by Indication and Region* continued

Indications	Regions: N. America	Europe	Asia	Oceania	Totals
Neurological continued					
Psychiatric					
ADHD	1	–	–	–	**1**
Anxiety	4	–	–	–	**4**
Bipolar disorder	1	–	–	–	**1**
Depression	6	–	5	–	**11**
Mood disorder	2	–	–	–	**2**
Obsessive-compulsive disorder	4	–	–	–	**4**
Opioid and other addictions	–	1	–	–	**1**
PTSD	1	–	–	–	**1**
Schizophrenia	–	–	1	–	**1**
Trauma					
Traumatic brain injury	2	–	1	–	**3**
Tumor					
Astrocytoma	3	–	–	–	**3**
Brain metastases, breast cancer	1	–	–	–	**1**
Brain metastases, lung cancer	4	–	–	–	**4**
Brain metastases, melanoma	–	1	–	–	**1**
Brain tumors, general	3	3	–	–	**6**
Glioblastoma	26	11	5	–	**42**
Neuroblastoma	1	–	–	–	**1**
Neurofibromatosis	2	1	–	–	**3**
Pontine glioma	5	–	–	–	**5**
Vascular					
Stroke, intracerebral hemorrhage	1	–	–	–	**1**
Stroke, thromboembolic	2	–	2	–	**4**

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Use the "search by disease research" and/or "search by research stage" dropdown menu.

Clinical Research Sites by Indication and Region* continued

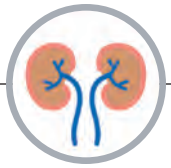
Indications	Regions: N. America	Europe	Asia	Oceania	Totals
Ophthalmological					
Glaucoma	1	5	1	–	**7**

Indications	Regions: N. America	Europe	Asia	Oceania	Totals
Pulmonary					
Lung cancer	1	–	–	–	**1**
Rhinitis	–	–	1	–	**1**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites.
Use the "search by disease research" and/or "search by research stage" dropdown menu.

Clinical Research Sites by Indication and Region* continued



Indications	Regions: N. America	Regions: Europe	Regions: Asia	Regions: Oceania	Totals
Urological					
Benign prostatic hyperplasia	–	2	–	–	**2**
Chyluria	–	–	1	–	**1**
Kidney disease, acute	–	–	1	–	**1**
Kidney stones	3	–	–	–	**3**
Kidney tumors	–	3	12	–	**15**
Prostate cancer	29	50	9	–	**88**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites.
Use the "search by disease research" and/or "search by research stage" dropdown menu.

Clinical Research Sites by Indication and Region* continued

Indications	Regions: N. America	Regions: Europe	Regions: Asia	Regions: Oceania	Totals
Women's health					
Breast tumors, benign	5	1	4	–	**10**
Breast tumors, malignant	8	8	12	–	**28**
Cervical tumors	1	2	1	–	**4**
Ectopic pregnancy	–	–	1	–	**1**
Endometrial tumors	–	1	–	–	**1**
Endometriosis	–	1	1	–	**2**
Lichen sclerosis	–	–	1	–	**1**
Ovarian tumors	1	1	–	–	**2**
Retained placenta	–	–	1	–	**1**
Uterine adenomyosis	–	6	19	2	**27**
Uterine fibroids	3	20	40	2	**65**
Vaginal tumors	–	2	–	–	**2**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites.
Use the "search by disease research" and/or "search by research stage" dropdown menu.

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Preclinical Research Sites

152 Preclinical research sites worldwide*

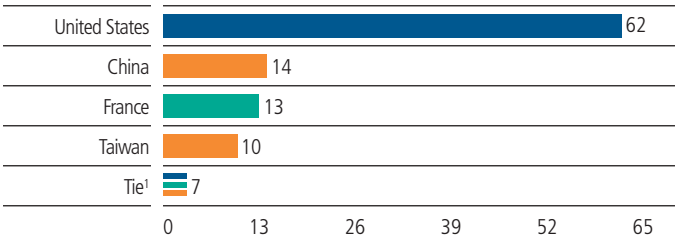
North America	Europe	Asia	South America	Oceania	Africa
69	41	39	–	3	–

Annual growth by region from 2013–2021

North America	Europe	Asia	South America	Oceania	Africa
5%	5%	11%	–	5%	–

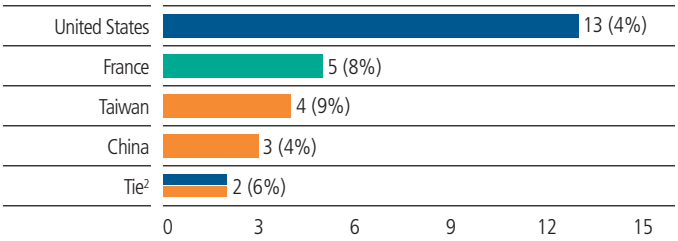
Top Countries for Preclinical Research

Number of sites



Top Countries with Preclinical Research Growth

Sites added, cumulative 2017 to 2022



Preclinical research in 2022 remained steady, with no significant changes from 2021 both in terms of overall numbers of sites and global distribution. The United States remains the dominant country for preclinical focused ultrasound research.

Preclinical research additional content

For more information about specific preclinical research sites and indications, please visit:
www.fusfoundation.org/the-technology/research-sites

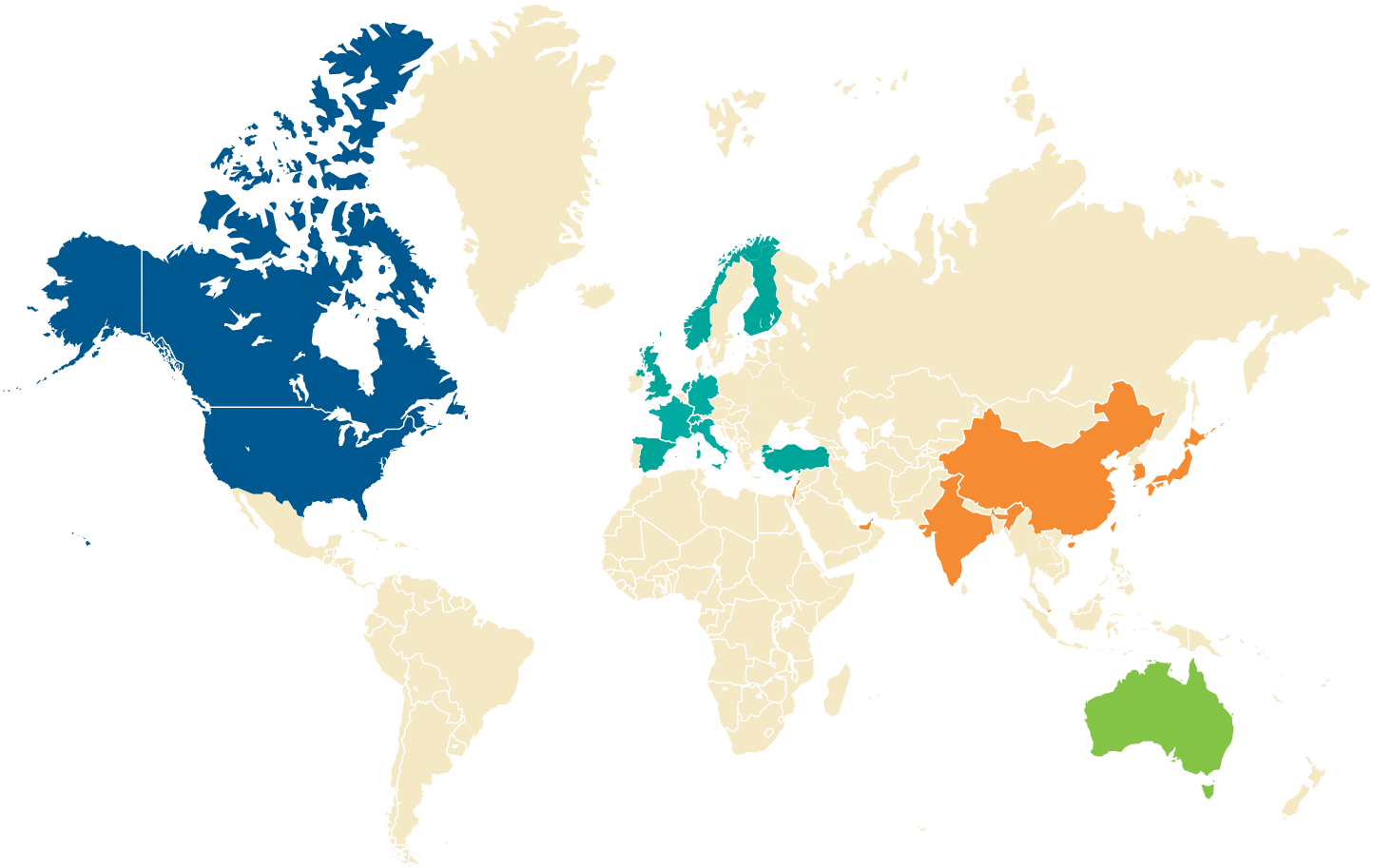
Use the "search by disease research" and/or "search by research stage" dropdown menu.

* Preclinical research sites conduct nonhuman FUS research to collect data in support of the safety or feasibility of clinical applications.

1 Three-way tie: Canada, Germany, and South Korea

2 Two-way tie: Canada and South Korea

Preclinical Research Sites by Country



North America

7 Canada
62 United States

Europe

1 Cyprus
1 Finland
13 France
7 Germany
2 Italy
1 The Netherlands
2 Norway
4 Spain
3 Switzerland
1 Turkey
6 United Kingdom

Asia

14 China
1 India
2 Israel
3 Japan
1 Singapore
7 South Korea
10 Taiwan
1 United Arab Emirates

Oceania

3 Australia

Preclinical Research Sites by Indication and Body System*

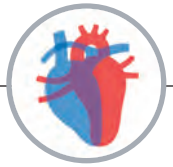
102 indications are being researched at preclinical sites worldwide.

26 **Cardiovascular sites** 15 indications	**4** **Endocrine disorders sites** 3 indications	**43** **Gastrointestinal sites** 8 indications	**24** **Miscellaneous sites** 9 indications
31 **Musculoskeletal sites** 12 indications	**81** **Neurological sites** 32 indications	**7** **Ophthalmological sites** 4 indications	**6** **Pulmonary sites** 2 indications
31 **Urological sites** 9 indications	**39** **Women's health sites** 8 indications		

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary above.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites. Use the "search by disease research" and/or "search by research stage" dropdown menu.

Preclinical Research Sites by Indication and Region*

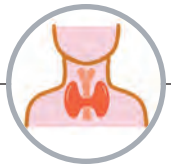


Indications	Regions: N. America	Regions: Europe	Regions: Asia	Regions: Oceania	Totals
Cardiovascular					
Cardiac					
Atrial fibrillation	1	1	1	–	**3**
Cardiac hypertrophy	–	–	1	–	**1**
Cardiac pacing	–	1	–	–	**1**
Fetal heart anomalies	1	–	–	–	**1**
Heart valve calcifications	–	1	–	–	**1**
Mitral regurgitation	–	1	–	–	**1**
Ventricular tachycardia	1	1	–	–	**2**
Peripheral					
Arteriovenous malformations	1	–	–	–	**1**
Atherosclerosis	4	1	1	–	**6**
Deep vein thrombosis	6	–	–	–	**6**
Hematoma	2	–	–	–	**2**
Hemophilia	1	–	–	–	**1**
Hypertension	1	–	–	–	**1**
Peripheral artery disease	2	–	–	–	**2**
Twin-twin transfusion syndrome	1	3	1	–	**5**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites. Use the "search by disease research" and/or "search by research stage" dropdown menu.

Preclinical Research Sites by Indication and Region* continued



Indications	Regions: N. America	Regions: Europe	Regions: Asia	Regions: Oceania	Totals
Endocrine disorders					
Diabetes	2	–	–	–	**2**
Thyroid cancer	2	–	–	–	**2**
Thyroid nodules	1	–	–	–	**1**

Indications	Regions: N. America	Regions: Europe	Regions: Asia	Regions: Oceania	Totals
Gastrointestinal					
Colorectal tumors	1	1	–	–	**2**
Gastric tumors	–	1	–	–	**1**
Inflammatory bowel disease	–	1	–	–	**1**
Liver metastases	2	3	–	–	**5**
Liver tumors	10	11	5	–	**26**
Pancreatic tumors	–	–	4	–	**4**
Pancreatic tumors, malignant	9	11	–	–	**20**
Periodontal disease	–	–	–	1	**1**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites. Use the "search by disease research" and/or "search by research stage" dropdown menu.

Preclinical Research Sites by Indication and Region* continued

Indications	Regions: N. America	Europe	Asia	Oceania	Totals
Miscellaneous					
Head & neck tumors	2	1	1	–	**4**
Heterotopic ossification	1	–	–	–	**1**
Infection	2	–	1	–	**3**
Melanoma	5	–	–	–	**5**
Multiple tumors[1]	4	2	–	–	**6**
Niemann-Pick disease	1	–	–	–	**1**
Obesity	1	–	–	–	**1**
Sinonasal disease	–	–	1	–	**1**
Wound healing	3	–	–	1	**4**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites. Use the "search by disease research" and/or "search by research stage" dropdown menu.

1 Protocols inclusive of more than one indication

Preclinical Research Sites by Indication and Region* continued

Indications	Regions: N. America	Regions: Europe	Regions: Asia	Regions: Oceania	Totals
Musculoskeletal					
Arthritis, facetogenic	2	1	1	–	**4**
Arthritis, knee	–	–	1	–	**1**
Bone cancer	1	–	–	–	**1**
Bone metastases	3	1	3	1	**8**
Bone tumors, benign	1	1	–	–	**2**
Muscle atrophy	3	–	–	–	**3**
Osteoid osteoma	1	1	2	–	**4**
Osteopenia	1	–	–	–	**1**
Rotator cuff injury	1	–	–	–	**1**
Soft tissue cancer	9	2	–	–	**11**
Soft tissue tumors, benign	2	1	2	–	**5**
Tendon contracture	1	–	–	–	**1**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites.
Use the "search by disease research" and/or "search by research stage" dropdown menu.

Preclinical Research Sites by Indication and Region* continued

Indications	Regions: N. America	Regions: Europe	Regions: Asia	Regions: Oceania	Totals
Neurological					
Movement disorder					
Epilepsy	11	4	3	–	**18**
Essential tremor	–	–	1	–	**1**
Parkinson's disease, dyskinesia	–	–	1	–	**1**
Parkinson's disease, tremor	2	–	–	–	**2**
Neurodegenerative					
Alzheimer's disease	8	6	4	1	**19**
Amyotrophic lateral sclerosis	1	1	–	–	**2**
Dementia	–	–	1	–	**1**
Huntington's disease	1	–	–	–	**1**
Parkinson's disease, underlying cause	6	3	4	–	**13**
Rett syndrome	–	1	–	–	**1**
Other					
Hydrocephalus	1	–	–	–	**1**
Neuromyelitis optica	1	–	–	–	**1**
Pain					
Cancer pain	1	2	–	–	**3**
Headache	–	–	1	–	**1**
Neuropathic pain	5	–	1	–	**6**
Neuropathy	–	–	1	–	**1**
Psychiatric					
Anxiety	2	1	–	–	**3**
Autism	–	1	–	–	**1**
Depression	4	2	–	–	**6**
Opioid and other addictions	2	1	–	–	**3**
Trauma					
Spinal cord injury	3	–	1	–	**4**
Traumatic brain injury	1	–	–	–	**1**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites. Use the "search by disease research" and/or "search by research stage" dropdown menu.

Preclinical Research Sites by Indication and Region* continued

Indications	Regions: N. America	Regions: Europe	Regions: Asia	Regions: Oceania	Totals
Neurological continued					
Tumor					
Astrocytoma	3	2	3	–	**8**
Brain metastases, breast cancer	3	1	–	–	**4**
Brain metastases, melanoma	1	–	–	–	**1**
Brain tumors, general	10	3	3	–	**16**
Glioblastoma	18	8	9	–	**35**
Neurofibromatosis	1	–	–	–	**1**
Pontine glioma	2	2	–	–	**4**
Vascular					
Cavernomas	1	–	–	–	**1**
Stroke, intracerebral hemorrhage	6	2	1	–	**9**
Stroke, thromboembolic	4	2	–	–	**6**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites. Use the "search by disease research" and/or "search by research stage" dropdown menu.

Preclinical Research Sites by Indication and Region* continued

Indications	Regions: N. America	Europe	Asia	Oceania	Totals
Ophthalmological					
Glaucoma	–	3	–	–	**3**
Macular degeneration	1	–	–	–	**1**
Presbyopia	–	1	1	–	**2**
Retinal injury	1	–	–	–	**1**

Indications	Regions: N. America	Europe	Asia	Oceania	Totals
Pulmonary					
Lung cancer	3	1	1	–	**5**
Tuberculosis	–	–	1	–	**1**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites.
Use the "search by disease research" and/or "search by research stage" dropdown menu.

Preclinical Research Sites by Indication and Region* continued

Indications	Regions: N. America	Regions: Europe	Regions: Asia	Regions: Oceania	Totals
Urological					
Acute tubular necrosis	1	–	–	–	**1**
Benign prostatic hyperplasia	1	–	1	–	**2**
Bladder tumors	2	–	–	–	**2**
Fetal bladder obstruction	–	–	1	–	**1**
Kidney disease, acute	1	–	–	–	**1**
Kidney stones	2	–	–	–	**2**
Kidney tumors	4	1	2	–	**7**
Prostate cancer	13	7	3	–	**23**
Urinary tract infection	–	1	–	–	**1**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites.
Use the "search by disease research" and/or "search by research stage" dropdown menu.

Preclinical Research Sites by Indication and Region* continued

Indications	Regions: N. America	Regions: Europe	Regions: Asia	Regions: Oceania	Totals
Women's health					
Breast tumors, benign	1	–	1	–	**2**
Breast tumors, malignant	15	4	6	–	**25**
Cervical tumors	–	–	1	–	**1**
Endometrial tumors	1	–	1	–	**2**
Endometriosis	–	1	–	–	**1**
Ovarian tumors	1	–	1	1	**3**
Uterine adenomyosis	–	–	2	1	**3**
Uterine fibroids	4	2	8	1	**15**

* A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary.

For more information about specific clinical research sites and indications, please visit: www.fusfoundation.org/the-technology/research-sites.
Use the "search by disease research" and/or "search by research stage" dropdown menu.

Mechanisms of Action Research Sites

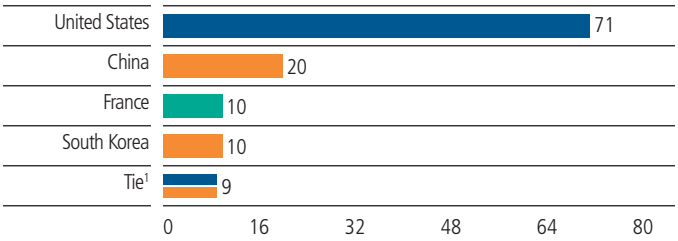
180 MOA research sites worldwide*

North America	Europe	Asia	South America	Oceania	Africa
80	42	55	–	3	–

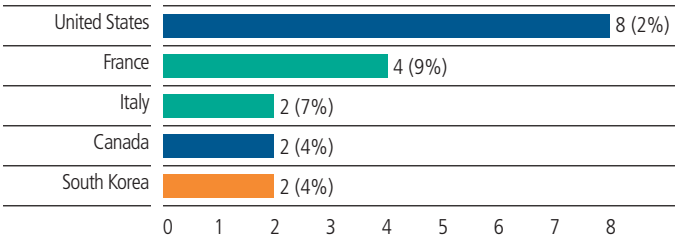
Annual growth by region from 2013–2021

North America	Europe	Asia	South America	Oceania	Africa
7%	9%	28%	–	20%	–

Top Countries for MOA Research
Number of sites



Top Countries with MOA Research Growth
Sites added, cumulative 2017 to 2022



Mechanism of action research also remained steady in 2022. No significant changes from 2021 both in terms of overall numbers of sites and global distribution. The United States remains the dominant country for mechanism of action focused ultrasound research.

MOA research additional content

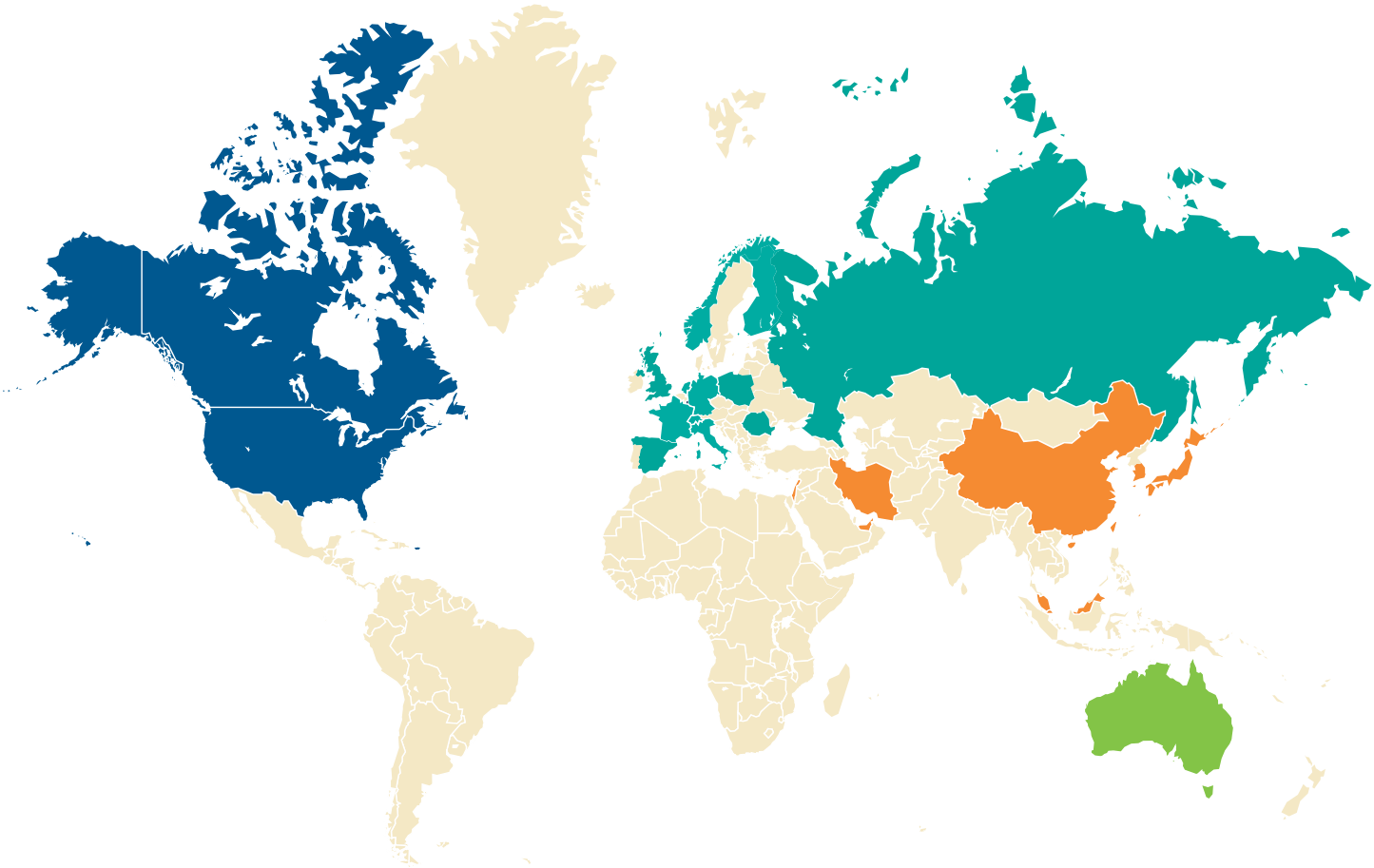
For more information about specific Mechanism of Action research sites and indications, please visit:
www.fusfoundation.org/the-technology/research-sites

Use the "search by disease research" and/or "search by research stage" dropdown menu and choose "Bioeffect."

* Mechanisms of action research sites conduct basic science research to understand how focused ultrasound affects the body.

1 Two-way tie: Canada and Japan

Mechanisms of Action Research Sites by Country



North America

9 Canada
71 United States

Europe

1 Bulgaria
1 Cyprus
10 France
6 Germany
6 Italy
2 The Netherlands
2 Norway
1 Russian Federation
2 Spain
4 Switzerland
7 United Kingdom

Asia

20 China
2 Iran
4 Israel
9 Japan
1 Malaysia
1 Singapore
10 South Korea
7 Taiwan
1 United Arab Emirates

Oceania

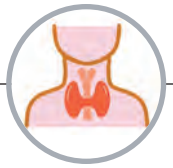
3 Australia

Number of Research Sites and MOAs under Investigation

Indications	MOAs[1]	Sites: Preclinical	Sites: Clinical	Sites: Commercial	Total[2]
Cardiovascular					
Cardiac					
Atrial fibrillation	2	3	–	–	**3**
Cardiac hypertrophy	1	1	–	–	**1**
Cardiac pacing	1	1	–	–	**1**
Fetal heart anomalies	1	1	–	–	**1**
Heart valve calcifications	1	1	9	–	**10**
Mitral regurgitation	1	1	–	–	**1**
Ventricular tachycardia	1	2	–	–	**2**
Peripheral					
Arteriovenous malformations	3	1	1	2	**4**
Atherosclerosis	5	7	–	–	**6**
Deep vein thrombosis	6	9	–	–	**6**
Hematoma	2	2	–	–	**2**
Hemophilia	1	1	–	–	**1**
Hypertension	2	1	3	–	**4**
Peripheral artery disease	3	2	1	–	**3**
Twin-twin transfusion syndrome	3	5	1	–	**5**
Varicose veins	2	–	6	9	**15**

1 Mechanisms of action
2 For each indication, a site may examine more than one mechanism of action or may perform more than one stage of research or treatment. The total reflects unique sites, and therefore may not necessarily be the sum of the values in the preceding three columns.

Number of Research Sites and MOAs under Investigation continued



Indications	MOAs[1]	Sites: Preclinical	Sites: Clinical	Sites: Commercial	Total[2]
Endocrine disorders					
Diabetes	1	2	–	–	**2**
Graves' disease	1	–	1	–	**1**
Thyroid cancer	2	2	–	–	**2**
Thyroid nodules	2	1	9	20	**30**

Number of Research Sites and MOAs under Investigation continued

Indications	MOAs[1]	Sites: Preclinical	Sites: Clinical	Sites: Commercial	Total[2]
Gastrointestinal					
Biliary tract cancer	1	–	1	–	**1**
Colorectal tumors	3	2	5	–	**7**
Dental infections	1	–	1	–	**1**
Esophageal tumors	1	–	1	–	**1**
Gastric tumors	2	1	1	–	**3**
Inflammatory bowel disease	1	1	–	1	**1**
Liver metastases	5	5	3	3	**11**
Liver tumors	11	31	36	137	**181**
Pancreatic tumors	3	4	4	41	**49**
Pancreatic tumors, benign	1	–	1	1	**2**
Pancreatic tumors, malignant	16	35	19	9	**40**
Periodontal disease	2	2	–	–	**1**

1 Mechanisms of action
2 For each indication, a site may examine more than one mechanism of action or may perform more than one stage of research or treatment. The total reflects unique sites, and therefore may not necessarily be the sum of the values in the preceding three columns.

Number of Research Sites and MOAs under Investigation continued

Indications	MOAs[1]	Sites: Preclinical	Sites: Clinical	Sites: Commercial	Total[2]
Miscellaneous					
Actinic keratosis	1	–	2	–	**2**
Basal cell carcinoma	1	–	3	–	**3**
Dercum's disease	1	–	1	–	**1**
Head & neck tumors	6	4	3	–	**6**
Heterotopic ossification	1	1	–	–	**1**
Hypersplenism	1	–	1	–	**1**
Infection	3	3	–	–	**3**
Kaposi's sarcoma	1	–	1	–	**1**
Lipoma	1	–	1	–	**1**
Melanoma	3	5	2	–	**6**
Multiple tumors[3]	7	6	5	–	**10**
Niemann-Pick disease	1	1	–	–	**1**
Obesity	*	1	–	–	**1**
Sinonasal disease	1	1	–	–	**1**
Wound healing	4	5	–	–	**4**

1 Mechanisms of action
2 For each indication, a site may examine more than one mechanism of action or may perform more than one stage of research or treatment. The total reflects unique sites, and therefore may not necessarily be the sum of the values in the preceding three columns.
3 Protocols inclusive of more than one indication.
* No mechanism of action was provided

Number of Research Sites and MOAs under Investigation continued

Indications	MOAs[1]	Sites: Preclinical	Sites: Clinical	Sites: Commercial	Total[2]
Musculoskeletal					
Arthritis, facetogenic	3	5	15	4	**19**
Arthritis, knee	2	1	1	–	**2**
Arthritis, sacroiliac	1	–	3	–	**3**
Bone cancer	2	1	7	8	**16**
Bone metastases	5	8	27	27	**46**
Bone tumors, benign	2	2	3	1	**6**
Desmoid tumors	1	–	8	11	**18**
Muscle atrophy	3	3	–	–	**3**
Osteoid osteoma	1	4	23	103	**107**
Osteopenia	2	2	–	–	**1**
Plantar fasciitis	1	–	1	–	**1**
Rotator cuff injury	1	1	–	–	**1**
Sacral chordoma	1	–	1	–	**1**
Soft tissue cancer	8	12	6	2	**15**
Soft tissue tumors, benign	2	5	21	92	**101**
Tendon contracture	2	2	–	–	**1**

1 Mechanisms of action
2 For each indication, a site may examine more than one mechanism of action or may perform more than one stage of research or treatment. The total reflects unique sites, and therefore may not necessarily be the sum of the values in the preceding three columns.

Number of Research Sites and MOAs under Investigation continued

Indications	MOAs[1]	Sites: Preclinical	Sites: Clinical	Sites: Commercial	Total[2]
Neurological					
Movement disorder					
Dystonia	2	–	4	1	**5**
Dystonia, hand	1	–	1	1	**1**
Epilepsy	10	21	10	2	**26**
Essential tremor	2	1	18	102	**109**
Parkinson's disease, dyskinesia	2	1	14	6	**19**
Parkinson's disease, tremor	3	2	14	57	**69**
Tremor, orthostatic	2	–	2	–	**1**
Neurodegenerative					
Alzheimer's disease	9	24	20	1	**28**
Amyotrophic lateral sclerosis	2	2	1	–	**2**
Dementia	1	1	–	–	**1**
Huntington's disease	1	1	–	–	**1**
Multiple sclerosis	1	–	1	–	**1**
Parkinson's disease, underlying cause	7	16	1	–	**14**
Rett syndrome	1	1	–	–	**1**
Other					
Hydrocephalus	1	1	–	–	**1**
Neuromyelitis optica	1	1	–	–	**1**
Pain					
Cancer pain	3	3	1	–	**4**
Headache	1	1	–	–	**1**
Neuropathic pain	4	6	6	3	**14**
Neuropathy	3	1	2	1	**4**
Painful amputation neuromas	1	–	1	–	**1**
Trigeminal neuralgia	1	–	1	1	**2**

1 Mechanisms of action
2 For each indication, a site may examine more than one mechanism of action or may perform more than one stage of research or treatment. The total reflects unique sites, and therefore may not necessarily be the sum of the values in the preceding three columns.

Number of Research Sites and MOAs under Investigation continued

Indications	MOAs[1]	Sites: Preclinical	Sites: Clinical	Sites: Commercial	Total[2]
Neurological continued					
Psychiatric					
ADHD	1	–	1	–	**1**
Anxiety	2	3	4	–	**7**
Autism	1	1	–	–	**1**
Bipolar disorder	1	–	1	–	**1**
Depression	2	6	11	1	**13**
Mood disorder	1	–	2	–	**2**
Obsessive-compulsive disorder	2	–	4	2	**5**
Opioid and other addictions	1	3	1	–	**4**
PTSD	1	–	1	–	**1**
Schizophrenia	1	–	1	–	**1**
Trauma					
Spinal cord injury	2	4	–	–	**4**
Traumatic brain injury	2	1	3	–	**4**
Tumor					
Astrocytoma	3	8	2	–	**10**
Brain metastases, breast cancer	5	6	1	–	**4**
Brain metastases, lung cancer	1	–	4	–	**4**
Brain metastases, melanoma	4	3	1	–	**2**
Brain tumors, general	21	31	6	–	**22**
Glioblastoma	21	47	37	–	**57**
Neuroblastoma	1	–	1	–	**1**
Neurofibromatosis	2	1	3	–	**4**
Pontine glioma	5	5	5	–	**8**
Vascular					
Cavernomas	1	1	–	–	**1**
Stroke, intracerebral hemorrhage	6	9	1	–	**10**
Stroke, thromboembolic	7	6	4	–	**10**

1 Mechanisms of action
2 For each indication, a site may examine more than one mechanism of action or may perform more than one stage of research or treatment. The total reflects unique sites, and therefore may not necessarily be the sum of the values in the preceding three columns.

Number of Research Sites and MOAs under Investigation continued

Indications	MOAs[1]	Sites: Preclinical	Sites: Clinical	Sites: Commercial	Total[2]
Ophthalmological					
Glaucoma	2	3	7	14	**22**
Macular degeneration	1	1	–	–	**1**
Presbyopia	2	2	–	–	**2**
Retinal injury	1	1	–	–	**1**

1 Mechanisms of action

2 For each indication, a site may examine more than one mechanism of action or may perform more than one stage of research or treatment. The total reflects unique sites, and therefore may not necessarily be the sum of the values in the preceding three columns.

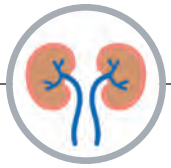
Number of Research Sites and MOAs under Investigation continued

Indications	MOAs[1]	Sites: Preclinical	Sites: Clinical	Sites: Commercial	Total[2]
Pulmonary					
Lung cancer	5	6	1	–	**5**
Rhinitis	1	–	1	–	**1**
Tuberculosis	1	1	–	–	**1**

1 Mechanisms of action

2 For each indication, a site may examine more than one mechanism of action or may perform more than one stage of research or treatment. The total reflects unique sites, and therefore may not necessarily be the sum of the values in the preceding three columns.

Number of Research Sites and MOAs under Investigation continued



Indications	MOAs[1]	Sites: Preclinical	Sites: Clinical	Sites: Commercial	Total[2]
Urological					
Acute tubular necrosis	1	1	–	–	**1**
Benign prostatic hyperplasia	3	2	2	45	**49**
Bladder tumors	2	2	–	–	**2**
Chyluria	1	–	1	–	**1**
Fetal bladder obstruction	1	1	–	–	**1**
Kidney disease, acute	2	1	1	–	**2**
Kidney stones	2	3	2	–	**2**
Kidney tumors	4	7	15	91	**97**
Prostate cancer	9	23	67	432	**461**
Urinary tract infection	1	1	–	–	**1**

1 Mechanisms of action
2 For each indication, a site may examine more than one mechanism of action or may perform more than one stage of research or treatment. The total reflects unique sites, and therefore may not necessarily be the sum of the values in the preceding three columns.

Number of Research Sites and MOAs under Investigation continued

Indications	MOAs[1]	Sites: Preclinical	Sites: Clinical	Sites: Commercial	Total[2]
Women's health					
Breast tumors, benign	2	2	9	13	**21**
Breast tumors, malignant	16	32	27	96	**125**
Cervical tumors	2	1	4	–	**5**
Cervicitis	1	–	–	1	**1**
Ectopic pregnancy	1	–	1	–	**1**
Endometrial tumors	1	2	1	1	**4**
Endometriosis	2	1	2	2	**4**
Lichen sclerosis	1	–	1	1	**2**
Ovarian tumors	2	3	2	–	**5**
Retained placenta	1	–	1	–	**1**
Urinary incontinence, stress	1	–	–	1	**1**
Uterine adenomyosis	3	3	27	115	**135**
Uterine fibroids	4	16	64	319	**347**
Vaginal tumors	1	–	2	–	**2**

1 Mechanisms of action
2 For each indication, a site may examine more than one mechanism of action or may perform more than one stage of research or treatment. The total reflects unique sites, and therefore may not necessarily be the sum of the values in the preceding three columns.

Technical Research Sites by Region

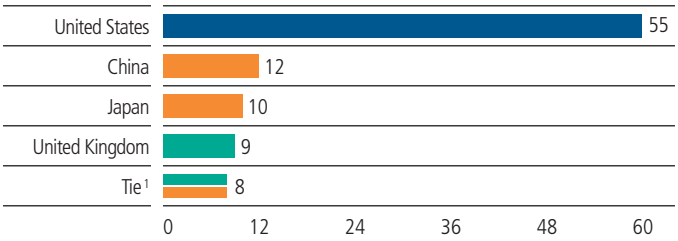
151 Technical research sites worldwide

North America	Europe	Asia	South America	Oceania	Africa
61	49	39	–	2	–

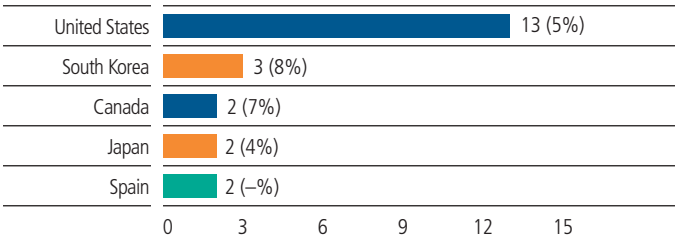
Annual growth by region from 2013–2022

5%	10%	33%	–	15%	–

Top Countries for Technical Research
Number of sites



Top Countries with Technical Research Growth
Sites added, cumulative 2017 to 2022



Technical research programs address high-priority scientific and engineering problems that can stand in the way of the adoption of focused ultrasound as a mainstream standard of care. Solutions developed by technical sites help make clinical treatments safer, faster, less expensive, and available to a wider patient population.

1 Three way tie: France, Germany, and South Korea

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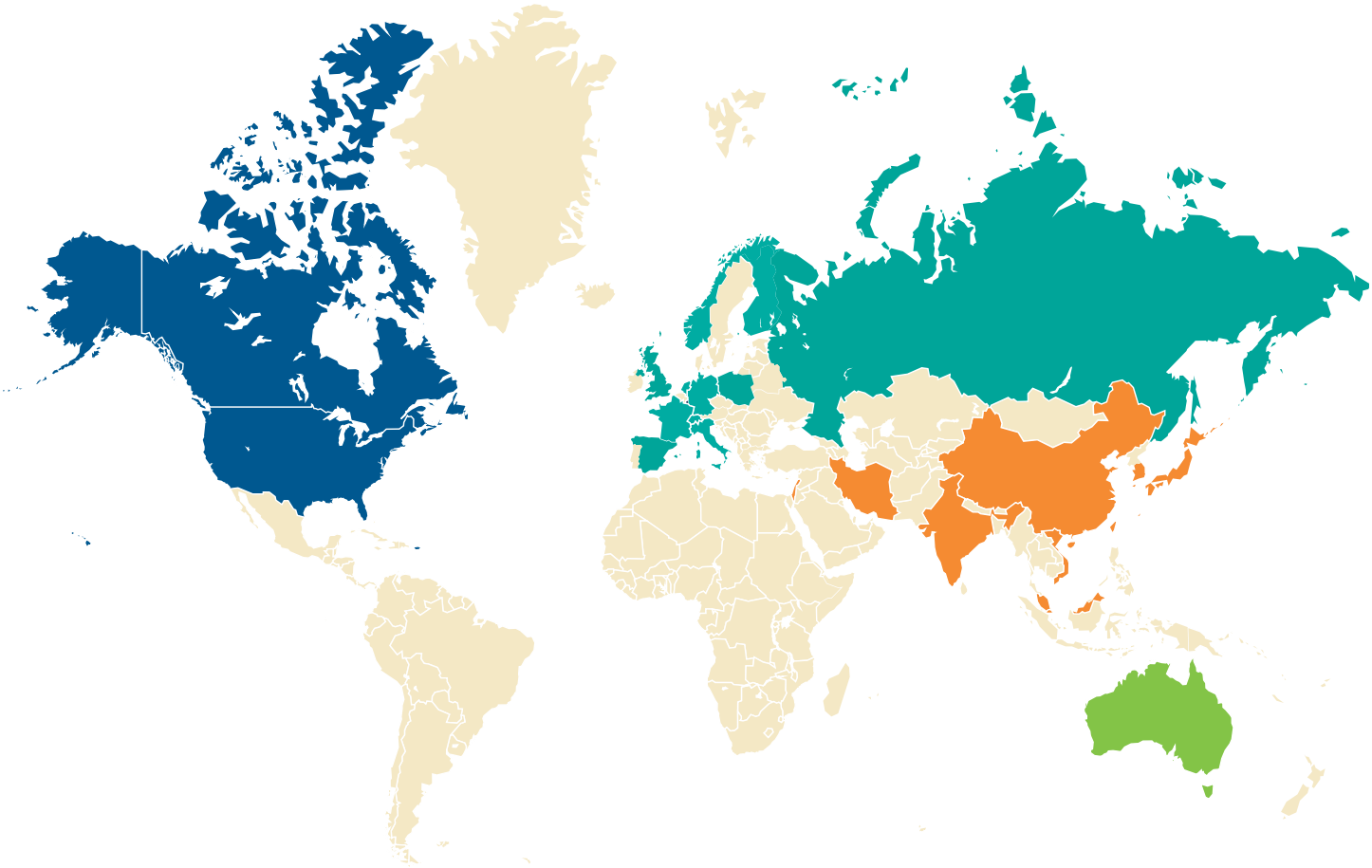
RESEARCH SITES

Technical Research Sites by Country



North America

6 Canada
55 United States

Europe

1 Cyprus
2 Finland
8 France
8 Germany
7 Italy
3 The Netherlands
1 Norway
2 Poland
1 Russian Federation
2 Spain
5 Switzerland
9 United Kingdom

Asia

12 China
1 India
1 Iran
1 Israel
10 Japan
1 Singapore
8 South Korea
4 Taiwan
1 Vietnam

Oceania

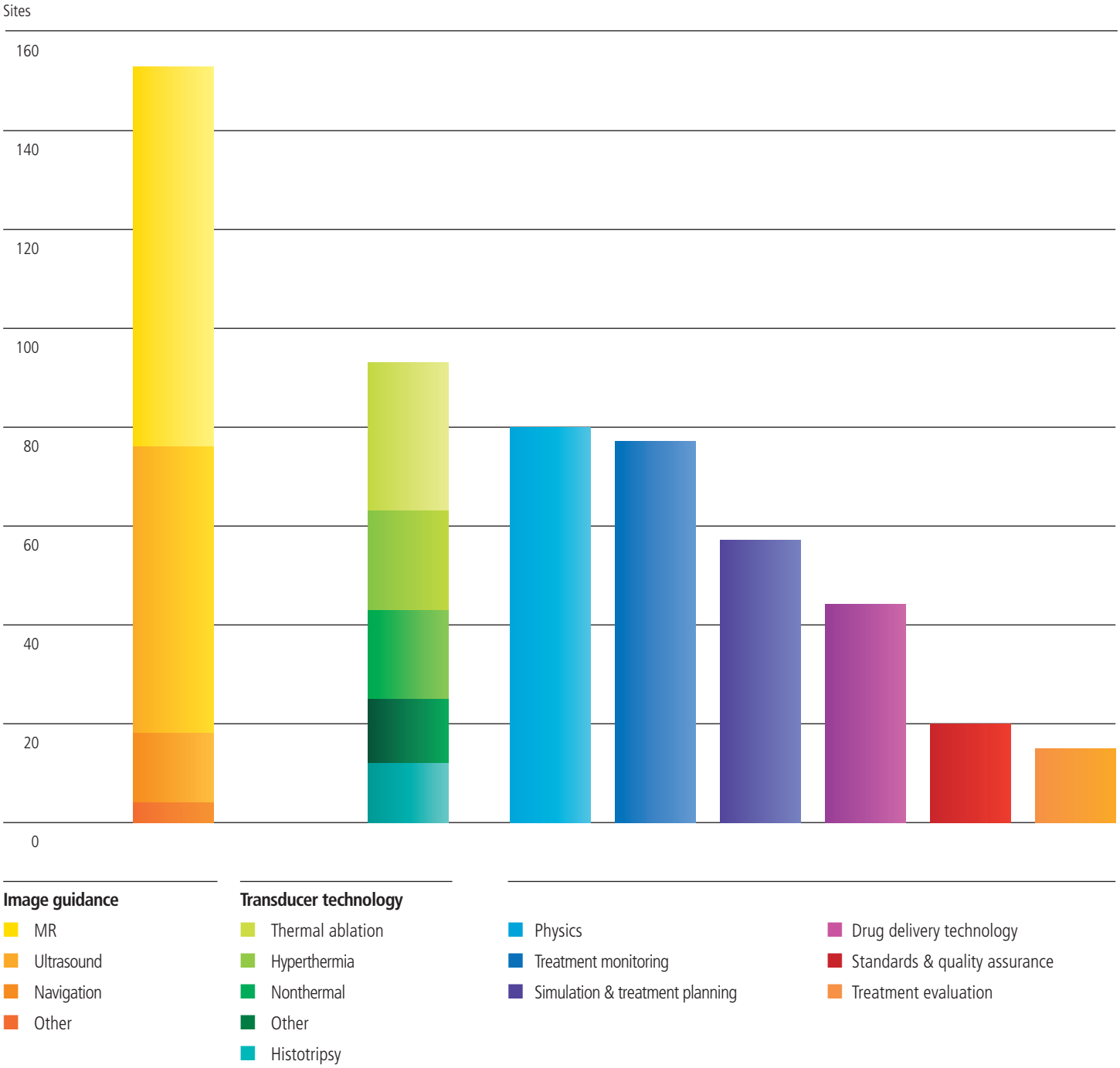
2 Australia

Technical Research Sites*

	Sites				Totals
	North America	Europe	Asia	Oceania	
Image guidance					**153**
MR	29	29	19	–	
Ultrasound	31	18	9	–	
Navigation	4	8	2	–	
Other	1	1	2	–	
Transducer technology					**93**
Thermal ablation	11	12	7	–	
Hyperthermia	7	10	3	–	
Nonthermal	11	3	4	–	
Other	8	4	–	1	
Histotripsy	7	3	2	–	
Physics	40	25	15	–	**80**
Treatment monitoring	32	29	15	1	**77**
Simulation & treatment planning	27	22	8	–	**57**
Drug delivery technology	25	13	4	2	**44**
Standards & quality assurance	9	8	3	–	**20**
Treatment evaluation	7	7	1	–	**15**

* Technical research sites may be working in more than one technical research area.

Technical Research Types*



*Technical research sites may be working in more than one technical research area.

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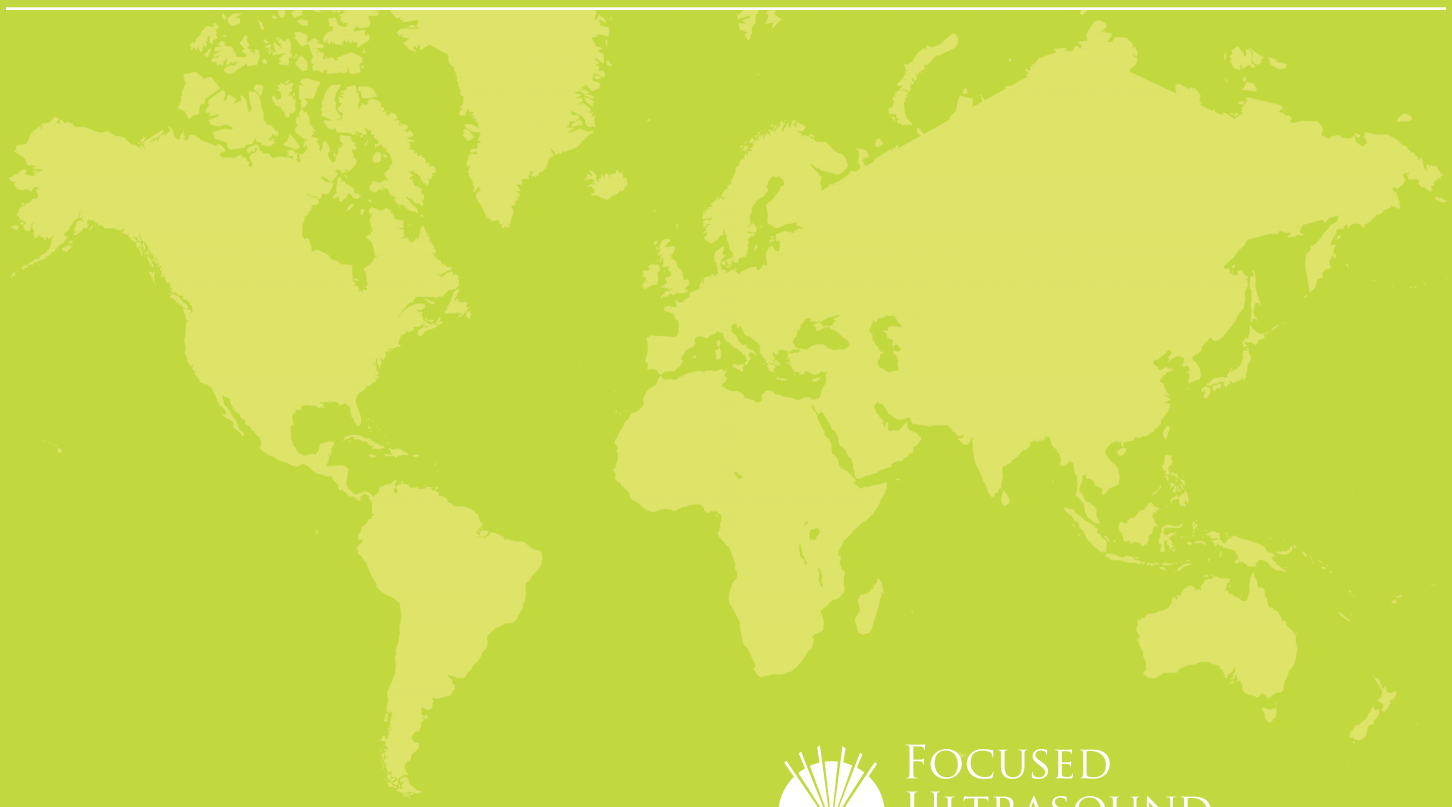
2023 Centers of Excellence



Focused Ultrasound Foundation

Overview

The ten research/treatment sites highlighted in this report are the Focused Ultrasound Foundation designated Centers of Excellence, COEs. They are also listed on our website.

Established in 2009, the COE program brings together the best people and technical resources at luminary sites across the globe. The Centers are created through partnerships of academia, industry, and the Foundation to showcase focused ultrasound technology and serve as hubs for collaboration. They are the powerhouses of focused ultrasound research; in 2022, they collectively published 202 scientific journal articles on their accomplishments. These sites, which include some of the most influential leaders in the field, are cultivators of the next generation of researchers and physicians for focused ultrasound and are creating the intellectual property that will spur the next iteration of commercialization efforts. We encourage you to review these pages in detail, look up the publications that might interest you, and reach out to the contacts we list for each site, if you are interested in a potential collaboration.

This portion of the 2022 State of the Field Report contains a summary of self-reported data from the COEs.

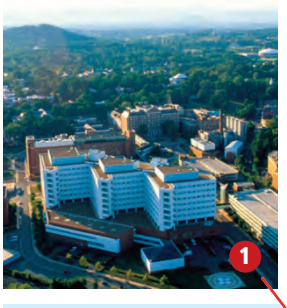
V. Centers of Excellence

V. 2 Overview

Centers

V. 3 Locations
V. 4 Years Established
V. 5 University Medical Center Utrecht
V. 7 Children's National Hospital
V. 9 Physics for Medicine Paris
V. 12 Inserm - LabTAU
V. 15 Stanford University School of Medicine
V. 19 Sunnybrook Health Sciences Centre
V. 24 University of Maryland School of Medicine
V. 26 Brigham and Women's Hospital
V. 29 ICR and The Royal Marsden
V. 31 University of Virginia Health System
V. 34 University of Virginia Focused Ultrasound Cancer Immunotherapy Center

Locations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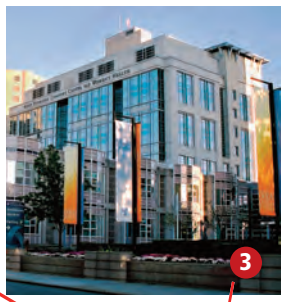
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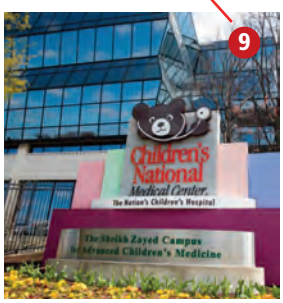
Centers of Excellence
1 University of Virginia Health System
2 The Institute of Cancer Research and The Royal Marsden
3 Brigham and Women's Hospital
4 University of Maryland School of Medicine
5 Sunnybrook Health Sciences Centre
6 Stanford University School of Medicine
7 Inserm - LabTAU
8 Physics for Medicine Paris
9 Children's National Hospital
10 University Medical Center Utrecht

6

7

8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Children's National
Medical Center
The Sheikh Zayed Campus for Advanced Children's Medicine

10

Years Established

Name	Location	Established
University Medical Center Utrecht	Utrecht, The Netherlands	2020
Children's National Hospital	Washington, DC	2020
Physics for Medicine Paris	Paris, France	2019
Inserm - LabTAU	Lyon, France	2017
Stanford University School of Medicine	Stanford, CA	2016
Sunnybrook Health Sciences Centre	Toronto, Canada	2016
University of Maryland School of Medicine	Baltimore, MD	2016
Brigham and Women's Hospital	Boston, MA	2015
The Institute of Cancer Research and The Royal Marsden	London, England	2013
University of Virginia Health System	Charlottesville, VA	2009

CENTERS OF EXCELLENCE

University Medical Center Utrecht

4	6
Commercial Treatments	Clinical Research

3	12	7	8
Preclinical Research	Mechanisms of Action Research	Technical Research	Publications

University Medical Center Utrecht | The Netherlands

The University Medical Center Utrecht, UMC Utrecht, is the fourth Center of Excellence in Europe. UMC Utrecht is striving to improve current cancer therapy with MRI-guided focused ultrasound, often in combination with other modalities, such as radiotherapy, chemotherapy, and surgery, leading to higher efficacy, fewer side effects, and lower costs. The emphasis of the clinical translation, in close collaboration with other nearby medical centers and international consortia, is on breast cancer, bone cancer, immune stimulation, and drug delivery for brain tumor treatment.

Contacts

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Commercial treatments

Musculoskeletal	Bone metastases, Desmoid tumors
Women's health	Endometriosis, Uterine fibroids

Clinical research

Cardiovascular	Peripheral artery disease
Musculoskeletal	Bone metastases, Desmoid tumors
Women's health	Breast tumors, malignant; Uterine fibroids

Preclinical research

Miscellaneous	Head & neck tumors
Neurological	Pontine glioma

Mechanisms of action research

Histotripsy	Immunomodulation, Tissue destruction
Hyperthermia	Drug delivery, Radiosensitization
Nonthermal	BBB opening; BBB opening, drug delivery; Drug delivery; Drug delivery, vehicle; Immunomodulation; Liquid biopsy; Tissue destruction
Thermal ablation	Tissue destruction

Technical research

- Drug delivery technology
- FUS Image guidance, MR
- FUS Image guidance, Ultrasound
- FUS Physics
- FUS Transducer technology, Histotripsy
- FUS Treatment monitoring

University Medical Center Utrecht continued

Research not involving thermal ablation, tissue destruction

Clinical Research - Women's health	
Breast tumors, malignant	Hyperthermia - Drug delivery
Preclinical Research - Miscellaneous	
Head & neck tumors	Nonthermal - Sonoporation
Preclinical Research - Neurological	
Pontine glioma	Nonthermal, BBB opening - Drug delivery
	Nonthermal - Drug delivery

Publications—2022

The Effect of Microbubble-Assisted Ultrasound on Molecular Permeability across Cell Barriers. Rousou C, de Maar J, Qiu B, van der Wurff-Jacobs K, Ruponen M, Urtti A, Oliveira S, Moonen C, Storm G, Mastrobattista E, Deckers R. Pharmaceutics. 2022 Feb 24;14(3):494. doi: 10.3390/pharmaceutics14030494. PMID: 35335871; PMCID: PMC8949944.

Increased MR-guided high intensity focused ultrasound (MR-HIFU) sonication efficiency of uterine fibroids after carbetocin administration. Anneveldt KJ, van 't Oever HJ, Verpalen IM, Nijholt IM, Bartels W, Dijkstra JR, van den Hoed RD, van 't Veer-Ten Kate M, de Boer E, Veersema S, Huirne JAF, Schutte JM, Boomsma MF. Eur J Radiol Open. 2022 Mar 21;9:100413. doi: 10.1016/j.ejro.2022.100413. PMID: 35340827; PMCID: PMC8942847.

Safety and feasibility study of non- invasive robot-assisted high-intensity focused ultrasound therapy for the treatment of atherosclerotic plaques in the femoral artery: protocol for a pilot study. Simons MV, Groen MHA, de Borst GJ, Leiner T, Doevendans PAF, Ebbini E, Slieker FJB, van Es R, Hazenberg CEVB. BMJ Open. 2022 May 2;12(5):e058418. doi: 10.1136/bmjopen-2021-058418. PMID: 35501090; PMCID: PMC9062820.

Ultrasound-directed enzyme-prodrug therapy (UDEPT) using self-immolative doxorubicin derivatives. Roemhild K, Besse HC, Wang B, Peña Q, Sun Q, Omata D, Ozbakir B, Bos C, Scheeren HW, Storm G, Metselaar JM, Yu H, Knüchel-Clarke R, Kiessling F, Moonen CTW, Deckers R, Shi Y, Lammers T. Theranostics. 2022 Jun 6;12(10):4791-4801. doi: 10.7150/thno.69168. PMID: 35832083; PMCID: PMC9254251.

Synthetic CT for the planning of MR-HIFU treatment of bone metastases in pelvic and femoral bones: a feasibility study. Lena B, Florkow MC, Ferrer CJ, van Stralen M, Seevinck PR, Vonken EPA, Boomsma MF, Slotman DJ, Viergever MA, Moonen CTW, Bos C, Bartels LW. Eur Radiol. 2022 Jul;32(7):4537-4546. doi: 10.1007/s00330-022-08568-y. Epub 2022 Feb 21. PMID: 35190891; PMCID: PMC9213310.

Publications—2022 continued

Early economic modeling of magnetic resonance image-guided high intensity focused ultrasound compared to radiotherapy for pain palliation of bone metastases. Simões Corrêa Galendi J, Yeo SY, Grüll H, Bratke G, Akuamoa-Boateng D, Baues C, Bos C, Verkooijen HM, Shukri A, Stock S, Müller D. Front Oncol. 2022 Sep 23;12:987546. doi: 10.3389/fonc.2022.987546. PMID: 36212449; PMCID: PMC9537476.

Diffusion-weighted MRI with deep learning for visualizing treatment results of MR-guided HIFU ablation of uterine fibroids. Slotman DJ, Bartels LW, Zijlstra A, Verpalen IM, van Osch JAC, Nijholt IM, Heijman E, van 't Veer-Ten Kate M, de Boer E, van den Hoed RD, Froeling M, Boomsma MF. Eur Radiol. 2022 Dec 6. doi: 10.1007/s00330-022-09294-1. Epub ahead of print. PMID: 36472702.

Focused Ultrasound and RadioTHERapy for non-invasive palliative pain treatment in patients with bone metastasis: a study protocol for the three armed randomized controlled FURTHER trial. Slotman DJ, Bartels MMTJ, Ferrer CJ, Bos C, Bartels LW, Boomsma MF, Phernambucq ECJ, Nijholt IM, Morganti AG, Siepe G, Buwenge M, Grüll H, Bratke G, Yeo SY, Blanco

Children's National Hospital

2	10
Commercial Treatments	Clinical Research

2	7	10	1
Preclinical Research	Mechanisms of Action Research	Technical Research	Publication

Children's National Hospital | Washington, DC

In September 2020, Children's National Hospital, CNH, in Washington, DC, became the first Center of Excellence focused exclusively on pediatrics. The COE includes a multidisciplinary team of clinicians and investigators from radiology, oncology, surgery, orthopedics, neurosurgery, and urology. In recent years, the CNH team has become a leader in the translation of focused ultrasound for treating pediatric solid tumors. They are currently investigating the treatment of malignant solid tumors with focused ultrasound alone and combined with chemotherapy. Moving forward, the team plans to further explore oncological applications of focused ultrasound, particularly to augment chemotherapy and immunotherapy for hard-to-treat pediatric cancers.

Contacts

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AeRang Kim, MD, PhD | Program Co-director | aekim@childrensnational.org

Commercial treatment

Musculoskeletal	Osteoid osteoma, Soft tissue cancer

Clinical research

Gastrointestinal	Liver tumors
Miscellaneous	Multiple tumors[1]
Musculoskeletal	Bone metastases, Osteoid osteoma, Soft tissue cancer
Neurological	Brain tumors, general; Neurofibromatosis; Pontine glioma

Preclinical research

Musculoskeletal	Osteoid osteoma, Soft tissue cancer

Mechanisms of action research

Histotripsy	Immunomodulation, Tissue destruction
Hyperthermia	Tissue destruction
Nonthermal	Drug delivery, vehicle; Neuromodulation
Thermal ablation	Immunomodulation, Tissue destruction

Technical research

- Drug delivery technology
- FUS Image guidance, MR
- FUS Image guidance, Navigation
- FUS Image guidance, Ultrasound
- FUS Simulation & treatment planning
- FUS Transducer technology, Histotripsy
- FUS Treatment evaluation
- FUS Treatment monitoring
- Standards & quality assurance

1 Protocols inclusive of more than one indication

Children's National Hospital continued

Research not involving thermal ablation, tissue destruction

Clinical research - Miscellaneous	
Multiple tumors[1]	Hyperthermia - Chemosensitization Hyperthermia - Drug delivery
Clinical research - Musculoskeletal	
Bone metastases	Thermal ablation - Chemosensitization
Clinical research - Neurological	
Pontine glioma	Nonthermal, BBB opening - Drug delivery Nonthermal - Sonodynamic therapy
Preclinical research - Musculoskeletal	
Soft tissue cancer	Histotripsy - Immunomodulation

Publications—2022

Focused Ultrasound for Pediatric Diseases. Janwadkar R, Leblang S, Ghanouni P, Brenner J, Ragheb J, Hennekens CH, Kim A, Sharma K. Pediatrics. 2022 Mar 1;149(3):e2021052714. doi: 10.1542/peds.2021-052714. PMID: 35229123.

1 Protocols inclusive of more than one indication

Physics for Medicine Paris

1	3	4	9	27
Clinical Research	Preclinical Research	Mechanisms of Action Research	Technical Research	Publications

Physics for Medicine Paris | France

In December 2019, Physics for Medicine Paris became the third Center of Excellence in Europe. The site focuses on accelerating the development of ultrasound-based technologies and translating these innovative technologies to the clinic, with an emphasis on cardiovascular and neurological disorders. Physics for Medicine Paris is a technological hub for new modalities of ultrasound guidance, monitoring, and treatment. The team also undertakes the training of many PhD students, assuring it a pivotal role in the education of young researchers.

Contacts

Mickael Tanter, **PhD** | Program Director | mickael.tanter@espci.fr

Jean-François Aubry, **PhD** | Scientific Director | jean-francois.aubry@espci.fr

Clinical research

Neurological	Essential tremor

Preclinical research

Cardiovascular	Heart valve calcifications
Neurological	Depression; Parkinson's disease, underlying cause

Mechanisms of action research

Histotripsy	Tissue destruction
Nonthermal	BBB opening, drug delivery; Neuromodulation
Thermal ablation	Tissue destruction

Technical research

- Drug delivery technology
- FUS Image guidance, MR
- FUS Image guidance, Navigation
- FUS Image guidance, Ultrasound
- FUS Physics
- FUS Simulation & treatment planning
- FUS Transducer technology, Histotripsy
- FUS Transducer technology, Thermal ablation
- FUS Treatment monitoring

Research not involving thermal ablation, tissue destruction

Preclinical research - Cardiovascular	
Heart valve calcifications	Histotripsy - Alteration of tissue mechanics
Preclinical research - Neurological	
Depression	Nonthermal - Neuromodulation
Parkinson's disease, underlying cause	Nonthermal - Neuromodulation

Physics for Medicine Paris continued

Publications—2022

Retinal functional ultrasound imaging (rfUS) for assessing neurovascular alterations: a pilot study on a rat model of dementia. Morisset C, Dizeux A, Larrat B, Selingue E, Boutin H, Picaud S, et al. Sci Rep 2022;12:19515. doi: 10.1038/s41598-022-23366-8. PMID: 36376408; PMCID: PMC9663720.

Fluoroscopy-Guided High-Intensity Focused Ultrasound Neurotomy of the Lumbar Zygapophyseal Joints: A Clinical Pilot Study. Perez J, Gofeld M, Leblang S, Hananel A, Aginsky R, Chen J, et al. Pain Med. 2022 Jan 3;23(1):67-75. doi: 10.1093/pm/pnab275. PMID: 34534337; PMCID: PMC8723143.

Assessing cardiac stiffness using ultrasound shear wave elastography. Caenen A, Pernot M, Nightingale KR, Voigt JU, Vos HJ, Segers P, D'hooge J. Phys Med Biol. 2022 Jan 17;67(2). doi: 10.1088/1361-6560/ac404d. PMID: 34874312.

Publications—2022 continued

Carotid Plaque Vulnerability Assessed by Combined Shear Wave Elastography and Ultrafast Doppler Compared to Histology. Goudot G, Sitruk J, Jimenez A, Julia P, Khider L, Alsac JM, El Batti S, Bruneval P, Amemyia K, Pedreira O, Mortelette H, Calvet D, Tanter M, Mirault T, Pernot M, Messas E. Transl Stroke Res. 2022 Feb;13(1):100-111. doi: 10.1007/s12975-021-00920-6. Epub 2021 Jun 28. PMID: 34181190.

Ret kinase-mediated mechanical induction of colon stem cells by tumor growth pressure stimulates cancer progression in vivo. Nguyen Ho-Bouldoires TH, Sollier K, Zamfirov L, Broders-Bondon F, Mitrossilis D, Bermeo S, et al. Commun Biol. 2022 Feb 17;5(1):137. doi: 10.1038/s42003-022-03079-4. PMID: 35177769; PMCID: PMC8854631.

Endothelial Zeb2 preserves the hepatic angioarchitecture and protects against liver fibrosis. de Haan W, Dheedene W, Apelt K, Décombas-Deschamps S, Vinckier S, Verhulst S, Conidi A, Deffieux T, Staring MW, Vandervoort P, Caluwé E, Lox M, Mannaerts I, Takagi T, Jaekers J, Berx G, Haigh J, Topal B, Zwijsen A, Higashi Y, van Grunsven LA, van IJcken WFJ, Mulugeta E, Tanter M, Lebrin FPG, Huylebroeck D, Luttun A. Cardiovasc Res. 2022 Mar 25;118(5):1262-1275. doi: 10.1093/cvr/cvab148. PMID: 33909875; PMCID: PMC8953454.

Ultrasound localization microscopy and functional ultrasound imaging reveal atypical features of the trigeminal ganglion vasculature. Réaux-Le-Goazigo A, Beliard B, Delay L, Rahal L, Claron J, Renaudin N, et al. Commun Biol. 2022 Apr 7;5(1):330. doi: 10.1038/s42003-022-03273-4. PMID: 35393515; PMCID: PMC8989975.

Boosting transducer matrix sensitivity for 3D large field ultrasound localization microscopy using a multi-lens diffracting layer: a simulation study. Favre H, Pernot M, Tanter M, Papadacci C. Phys Med Biol. 2022 Apr 7;67(8). doi: 10.1088/1361-6560/ac5f72. PMID: 35313289.

Ultrafast Doppler imaging and ultrasound localization microscopy reveal the complexity of vascular rearrangement in chronic spinal lesion. Beliard B, Ahmanna C, Tiran E, Kanté K, Deffieux T, Tanter M, et al. Sci Rep. 2022 Apr 21;12(1):6574. doi: 10.1038/s41598-022-10250-8. PMID: 35449222; PMCID: PMC9023600.

Intensity distribution segmentation in ultrafast Doppler combined with scanning laser confocal microscopy for assessing vascular changes associated with ageing in murine hippocampi. Anzibar Fialho M, Vázquez Alberdi L, Martínez M, Calero M, Baranger J, Tanter M, et al. Sci Rep. 2022 Apr 26;12(1):6784. doi: 10.1038/s41598-022-10457-9. Erratum in: Sci Rep. 2022 May 10;12(1):7626. PMID: 35473942; PMCID: PMC9042937.

In vivo whole brain microvascular imaging in mice using transcranial 3D Ultrasound Localization Microscopy. Demeulenaere O, Bertolo A, Pezet S, Ialy-Radio N, Osmanski B, Papadacci C, et al. EBioMedicine. 2022 May;79:103995. doi: 10.1016/j.ebiom.2022.103995. Epub 2022 Apr 20. PMID: 35460988; PMCID: PMC9048085.

Publisher Correction: Intensity distribution segmentation in ultrafast Doppler combined with scanning laser confocal microscopy for assessing vascular changes associated with ageing in murine hippocampi. Fialho MA, Alberdi LV, Martínez M, Calero M, Baranger J, Tanter M, et al. Sci Rep. 2022 May 10;12(1):7626. doi: 10.1038/s41598-022-11822-4. Erratum for: Sci Rep. 2022 Apr 26;12(1):6784. PMID: 35538217; PMCID: PMC9091278.

Publications—2022 continued

Covariations between pupil diameter and supplementary eye field activity suggest a role in cognitive effort implementation. Claron J, Royo J, Arcizet F, Deffieux T, Tanter M, Pouget P. PLoS Biol. 2022 May 26;20(5):e3001654. doi: 10.1371/journal.pbio.3001654. PMID: 35617290; PMCID: PMC9135265.

Increased Capillary Permeability in Heart Induces Diastolic Dysfunction Independently of Inflammation, Fibrosis, or Cardiomyocyte Dysfunction. Abelanet A, Camoin M, Rubin S, Bougaran P, Delobel V, Pernot M, Forfar I, Guilbeau-Frugier C, Galès C, Bats ML, Renault MA, Dufourcq P, Couffinhal T, Duplàa C. Arterioscler Thromb Vasc Biol. 2022 Jun;42(6):745-763. doi: 10.1161/ATVBAHA.121.317319. Epub 2022 May 5. PMID: 35510550.

Coronary Flow Assessment Using 3-Dimensional Ultrafast Ultrasound Localization Microscopy. Demeulenaere O, Sandoval Z, Mateo P, Dizeux A, Villemain O, Gallet R, et al. JACC Cardiovasc Imaging. 2022 Jul;15(7): 1193-1208. doi: 10.1016/j.jcmg.2022.02.008. Epub 2022 Apr 13. PMID: 35798395.

Altered cortical trigeminal fields excitability by spreading depolarization revealed with in vivo functional ultrasound imaging combined with electrophysiology. Bourgeais-Rambur L, Beynac L, Mariani J-C, Tanter M, Deffieux T, Lenkei Z, et al. J Neurosci. 2022 Jul 8;42(32):6295–308. doi: 10.1523/JNEUROSCI.1825-21.2022. Epub ahead of print. PMID: 35817577; PMCID: PMC9374159.

Functional ultrasound localization microscopy reveals brain-wide neurovascular activity on a microscopic scale. Renaudin N, Demené C, Dizeux A, Ialy-Radio N, Pezet S, Tanter M. Nat Methods. 2022 Aug;19(8):1004-1012. doi: 10.1038/s41592-022-01549-5. Epub 2022 Aug 4. PMID: 35927475; PMCID: PMC9352591.

Benchmark problems for transcranial ultrasound simulation: Intercomparison of compressional wave models. Aubry JF, Bates O, Boehm C, Butts Pauly K, Christensen D, Cueto C, Gélat P, Guasch L, Jaros J, Jing Y, Jones R, Li N, Marty P, Montanaro H, Neufeld E, Pichardo S, Pinton G, Pulkkinen A, Stanziola A, Thielscher A, Treeby B, van 't Wout E. J Acoust Soc Am. 2022 Aug;152(2):1003. doi: 10.1121/10.0013426. PMID: 36050189; PMCID: PMC9553291.

Proof of Concept of 3-D Backscatter Tensor Imaging Tomography for Non-invasive Assessment of Human Breast Cancer Collagen Organization. Guillaumin J-B, Djerroudi L, Aubry J-F, Tardivon A, Tanter M, Vincent-Salomon A, et al. Ultrasound Med Biol. 2022 Sep;48(9):1867-1878. doi: 10.1016/j.ultrasmedbio.2022.05.017. Epub 2022 Jun 23. PMID: 35752513.

Quantitative stiffness assessment of cardiac grafts using ultrasound in a porcine model: A tissue biomarker for heart transplantation. Pedreira O, Papadacci C, Augeul L, Loufouat J, Lo-Grasso M, Tanter M, et al. EBioMedicine. 2022 Sep;83:104201. doi: 10.1016/j.ebiom.2022.104201. Epub 2022 Aug 3. PMID: 35932640; PMCID: PMC9358428.

Local Arterial Stiffness Assessment: Comparison of Pulse Wave Velocity Assessed by Ultrafast Ultrasound Imaging versus the Bramwell-Hill Equation. Rasouli R, Baranger J, Slorach C, Nguyen M, Segers P, Guerra V, Pernot M, Hui W, Mertens L, Villemain O. J Am Soc Echocardiogr. 2022 Nov;35(11):1185-1188. doi: 10.1016/j.echo.2022.07.011. Epub 2022 Jul 19. PMID: 35863547.

Publications—2022 continued

Global dissociation of the posterior amygdala from the rest of the brain during REM sleep. Matei M, Bergel A, Pezet S, Tanter M. Commun Biol. 2022 Nov 28;5(1):1306. doi: 10.1038/s42003-022-04257-0. PMID: 36443640; PMCID: PMC9705305.

To Be, or Not to Be Diastolic: About Natural Mechanical Waves After Mitral Valve Closure. Villemain O, Pernot M. JACC Cardiovasc Imaging. 2022 Dec;15(12):2035-2037. doi: 10.1016/j.jcmg.2022.09.016. Epub 2022 Nov 16. PMID: 36481070.

Ultrasound Matrix Imaging-Part I: The Focused Reflection Matrix, the F-Factor and the Role of Multiple Scattering. Lambert W, Robin J, Cobus LA, Fink M, Aubry A. IEEE Trans Med Imaging. 2022 Dec;41(12):3907-3920. doi: 10.1109/TMI.2022.3199498. Epub 2022 Dec 2. PMID: 35976836.

Ultrasound Matrix Imaging-Part II: The Distortion Matrix for Aberration Correction Over Multiple Isoplanatic Patches. Lambert W, Cobus LA, Robin J, Fink M, Aubry A. IEEE Trans Med Imaging. 2022 Dec;41(12):3921-3938. doi: 10.1109/TMI.2022.3199483. Epub 2022 Dec 2. PMID: 35976837.

A guide for assessment of myocardial stiffness in health and disease. Villalobos Lizardi, J.C., Baranger, J., Nguyen, M.B. et al. Nat Cardiovasc Res 1, 8–22 (2022). https://doi.org/10.1038/s44161-021-00007-3.

Volumetric ultrasound localization microscopy of the whole rat brain microvasculature. Heiles B, Chavignon A, Bergel A, Hingot V, Serroune H, Maresca D, et al. IEEE Open Journal of Ultrasonics, Ferroelectrics, and Frequency Control 2022;2:261–82. https://doi.org/10.1109/OJUFFC.2022.3214185.

Inserm - LabTAU

1	3
Commercial Treatment	Clinical Research

14	11	7	20
Preclinical Research	Mechanisms of Action Research	Technical Research	Publications

INSERM - LabTAU | Lyon, France

In February 2017, INSERM Unit 1032, the Laboratory of Therapeutic Applications of Ultrasound, LabTAU, at the French National Institute for Health and Medical Research, INSERM, was named a Focused Ultrasound Center of Excellence. LabTAU conducts significant translational and clinical research with a multidisciplinary, highly qualified, and complementary team of physicians and scientists. The COE has special expertise in commercializing technology and creating strategic interfaces between engineering and medicine.

Contact

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Commercial treatment

Urological	Prostate cancer, *Hôpital Edouard Herriot*

Clinical research

Cardiovascular	Varicose veins
Neurological	Glioblastoma, *Hôpitaux Universitaires Pitié-Salpêtrière & Hôpital Pierre Wertheimer*
Urological	Prostate cancer, *Hôpital Edouard Herriot*
Women's health	Endometriosis, *Hôpital Croix-Rousse*

Preclinical research

Cardiovascular	Twin-twin transfusion syndrome, Ventricular tachycardia
Gastrointestinal	Liver tumors; Pancreatic tumors, malignant
Musculoskeletal	Osteoradionecrosis
Neurological	Cancer pain
Ophthalmological	Presbyopia
Urological	Prostate cancer
Women's health	Breast tumors, malignant; Endometriosis

Mechanisms of action research

Histotripsy	Tissue destruction
Nonthermal	BBB opening; BBB opening, drug delivery; Chemosensitization; Drug delivery; Immunomodulation; Neuromodulation; Sonodynamic therapy; Sonoporation; Tissue destruction
Thermal ablation	Tissue destruction

Technical research

- Drug delivery technology
- FUS Image guidance, MR
- FUS Image guidance, Ultrasound
- FUS Physics
- FUS Simulation & treatment planning
- FUS Transducer technology, Other
- FUS Treatment monitoring

Research not involving thermal ablation, tissue destruction

Clinical research - Cardiovascular	
Varicose veins	Thermal ablation - Vascular occlusion
Clinical research - Neurological	
Glioblastoma	Nonthermal, BBB opening Nonthermal, BBB opening - Drug delivery
Preclinical research - Gastrointestinal	
Pancreatic tumors, malignant	Nonthermal - Drug delivery Nonthermal - Sonodynamic therapy Nonthermal - Tissue destruction Thermal ablation - Immunomodulation
Preclinical research - Neurological	
Cancer pain	Nonthermal - Neuromodulation
Preclinical research - Ophthalmological	
Presbyopia	Nonthermal - Tissue destruction
Preclinical research - Women's health	
Breast tumors, malignant	Nonthermal - Immunomodulation

Publications—2022

High intensity focused ultrasound: a future alternative to surgery for the treatment of localized pancreatic tumors? Fabritius M, Lambin T, Cao E, Robert J, Milot L, Lafon C, Pioche M. Endoscopy. 2022 Jan;54(1):E17-E18. doi: 10.1055/a-1338-0293. Epub 2021 Feb 16. Erratum in: Endoscopy. 2021 Feb 22. PMID: 33592643.

Correction: High intensity focused ultrasound: a future alternative to surgery for the treatment of localized pancreatic tumors? Fabritius M, Lambin T, Cao E, Robert J, Milot L, Lafon C, Pioche M. Endoscopy. 2022 Jan;54(1): C2. doi: 10.1055/a-1394-0547. Epub 2021 Feb 22. Erratum for: Endoscopy. 2022 Jan;54(1):E17-E18. PMID: 33618371.

Neurostimulation success rate of repetitive-pulse focused ultrasound in an in vivo giant axon model: An acoustic parametric study. Vion-Bailly J, Suarez-Castellanos IM, Chapelon JY, Carpentier A, N'Djin WA. Med Phys. 2022 Jan;49(1):682-701. doi: 10.1002/mp.15358. Epub 2021 Dec 7. PMID: 34796512.

Detection of ISUP ≥2 prostate cancers using multiparametric MRI: prospective multicentre assessment of the non-inferiority of an artificial intelligence system as compared to the PI-RADS V.2.1 score (CHANGE study). Rouvière O, Souchon R, Lartizien C, Mansuy A, Magaud L, Colom M, Dubreuil-Chambardel M, Debeer S, Jaouen T, Duran A, Rippert P, Riche B, Monini C, Vlaeminck-Guillem V, Haesebaert J, Rabilloud M, Crouzet S. BMJ Open. 2022 Feb 9;12(2):e051274. doi: 10.1136/bmjopen-2021-051274. PMID: 35140147; PMCID: PMC8830410.

Locoregional therapies and their effects on the tumoral microenvironment of pancreatic ductal adenocarcinoma. Lambin T, Lafon C, Drainville RA, Pioche M, Prat F. World J Gastroenterol. 2022 Apr 7;28(13):1288-1303. doi: 10.3748/wjg.v28.i13.1288. PMID: 35645539; PMCID: PMC9099187.

Publications—2022 continued

Pancreatic Ductal Adenocarcinoma: Current and Emerging Therapeutic Uses of Focused Ultrasound. Lafond M, Lambin T, Drainville RA, Dupré A, Pioche M, Melodelima D, Lafon C. Cancers (Basel). 2022 May 24;14(11):2577. doi: 10.3390/cancers14112577. PMID: 35681557; PMCID: PMC9179649.

Development of a Numerical Model of High-Intensity Focused Ultrasound Treatment in Mobile and Elastic Organs: Application to a Beating Heart. Cao E, Greillier P, Loyet R, Chavrier F, Robert J, Bessière F, Dillenseger JL, Lafon C. Ultrasound Med Biol. 2022 Jul;48(7):1215-1228. doi: 10.1016/j.ultrasmedbio.2022.02.017. Epub 2022 Apr 14. PMID: 35430101.

Enhanced Stable Cavitation and Nonlinear Acoustic Properties of Poly (butyl cyanoacrylate) Polymeric Microbubbles after Bioconjugation. Barmin RA, Dasgupta A, Rix A, Weiler M, Appold L, Rütten S, Padilla F, Kuehne AJC, Pich A, De Laporte L, Kiessling F, Pallares RM, Lammers T. ACS Biomater Sci Eng. 2022 Oct 31. doi: 10.1021/acsbiomaterials2c01021. Epub ahead of print. PMID: 36315422.

Non-invasive High-Intensity Focused Ultrasound Treatment of Liver Tissues in an In Vivo Porcine Model: Fast, Large and Safe Ablations Using a Toroidal Transducer. Cambronero S, Dupré A, Mastier C, Melodelima D. Ultrasound Med Biol. 2023 Jan;49(1):212-224. doi: 10.1016/j.ultrasmedbio.2022.08.015. Epub 2022 Oct 28. PMID: 36441030.

Combination of Focused Ultrasound, Immunotherapy, and Chemotherapy: New Perspectives in Breast Cancer Therapy. Dahan M, Cortet M, Lafon C, Padilla F. J Ultrasound Med. 2023 Feb;42(3):559-573. doi: 10.1002/jum.16053. Epub 2022 Jul 23. PMID: 35869903.

Inserm – LabTAU continued

Publications—2022 continued

Gravitational lens effect revisited through membrane waves. Catheline S, Delattre V, Laloy-Borgna G, Faure F, Fink M. American Journal of Physics. 2022;90:47-50. doi: 10.1119/10.0006612.

Stimulation of dental implant osseointegration by low-Intensity pulsed ultrasound: An in vivo preliminary study in a porcine model. Chauvel-Picard J, Gourmet R, Vercherin P, Béra, JC, Gleizal A. Journal of Prosthodontic Research. 2022;66(4): 639-45. doi: 10.2186/jpr.JPR_D_21_00115.

Proof of Concept: Protein Delivery into Human Erythrocytes Using Stable Cavitation. Chettab K, Matera EL, Lafond M, Coralie D, Favin-Lévêque C, Goy C, Strakhova R, Mestas JL, Lafon C, Dumontet C. Molecular Pharmaceutics. 2022;19(3): 929-35. doi: 10.1021/acs.molpharmaceut.1c00907.

Nonspherical dynamics and microstreaming of a wall-attached microbubble. Fauconnier M, Mauger C, Béra JC, Inserra C. Journal of Fluid Mechanics. 2022; 935: pA22-1-pA22. doi: 10.1017/jfm.2021.1089.

Seismic surface wave focal spot imaging: numerical resolution experiments. Giammarinaro B, Tsarsitalidou C, Hillers G, de Rosny J, Seydoux L, Catheline S, Campillo M, Roux P. Geophysical Journal International. 2022;232(1): 201-22. doi: 10.1093/gji/ggac247.

Reproducibility of apparent diffusion coefficient measurement in normal prostate peripheral zone at 1.5T MRI. Hoang-Dinh A, Nguyen-Quang T, Bui-Van L, Gonindard-Melodelima C, Souchon R, Rouviere O. Diagnostic and interventional imaging, 2022;103(11):545-54. doi: 10.1016/j.diii.2022.06.001.

Publications—2022 continued

Evaluating chemical-crosslinking induced microstructural changes in the posterior sclera with high-frequency quantitative ultrasound. Hoerig C, Aichele J, Catheline S, Hoang QV, Mamou J. Invest. Ophthalmol. Vis. Sci. 2022;63(7):4409 – F0088.

Spectral Analysis of Tissue Displacement for Cardiac Activation Mapping: Ex-vivo Working Heart and In-vivo Study. Robert J, Bessiere F, Cao E, Loyer V, Abell E, Vaillant F, Quesson B, Catheline S, Lafon C. IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control. 2022;69(3):942-56. doi: 10.1109/TUFFC.2021.3137989.

Prostate Cancer Diagnosis Without Histological Proof: Is Treating Images Reasonable? Rouvière O, Crouzet S. European Urology Open Science. 2022;46:1-2. doi: 10.1016/j.euros.2022.09.016.

Combined model-based and deep learning-based automated 3D zonal segmentation of the prostate on T2-weighted MR images: clinical evaluation. Rouvière O, Moldovan PC, Vlachomitrou A, Gouttard S, Riche B, Groth A, Rabotnikov M, Ruffion A, Colombel M, Crouzet S, Weese J, Rabilloud M. European radiology. 2022;32(5):3248-59. doi: 10.1007/s00330-021-08408-5.

Stanford University School of Medicine

12 Commercial Treatments	**4** Clinical Research
10 Preclinical Research	**17** Mechanisms of Action Research
8 Technical Research	**33** Publications

Stanford University School of Medicine | California

Established in 2016, Stanford's COE focuses on several clinical and preclinical projects. These include industry-sponsored trials using focused ultrasound to treat bone metastases, uterine fibroids, essential tremor, and prostate cancer, as well as investigator-initiated trials to treat soft tissue tumors. Preclinical projects have included developing referenceless methods for MR (Magnetic Resonance) thermometry in the brain and respiratory-compensated focused ultrasound in treatment of porcine liver during free-breathing. These clinical and preclinical projects involve close collaboration with colleagues in radiology, obstetrics and gynecology, medical and radiation oncology, neurosurgery, neurology, orthopedic surgery, urology, pathology, immunology, and electrical and mechanical engineering.

Stanford University | California
University of California Davis | California

A collaboration between Stanford and UC Davis investigating the use of focused ultrasound for the treatment of liver cancer in canines is underway. The research team is using focused ultrasound to deliver microRNA to the tumors, demonstrating efficient drug delivery and a significant change in the immunogenicity of the tumor.

4
Veterinary Research

Contacts

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Commercial treatments

Cardiovascular	Arteriovenous malformations
Musculoskeletal	Bone cancer, Bone metastases, Desmoid tumors, Osteoid osteoma
Neurological	Essential tremor; Parkinson's disease, tremor
Urological	Prostate cancer
Women's health	Uterine adenomyosis, Uterine fibroids

Stanford University School of Medicine continued

Clinical research

Gastrointestinal	Pancreatic tumors, malignant
Musculoskeletal	Bone metastases, Osteoid osteoma
Neurological	Epilepsy

Preclinical research

Gastrointestinal	Pancreatic tumors, malignant
Miscellaneous	Melanoma
Musculoskeletal	Muscle atrophy
Neurological	Epilepsy, Glioblastoma, Neuropathic pain
Urological	Kidney disease, acute
Women's health	Breast tumors, malignant; Ovarian tumors

Mechanisms of action research

Hyperthermia	Drug delivery
Nonthermal	BBB opening; BBB opening, drug delivery; Drug delivery; Drug delivery, immunotherapeutic; Drug delivery, vehicle; Gene delivery; Neuromodulation; Sonoporation; Stem cell delivery; Stem cell trafficking; Tissue destruction
Thermal ablation	Amplification of cancer biomarkers, Chemosensitization, Immune cell trafficking, Immunomodulation, Tissue destruction

Technical research

- Drug delivery technology
- FUS Image guidance, MR
- FUS Physics
- FUS Simulation & treatment planning
- FUS Transducer technology, Nonthermal
- FUS Transducer technology, Thermal ablation
- FUS Treatment evaluation
- FUS Treatment monitoring

Research not involving thermal ablation, tissue destruction

Clinical research - Gastrointestinal	
Pancreatic tumors, malignant	Thermal ablation - Immunomodulation
Preclinical research - Gastrointestinal	
Pancreatic tumors, malignant	Thermal ablation - Immunomodulation
Preclinical Research - Miscellaneous	
Melanoma	Thermal ablation - Immunomodulation
Preclinical research - Musculoskeletal	
Muscle atrophy	Nonthermal - Gene delivery
Preclinical research - Neurological	
Epilepsy	Nonthermal, BBB opening - Drug delivery
Glioblastoma	Nonthermal, BBB opening - Drug delivery
Neuropathic pain	Nonthermal - Drug delivery, vehicle
Preclinical research - Urological	
Kidney disease, acute	Nonthermal - Stem cell delivery
Preclinical research - Women's health	
Breast tumors, malignant	Nonthermal - Gene delivery Thermal ablation - Immunomodulation
Ovarian tumors	Thermal ablation - Immunomodulation
Veterinary research - Gastrointestinal	
Liver tumors	Nonthermal - Drug delivery, vehicle Nonthermal - Gene delivery Nonthermal - Immunomodulation

Stanford University School of Medicine continued

Publications—2022

A Review of Imaging Methods to Assess Ultrasound-Mediated Ablation. Fite BZ, Wang J, Ghanouni P, Ferrara KW. BME Front. 2022;2022:9758652. doi: 10.34133/2022/9758652. Epub 2022 May 2. PMID: 35957844; PMCID: PMC9364780.

Current management and recent progress in desmoid tumors. Zhou MY, Bui NQ, Charville GW, Ghanouni P, Ganjoo KN. Cancer Treat Res Commun. 2022;31:100562. doi: 10.1016/j.ctarc.2022.100562. Epub 2022 Apr 16. PMID: 35460976.

Focused ultrasound for functional neurosurgery. Lev-Tov L, Barbosa DAN, Ghanouni P, Halpern CH, Buch VP. J Neurooncol. 2022 Jan;156(1):17-22. doi: 10.1007/s11060-021-03818-3. Epub 2021 Aug 12. PMID: 34383232.

Focused ultrasound: growth potential and future directions in neurosurgery. Janwadkar R, Leblang S, Ghanouni P, Brenner J, Ragheb J, Hennekens CH, Kim A, Zhang M, Rodrigues A, Zhou Q, Li G.. J Neurooncol. 2022 Jan;156(1):23-32. doi: 10.1007/s11060-021-03820-9. Epub 2021 Aug 19. PMID: 34410576.

Ultrasound-Guided Microbubble-Mediated Locoregional Delivery of Multiple MicroRNAs Improves Chemotherapy in Hepatocellular Carcinoma. Wang H, Hu Z, Sukumar UK, Bose RJ, Telichko A, Dahl JJ, Paulmurugan R. Nanotheranostics. 2022 Jan 1;6(1):62-78. doi: 10.7150/ntno.63320. PMID: 34976581; PMCID: PMC8671967.

CAR T Cell Therapy in Primary Brain Tumors: Current Investigations and the Future. Lin YJ, Mashouf LA, Lim M. Front Immunol. 2022 Feb 21;13:817296. doi: 10.3389/fimmu.2022.817296. PMID: 35265074; PMCID: PMC8899093.

Increasing the transmission efficiency of transcranial ultrasound using a dual-mode conversion technique based on Lamb waves. Kang KC, Kim YH, Kim JN, Kabir M, Zhang Y, Ghanouni P, Park KK, Firouzi K, Khuri-Yakub BT. J Acoust Soc Am. 2022 Mar;151(3):2159. doi: 10.1121/10.0009849. PMID: 35364946; PMCID: PMC8957390.

Patterned Interference Radiation Force for Transcranial Neuromodulation. Kim YH, Kang KC, Kim JN, Pai CN, Zhang Y, Ghanouni P, Park KK, Firouzi K, Khuri-Yakub BT. Ultrasound Med Biol. 2022 Mar;48(3):497-511. doi: 10.1016/j.ultrasmedbio.2021.11.006. Epub 2021 Dec 23. PMID: 34955292

Ultrasonic Deep Brain Neuromodulation in Acute Disorders of Consciousness: A Proof-of-Concept. Cain JA, Spivak NM, Coetzee JP, Crone JS, Johnson MA, Lutkenhoff ES, Real C, Buitrago-Blanco M, Vespa PM, Schnakers C, Monti MM. Brain Sci. 2022 Mar 23;12(4):428. doi: 10.3390/brainsci12040428. PMID: 35447960; PMCID: PMC9032970.

Dose-dependent effects of high intensity focused ultrasound on compound action potentials in an ex vivo rodent peripheral nerve model: comparison to local anesthetics. Anderson TA, Delgado J, Sun S, Behzadian N, Vilches-Moure J, Szlavik RB, Butts-Pauly K, Yeomans D. Reg Anesth Pain Med. 2022 Apr;47(4):242-248. doi: 10.1136/rapm-2021-103115. Epub 2022 Feb 3. Erratum in: Reg Anesth Pain Med. 2022 Jul;47(7):e3. PMID: 35115412.

The roles of thermal and mechanical stress in focused ultrasound-mediated immunomodulation and immunotherapy for central nervous system tumors. Kim C, Lim M, Woodworth GF, Arvanitis CD. J Neurooncol. 2022 Apr;157(2):221-236. doi: 10.1007/s11060-022-03973-1. Epub 2022 Mar 2. PMID: 35235137; PMCID: PMC9119565.

Publications—2022 continued

Toward Reduction in False-Positive Thyroid Nodule Biopsies with a Deep Learning-based Risk Stratification System Using US Cine-Clip Images. Yamashita R, Kapoor T, Alam MN, Galimzianova A, Syed SA, Ugur Akdogan M, Alkim E, Wentland AL, Madhuripan N, Goff D, Barbee V, Sheybani ND, Sagreiya H, Rubin DL, Desser TS.. Radiol Artif Intell. 2022 May 11;4(3):e210174. doi: 10.1148/ryai.210174. PMID: 35652118; PMCID: PMC9152684.

FN3 linked nanobubbles as a targeted contrast agent for US imaging of cancer-associated human PD-L1. Kumar US, Natarajan A, Massoud TF, Paulmurugan R. J Control Release. 2022 Jun;346:317-327. doi: 10.1016/j.jconrel.2022.04.030. Epub 2022 Apr 29. PMID: 35469983.

A theranostic 3D ultrasound imaging system for high resolution image-guided therapy. Bendjador H, Foiret J, Wodnicki R, Stephens DN, Krut Z, Park EY, Gazit Z, Gazit D, Pelled G, Ferrara KW. Theranostics. 2022 Jun 27; 12(11):4949-4964. doi: 10.7150/thno.71221. PMID: 35836805; PMCID: PMC9274734.

MRI-guided focused ultrasound focal therapy for patients with intermediate-risk prostate cancer: a phase 2b, multicentre study. Ehdaie B, Tempany CM, Holland F, Sjoberg DD, Kibel AS, Trinh QD, Durack JC, Akin O, Vickers AJ, Scardino PT, Sperling D, Wong JYC, Yuh B, Woodrum DA, Mynderse LA, Raman SS, Pantuck AJ, Schiffman MH, McClure TD, Sonn GA, Ghanouni P. Lancet Oncol. 2022 Jul;23(7):910-918. doi: 10.1016/S1470-2045(22)00251-0. Epub 2022 Jun 14. PMID: 35714666; PMCID: PMC9400094.

Pulsed-Focused Ultrasound Provides Long-Term Suppression of Epileptiform Bursts in the Kainic Acid-Induced Epilepsy Rat Model. Chu PC, Yu HY, Lee CC, Fisher R, Liu HL. Neurotherapeutics. 2022 Jul;19(4):1368-1380. doi: 10.1007/s13311-022-01250-7. Epub 2022 May 17. PMID: 35581489; PMCID: PMC9587190.

Comparison between MR and CT imaging used to correct for skull-induced phase aberrations during transcranial focused ultrasound. Leung SA, Moore D, Gilbo Y, Snell J, Webb TD, Meyer CH, Miller GW, Ghanouni P, Butts Pauly K. Sci Rep. 2022 Aug 4;12(1):13407. doi: 10.1038/s41598-022-17319-4. PMID: 35927449; PMCID: PMC9352781.

Magnetic resonance imaging-guided focused ultrasound thalamotomy for essential tremor: 5-year follow-up results. Cosgrove GR, Lipsman N, Lozano AM, Chang JW, Halpern C, Ghanouni P, Eisenberg H, Fishman P, Taira T, Schwartz ML, McDannold N, Hayes M, Ro S, Shah B, Gwinn R, Santini VE, Hynynen K, Elias WJ. J Neurosurg. 2022 Aug 5:1-6. doi: 10.3171/2022.6.JNS212483. Epub ahead of print. PMID: 35932269.

Management of Patients with Newly Diagnosed Desmoid Tumors in a First-Line Setting. Testa S, Bui NQ, Charville GW, Avedian RS, Steffner R, Ghanouni P, Mohler DG, Ganjoo KN. Cancers (Basel). 2022 Aug 12;14(16):3907. doi: 10.3390/cancers14163907. PMID: 36010900; PMCID: PMC9405618.

Improving Transcranial Acoustic Targeting: The Limits of CT-Based Velocity Estimates and the Role of MR. Webb TD, Fu F, Leung SA, Ghanouni P, Dahl JJ, Does MD, Pauly KB. IEEE Trans Ultrason Ferroelectr Freq Control. 2022 Sep;69(9):2630-2637. doi: 10.1109/TUFFC.2022.3192224. Epub 2022 Aug 26. PMID: 35853046; PMCID: PMC9519088.

Stanford University School of Medicine continued

Publications—2022

Noninvasive ultrasonic induction of cerebrospinal fluid flow enhances intrathecal drug delivery. Aryal M, Azadian MM, Hart AR, Macedo N, Zhou Q, Rosenthal EL, Airan RD. J Control Release. 2022 Sep;349:434-442. doi: 10.1016/j.jconrel.2022.06.067. Epub 2022 Jul 15. PMID: 35798095.

Improving in situ acoustic intensity estimates using MR acoustic radiation force imaging in combination with multifrequency MR elastography. Li N, Gaur P, Quah K, Butts Pauly K. Magn Reson Med. 2022 Oct;88(4): 1673-1689. doi: 10.1002/mrm.29309. Epub 2022 Jun 28. PMID: 35762849; PMCID: PMC9439407.

Tempering optimism for MRI-guided focused ultrasound therapy - Authors' reply. Ehdaie B, Sonn GA, Ghanouni P. Lancet Oncol. 2022 Oct;23 (10):e439. doi: 10.1016/S1470-2045(22)00557-5. PMID: 36174620.

Therapeutic US Applications for the Abdomen and Pelvis. Sailer A, Ghanouni P, Schade GR, Napoli A, Vidal-Jove J, Raman SS, Mendiratta-Lala M, Ghai S, Abreu A, Sundaram KM, Westphalen A, Arora S. Radiographics. 2022 Oct;42(6):E182-E183. doi: 10.1148/rg.220044. PMID: 36190852; PMCID: PMC9539095.

Palette of Rechargeable Mechanoluminescent Fluids Produced by a Biomineral-Inspired Suppressed Dissolution Approach. Yang F, Wu X, Cui H, Jiang S, Ou Z, Cai S, Hong G. J Am Chem Soc. 2022 Oct 12;144(40): 18406-18418. doi: 10.1021/jacs.2c06724. Epub 2022 Oct 3. PMID: 36190898.

A Pilot Study of 68Ga-PSMA11 and 68Ga-RM2 PET/MRI for Evaluation of Prostate Cancer Response to High Intensity Focused Ultrasound (HIFU) Therapy. Duan H, Ghanouni P, Daniel B, Rosenberg J, Davidzon GA, Mari Aparici C, Kunder C, Sonn G, Iagaru A. J Nucl Med. 2022 Nov 3:jnumed.122.264783. doi: 10.2967/jnumed.122.264783. Epub ahead of print. PMID: 36328488

Evaluation of post-ablation mpMRI as a predictor of residual prostate cancer after focal high intensity focused ultrasound (HIFU) ablation. Khandwala YS, Morisetty S, Ghanouni P, Fan RE, Soerensen SJC, Rusu M, Sonn GA. Urol Oncol. 2022 Nov;40(11):489.e9-489.e17. doi: 10.1016/j.urolonc.2022.07.017. Epub 2022 Sep 2. PMID: 36058811.

Publications—2022 continued

The Association of Tissue Change and Treatment Success During High-intensity Focused Ultrasound Focal Therapy for Prostate Cancer. Khandwala YS, Soerensen SJC, Morisetty S, Ghanouni P, Fan RE, Vesal S, Rusu M, Sonn GA. Eur Urol Focus. 2022 Nov 10:S2405-4569(22)00237-1. doi: 10.1016/j.euf.2022.10.010. Epub ahead of print. PMID: 36372735.

Multiomic analysis for optimization of combined focal and immunotherapy protocols in murine pancreatic cancer. Wang J, Fite BZ, Kare AJ, Wu B, Raie M, Tumbale SK, Zhang N, Davis RR, Tepper CG, Aviran S, Newman AM, King DA, Ferrara KW. Theranostics. 2022 Nov 14;12(18):7884-7902. doi: 10.7150/thno.73218. PMID: 36451859; PMCID: PMC9706583.

A tool for monitoring cell type-specific focused ultrasound neuromodulation and control of chronic epilepsy. Murphy KR, Farrell JS, Gomez JL, Stedman QG, Li N, Leung SA, Good CH, Qiu Z, Firouzi K, Butts Pauly K, Khuri-Yakub BPT, Michaelides M, Soltesz I, de Lecea L. Proc Natl Acad Sci U S A. 2022 Nov 16;119(46):e2206828119. doi: 10.1073/pnas.2206828119. Epub 2022 Nov 7. PMID: 36343238; PMCID: PMC9674244.

Correction: Facilitating islet transplantation using a three-step approach with mesenchymal stem cells, encapsulation, and pulsed focused ultrasound. Razavi M, Ren T, Zheng F, Telichko A, Wang J, Dahl JJ, Demirci U, Thakor AS. Stem Cell Res Ther. 2022 Dec 20;13(1):526. doi: 10.1186/s13287-022-03210-6. Erratum for: Stem Cell Res Ther. 2020 Sep 18;11(1):405. PMID: 36536426; PMCID: PMC9764474.

Three-layer model with absorption for conservative estimation of the maximum acoustic transmission coefficient through the human skull for transcranial ultrasound stimulation. Attali D, Tiennot T, Schafer M, Fouragnan E, Sallet J, Caskey CF, Chen R, Pauly KB, Aubry JF. Brain Stimul. 2023 Jan- Feb;16(1):48-55. doi: 10.1016/j.brs.2022.12.005. Epub 2022 Dec 19. PMID: 36549480

Changes in the Cerebello-Thalamo-Cortical Network After Magnetic Resonance-Guided Focused Ultrasound Thalamotomy. Thaler C, Tian Q, Wintermark M, Ghanouni P, Halpern CH, Henderson JM, Airan RD, Zeineh M, Goubran M, Leuze C, Fiehler J, Butts Pauly K, McNab JA. Brain Connect. 2023 Feb;13(1):28-38. doi: 10.1089/brain.2021.0157. Epub 2022 Jul 7. PMID: 35678063; PMCID: PMC9942176.

Sunnybrook Health Sciences Centre

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Commercial Treatments	Clinical Research

17	14	12	52
Preclinical Research	Mechanisms of Action Research	Technical Research	Publications

Sunnybrook Health Sciences Centre | Toronto, Canada

Established as a COE in 2016, the Sunnybrook Health Sciences Centre is conducting research for focused ultrasound in neurology, neurosurgery, urology, orthopedics, gynecology, radiation oncology, and biomedical engineering, and has studies underway for Alzheimer's disease, obsessive-compulsive disorder, depression, Parkinson's disease, ALS, breast cancer brain metastases, and others.

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Commercial treatment

Neurological	Essential tremor
Urological	Prostate cancer

Clinical research

Gastrointestinal	Pancreatic tumors, malignant
Miscellaneous	Head & neck tumors
Musculoskeletal	Bone cancer
Neurological	Alzheimer's disease; Amyotrophic lateral sclerosis; Brain metastases, breast cancer; Brain metastases, lung cancer; Depression; Essential tremor; Glioblastoma; Multiple sclerosis; Obsessive-compulsive disorder; Pontine glioma
Urological	Prostate cancer
Women's health	Breast tumors, malignant

Preclinical research

Cardiovascular	Atrial fibrillation, Deep vein thrombosis
Gastrointestinal	Colorectal tumors
Musculoskeletal	Bone metastases
Neurological	Alzheimer's disease; Amyotrophic lateral sclerosis; Brain metastases, breast cancer; Depression; Epilepsy; Glioblastoma; Parkinson's disease, underlying cause; Spinal cord injury; Stroke, intracerebral hemorrhage; Stroke, thromboembolic
Ophthalmological	Retinal injury
Women's health	Breast tumors, malignant

Sunnybrook Health Sciences Centre continued

Mechanisms of action research	
Hyperthermia	Drug delivery, radiosensitization
Nonthermal	BBB opening; BBB opening, drug delivery; Chemosensitization; Clot lysis; Drug delivery; Drug delivery, immunotherapeutic; Neuromodulation; Sonoporation; Stem cell delivery; Vascular occlusion
Thermal ablation	Immune cell trafficking, Tissue destruction

Technical research
Drug delivery technology
FUS Image guidance, MR
FUS Image guidance, Ultrasound
FUS Physics
FUS Simulation & treatment planning
FUS Transducer technology, Histotripsy
FUS Transducer technology, Hyperthermia
FUS Transducer technology, Nonthermal
FUS Transducer technology, Other
FUS Transducer technology, Thermal ablation
FUS Treatment monitoring
Standards & quality assurance

Research not involving thermal ablation, tissue destruction	
Clinical research - Gastrointestinal	
Pancreatic tumors, malignant	Nonthermal - Drug delivery Nonthermal - Immunomodulation
Clinical research - Miscellaneous	
Head & neck tumors	Hyperthermia - Radiosensitization Nonthermal - Radiosensitization
Clinical research - Neurological	
Alzheimer's disease	Nonthermal, BBB opening - Drug delivery
Amyotrophic lateral sclerosis	Nonthermal, BBB opening - Drug delivery
Brain metastases, breast cancer	Nonthermal, BBB opening - Drug delivery
Brain metastases, lung cancer	Nonthermal, BBB opening - Drug delivery, immunotherapeutic
Glioblastoma	Nonthermal, BBB opening - Drug delivery Nonthermal - Liquid biopsy
Pontine glioma	Nonthermal, BBB opening - Drug delivery, immunotherapeutic
Clinical research - Women's health	
Breast tumors, malignant	Hyperthermia - Radiosensitization Nonthermal - Radiosensitization
Preclinical research - Cardiovascular	
Deep vein thrombosis	Histotripsy - Tissue destruction
Preclinical research - Neurological	
Alzheimer's disease	Nonthermal, BBB opening - Drug delivery Nonthermal, BBB opening - Gene delivery
Amyotrophic lateral sclerosis	Nonthermal, BBB opening - Drug delivery
Brain metastases, breast cancer	Nonthermal, BBB opening - Drug delivery
Epilepsy	Nonthermal - Neuromodulation
Glioblastoma	Nonthermal, BBB opening - Drug delivery
Parkinson's disease, underlying cause	Nonthermal, BBB opening - Drug delivery
Spinal cord injury	Nonthermal, BBB opening - Drug delivery
Stroke, intracerebral hemorrhage	Nonthermal, BBB opening - Drug delivery
Stroke, thromboembolic	Nonthermal, BBB opening - Drug delivery
Preclinical research - Ophthalmological	
Retinal injury	Nonthermal - Gene delivery

Sunnybrook Health Sciences Centre continued

Publications—2022

Dysgeusia induced and resolved by focused ultrasound thalamotomy: case report. De Vloo P, Boutet A, Elias GJB, Gramer RM, Joel SE, Llinas M, Kucharczyk W, Fasano A, Hamani C, Lozano AM. J Neurosurg. 2021 Jun 18;136(1):215-220. doi: 10.3171/2020.11.JNS202882. PMID: 34144526.

Novel Treatment Approaches for Brain Tumour from a Blood-Brain Barrier Perspective. Wu SK, Tsai CL, Hynynen K. Handb Exp Pharmacol. 2022;273:351-364. doi: 10.1007/164_2020_408. PMID: 33454856.

Current state of therapeutic focused ultrasound applications in neuro-oncology. Meng Y, Pople CB, Budiansky D, Li D, Suppiah S, Lim-Fat MJ, Perry J, Sahgal A, Lipsman N. J Neurooncol. 2022 Jan;156(1):49-59. doi: 10.1007/s11060-021-03861-0. Epub 2021 Oct 18. PMID: 34661791.

Neutrophil Recruitment and Leukocyte Response Following Focused Ultrasound and Microbubble Mediated Blood-Brain Barrier Treatments. Poon C, Pellow C, Hynynen K. Focus (Am Psychiatr Publ). 2022 Jan;20(1):100-116. doi: 10.1176/appi.focus.20104. Epub 2022 Jan 25. PMID: 35746942; PMCID: PMC9063606.

Untapped Neuroimaging Tools for Neuro-Oncology: Connectomics and Spatial Transcriptomics. Germann J, Zadeh G, Mansouri A, Kucharczyk W, Lozano AM, Boutet A. Cancers (Basel). 2022 Jan 18;14(3):464. doi: 10.3390/cancers14030464. PMID: 35158732; PMCID: PMC8833690.

MORPHIOUS: an unsupervised machine learning workflow to detect the activation of microglia and astrocytes. J Neuroinflammation. Silburt J, Aubert I. 2022 Jan 29;19(1):24. doi: 10.1186/s12974-021-02376-9. PMID: 35093113; PMCID: PMC8800241.

Focused Ultrasound Stimulation of Microbubbles in Combination with Radiotherapy for Acute Damage of Breast Cancer Xenograft Model. Sharma D, Hussein F, Law N, Farhat G, Tarapacki C, Sannachi L, Giles A, Czarnota GJ. Technol Cancer Res Treat. 2022 Jan-Dec;21:15330338221132925. doi: 10.1177/15330338221132925. PMID: 36412102; PMCID: PMC9706051.

Lesional psychiatric neurosurgery: meta-analysis of clinical outcomes using a transdiagnostic approach. Davidson B, Eapen-John D, Mithani K, Rabin JS, Meng Y, Cao X, Pople CB, Giacobbe P, Hamani C, Lipsman N. J Neurol Neurosurg Psychiatry. 2022 Feb;93(2):207-215. doi: 10.1136/jnnp-2020-325308. Epub 2021 Jul 14. PMID: 34261748.

Microscopy to Visualize Focused Ultrasound and Microbubble Treatments to Increase Blood-Brain Barrier Permeability. Poon C, Mühlenpfordt M, Olsman M, Kotopoulis S, de Lange Davies C, Hynynen K. Real-Time Intravital Multiphoton. J Vis Exp. 2022 Feb 5;(180). doi: 10.3791/62235. PMID: 35188113.

Milestones in Tremor Research: 10 Years Later. Erro R, Fasano A, Barone P, Bhatia KP. Mov Disord Clin Pract. 2022 Feb 26;9(4):429-435. doi: 10.1002/mdc3.13418. PMID: 35582314; PMCID: PMC9092753.

Establishing density-dependent longitudinal sound speed in the vertebral lamina. Xu R, O'Reilly MA. J Acoust Soc Am. 2022 Mar;151(3):1516. doi: 10.1121/10.0009316. PMID: 35364923.

High-Pressure Low-Frequency Lateral Mode Phased-Array Transducer System for the Treatment of Deep Vein Thrombosis: An In Vitro Study. Dadgar MM, Hynynen K. IEEE Trans Ultrason Ferroelectr Freq Control. 2022 Mar; 69(3):1088-1099. doi: 10.1109/TUFFC.2022.3141871. Epub 2022 Mar 2. PMID: 35020593.

Publications—2022 continued

Targeted Nanoparticle for Co-delivery of HER2 siRNA and a Taxane to Mirror the Standard Treatment of HER2+ Breast Cancer: Efficacy in Breast Tumor and Brain Metastasis. Ngamcherdtrakul W, Bejan DS, Cruz-Muñoz W, Reda M, Zaidan HY, Siriwon N, Marshall S, Wang R, Nelson MA, Rehwaldt JPC, Gray JW, Hynynen K, Yantasee W. Small. 2022 Mar;18(11):e2107550. doi: 10.1002/smll.202107550. Epub 2022 Jan 27. PMID: 35083840; PMCID: PMC8959011.

Commentary: Feasibility of Magnetic Resonance-Guided Focused Ultrasound Thalamotomy for Essential Tremor in the Setting of Prior Craniotomy. Yamamoto K, Lozano AM, Fasano A. Oper Neurosurg (Hagerstown). 2022 Mar 1;22(3):e147-e149. doi: 10.1227/ONS.0000000000000087. PMID: 35030144.

Toward focused ultrasound neuromodulation in deep brain stimulator implanted patients: Ex-vivo thermal, kinetic and targeting feasibility assessment. Sarica C, Fomenko A, Nankoo JF, Darmani G, Vetkas A, Yamamoto K, Lozano AM, Chen R. Brain Stimul. 2022 Mar-Apr;15(2): 376-379. doi: 10.1016/j.brs.2021.12.012. Epub 2022 Feb 1. PMID: 35121189.

A robotic magnetic resonance-guided high-intensity focused ultrasound platform for neonatal neurosurgery: Assessment of targeting accuracy and precision in a brain phantom. Raghuram H, Keunen B, Soucier N, Looi T, Pichardo S, Waspe AC, Drake JM. Med Phys. 2022 Apr;49(4):2120-2135. doi: 10.1002/mp.15540. Epub 2022 Mar 1. PMID: 35174892.

Commonly used outcome measures in neurosurgical trials for major depressive disorder might not capture clinically meaningful treatment effects. Rabin JS, Nyman AJ, Davidson B, Zakzanis KK, Giacobbe P, Hamani C, Nestor S, Lipsman N. J Neurol Neurosurg Psychiatry. 2022 Apr;93(4):455-456. doi: 10.1136/jnnp-2021-327688. Epub 2022 Jan 25. PMID: 35078915; PMCID: PMC8921571.

Comparison of computer simulations and clinical treatment results of magnetic resonance-guided focused ultrasound surgery (MRgFUS) of uterine fibroids. Hyvärinen M, Huang Y, David E, Hynynen K. Med Phys. 2022 Apr;49(4):2101-2119. doi: 10.1002/mp.15263. Epub 2022 Mar 2. PMID: 34601729; PMCID: PMC9314069.

Application of Ultrasound Combined with Microbubbles for Cancer Therapy. Sharma D, Leong KX, Czarnota GJ. Int J Mol Sci. 2022 Apr 15;23(8):4393. doi: 10.3390/ijms23084393. PMID: 35457210; PMCID: PMC9026557.

Functional tremor developing after successful MRI-guided focused ultrasound thalamotomy for essential tremor. Alshimemeri S, Vargas-Méndez D, Chen R, Lipsman N, Schwartz ML, Lozano AM, Fasano A. J Neurol Neurosurg Psychiatry. 2022 Apr 26:jnnp-2021-327524. doi: 10.1136/jnnp-2021-327524. Epub ahead of print. PMID: 35473713.

An Ultrasound-Guided Hemispherical Phased Array for Microbubble-Mediated Ultrasound Therapy.Deng L, Yang SD, O'Reilly MA, Jones RM, Hynynen K. IEEE Trans Biomed Eng. 2022 May;69(5):1776-1787. doi: 10.1109/TBME.2021.3132014. Epub 2022 Apr 21. PMID: 34855582; PMCID: PMC9092225.

Sunnybrook Health Sciences Centre continued

Publications—2022 continued

Development of a novel castration-resistant orthotopic prostate cancer model in New Zealand White rabbit. Wang Y, Abenojar EC, Wang J, de Leon AC, Tavri S, Wang X, Gopalakrishnan R, Walker E, MacLennan GT, Giles A, Czarnota GJ, Basilion JP, Exner AA. Prostate. 2022 May;82(6):695-705. doi: 10.1002/pros.24314. Epub 2022 Feb 15. PMID: 35167141; PMCID: PMC8994852.

Effect of Public Interest in Magnetic Resonance Imaging-Guided Focused Ultrasound on Enrolment for Deep Brain Stimulation. Balachandar A, Matta R, Shetty A, Algarni M, Lozano AM, Fasano A. Mov Disord. 2022 May;37(5):1103-1104. doi: 10.1002/mds.28963. Epub 2022 Mar 2. PMID: 35234316.

Alpha- Synuclein Targeting Therapeutics for Parkinson's Disease and Related Synucleinopathies. Menon S, Armstrong S, Hamzeh A, Visanji NP, Sardi SP, Tandon A. Front Neurol. 2022 May 9;13:852003. doi: 10.3389/fneur.2022.852003. PMID: 35614915; PMCID: PMC9124903.

Human Studies of Transcranial Ultrasound neuromodulation: A systematic review of effectiveness and safety. Sarica C, Nankoo JF, Fomenko A, Grippe TC, Yamamoto K, Samuel N, Milano V, Vetkas A, Darmani G, Cizmeci MN, Lozano AM, Chen R. Brain Stimul. 2022 May-Jun;15(3):737-746. doi: 10.1016/j.brs.2022.05.002. Epub 2022 May 6. PMID: 35533835

An ultrasonically actuated fine needle creates cavitation in bovine liver. Perra E, Hayward N, Pritzker KPH, Nieminen HJ. J Acoust Soc Am. 2022 Jun;151(6):3690. doi: 10.1121/10.0010534. PMID: 35778205.

Ultrasound-triggered oxygen-loaded nanodroplets enhance and monitor cerebral damage from sonodynamic therapy. Lea-Banks H, Wu SK, Lee H, Hynynen K. Nanotheranostics. 2022 Jun 27;6(4):376-387. doi: 10.7150/ntno.71946. PMID: 35795341; PMCID: PMC9254362.

An Acoustic Measurement Library for Non- Invasive Trans-Rodent Skull Ultrasonic Focusing at High Frequency. Rahimi S, Jones RM, Hynynen K. IEEE Trans Biomed Eng. 2022 Jul;69(7):2184-2191. doi: 10.1109/TBME.2021.3138352. Epub 2022 Jun 17. PMID: 34951839.

An ultrasonically actuated needle promotes the transport of nanoparticles and fluids. Perra E, Hayward N, Pritzker KPH, Nieminen HJ. J Acoust Soc Am. 2022 Jul;152(1):251. doi: 10.1121/10.0012190. PMID: 35931509.

Salvage partial gland ablation for recurrent prostate cancer following primary partial gland ablation: Functional and oncological outcomes. Qaoud Y, Herrera-Caceres JO, Bass R, Berjaoui MB, Tiwari R, Kenk M, Lajkosz K, Finelli A, Perlis N, Klotz L, Fleshner N. Urol Oncol. 2022 Jul;40(7): 343.e1-343.e6. doi: 10.1016/j.urolonc.2022.03.019. Epub 2022 May 9. PMID: 35537905.

Magnetic resonance imaging-guided focused ultrasound thalamotomy for essential tremor: 5-year follow-up results. Cosgrove GR, Lipsman N, Lozano AM, Chang JW, Halpern C, Ghanouni P, Eisenberg H, Fishman P, Taira T, Schwartz ML, McDannold N, Hayes M, Ro S, Shah B, Gwinn R, Santini VE, Hynynen K, Elias WJ. J Neurosurg. 2022 Aug 5:1-6. doi: 10.3171/2022.6.JNS212483. Epub ahead of print. PMID: 35932269.

Publications—2022 continued

Ipsilateral and axial tremor response to focused ultrasound thalamotomy for essential tremor: clinical outcomes and probabilistic mapping. Yamamoto K, Sarica C, Elias GJB, Boutet A, Germann J, Loh A, Joel SE, Bigioni L, Gwun D, Gramer R, Li SX, Zemmar A, Vetkas A, Algarni M, Devenyi G, Chakravarty M, Hynynen K, Scantlebury N, Schwartz ML, Lozano AM, Fasano A. J Neurol Neurosurg Psychiatry. 2022 Aug 22:jnnp-2021-328459. doi: 10.1136/jnnp-2021-328459. Epub ahead of print. PMID: 35995551.

Ultrasound delivery of a TrkA agonist confers neuroprotection to Alzheimer-associated pathologies. Xhima K, Markham-Coultes K, Hahn Kofoed R, Saragovi HU, Hynynen K, Aubert I. Brain. 2022 Aug 27;145(8):2806-2822. doi: 10.1093/brain/awab460. PMID: 34919633; PMCID: PMC9420023.

A Cautionary Tale of Magnetic Resonance-Guided Focused Ultrasound Thalamotomy-Induced White Matter Lesions. Boutet A, Loh A, Germann J, Machnowska M, Scantlebury N, Vetkas A, Elias GJB, Lozano AM, Katzberg HD, Fasano A, Schwartz ML. Mov Disord. 2022 Sep;37(9):1953-1955. doi: 10.1002/mds.29040. Epub 2022 May 26. PMID: 35616482.

The engineered AAV2-HBKO promotes non-invasive gene delivery to large brain regions beyond ultrasound targeted sites. Kofoed RH, Noseworthy K, Wu K, Sivadas S, Stanek L, Elmer B, Hynynen K, Shihabuddin LS, Aubert I. Mol Ther Methods Clin Dev. 2022 Sep 26;27:167-184. doi: 10.1016/j.omtm.2022.09.011. PMID: 36284767; PMCID: PMC9574578.

A robotic MR-guided high-intensity focused ultrasound platform for intraventricular hemorrhage: assessment of clot lysis efficacy in a brain phantom. Raghuram H, Looi T, Pichardo S, Waspe AC, Drake JM. J Neurosurg Pediatr. 2022 Sep 16;30(6):586-594. doi: 10.3171/2022.8.PEDS22144. PMID: 36115058.

Magnetic resonance- guided focused ultrasound for the treatment of tremor. Yamamoto K, Sarica C, Loh A, Vetkas A, Samuel N, Milano V, Zemmar A, Germann J, Cheyuo C, Boutet A, Elias GJ, Ito H, Taira T, Lozano AM. Expert Rev Neurother. 2022 Oct;22(10):849-861. doi: 10.1080/14737175.2022.2147826. Epub 2022 Dec 5. PMID: 36469578.

Putaminal Recombinant Glucocerebrosidase Delivery with Magnetic Resonance-Guided Focused Ultrasound in Parkinson's Disease: A Phase I Study. Meng Y, Pople CB, Huang Y, Jones RM, Ottoy J, Goubran M, Oliveira LM, Davidson B, Lawrence LSP, Lau AZ, Bethune A, Maralani P, Abrahao A, Hamani C, Hynynen K, Kalia SK, Lipsman N, Kalia LV. Mov Disord. 2022 Oct;37(10):2134-2139. doi: 10.1002/mds.29190. Epub 2022 Sep 11. PMID: 36089809.

Effect of Ultrasound-Stimulated Microbubbles and Hyperthermia on Tumor Vasculature of Breast Cancer Xenograft. Sharma D, Cartar H, Quiaoit K, Law N, Giles A, Czarnota GJ. J Ultrasound Med. 2022 Nov;41(11): 2659-2671. doi: 10.1002/jum.15950. Epub 2022 Feb 10. PMID: 35142383; PMCID: PMC9790356.

Efficacy of gene delivery to the brain using AAV and ultrasound depends on serotypes and brain areas. Kofoed RH, Dibia CL, Noseworthy K, Xhima K, Vacaresse N, Hynynen K, Aubert I. J Control Release. 2022 Nov;351: 667-680. doi: 10.1016/j.jconrel.2022.09.048. Epub 2022 Oct 6. PMID: 36179767.

Sunnybrook Health Sciences Centre continued

Publications—2022 continued

Cognitive effects of unilateral thalamotomy for tremor: a meta-analysis. Rohringer CR, Sewell IJ, Gandhi S, Isen J, Davidson B, McSweeney M, Swardfager W, Scantlebury N, Swartz RH, Hamani C, Giacobbe P, Nestor SM, Yunusova Y, Lam B, Schwartz ML, Lipsman N, Abrahao A, Rabin JS. Brain Commun. 2022 Nov 4;4(6):fcac287. doi: 10.1093/braincomms/fcac287. PMID: 36440102; PMCID: PMC9683603.

Connectomic neuromodulation for Alzheimer's disease: A systematic review and meta-analysis of invasive and non-invasive techniques. Cheyuo C, Germann J, Yamamoto K, Vetkas A, Loh A, Sarica C, Milano V, Zemmar A, Flouty O, Harmsen IE, Hodaie M, Kalia SK, Tang-Wai D, Lozano AM. Transl Psychiatry. 2022 Nov 21;12(1):490. doi: 10.1038/s41398-022-02246-9. PMID: 36411282; PMCID: PMC9678946.

Cavitation Feedback Control of Focused Ultrasound Blood-Brain Barrier Opening for Drug Delivery in Patients with Parkinson's Disease. Huang Y, Meng Y, Pople CB, Bethune A, Jones RM, Abrahao A, Hamani C, Kalia SK, Kalia LV, Lipsman N, Hynynen K. Pharmaceutics. 2022 Nov 26;14(12):2607. doi: 10.3390/pharmaceutics14122607. PMID: 36559101; PMCID: PMC9781334.

Automatic detection of foreign body objects in neurosurgery using a deep learning approach on intraoperative ultrasound images: From animal models to first in-human testing. Abramson HG, Curry EJ, Mess G, Thombre R, Kempski-Leadingham KM, Mistry S, Somanathan S, Roy L, Abu-Bonsrah N, Coles G, Doloff JC, Brem H, Theodore N, Huang J, Manbachi A. Front Surg. 2022 Nov 30;9:1040066. doi: 10.3389/fsurg.2022.1040066. PMID: 36532130; PMCID: PMC9748097.

Multi-modal investigation of transcranial ultrasound-induced neuroplasticity of the human motor cortex. Samuel N, Zeng K, Harmsen IE, Ding MYR, Darmani G, Sarica C, Santyr B, Vetkas A, Pancholi A, Fomenko A, Milano V, Yamamoto K, Saha U, Wennberg R, Rowland NC, Chen R, Lozano AM. Brain Stimul. 2022 Nov- Dec;15(6):1337-1347. doi: 10.1016/j.brs.2022.10.001. Epub 2022 Oct 11. PMID: 36228977

Microbubble drug conjugate and focused ultrasound blood brain barrier delivery of AAV-2 SIRT-3. Trinh D, Nash J, Goertz D, Hynynen K, Bulner S, Iqbal U, Keenan J. Drug Deliv. 2022 Dec;29(1):1176-1183. doi: 10.1080/10717544.2022.2035855. PMID: 35393905; PMCID: PMC9004516.

Publications—2022 continued

Formulation of a kit under Good Manufacturing Practices (GMP) for preparing [111In]In-BnDTPA- trastuzumab-NLS injection: a theranostic agent for imaging and Meitner-Auger Electron (MAE) radioimmunotherapy of HER2-positive breast cancer. Chan C, Prozzo V, Aghevlian S, Reilly RM. EJNMMI Radiopharm Chem. 2022 Dec 21;7(1):33. doi: 10.1186/s41181-022-00186-9. PMID: 36542157; PMCID: PMC9772372.

Laser interstitial thermal therapy for the treatment of insular lesions: A systematic review.Vetkas A, Germann J, Boutet A, Samuel N, Sarica C, Yamamoto K, Santyr B, Cheyuo C, Conner CR, Lang SM, Lozano AM, Ibrahim GM, Valiante T, Kongkham PN, Kalia SK. Front Neurol. 2023 Jan 4; 13:1024075. doi: 10.3389/fneur.2022.1024075. PMID: 36686528; PMCID: PMC9845884.

Magnetic resonance imaging-guided ultrasound ablation for prostate cancer - A contemporary review of performance Alabousi M, Ghai S. Front Oncol. 2023 Jan 4;12:1069518. doi: 10.3389/fonc.2022.1069518. PMID: 36686753; PMCID: PMC9846805.

Anesthetic-loaded nanodroplets with focused ultrasound reduces agitation in Alzheimer's mice. Gouveia FV, Lea-Banks H, Aubert I, Lipsman N, Hynynen K, Hamani C. Ann Clin Transl Neurol. 2023 Jan 30. doi: 10.1002/acn3.51737. Epub ahead of print. PMID: 36715553.

Three-layer model with absorption for conservative estimation of the maximum acoustic transmission coefficient through the human skull for transcranial ultrasound stimulation. Attali D, Tiennot T, Schafer M, Fouragnan E, Sallet J, Caskey CF, Chen R, Darmani G, Bubrick EJ, Butler C, Stagg CJ, Klein-Flügge M, Verhagen L, Yoo SS, Pauly KB, Aubry JF. Brain Stimul. 2023 Jan- Feb;16(1):48-55. doi: 10.1016/j.brs.2022.12.005. Epub 2022 Dec 19. PMID: 36549480

Blood-brain barrier opening of the default mode network in Alzheimer's disease with magnetic resonance-guided focused ultrasound. Meng Y, Goubran M, Rabin JS, McSweeney M, Ottoy J, Pople CB, Huang Y, Storace A, Ozzoude M, Bethune A, Lam B, Swardfager W, Heyn C, Abrahao A, Davidson B, Hamani C, Aubert I, Zetterberg H, Ashton NJ, Karikari TK, Blennow K, Black SE, Hynynen K, Lipsman N. Brain. 2023 Mar 1; 146(3):865-872. doi: 10.1093/brain/awac459. PMID: 36694943.

University of Maryland School of Medicine

2	3
Commercial Treatments	Clinical Research

14	12	7	10
Preclinical Research	Mechanisms of Action Research	Technical Research	Publications

University of Maryland School of Medicine | Baltimore, MD

The COE at the University of Maryland, UMD, was established in 2016. At present, the UMD departments of neurosurgery, radiology, and neurology are collaborating to study the treatment of movement disorders, chronic neuropathic pain, brain tumors, and the use of enhanced drug delivery. In addition, their immunomodulation studies range from investigating cell systems to animal models and human clinical trials

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Commercial treatment

Neurological	Essential tremor; Parkinson's disease, tremor

Clinical research

Neurological	Brain metastases, lung cancer; Glioblastoma; Trigeminal neuralgia

Preclinical research

Miscellaneous	Infection
Neurological	Brain tumors, general; Epilepsy; Glioblastoma; Opioid and other addictions

Mechanisms of action research

Histotripsy	Immune cell trafficking
Nonthermal	BBB opening; BBB opening, drug delivery; BBB opening, drug delivery, immunotherapeutic; Chemosensitization; Immunomodulation; Liquid biopsy; Neuromodulation; Radiosensitization; Sonodynamic therapy; Tissue destruction
Thermal ablation	Tissue destruction

Technical research

- Drug delivery technology
- FUS Image guidance, MR
- FUS Image guidance, Ultrasound
- FUS Physics
- FUS Simulation & treatment planning
- FUS Treatment monitoring
- Standards & quality assurance

University of Maryland School of Medicine continued

Research not involving thermal ablation, tissue destruction

Clinical research - Neurological	
Brain metastases, lung cancer	Nonthermal, BBB opening - Drug delivery, immunotherapeutic
Glioblastoma	Nonthermal - Liquid biopsy
Preclinical research - Miscellaneous	
Infection	Nonthermal, BBB opening - Drug delivery
Preclinical research - Neurological	
Brain tumors, general	Nonthermal - Amplification of cancer biomarkers Nonthermal, BBB opening Nonthermal, BBB opening - Drug delivery Nonthermal, BBB opening - Drug delivery, immunotherapeutic Nonthermal - Gene delivery Nonthermal - Immunomodulation Nonthermal - Liquid biopsy
Epilepsy	Nonthermal - Gene delivery Nonthermal - Neuromodulation
Glioblastoma	Nonthermal - Immune cell trafficking Nonthermal - Immunomodulation
Opioid and other addictions	Nonthermal - Neuromodulation

Publications—2022

Towards controlled drug delivery in brain tumors with microbubble-enhanced focused ultrasound. Schoen S Jr, Kilinc MS, Lee H, Guo Y, Degertekin FL, Woodworth GF, Arvanitis C. Adv Drug Deliv Rev. 2022 Jan;180:114043. doi: 10.1016/j.addr.2021.114043. Epub 2021 Nov 18. PMID: 34801617; PMCID: PMC8724442.

Technical Comparison of Treatment Efficiency of Magnetic Resonance-Guided Focused Ultrasound Thalamotomy and Pallidotomy in Skull Density Ratio-Matched Patient Cohorts. Ahmed AK, Guo S, Kelm N, Clanton R, Melhem ER, Gullapalli RP, Ksendzovsky A, Eisenberg HM, Miller TR, Gandhi D. Front Neurol. 2022 Jan 21;12:808810. doi: 10.3389/fneur.2021.808810. PMID: 35126300; PMCID: PMC8813961.

Magnetic Nanoparticle-Mediated Heating for Biomedical Applications. Kwizera EA, Stewart S, Mahmud MM, He X. J Heat Transfer. 2022 Mar;144(3):030801. doi: 10.1115/1.4053007. Epub 2022 Jan 18. PMID: 35125512; PMCID: PMC8813031.

A Novel Matrix-Array-Based MR-Conditional Ultrasound System for Local Hyperthermia of Small Animals. Tretbar SH, Fournelle M, Speicher D, Becker FJ, Anastasiadis P, Landgraf L, Roy U, Melzer A. IEEE Trans Biomed Eng. 2022 Feb;69(2):758-770. doi: 10.1109/TBME.2021.3104865. Epub 2022 Jan 20. PMID: 34398748.

The roles of thermal and mechanical stress in focused ultrasound-mediated immunomodulation and immunotherapy for central nervous system tumors. Kim C, Lim M, Woodworth GF, Arvanitis CD. J Neurooncol. 2022 Apr; 157(2):221-236. doi: 10.1007/s11060-022-03973-1. Epub 2022 Mar 2. PMID: 35235137; PMCID: PMC9119565.

Publications—2022 continued

Application of optical coherence tomography in decision-making of post-thrombectomy adjunctive treatments. Li D, Tang T, Hu T, Walczak P, Gandhi D, Li S. J Neurointerv Surg. 2022 Jul 26:neurintsurg-2022-019195. doi: 10.1136/jnis-2022-019195. Epub ahead of print. PMID: 35882553.

Magnetic resonance imaging-guided focused ultrasound thalamotomy for essential tremor: 5-year follow-up results. Cosgrove GR, Lipsman N, Lozano AM, Chang JW, Halpern C, Ghanouni P, Eisenberg H, Fishman P, Taira T, Schwartz ML, McDannold N, Hayes M, Ro S, Shah B, Gwinn R, Santini VE, Hynynen K, Elias WJ. J Neurosurg. 2022 Aug 5:1-6. doi: 10.3171/2022.6.JNS212483. Epub ahead of print. PMID: 35932269.

Nanotherapeutic treatment of the invasive glioblastoma tumor microenvironment. Pandey N, Anastasiadis P, Carney CP, Kanvinde PP, Woodworth GF, Winkles JA, Kim AJ. Adv Drug Deliv Rev. 2022 Sep;188:114415. doi: 10.1016/j.addr.2022.114415. Epub 2022 Jul 3. PMID: 35787387.

Slow is smooth, smooth is fast. Colasurdo M, Gandhi D. J Neurointerv Surg. 2022 Nov 15:jnis-2022-019843. doi: 10.1136/jnis-2022-019843. Epub ahead of print. PMID: 36379703.

Trial of Globus Pallidus Focused Ultrasound Ablation in Parkinson's Disease. Krishna V, Fishman PS, Eisenberg HM, Kaplitt M, Baltuch G, Chang JW, Chang WC, Martinez Fernandez R, Del Alamo M, Halpern CH, Ghanouni P, Eleopra R, Cosgrove R, Guridi J, Gwinn R, Khemani P, Lozano AM, McDannold N, Fasano A, Constantinescu M, Schlesinger I, Dalvi A, Elias WJ. N Engl J Med. 2023 Feb 23;388(8):683-693. doi: 10.1056/NEJMoa2202721. PMID: 36812432.

Brigham and Women's Hospital

5	4
Commercial Treatments	Clinical Research

7	12	6	17
Preclinical Research	Mechanisms of Action Research	Technical Research	Publications

Brigham and Women's Hospital | Boston, MA

Brigham and Women's Hospital was named a COE in 2015. More than 50 focused ultrasound researchers in three different laboratories span the Boston campus of Brigham and Women's Hospital where, in conjunction with Harvard Medical School, they are pioneering innovative uses of focused ultrasound and advancing these new approaches from bench to bedside.

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Commercial treatments

Musculoskeletal	Bone metastases
Neurological	Essential tremor
Urological	Prostate cancer
Women's health	Uterine fibroids

Clinical research

Neurological	Epilepsy, Glioblastoma
Urological	Prostate cancer

Preclinical research

Miscellaneous	Niemann-Pick disease
Neurological	Alzheimer's disease; Epilepsy; Glioblastoma; Huntington's disease; Parkinson's disease, tremor

Mechanisms of action research

Hyperthermia	Tissue destruction
Nonthermal	Amplification of cancer biomarkers; BBB opening, drug delivery; BBB opening, gene delivery; Drug delivery, vehicle; Immunomodulation; Liquid biopsy; Neuromodulation; Radiosensitization; Stem cell delivery; Tissue destruction
Thermal ablation	Tissue destruction

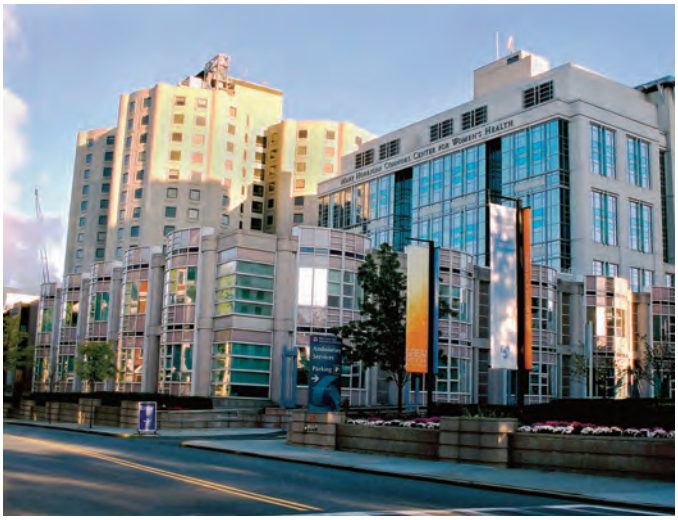
Technical research

- FUS Image guidance, MR
- FUS Image guidance, Ultrasound
- FUS Physics
- FUS Simulation & treatment planning
- FUS Treatment evaluation
- FUS Treatment monitoring

Brigham and Women's Hospital continued

Research not involving thermal ablation, tissue destruction

Clinical research - Neurological	
Epilepsy	Nonthermal - Neuromodulation
Glioblastoma	Nonthermal, BBB opening - Drug delivery
Preclinical research - Miscellaneous	
Niemann-Pick disease	Nonthermal, BBB opening - Gene delivery
Preclinical research - Neurological	
Alzheimer's disease	Nonthermal, BBB opening - Drug delivery
Epilepsy	Nonthermal - Neuromodulation
Glioblastoma	Nonthermal, BBB opening - Drug delivery Nonthermal - Tissue destruction
Huntington's disease	Nonthermal, BBB opening - Drug delivery
Parkinson's disease, tremor	Nonthermal - Neuromodulation



Publications—2022

Short-Term Efficacy of Transcranial Focused Ultrasound to the Hippocampus in Alzheimer's Disease: A Preliminary Study. Jeong H, Song IU, Chung YA, Park JS, Na SH, Im JJ, Bikson M, Lee W, Yoo SS. J Pers Med. 2022 Feb 9; 12(2):250. doi: 10.3390/jpm12020250. PMID: 35207738; PMCID: PMC8878180.

Magnetic Resonance Image Guided Focused Ultrasound Thalamotomy. A Single Center Experience With 160 Procedures. Lak AM, Segar DJ, McDannold N, White PJ, Cosgrove GR. Front Neurol. 2022 Feb 18;13:743649. doi: 10.3389/fneur.2022.743649. PMID: 35250802; PMCID: PMC8894664.

Low Intensity Focused Ultrasound for Epilepsy- A New Approach to Neuromodulation. Bubrick EJ, McDannold NJ, White PJ. Epilepsy Curr. 2022 Mar 29;22(3):156-160. doi: 10.1177/15357597221086111. PMID: 36474831; PMCID: PMC9684587.

The Evolution of Modern Ablative Surgery for the Treatment of Obsessive-Compulsive and Major Depression Disorders. Mustroph ML, Cosgrove GR, Williams ZM. Front Integr Neurosci. 2022 Apr 6;16:797533. doi: 10.3389/fnint.2022.797533. PMID: 35464603; PMCID: PMC9026193.

Somatotopic Organization of Hyperdirect Pathway Projections from the Primary Motor Cortex in the Human Brain. Pujol S, Cabeen RP, Yelnik J, François C, Fernandez Vidal S, Karachi C, Bardinet E, Cosgrove GR, Kikinis R. Front Neurol. 2022 Apr 25;13:791092. doi: 10.3389/fneur.2022.791092. PMID: 35547388; PMCID: PMC9081715.

Two-step aberration correction: application to transcranial histotripsy. Lu N, Hall TL, Sukovich JR, Choi SW, Snell J, McDannold N, Xu Z. Phys Med Biol. 2022 Jun 10;67(12):10.1088/1361-6560/ac72ed. doi: 10.1088/1361-6560/ac72ed. PMID: 35609619; PMCID: PMC9234948.

Publications—2022 continued

Neuromodulation Using Transcranial Focused Ultrasound on the Bilateral Medial Prefrontal Cortex. Kim YG, Kim SE, Lee J, Hwang S, Yoo SS, Lee HW. J Clin Med. 2022 Jun 30;11(13):3809. doi: 10.3390/jcm11133809. PMID: 35807094; PMCID: PMC9267901.

MRI-guided focused ultrasound focal therapy for patients with intermediate-risk prostate cancer: a phase 2b, multicentre study. Ehdaie B, Tempany CM, Holland F, Sjoberg DD, Kibel AS, Trinh QD, Durack JC, Akin O, Vickers AJ, Scardino PT, Sperling D, Wong JYC, Yuh B, Woodrum DA, Mynderse LA, Raman SS, Pantuck AJ, Schiffman MH, McClure TD, Sonn GA, Ghanouni P. Lancet Oncol. 2022 Jul;23(7):910-918. doi: 10.1016/S1470-2045(22)00251-0. Epub 2022 Jun 14. PMID: 35714666; PMCID: PMC9400094.

Acute Effects of Focused Ultrasound-Induced Blood-Brain Barrier Opening on Anti- Pyroglu3 Abeta Antibody Delivery and Immune Responses. Bathini P, Sun T, Schenk M, Schilling S, McDannold NJ, Lemere CA. Biomolecules. 2022 Jul 6;12(7):951. doi: 10.3390/biom12070951. PMID: 35883506; PMCID: PMC9313174.

Enhancement of cerebrospinal fluid tracer movement by the application of pulsed transcranial focused ultrasound. Yoo SS, Kim HC, Kim J, Kim E, Kowsari K, Van Reet J, Yoon K. Sci Rep. 2022 Jul 28;12(1):12940. doi: 10.1038/s41598-022-17314-9. PMID: 35902724; PMCID: PMC9334279.

Magnetic resonance imaging-guided focused ultrasound thalamotomy for essential tremor: 5-year follow-up results.Cosgrove GR, Lipsman N, Lozano AM, Chang JW, Halpern C, Ghanouni P, Eisenberg H, Fishman P, Taira T, Schwartz ML, McDannold N, Hayes M, Ro S, Shah B, Gwinn R, Santini VE, Hynynen K, Elias WJ. J Neurosurg. 2022 Aug 5:1-6. doi: 10.3171/2022.6.JNS212483. Epub ahead of print. PMID: 35932269.

Effects of Osmolarity on Ultrasound-Induced Membrane Depolarization in Isolated Crayfish Motor Axon. Yu F, Müller WS, Ehnholm G, Okada Y, Lin JW. Ultrasound Med Biol. 2022 Oct;48(10):2040-2051. doi: 10.1016/j.ultrasmedbio.2022.05.028. Epub 2022 Jul 23. PMID: 35882572.

Brigham and Women's Hospital continued

Publications—2022 continued

High Incidence of Intracerebral Hemorrhaging Associated with the Application of Low-Intensity Focused Ultrasound Following Acute Cerebrovascular Injury by Intracortical Injection. Kim E, Van Reet J, Kim HC, Kowsari K, Yoo SS. Pharmaceutics. 2022 Oct 6;14(10):2120. doi: 10.3390/pharmaceutics14102120. PMID: 36297554; PMCID: PMC9609794.

Deep Neural Network for Navigation of a Single-Element Transducer During Transcranial Focused Ultrasound Therapy: Proof of Concept. Choi M, Jang M, Yoo SS, Noh G, Yoon K. IEEE J Biomed Health Inform. 2022 Nov;26(11):5653-5664. doi: 10.1109/JBHI.2022.3198650. Epub 2022 Nov 10. PMID: 35969551.

Effects of focused ultrasound pulse duration on stimulating cortical and subcortical motor circuits in awake sheep. Kim HC, Lee W, Kowsari K, Weisholtz DS, Yoo SS. PLoS One. 2022 Dec 13;17(12):e0278865. doi: 10.1371/journal.pone.0278865. PMID: 36512563; PMCID: PMC9746960.

Transcranial MR-Guided Focused Ultrasound and Hyperostosis Calvariae Diffusa: Case Report and Systematic Review of the Literature. Bernstock JD, Torio EF, Raghu ALB, Chua M, Chen JA, Segar D, Gupta S, White PJ, McDannold N, Golby AJ, Cosgrove GR. Stereotact Funct Neurosurg. 2022;100(5-6):331-339. doi: 10.1159/000527232. Epub 2022 Dec 15. PMID: 36521432.

Three-layer model with absorption for conservative estimation of the maximum acoustic transmission coefficient through the human skull for transcranial ultrasound stimulation. Attali D, Tiennot T, Schafer M, Fouragnan E, Sallet J, Caskey CF, Chen R, Darmani G, Bubrick EJ, Butler C, Stagg CJ, Klein-Flügge M, Verhagen L, Yoo SS, Pauly KB, Aubry JF. Brain Stimul. 2023 Jan- Feb;16(1):48-55. doi: 10.1016/j.brs.2022.12.005. Epub 2022 Dec 19. PMID: 36549480.

ICR and The Royal Marsden

1	2
Commercial Treatment	Clinical Research

6	11	8	7
Preclinical Research	Mechanisms of Action Research	Technical Research	Publications

The Institute of Cancer Research and The Royal Marsden | London, England

In 2013, the Focused Ultrasound Foundation and Philips entered an innovative public-private collaboration with the Institute of Cancer Research, ICR, and The Royal Marsden National Health Service Foundation Trust to create a COE in London. The Center created a state-of-the-art resource for clinicians and scientists working on focused ultrasound therapy, developing clinical evidence in oncology, and establishing best practices, treatment standards, and protocols.

1
Veterinary Research

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Commercial treatment

Urological	Prostate cancer

Clinical research

Gastrointestinal	Colorectal tumors
Urological	Prostate cancer

Preclinical research

Cardiovascular	Twin-twin transfusion syndrome
Gastrointestinal	Liver metastases; Liver tumors; Pancreatic tumors, malignant
Neurological	Cancer pain, Glioblastoma

Mechanisms of action research

Histotripsy	Tissue destruction
Hyperthermia	Drug delivery, Radiosensitization
Nonthermal	Chemosensitization; Drug delivery; Drug delivery, immunotherapeutic; Tissue destruction; Vascular occlusion
Thermal ablation	Immune cell trafficking, Immunomodulation, Tissue destruction

Technical research

- Drug delivery technology
- FUS Image guidance, MR
- FUS Image guidance, Ultrasound
- FUS Physics
- FUS Simulation & treatment planning
- FUS Transducer technology, Thermal ablation
- FUS Treatment monitoring
- Standards & quality assurance

ICR and The Royal Marsden continued

Research not involving thermal ablation, tissue destruction

Clinical research - Gastrointestinal	
Colorectal tumors	Nonthermal - Drug delivery
Preclinical research - Cardiovascular	
Twin-twin transfusion syndrome	Nonthermal - Vascular occlusion
Preclinical research - Gastrointestinal	
Pancreatic tumors, malignant	Nonthermal - Immunomodulation
Preclinical research - Neurological	
Glioblastoma	Nonthermal - Drug delivery, vehicle
Veterinary research - Urological	
Bladder tumors	Thermal ablation - Immunomodulation

Publications—2022

Latest Advances in the Use of Therapeutic Focused Ultrasound in the Treatment of Pancreatic Cancer. Mouratidis PXE, ter Haar G. Cancers (Basel). 2022 Jan 27;14(3):638. doi: 10.3390/cancers14030638. PMID: 35158903; PMCID: PMC8833696.

Methods of monitoring thermal ablation of soft tissue tumors - A comprehensive review. Geoghegan R, ter Haar G, Nightingale K, Marks L, Natarajan S. Med Phys. 2022 Feb;49(2):769-791. doi: 10.1002/mp.15439. Epub 2022 Jan 10. PMID: 34965307.

Characterization of Acoustic, Cavitation, and Thermal Properties of Poly (vinyl alcohol) Hydrogels for Use as Therapeutic Ultrasound Tissue Mimics. Braunstein L, Brüningk SC, Rivens I, Civale J, ter Haar G. Ultrasound Med Biol. 2022 Jun;48(6):1095-1109. doi: 10.1016/j.ultrasmedbio.2022.02.007. Epub 2022 Mar 22. PMID: 35337687.

Drug Delivery to the Pons Using Short-Pulse Focused Ultrasound and Microbubble Exposure for the Treatment of Diffuse Midline Glioma. Chattenton D, Rivens I, Jiang Z, Carvalho DM, Sujarittam K, Boult JKR, Robinson SP, Jones C, ter Haar G, Choi J. Neuro-Oncology, Volume 24, Issue Supplement_1, June 2022, Page i35, https://doi.org/10.1093/neuonc/noac079.127.

Recommendations for Reporting Therapeutic Ultrasound Treatment Parameters. Padilla F, ter Haar G. Ultrasound Med Biol. 2022 Jul;48(7):1299-1308. doi: 10.1016/j.ultrasmedbio.2022.03.001. Epub 2022 Apr 21. PMID: 35461726.

Tissue specific considerations in implementing high intensity focussed ultrasound under magnetic resonance imaging guidance. deSouza NM, Gedroyc W, Rivens I, ter Haar G. Front Oncol. 2022 Nov 1;12:1037959. doi: 10.3389/fonc.2022.1037959. PMID: 36387108; PMCID: PMC9663991.

First in-human use of high-intensity focused ultrasound to occlude placental vessels non-invasively in TTTS. Shaw CJ, Rivens I, Symonds-Tayler R, Giussani D, ter Haar G, Lees C. Ultrasound Obstet Gynecol, 2022;60: 41-41. https://doi.org/10.1002/uog.25095.

University of Virginia Health System

4	13
Commercial Treatments	Clinical Research

25	34	5	27
Preclinical Research	Mechanisms of Action Research	Technical Research	Publications

University of Virginia Health System | Charlottesville, VA

The Foundation's first COE was inaugurated at the University of Virginia in September 2009 through a public private partnership between the Foundation, the Commonwealth of Virginia, the University of Virginia, Insightec, and GE. The COE has a strong history in brain research, having pioneered clinical trials for essential tremor and Parkinsonian tremor, as well as technical and preclinical studies for neurological disorders. The center also treats uterine fibroids and bone metastases and conducts cancer research.

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Commercial treatments

Neurological	Essential tremor; Parkinson's disease, dyskinesia; Parkinson's disease, tremor
Women's health	Uterine fibroids

Clinical research

Gastrointestinal	Esophageal tumors, Gastric tumors
Miscellaneous	Melanoma, Multiple tumors[1]
Neurological	Cancer pain, Epilepsy
Pulmonary	Lung cancer
Women's health	Breast tumors, benign; Breast tumors, malignant; Cervical tumors; Ovarian tumors

Preclinical research

Cardiovascular	Arteriovenous malformations, Peripheral artery disease
Gastrointestinal	Pancreatic tumors, malignant
Miscellaneous	Melanoma
Neurological	Brain metastases, breast cancer; Brain metastases, melanoma; Brain tumors, general; Cavernomas; Epilepsy; Glioblastoma; Parkinson's disease, underlying cause; Stroke, thromboembolic
Pulmonary	Lung cancer
Women's health	Breast tumors, malignant

1 Protocols inclusive of more than one indication.

University of Virginia Health System continued

Mechanisms of action research

Histotripsy	Amplification of cancer biomarkers, Chemosensitization, Immune cell trafficking, Immunomodulation, Liquid biopsy, Tissue destruction
Hyperthermia	Drug delivery
Miscellaneous	Melanoma
Nonthermal	Amplification of cancer biomarkers; Angiogenesis; BBB opening; BBB opening, drug delivery; BBB opening, drug delivery, vehicle; BBB opening, gene delivery; BBB opening, immune cell delivery; BNB opening, drug delivery; Clot lysis; Drug delivery; Drug delivery, immunotherapeutic
Thermal ablation	Chemosensitization, Immunomodulation, Tissue destruction

Technical research

Drug delivery technology
FUS Image guidance, MR
FUS Image guidance, Ultrasound
FUS Treatment evaluation
FUS Treatment monitoring

1 Inclusive of more than one indication

Research not involving thermal ablation, tissue destruction

Clinical research - Gastrointestinal	
Esophageal tumors	Thermal ablation - Immunomodulation
Gastric tumors	Thermal ablation - Immunomodulation
Clinical research - Miscellaneous	
Melanoma	Thermal ablation - Immunomodulation
Multiple tumors[1]	Thermal ablation - Immunomodulation
Clinical Research - Pulmonary	
Lung cancer	Thermal ablation - Immunomodulation
Clinical Research - Women's health	
Breast tumors, malignant	Nonthermal - Immunomodulation
Cervical tumors	Thermal ablation - Immunomodulation
Ovarian tumors	Thermal ablation - Immunomodulation
Preclinical research - Cardiovascular	
Arteriovenous malformations	Nonthermal - Tissue destruction
Peripheral artery disease	Nonthermal - Drug delivery, vehicle
Preclinical research - Gastrointestinal	
Pancreatic tumors, malignant	Thermal ablation - Immunomodulation
Preclinical research - Miscellaneous	
Melanoma	Thermal ablation - Immunomodulation
Preclinical research - Neurological	
Brain metastases, breast cancer	Nonthermal, BBB opening - Drug delivery; immunotherapeutic Nonthermal - Immunomodulation
Brain metastases, melanoma	Nonthermal, BBB opening - Drug delivery; immunotherapeutic Nonthermal - Immunomodulation Nonthermal - Sonodynamic therapy
Brain tumors, general	Nonthermal, BBB opening - Gene delivery
Cavernomas	Nonthermal - Sonodynamic therapy
Epilepsy	Nonthermal, BBB opening - Drug delivery Nonthermal - Neuromodulation
Glioblastoma	Nonthermal, BBB opening - Drug delivery Nonthermal, BBB opening - Gene delivery Nonthermal - Drug delivery, vehicle Nonthermal - Immunomodulation Nonthermal - Radiosensitization Nonthermal - Sonodynamic therapy Nonthermal - Vascular occlusion
Parkinson's disease, underlying cause	Nonthermal, BBB opening - Drug delivery
Stroke, thromboembolic	Nonthermal - Sonoporation
Preclinical research - Women's health	
Breast tumors, malignant	Thermal ablation - Immunomodulation

University of Virginia Health System continued

Publications—2022

Low-Cost 3-D Hydrophone Scanning Tank with MATLAB GUI Control. Clinard S, Wettstone E, Moore D, Snell J, Padilla F, Eames M. Ultrasound Med Biol. 2022 Jan;48(1):157-163. doi: 10.1016/j.ultrasmedbio.2021.09.022. Epub 2021 Oct 23. PMID: 34702638.

Hybrid Workshops During the COVID-19 Pandemic-Dawn of a New Era in Neurosurgical Learning Platforms. Garg K, Mishra S, Raheja A, Verma S, Tandon V, Agrawal S, Suri A, Chandra PS, Prada F, Servadei F, Kale SS, Srivastava P. World Neurosurg. 2022 Jan;157:e198-e206. doi: 10.1016/j.wneu.2021.09.132. Epub 2021 Oct 6. PMID: 34624519; PMCID: PMC8523585.

Pilot study of focused ultrasound for drug-resistant epilepsy. Lee CC, Chou CC, Hsiao FJ, Chen YH, Lin CF, Chen CJ, Peng SJ, Liu HL, Yu HY. Epilepsia. 2022 Jan;63(1):162-175. doi: 10.1111/epi.17105. Epub 2021 Nov 2. PMID: 34729772; PMCID: PMC9297900.

Cranial sonolucent prosthesis: a window of opportunity for neuro- oncology (and neuro-surgery). Del Bene M, Raspagliesi L, Carone G, Gaviani P, Silvani A, Solbiati L, Prada F, DiMeco F. J Neurooncol. 2022 Feb;156(3):529-540. doi: 10.1007/s11060-021-03929-x. Epub 2022 Jan 26. PMID: 35079911.

Development of and Gathering Validity Evidence for a Theoretical Test in Contrast-Enhanced Ultrasound. Jacobsen N, Nolsøe CP, Konge L, Graumann O, Dietrich CF, Sidhu PS, Gilja OH, Meloni MF, Berzigotti A, Harvey CJ, Deganello A, Prada F, Lerchbaumer MH, Laursen CB. Ultrasound Med Biol. 2022 Feb;48(2):248-256. doi: 10.1016/j.ultrasmedbio.2021.10.016. Epub 2021 Nov 21. PMID: 34815128.

Ultrasounds induce blood-brain barrier opening across a sonolucent polyolefin plate in an in vitro isolated brain preparation. Librizzi L, Uva L, Raspagliesi L, Gionso M, Regondi MC, Durando G, DiMeco F, de Curtis M, Prada F. Sci Rep. 2022 Feb 21;12(1):2906. doi: 10.1038/s41598-022-06791-7. PMID: 35190597; PMCID: PMC8861168.

Computational model of brain endothelial cell signaling pathways predicts therapeutic targets for cerebral pathologies. Gorick CM, Saucerman JJ, Price RJ. J Mol Cell Cardiol. 2022 Mar;164:17-28. doi: 10.1016/j.yjmcc.2021.11.005. Epub 2021 Nov 16. PMID: 34798125; PMCID: PMC8958390.

Focused ultrasound and other lesioning in the treatment of tremor. Binder DK, Shah BB, Elias WJ. J Neurol Sci. 2022 Apr 15;435:120193. doi: 10.1016/j.jns.2022.120193. Epub 2022 Feb 19. PMID: 35259650.

Multiparametric Intraoperative Ultrasound in Oncological Neurosurgery: A Pictorial Essay. Prada F, Ciocca R, Corradino N, Gionso M, Raspagliesi L, Vetrano IG, Doniselli F, Del Bene M, DiMeco F. Front Neurosci. 2022 Apr 19; 16:881661. doi: 10.3389/fnins.2022.881661. PMID: 35516800; PMCID: PMC9063404.

Neuropathology of Parkinson's disease after focused ultrasound thalamotomy. Koga S, Ishaque M, Jeffrey Elias W, Shah BB, Murakami A, Dickson DW. NPJ Parkinsons Dis. 2022 May 12;8(1):59. doi: 10.1038/s41531-022-00319-6. PMID: 35550514; PMCID: PMC9098516.

Publications—2022 continued

Toward Reduction in False-Positive Thyroid Nodule Biopsies with a Deep Learning-based Risk Stratification System Using US Cine-Clip Images. Yamashita R, Kapoor T, Alam MN, Galimzianova A, Syed SA, Ugur Akdogan M, Alkim E, Wentland AL, Madhuripan N, Goff D, Barbee V, Sheybani ND, Sagreiya H, Rubin DL, Desser TS. Radiol Artif Intell. 2022 May 11;4(3): e210174. doi: 10.1148/ryai.210174. PMID: 35652118; PMCID: PMC9152684.

Recommendations for Reporting Therapeutic Ultrasound Treatment Parameters. Padilla F, Ter Haar G. Ultrasound Med Biol. 2022 Jul;48(7):1299-1308. doi: 10.1016/j.ultrasmedbio.2022.03.001. Epub 2022 Apr 21. PMID: 35461726.

Magnetic resonance imaging-guided focused ultrasound thalamotomy for essential tremor: 5-year follow-up results. Cosgrove GR, Lipsman N, Lozano AM, Chang JW, Halpern C, Ghanouni P, Eisenberg H, Fishman P, Taira T, Schwartz ML, McDannold N, Hayes M, Ro S, Shah B, Gwinn R, Santini VE, Hynynen K, Elias WJ. J Neurosurg. 2022 Aug 5:1-6. doi: 10.3171/2022.6.JNS212483. Epub ahead of print. PMID: 35932269.

Comparison between MR and CT imaging used to correct for skull-induced phase aberrations during transcranial focused ultrasound. Leung SA, Moore D, Gilbo Y, Snell J, Webb TD, Meyer CH, Miller GW, Ghanouni P, Butts Pauly K. Sci Rep. 2022 Aug 4;12(1):13407. doi: 10.1038/s41598-022-17319-4. PMID: 35927449; PMCID: PMC9352781.

Patient-Reported Outcomes and Predictive Factors following Focused Ultrasound Thalamotomy for Essential Tremor. Moosa S, Craver A, Asuzu D, Eames M, Wang TR, Elias WJ. Stereotact Funct Neurosurg. 2022;100(5-6): 291-299. doi: 10.1159/000525763. Epub 2022 Aug 26. PMID: 36030772.

Cytoreductive Surgical Treatment of Pleural Mesothelioma in a Porcine Model Using Magnetic-Resonance-Guided Focused Ultrasound Surgery (MRgFUS) and Radiofrequency Ablation (RFA). Costa M, Fernandes C, Eames M, Hananel A, Mugler JP 3rd, Huaromo J, Yang JB, Mata J. Tomography. 2022 Sep 3;8(5):2232-2242. doi: 10.3390/tomography8050187. PMID: 36136883; PMCID: PMC9498358.

Enhanced Stable Cavitation and Nonlinear Acoustic Properties of Poly (butyl cyanoacrylate) Polymeric Microbubbles after Bioconjugation. Barmin RA, Dasgupta A, Rix A, Weiler M, Appold L, Rütten S, Padilla F, Kuehne AJC, Pich A, De Laporte L, Kiessling F, Pallares RM, Lammers T. ACS Biomater Sci Eng. 2022 Oct 31. doi: 10.1021/acsbiomaterials.2c01021. Epub ahead of print. PMID: 36315422.

Iron-based coupling media for MRI-guided ultrasound surgery. Allen SP, Fergusson A, Edsall C, Chen S, Moore D, Vlaisavljevich E, Davis RM, Meyer CH. Med Phys. 2022 Dec;49(12):7373-7383. doi: 10.1002/mp.15979. Epub 2022 Nov 7. PMID: 36156266; PMCID: PMC9946126.

Low-Cost Thermochromic Quality Assurance Phantom for Therapeutic Ultrasound Devices: A Proof of Concept. Eames M, Larrabee Z, Hananel A, Padilla F, Aubry JF. Ultrasound Med Biol. 2023 Jan;49(1):269-277. doi: 10.1016/j.ultrasmedbio.2022.09.001. Epub 2022 Oct 27. PMID: 36441031.

Ultrasound Elastography in Neurosurgery: Current Applications and Future Perspectives. Albakr A, Ben-Israel D, Yang R, Kruger A, Alhothali W, Al Towim A, Lama S, Ajlan A, Riva-Cambrin J, Prada F, Al-Habib A, Sutherland GR. World Neurosurg. 2023 Feb;170:195-205.e1. doi: 10.1016/j.wneu.2022.10.108. Epub 2022 Nov 4. PMID: 36336268.

University of Virginia Health System continued

The University of Virginia Focused Ultrasound Cancer Immunotherapy Center Charlottesville, VA

In 2022, UVA Health and the Focused Ultrasound Foundation launched the Focused Ultrasound Cancer Immunotherapy Center, the world's first center dedicated specifically to advancing a focused ultrasound and cancer immunotherapy treatment approach that could revolutionize 21st-century cancer care. The center is designed to capitalize on UVA's strengths including cancer immunotherapy, focused ultrasound, and medical imaging.

Research not involving thermal ablation, tissue destruction	
Clinical research - Gastrointestinal	
Esophageal tumors	Thermal ablation - Immunomodulation
Gastric tumors	Thermal ablation - Immunomodulation
Clinical research - Miscellaneous	
Melanoma	Thermal ablation - Immunomodulation
Multiple tumors[1]	Thermal ablation - Immunomodulation
Clinical research - Pulmonary	
Lung cancer	Thermal ablation - Immunomodulation
Clinical research - Women's health	
Breast tumors, malignant	Nonthermal - Immunomodulation
Cervical tumors	Thermal ablation - Immunomodulation
Ovarian tumors	Thermal ablation - Immunomodulation
Preclinical research - Gastrointestinal	
Pancreatic tumors, malignant	Thermal ablation - Immunomodulation
Preclinical research - Miscellaneous	
Melanoma	Thermal ablation - Immunomodulation
Preclinical research - Neurological	
Brain metastases, breast cancer	Nonthermal, BBB opening - Drug delivery; immunotherapeutic Nonthermal - Immunomodulation
Brain metastases, melanoma	Nonthermal, BBB opening - Drug delivery; immunotherapeutic Nonthermal - Immunomodulation
Brain tumors, general	Nonthermal, BBB opening - Gene delivery
Glioblastoma	Nonthermal, BBB opening - Gene delivery Nonthermal - Immunomodulation
Preclinical research - Women's health	
Breast tumors, malignant	Thermal ablation - Immunomodulation

Mechanisms of action research	
Histotripsy	Immune cell trafficking, Immunomodulation
Nonthermal	BBB opening, immune cell delivery; Drug delivery, immunotherapeutic; Immune cell delivery; Immune cell trafficking; Immunomodulation
Thermal ablation	Immunomodulation

1 Inclusive of more than one indication

Publications—2022 continued

Profiling of the immune landscape in murine glioblastoma following blood brain/tumor barrier disruption with MR image-guided focused ultrasound. Sheybani ND, Witter AR, Garrison WJ, Miller GW, Price RJ, Bullock TNJ. J Neurooncol. 2022 Jan;156(1):109-122. doi: 10.1007/s11060-021-03887-4. Epub 2021 Nov 3. PMID: 34734364; PMCID: PMC8714701.

Sonodynamic therapy for gliomas. Bunevicius A, Pikis S, Padilla F, Prada F, Sheehan J. J Neurooncol. 2022 Jan;156(1):1-10. doi: 10.1007/s11060-021-03807-6. Epub 2021 Jul 12. PMID: 34251601.

Focused ultrasound for the treatment of glioblastoma. Roberts JW, Powlovich L, Sheybani N, LeBlang S. J Neurooncol. 2022 Apr;157(2):237-247. doi: 10.1007/s11060-022-03974-0. Epub 2022 Mar 10. PMID: 35267132; PMCID: PMC9021052.

Sonodynamic therapy: Rapid progress and new opportunities for non-invasive tumor cell killing with sound. Nowak KM, Schwartz MR, Breza VR, Price RJ. Cancer Lett. 2022 Apr 28;532:215592. doi: 10.1016/j.canlet.2022.215592. Epub 2022 Feb 11. PMID: 35151824; PMCID: PMC8918024.

Letter to the editor regarding Translation of focused ultrasound for blood-brain barrier opening in glioma. Price RJ, Bullock TNJ, Sheybani ND. J Control Release. 2022 Sep;349:16-17. doi: 10.1016/j.jconrel.2022.06.041. Epub 2022 Jul 4. PMID: 35780955.

Applications of focused ultrasound-mediated blood-brain barrier opening. Gorick CM, Breza VR, Nowak KM, Cheng VWT, Fisher DG, Debski AC, Hoch MR, Demir ZEF, Tran NM, Schwartz MR, Sheybani ND, Price RJ. Adv Drug Deliv Rev. 2022 Dec;191:114583. doi: 10.1016/j.addr.2022.114583. Epub 2022 Oct 19. PMID: 36272635; PMCID: PMC9712235.

Combination of Focused Ultrasound, Immunotherapy, and Chemotherapy: New Perspectives in Breast Cancer Therapy. Dahan M, Cortet M, Lafon C, Padilla F. J Ultrasound Med. 2023 Feb;42(3):559-573. doi: 10.1002/jum.16053. Epub 2022 Jul 23. PMID: 35869903.

2023 Awareness

Focused Ultrasound Foundation

Overview

This chapter includes an overview of the number of presentations and publications that were presented at scientific symposia or journals in 2022. We continue to see growth in the absolute numbers of abstracts and publications, where these abstracts are presented, and new journals publishing focused ultrasound articles. The largest growth of presented abstracts is occurring within the physician specialty societies, and thus indicates a wider exposure of focused ultrasound research and rising levels of interest from practicing clinicians. This is an encouraging trend, and we are hopeful it will lead to increased patient access to the technology in future years.

Additionally, the increasing transparency and openness practices (TOP) within the scientific publishing field are gaining momentum. This means that clinicians and researchers who are new to focused ultrasound have increasing access to the body of focused ultrasound scientific literature–entire articles, not just the abstract. As a result of open access publishing, a simple search allows readers instant access, whereas previously, often the information/full article were restricted behind a pay wall available only to subscribers.

This chapter emphasizes awareness for the scientific community, but we would be remiss if we did not also mention that in May 2022 National Geographic ran a lead story, "New Method Delivers Life-Saving Drugs to the Brain–Using Sound Waves." The story provides an in-depth look at focused ultrasound for drug delivery, blood-brain barrier opening, and more. It can be found here: nationalgeographic.co.uk/science-and-technology/2022/05/new-method-delivers-life-saving-drugs-to-the-brain-using-sound-waves

VI. Awareness

VI. 2 Overview

Abstracts

VI. 3 Presented at FUS Meetings
VI. 3 Presented at Other Symposia

Publications

VI. 5 FUS Publications
VI. 5 FUS Publications and Citations
VI. 6 Cumulative Top Twenty-five Source Titles
VI. 7 2022 Top Source Titles
VI. 8 Cumulative Top Twenty-five Research Areas
VI. 9 2022 Top Ten Research Areas

Abstracts Presented at FUS Meetings

Meetings	2017	2018	2019	2020	2021	2022
Focused Ultrasound Foundation Symposium, FUSF[1]	–	250	–	257	–	202
International Symposium on Therapeutic Ultrasound, ISTU[2]	207	257	197	*	241	281
iTRUSST Focused Ultrasound Neuromodulation	–	–	–	–	60	35
Totals	**207**	**507**	**197**	**257**	**301**	**518**

FUS Abstracts Presented at Other Symposia

Symposium	2017	2018	2019	2020	2021	2022
Acoustical Society of America	48	39	22	13	30	76
American Association for Cancer Research	–	–	–	7	5	7
American Association of Neurological Surgeons[3]	–	–	–	–	–	9
American Association of Physicists in Medicine	16	5	7	6	4	3
American Epilepsy Society[3]	–	–	–	–	–	7
American Institute of Ultrasound in Medicine	–	9	6	*	5	12
American Society of Clinical Oncology	–	–	–	4	1	–
American Society for Radiation Oncology	5	3	–	2	2	3
American Society for Stereotactic and Functional Neurosurgery	–	6	–	*	–	9
American Urological Association	7	4	16	*	5	13
Biomedical Engineering Society	16	14	26	9	7	1
Cardiovascular and Interventional Radiology Society of Europe	–	–	–	10	8	6
Congress of Neurological Surgeons[3]	–	–	–	–	–	7
European Association of Neuro Oncology[3]	–	–	–	–	–	3
European Association of Urology	–	–	–	5	6	6
European Conference on Interventional Oncology	–	–	–	–	7	2
European Congress of Radiology	13	22	10	15	2	3

1 Held biennially
2 In 2019 the European Symposium on Focused Ultrasound, EUFUS, combined with the International Symposium on Therapeutic Ultrasound, ISTU and is now held under the title of ISTU.
3 New meetings being followed as of 2022 for focused ultrasound content.
* Cancelled due to COVID-19 pandemic.

FUS Abstracts Presented at Other Symposia continued

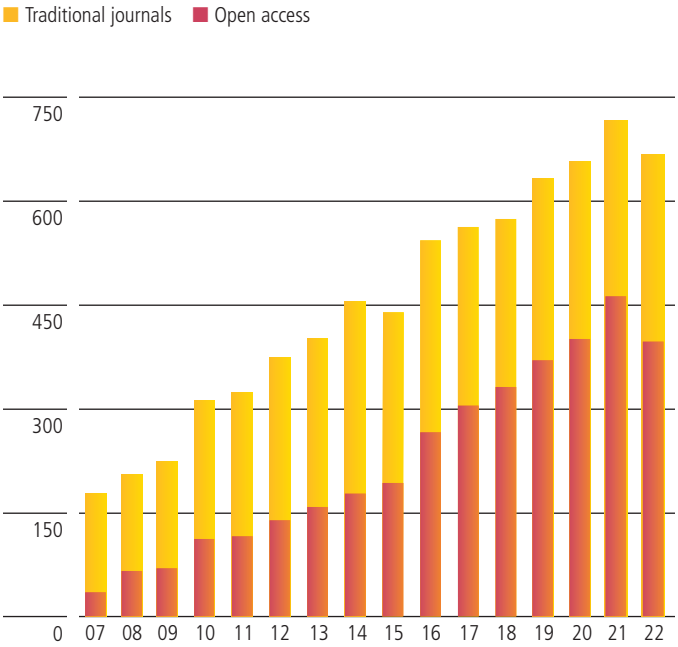
Symposium	2017	2018	2019	2020	2021	2022
European Society of Hyperthermic Oncology[3]	–	–	–	–	–	9
IEEE International Engineering in Medicine and Biology	5	11	11	2	2	1
IEEE International Ultrasonics Symposium	71	19	49	57	72	45
International Skeletal Society[3]	–	–	–	–	–	1
International Bubble Conference[3]	–	–	–	–	–	2
International Society for Magnetic Resonance in Medicine	–	–	–	33	12	32
International Stereotactic Radiosurgery Society[3]	–	–	–	–	–	6
Japanese Society for Therapeutic Ultrasound	39	35	48	52	*	–
Korean Society for Therapeutic Ultrasound	15	17	22	6	–	29
Radiological Society of North America	17	14	26	7	4	26
Society for Thermal Medicine	10	10	9	*	5	10
Society of Interventional Radiology	2	1	5	*	3	21
Society of Neuro-Oncology[3]	–	–	–	–	–	10
Society of Pediatric Interventional Radiology[3]	–	–	–	–	–	2
Taiwan Associated of Interventional Therapeutic Ultrasound	–	–	12	5	9	8
World Society for Stereotactic and Functional Neurosurgery[3]	–	–	–	–	–	25
Totals	**243**	**260**	**222**	**273**	**189**	**394**

In 2022 abstracts presented at scientific meetings rebounded to growth similar to pre-pandemic levels. This year we started tracking 12 new meetings. 81 abstracts presented at these scientific meetings along with 313 abstracts at other symposia and an additional 518 abstracts as focused ultrasound specific meetings leads to a whooping total of 912 abstracts. The largest growth in abstracts is happening in physician specialty societies. This tracks well with our noted transition of the field from preclinical to first-in-human research.

3 New meetings being followed as of 2022 for focused ultrasound content.

* Cancelled due to COVID-19 pandemic.

FUS Publications*



* New source in 2022: Web of Science Core Collection as of February 14, 2023

FUS Publications and Citations*

Cumulative

8,377
FUS publications

234,640
Citations of FUS publications

2022

677
FUS publications

26,848
Citations of FUS publications

* New source in 2022: Web of Science Core Collection as of February 14, 2023

Readers will note that our numbers for publications and citations have changed from last year's report. This year we used a new indexed data source, Web of Science Core Collection, while reports from previous years were restricted to search in the Medline database.

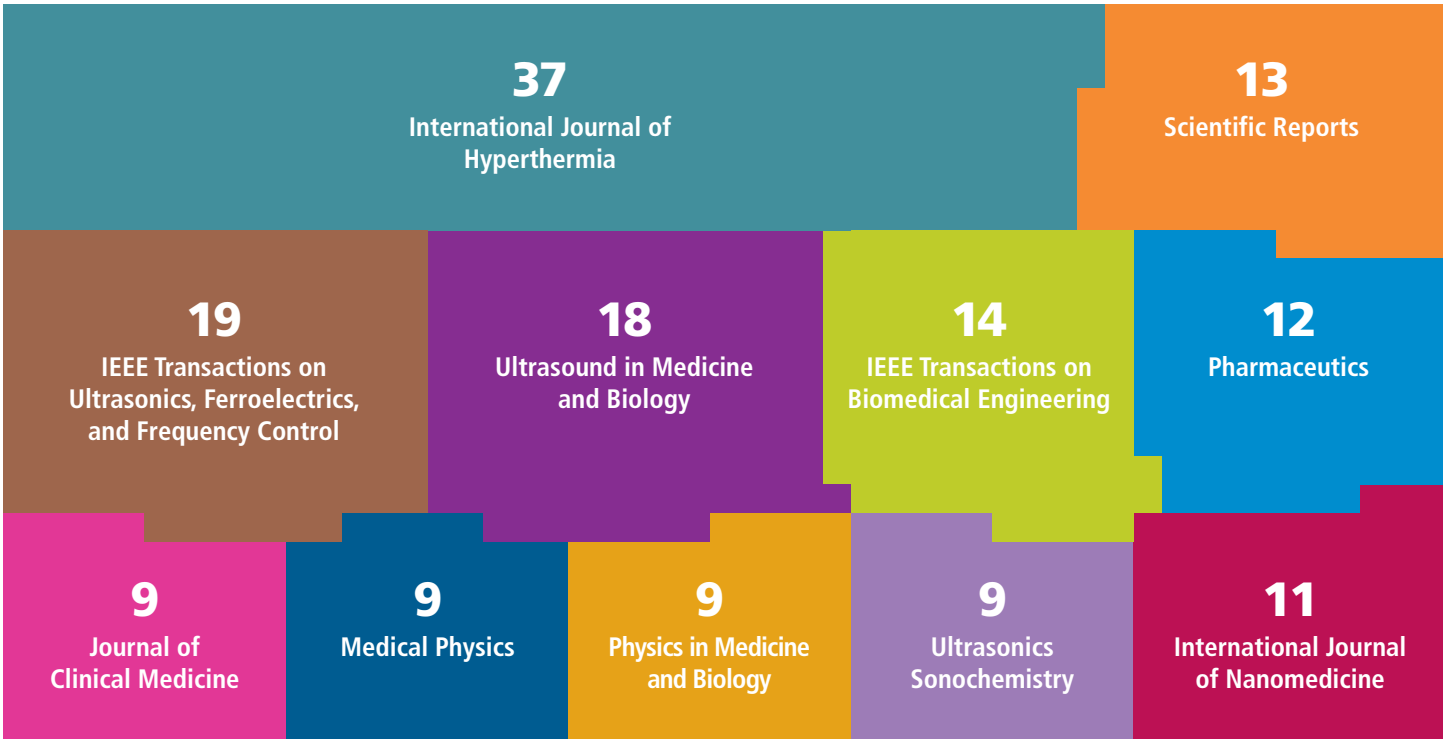
Publications—Cumulative Top Twenty-five Source Titles

Records	Scientific publication titles
577	Ultrasound in Medicine and Biology
336	International Journal of Hyperthermia
277	IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control
257	Physics in Medicine and Biology
185	Journal of the Acoustical Society of America
164	Medical Physics
151	Ultrasonics
143	Journal of Controlled Release
143	Scientific Reports
135	Magnetic Resonance in Medicine
120	Ultrasonics Sonochemistry
111	IEEE Transactions on Biomedical Engineering
108	Japanese Journal of Applied Physics
96	Plos One
73	European Radiology
73	Radiology
71	Journal of Neurosurgery
70	Theranostics
68	Journal of Ultrasound in Medicine
61	Journal of Urology
60	Journal of Magnetic Resonance Imaging JMRI
58	BJU International
55	Journal of Endourology
53	Applied Physics Letters
51	European Urology

* New source in 2022: Web of Science Core Collection as of February 14, 2023

Of interest, the Transparency and Openness Promotion, TOP, scores for the journals on our list of 2022 top source titles, page VI.7, have increased significantly in several journals. We are hopeful this trend will continue as we strongly believe open science practices are good for the focused ultrasound research community.

Publications—2022 Top Source Titles



Publications—2022 Top Source Titles

Records	Impact factor	TOP score '21	TOP score '22	Scientific publication titles	
37	3.8	1	4	International Journal of Hyperthermia	
19	3.3	1	1	IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control	
18	3.7	2	4	Ultrasound in Medicine and Biology	
14	4.8	0	0	IEEE Transactions on Biomedical Engineering	
13	5.0	13	14	Scientific Reports	
12	6.5	9	9	Pharmaceutics	
11	7.0	3	3	International Journal of Nanomedicine	
9	5.0	—	10	Journal of Clinical Medicine	tie
9	4.5	1	1	Medical Physics	tie
9	4.2	1	2	Physics in Medicine and Biology	tie
9	9.3	1	2	Ultrasonics Sonochemistry	tie

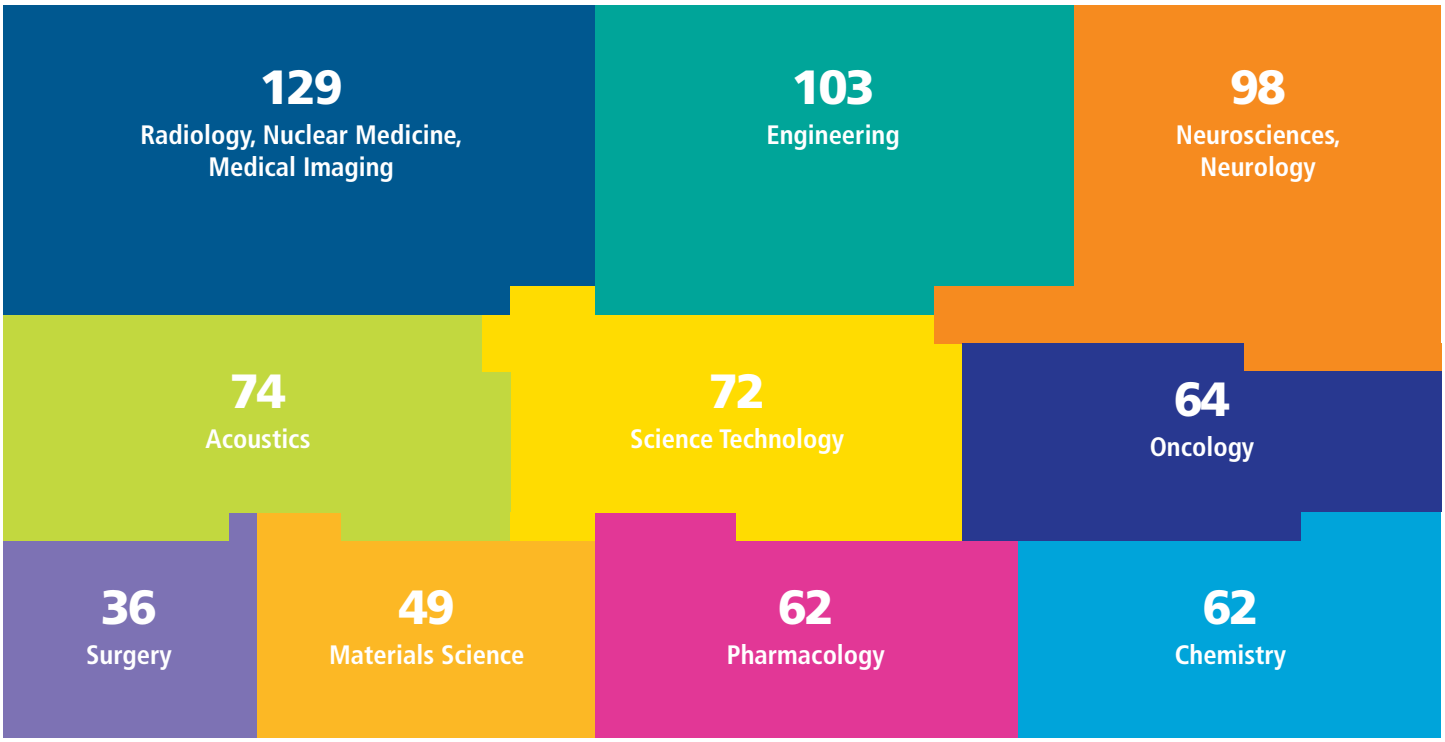
* New source in 2022: Web of Science Core Collection as of February 14, 2023

Publications—Cumulative Top Twenty-five Research Areas

Records	Scientific research areas
2659	Radiology, Nuclear Medicine, Medical Engineering
1551	Acoustics
1226	Engineering
749	Oncology
650	Science Technology
644	Neurosciences, Neurology
627	Chemistry
521	Physics
503	Surgery
479	Urology, Nephrology
431	Materials Science
405	Pharmacology
304	Research, Experimental Medicine
204	Obstetrics, Gynecology
200	Biochemistry, Molecular Biology
188	Audiology, Speech Language, Pathology
716	Dermatology
168	Cardiology
132	Computer Science
131	General Internal Medicine
115	Optics
111	Biophysics
101	Instrumentation
86	Biotechnology, Applied Microbiology
67	Cell Biology

* New source in 2022: Web of Science Core Collection as of February 14, 2023

Publications—2022 Top Ten Research Areas



Publications—2022 Top Ten Research Areas

Records	Scientific research areas
129	Radiology, Nuclear Medicine, Medical Imaging
103	Engineering
98	Neurosciences, Neurology
74	Acoustics
72	Science Technology
64	Oncology
62	Chemistry (tie)
62	Pharmacology (tie)
49	Materials Science
36	Surgery

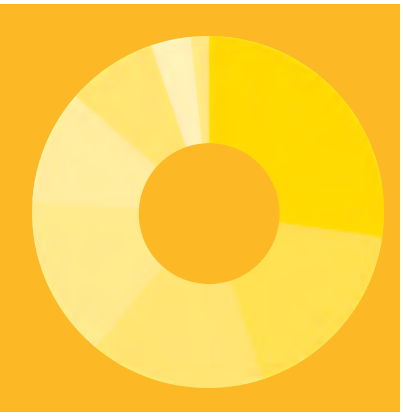
* New source in 2022: Web of Science Core Collection as of February 14, 2023

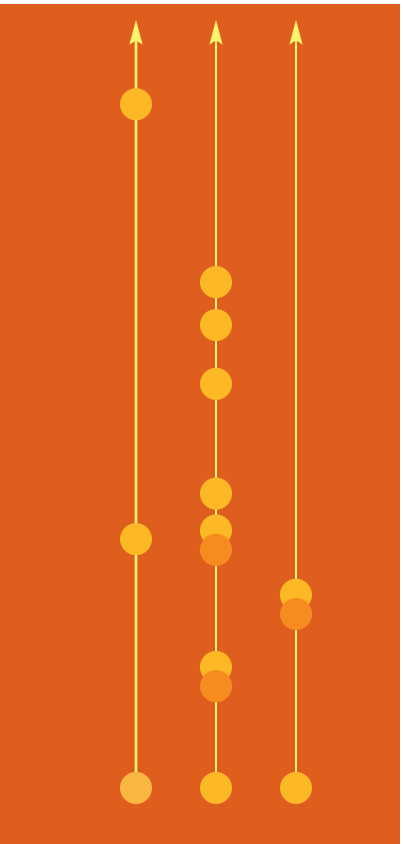
2023 Patient Access

Focused Ultrasound Foundation

Overview

In 2022, with nearly 100,000 patients treated, the field exceeded 500,000 cumulative patient treatments. Pancreatic cancer is the leading cancer indication for focused ultrasound treatments in 2022. Urological and women's health are the two body systems that have the most treatment sites with more than 500 each. This is not surprising as prostate disease and uterine fibroids were some of the earliest indications to have regulatory approval around the world.





VII. Patient Access

VII. 2 Overview
VII. 3 Treatment Highlights

Commercial Treatments

VII. 4 Sites by Region
VII. 5 Sites by Country

Patient Treatments

VII. 6 By Indication
- VII. 6 Cumulative
- VII. 7 2022
- VII. 7 Annual

VII. 8 Oncology Treatments by Indication
- VII. 8 Cumulative
- VII. 9 2022
- VII. 9 Annual

VII.10 Brain Treatments by Indication
- VII.10 Cumulative
- VII.11 2022
- VII.11 Annual

VII.12 Other Treatments by Indication
- VII.12 Cumulative
- VII.13 2022

Treatment Sites

VII.14 By Indication and Body System
VII.15 By Indication and Region
- VII.15 Cardiovascular
- VII.15 Endocrine disorders
- VII.16 Gastrointestinal
- VII.16 Musculoskeletal
- VII.17 Neurological
- VII.18 Ophthalmological
- VII.18 Urological
- VII.19 Women's health

Treatment Highlights

2022

A leading indication

24,000

Pancreatic cancer treatments

Body systems with the most treatment sites

568

Urological
3 indications

549

Women's health
9 indications

Commercial Treatment Sites by Region

Number of Sites

2022

932

Commercial Treatment Sites

219
North America
25% Annual Growth from 2013–2022

290
Europe
4% Annual Growth from 2013–2022

405
Asia
12% Annual Growth from 2013–2022

7
South America
4% Annual Growth from 2013–2022

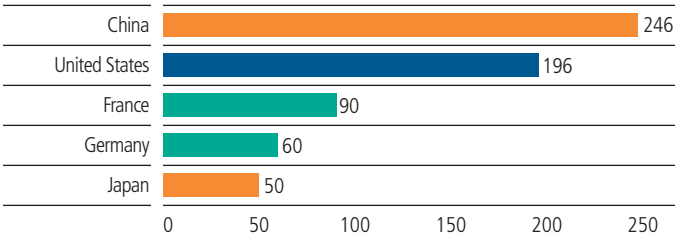
4
Oceania
19% Annual Growth from 2013–2022

7
Africa
15% Annual Growth from 2013–2022

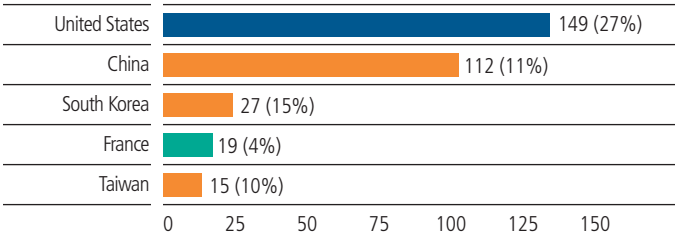
Top Countries

2022

Top Countries for Treatment
Number of sites



Top Countries with Commercial Treatment Growth
Sites added, cumulative 2017 to 2022



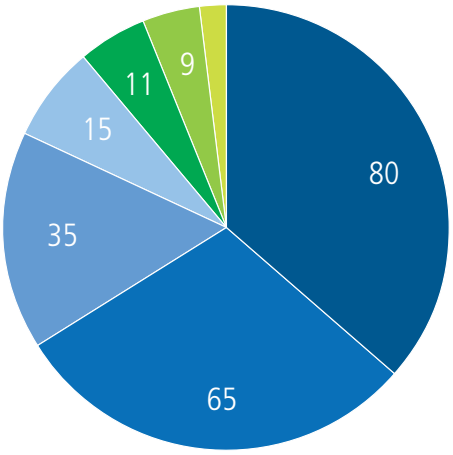
In 2022 there were 32 new commercial treatment sites of which 28 were in the United States. While China remains the top country in the world for commercial treatment with 246 sites, the United States is quickly closing the gap with 196 sites.

Commercial Treatment Sites by Country

North America

219

Treatment Sites



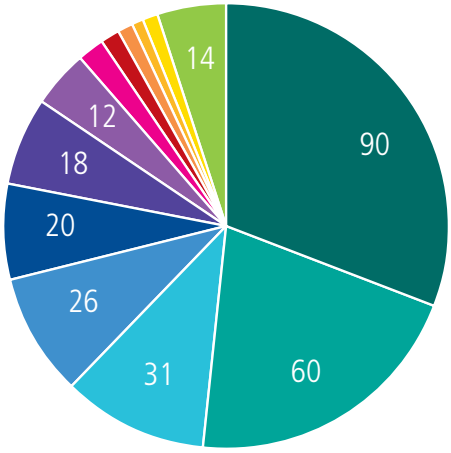
US, Central	80
Eastern	65
Pacific	35
Mountain	15
Canada	11
Mexico	9
Other*	4

*Cayman Islands, Cuba, Dominica, and Dominican Republic

Europe

290

Treatment Sites



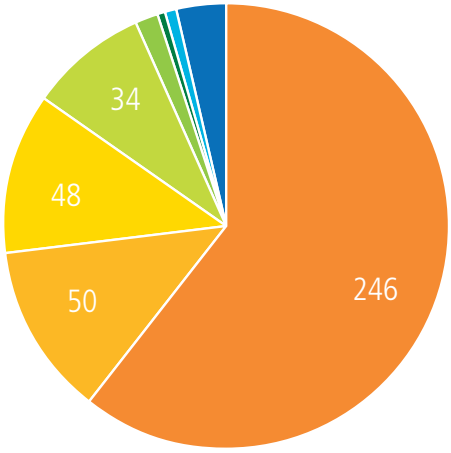
France	90
Germany	60
Russian Federation	31
Italy	26
United Kingdom	20
Spain	18
Switzerland	12
Poland	6
The Netherlands	4
Greece	3
Norway	3
Turkey	3
Other*	14

*Austria, Belgium, Bulgaria, Czech Republic, Denmark, Finland, Georgia, Latvia, Monaco, Portugal, Romania, and Ukraine

Asia

405

Treatment Sites



China	246
Japan	50
South Korea	48
Taiwan	34
India	7
Israel	3
Thailand	3
Other*	14

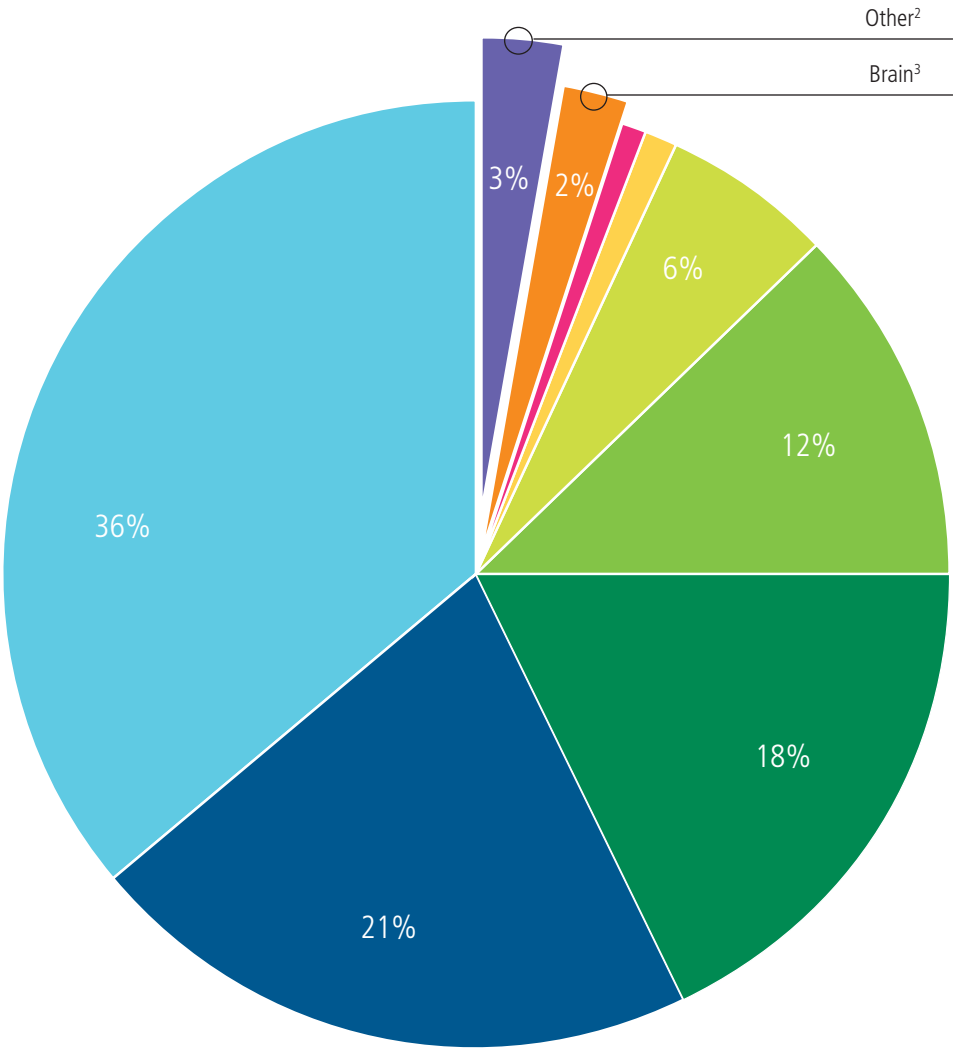
*Kazakhstan, Iran, Lebanon, Malaysia, Myanmar, Philippines, Qatar, Singapore, Uzbekistan, and Vietnam

Patient Treatments by Indication—Cumulative

565,210 total treatments[1]

Uterine fibroids	201,084	36%
Liver tumors	121,435	21%
Prostate diseases	99,010	18%
Pancreatic tumors	70,246	12%
Uterine adenomyosis	33,518	6%
Other[2]	15,838	3%
Brain[3]	12,340	2%
Glaucoma	6,179	1%
Cancer, unspecified	5,560	1%

All indications



2022 was the biggest year for pancreatic cancer treatments to date with 24,000 patients treated last year.

1 The number of patient treatments reported is lower than the actual number of procedures because of incomplete reporting from manufacturers and treatment sites. Companies reporting patient treatment values this year were: Arrayus, Cardiawave, CarThera, EDAP TMS, EpiSonica, FUSMobile, HistoSonics, Insightec, NaviFUS, Profound Medical, Shanghai A&S, Shenzhen PRO-HITU Medical, Sonablate, Theraclion, TOOsonix, and VeinSound.

2 For an expanded list of these indications, please refer to Cumulative Other Treatments by Indication, on p. VII.12.

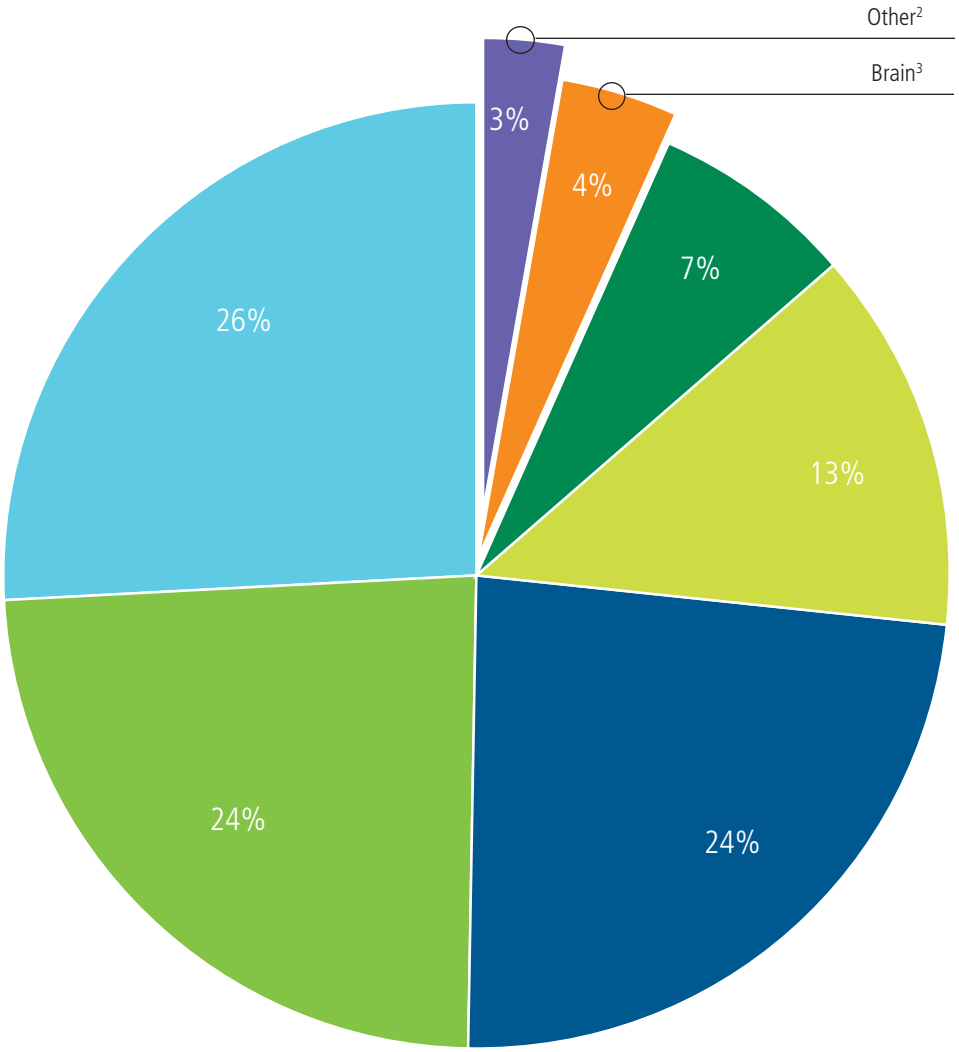
3 For an expanded list of these indications, please refer to Cumulative Brain Treatments by Indication, on p. VII.10.

Patient Treatments by Indication—2022

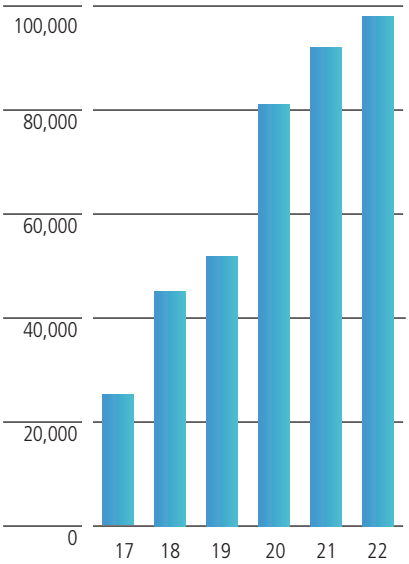
98,048 total treatments[1]

Uterine fibroids	25,273	26%
Pancreatic tumors	24,000	24%
Liver tumors	23,421	24%
Uterine adenomyosis	12,362	13%
Prostate diseases	6,385	7%
Other[2]	2,684	3%
Brain[3]	3,923	4%
– Glaucoma	—	—
– Cancer, unspecified	—	—

All indications



Annual Patient Treatments



1 The number of patient treatments reported is lower than the actual number of procedures because of incomplete reporting from manufacturers and treatment sites. Companies reporting patient treatment values this year were: Arrayus, Cardiawave, CarThera, EDAP TMS, EpiSonica, FUSMobile, HistoSonics, Insightec, NaviFUS, Profound Medical, Shanghai A&S, Shenzhen PRO-HITU Medical, Sonablate, Theraclion, TOOsonix, and VeinSound.

2 For an expanded list of these indications, please refer to Other Treatments by Indication, on p. VII.13.

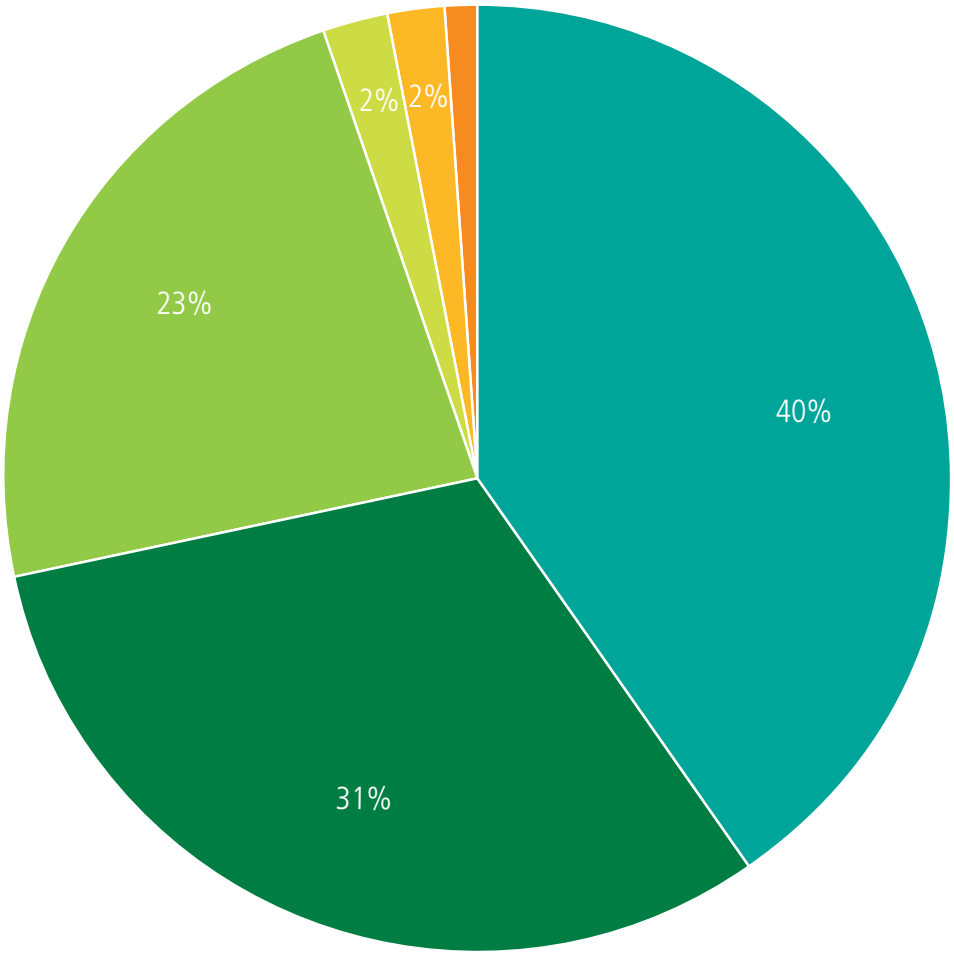
3 For an expanded list of these indications, please refer to Brain Treatments by Indication, on p. VII.11.

Oncology Treatments by Indication—Cumulative

301,528 total treatments

Liver tumors	121,446	40%
Prostate cancer	93,232	31%
Pancreatic tumors	70,246	23%
Cancer, unspecified	5,560	2%
Soft tissue cancer	5,137	2%
Bone metastases	4,064	1%
– Other[1]	1,293	—
– Brain tumors	550	—

Oncology indications



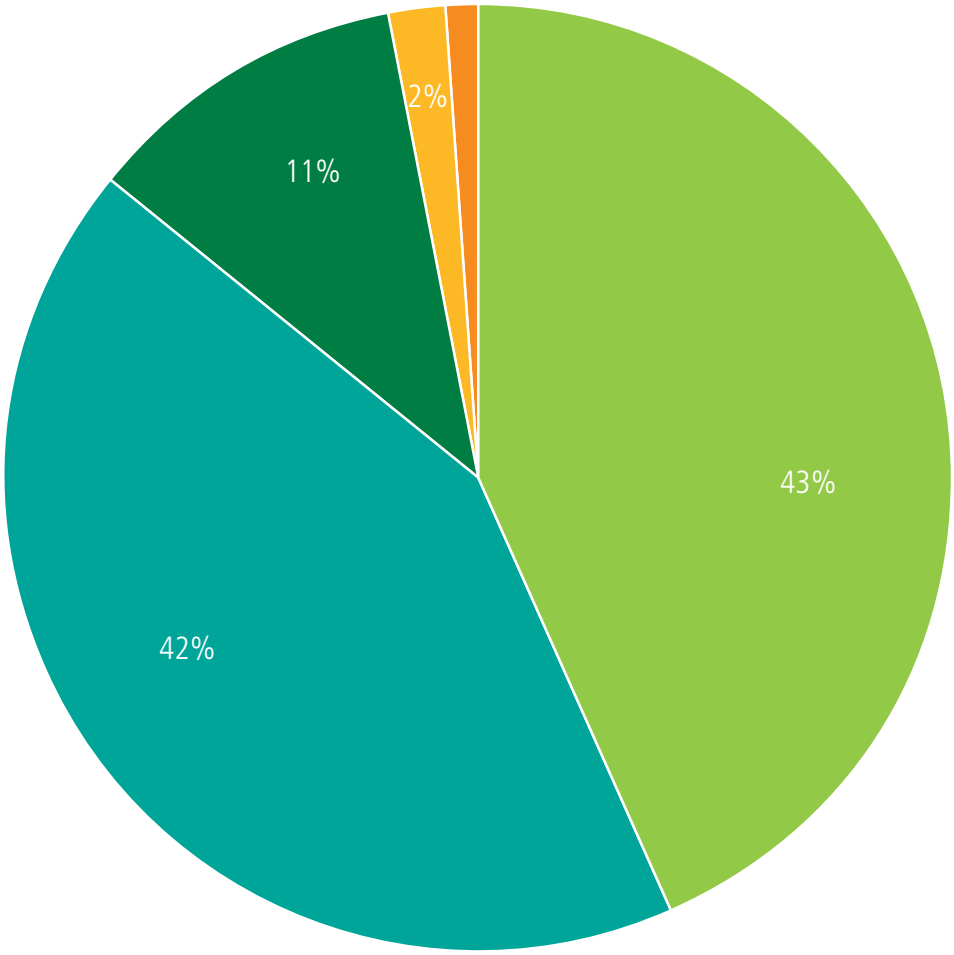
1 Includes, in descending order of patient treatments: breast tumors, malignant; endometrial tumors; neurofibromatosis; kidney tumors; bone cancer; basal cell carcinoma; abdominal paraganglioma; hemangioma; abdominal tumors; granular cell tumors of the gluteals; Kaposi's sarcoma; cervical tumors; sacral chordoma; schwannoma; and spleen tumors

Oncology Treatments by Indication—2022

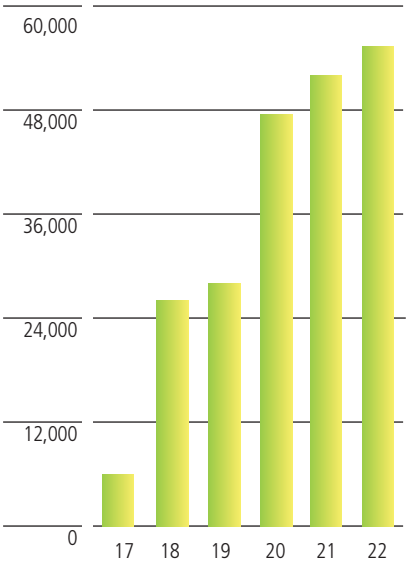
55,386 total treatments

Liver tumors	23,430	42%
Prostate cancer	5,845	11%
Pancreatic tumors	24,000	43%
Soft tissue cancer	1,330	2%
Bone metastases	477	1%
– Other[1]	131	—
– Brain tumors	173	—

Oncology indications



Annual Oncology Treatments



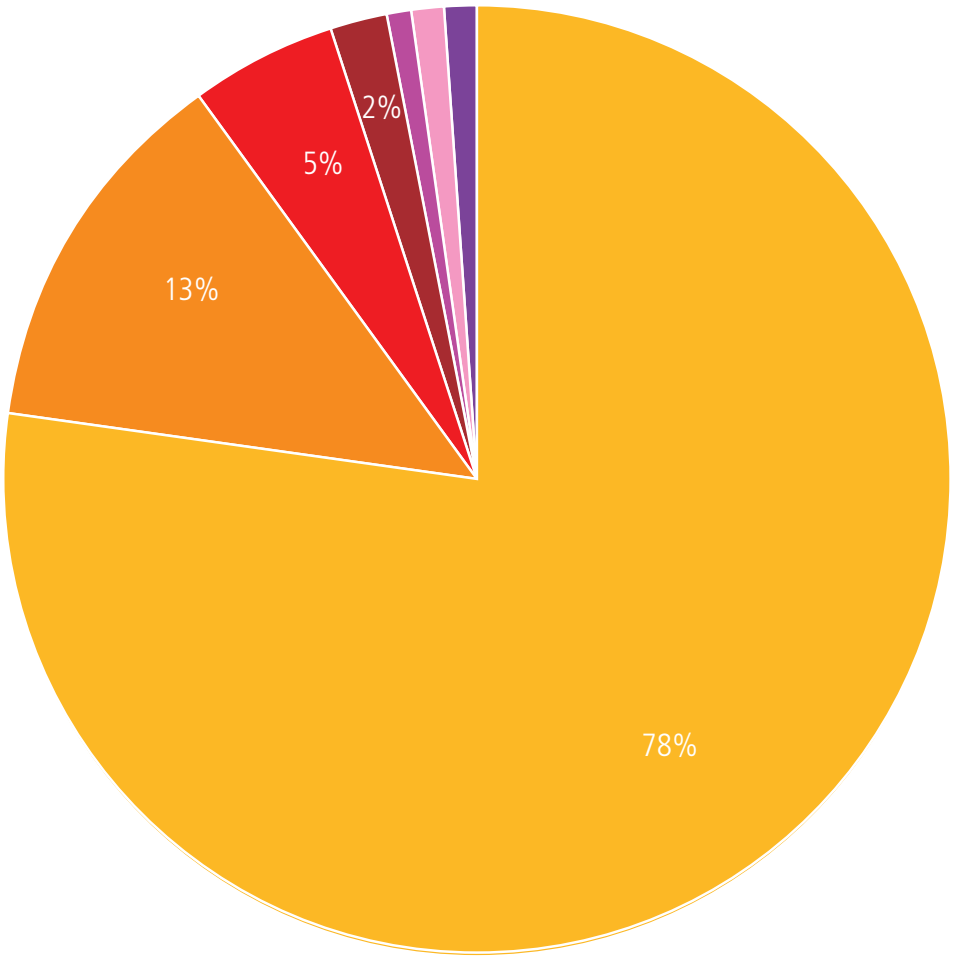
1 Includes, in descending order of patient treatments: endometrial tumors; glioblastoma; brain tumors, general; glioblastoma multiforme; diffuse intrinsic pontine glioma (DIPG); basal cell carcinoma; and bone cancer

Brain Treatments by Indication—Cumulative

12,340 total brain treatments

Essential tremor	9,675	78%
Parkinson's disease	1,544	13%
Brain tumors[1]	550	5%
Neuropathic pain	218	2%
Alzheimer's disease	152	1%
Other movement disorders[2]	91	1%
Mental health[3]	81	1%
Other brain[4]	29	—

Brain indications



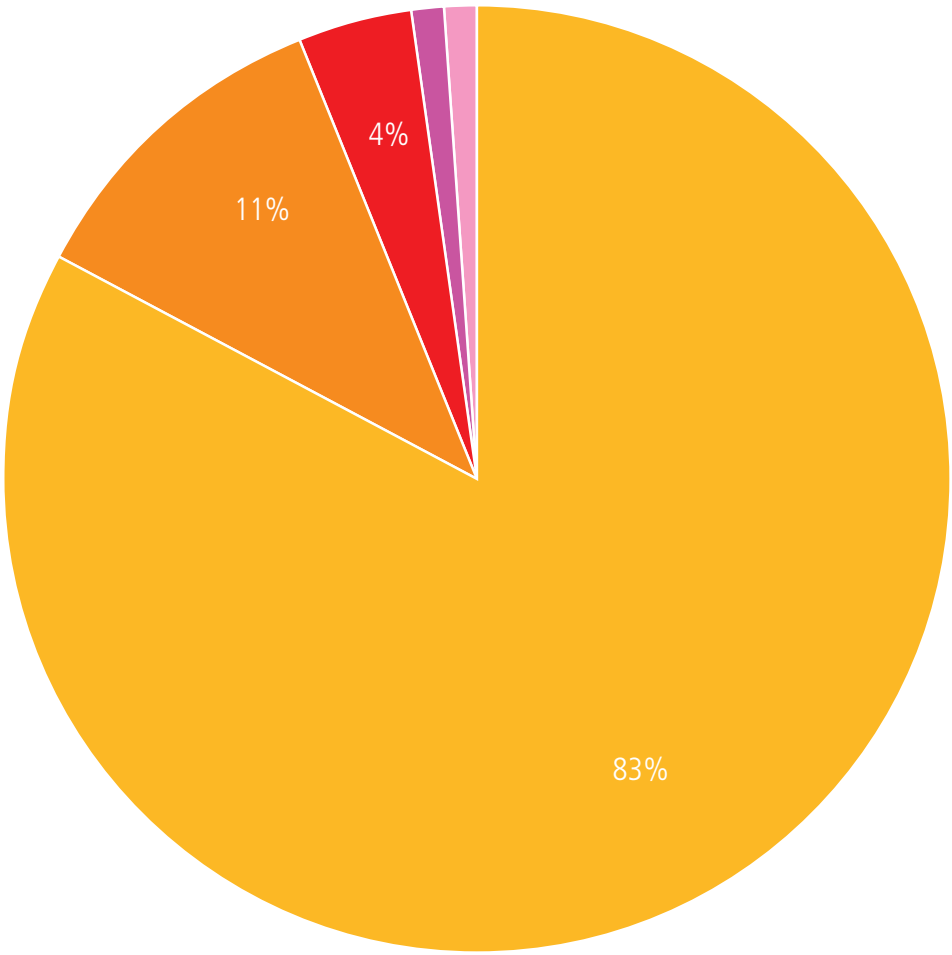
1 Includes, in descending order of patient treatments: glioblastoma; brain tumors, general; astrocytoma; pontine glioma; and ganglioglioma
2 Includes, in descending order of patient treatments: epilepsy; dystonia; and dystonia, hand
3 Includes, in descending order of patient treatments: depression, obsessive compulsive disorder (OCD), and anxiety
4 Includes, in descending order of patient treatments: traumatic brain injury, and blood-brain barrier opening (safety / feasibility)

Brain Treatments by Indication—2022

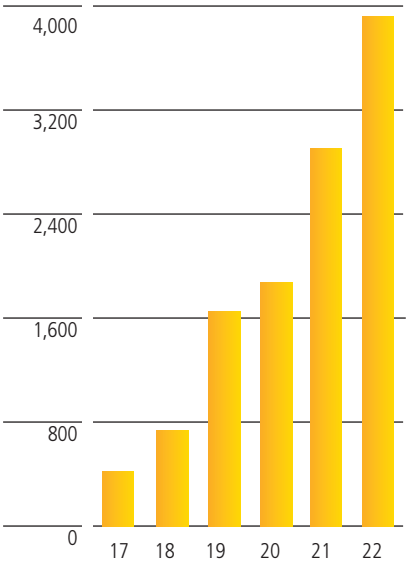
3,923 total brain treatments

Essential Tremor	3,249	83%
Parkinson's disease	446	11%
Brain tumors[1]	173	4%
Neuropathic pain	11	—
Alzheimer's disease	19	1%
Other movement disorders[2]	23	1%
Mental health[3]	2	—
Other	—	—

Brain indications



Annual Brain Treatments



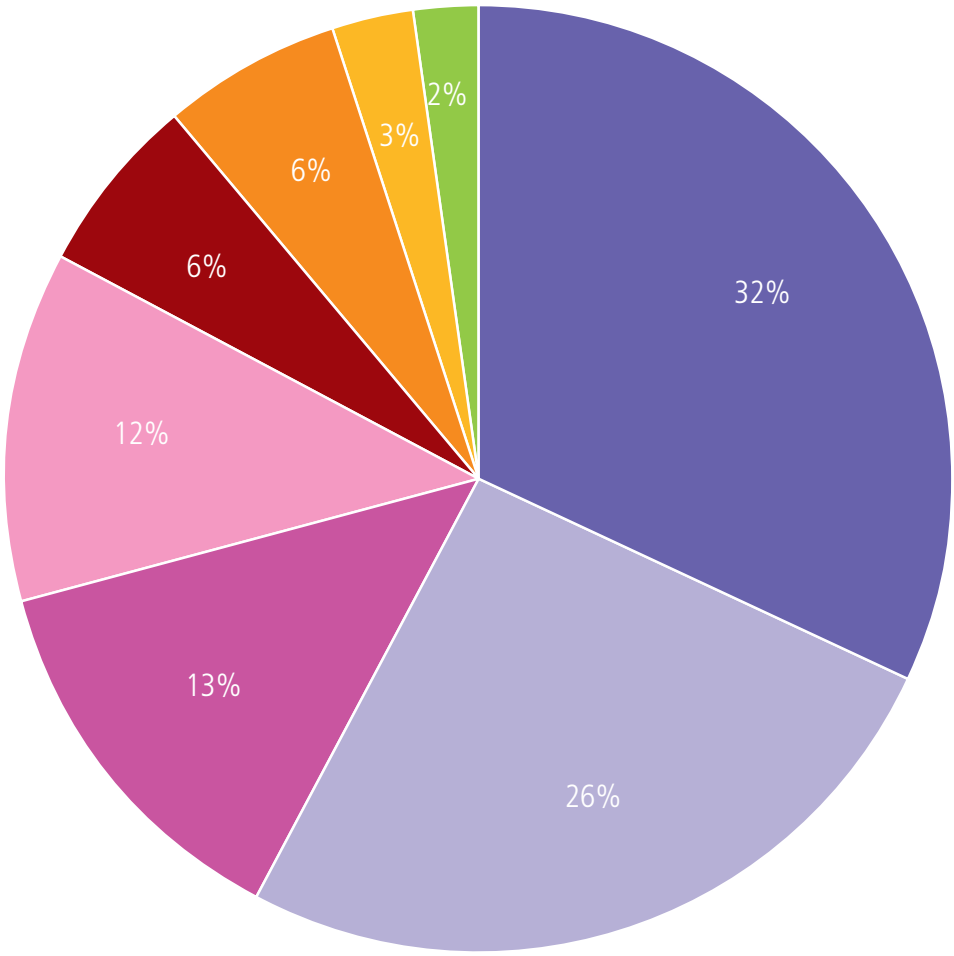
1 Includes, in descending order of patient treatments: glioblastoma and brain tumors, general
2 Includes, in descending order of patient treatments: dystonia, hand; epilepsy; and dystonia
3 Includes, in descending order of patient treatments: obsessive compulsive disorder (OCD)

Other Treatments by Indication—Cumulative

15,838 total treatments

Soft tissue cancer	5,137	32%
Bone metastases	4,064	26%
Thyroid nodules	2,057	13%
Other[1]	1,907	12%
Varicose veins	995	6%
Breast tumors, malignant	916	6%
Arthritis, facetogenic	438	3%
Osteoid osteoma	324	2%

Other indications



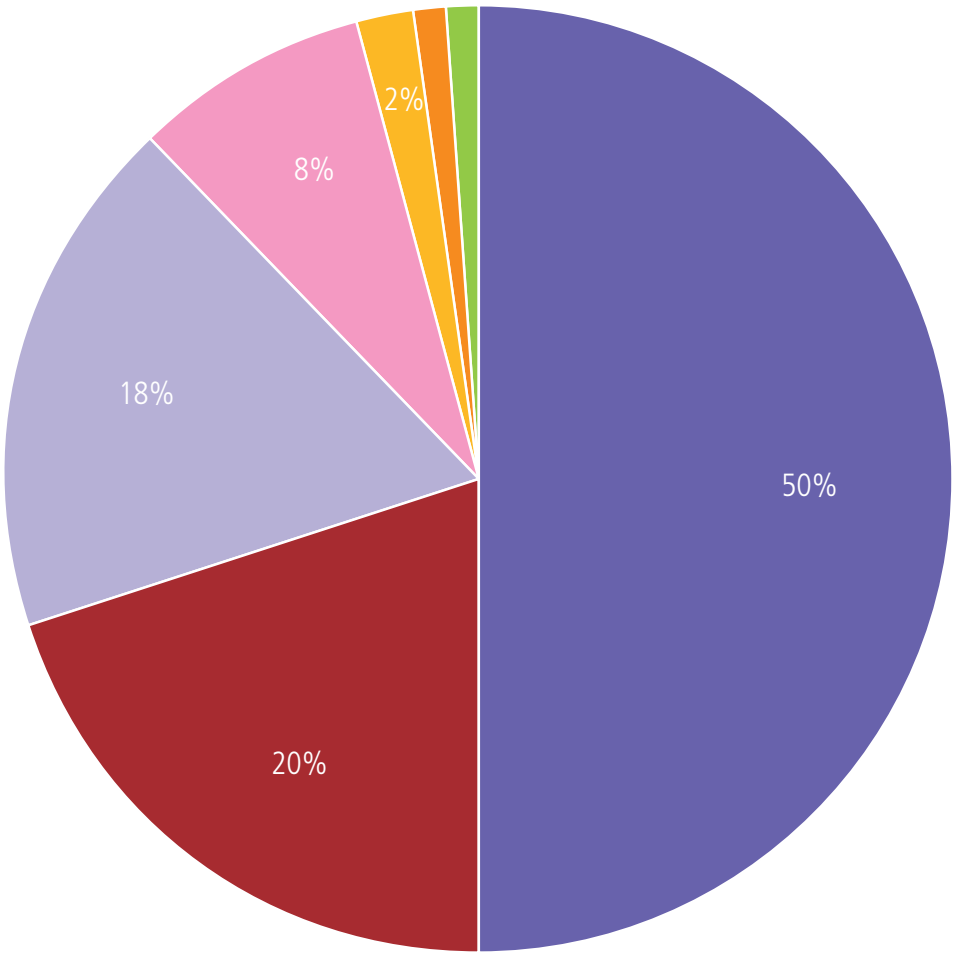
1 Includes, in descending order of patient treatments: breast tumors, benign; endometrial tumors; desmoid tumors; endometriosis; hypertension; heart valve calcifications; hyperparathyroidism; actinic keratosis; arthritis; dermatology research; tattoo removal; neurofibromatosis; bone tumors, benign; kidney tumors; bone cancer; basal cell carcinoma; seborrheic keratosis; vascular malformations and angiomas; painful amputation neuromas; abdominal paraganglioma; hemangioma; peripheral artery disease; Verruca vulgaris; abdominal tumors; amyotrophic lateral sclerosis; arteriovenous malformations; granular cell tumors of the gluteals; Kaposi's sarcoma; cervical tumors; sacral chordoma; schwannoma; soft tissue tumors, benign; and spleen tumors

Other Treatments by Indication—2022

Other indications

2,684 total treatments

Soft tissue cancer	1,330	50%
Bone metastases	477	18%
Thyroid nodules	—	—
Other[1]	217	8%
Varicose veins	550	20%
Breast tumors, malignant	20	1%
Arthritis, facetogenic	60	2%
Osteoid osteoma	30	1%



1 Includes, in descending order of patient treatments: endometrial tumors, desmoid tumors, endometriosis, neurofibromatosis, heart valve calcifications, basal cell carcinoma, and Kaposi's sarcoma

Commercial Treatment Sites by Indication and Body System*

11 Cardiovascular sites 2 indications	**20** Endocrine disorders sites 1 indication	**192** Gastrointestinal sites 6 indications	**248** Musculoskeletal sites 8 indications
179 Neurological sites 13 indications	**14** Ophthalmological sites 1 indication	**568** Urological sites 3 indications	**549** Women's health sites 9 indications

Growth of Commercial Treatment Sites

Neurological Body system with the greatest growth in 2022		United States Country with the greatest growth in 2022	
23 new sites	**179** total sites	**28** new sites	**196** total sites

The area of largest growth in 2022 was neurological sites, with 23 additional sites.

Commercial treatment additional content

For more information about specific commercial treatment sites and indications, please visit:
www.fusfoundation.org/the-technology/treatment-sites
Use the "search by disease" dropdown menu and/or location.

*Indications being performed off label in a region are shown in bold italic. A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary at the top.

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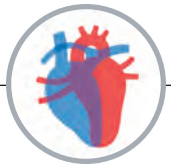
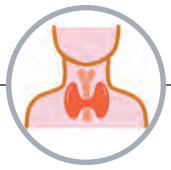
Use the "search by disease" dropdown menu and/or location.

Commercial Treatment Sites by Indication and Region*



Indications	Regions: N. America	Europe	Asia	S. America	Oceania	Africa	Totals
Cardiovascular							
Peripheral							
Arteriovenous malformations	***1***	***1***	–	–	–	–	**2**
Varicose veins	–	9	–	–	–	–	**9**



Indications	Regions: N. America	Europe	Asia	S. America	Oceania	Africa	Totals
Endocrine disorders							
Thyroid nodules	–	13	7	–	–	–	**20**

*Indications being performed off label in a region are shown in bold italic. A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary at the top.

For more information about specific commercial treatment sites and indications, please visit: www.fusfoundation.org/the-technology/treatment-sites. Use the "search by disease" dropdown menu and/or location.

Commercial Treatment Sites by Indication and Region* continued

Indications	Regions: N. America	Europe	Asia	S. America	Oceania	Africa	Totals
Gastrointestinal							
Gastric tumors	–	***1***	–	–	–	–	**1**
Liver metastases	–	–	***2***	–	–	***1***	**3**
Liver tumors	***2***	8	126	–	–	***1***	**137**
Pancreatic tumors	–	–	41	–	–	–	**41**
Pancreatic tumors, benign	–	–	***1***	–	–	–	**1**
Pancreatic tumors, malignant	***1***	3	4	–	–	***1***	**9**

Indications	Regions: N. America	Europe	Asia	S. America	Oceania	Africa	Totals
Musculoskeletal							
Arthritis, facetogenic	***1***	1	1	–	1	–	**4**
Bone cancer	***3***	2	2	–	–	***1***	**8**
Bone metastases	6	14	5	–	1	***1***	**27**
Bone tumors, benign	–	1	–	–	–	–	**1**
Desmoid tumors	***4***	5	–	–	***1***	***1***	**11**
Osteoid osteoma	5	11	85	–	***1***	***1***	**103**
Soft tissue cancer	***1***	1	–	–	–	–	**2**
Soft tissue tumors, benign	***1***	5	85	–	–	–	**92**

*Indications being performed off label in a region are shown in bold italic. A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary at the top.

For more information about specific commercial treatment sites and indications, please visit: www.fusfoundation.org/the-technology/treatment-sites. Use the "search by disease" dropdown menu and/or location.

Commercial Treatment Sites by Indication and Region* continued

Indications	Regions: N. America	Europe	Asia	S. America	Oceania	Africa	Totals
Neurological							
Movement disorder							
Dystonia	–	***1***	–	–	–	–	**1**
Dystonia, hand	–	–	***1***	–	–	–	**1**
Epilepsy	–	***1***	***1***	–	–	–	**2**
Essential tremor	51	25	23	1	2	–	**102**
Parkinson's disease, dyskinesia	2	3	1	–	–	–	**6**
Parkinson's disease, tremor	35	10	10	1	1	–	**57**
Neurodegenerative							
Alzheimer's disease	–	–	***1***	–	–	–	**1**
Pain							
Neuropathic pain	–	2	–	–	1	–	**3**
Neuropathy	–	***1***	–	–	–	–	**1**
Trigeminal neuralgia	–	***1***	–	–	–	–	**1**
Psychiatric							
Depression	–	–	1	–	–	–	**1**
Obsessive-compulsive disorder	***1***	–	1	–	–	–	**2**

*Indications being performed off label in a region are shown in bold italic. A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary at the top.

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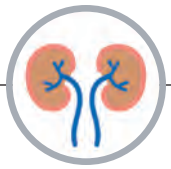
Commercial Treatment Sites by Indication and Region* continued

Indications	Regions: N. America	Europe	Asia	S. America	Oceania	Africa	Totals
Ophthalmological							
Glaucoma	–	14	–	–	–	–	**14**



Indications	Regions: N. America	Europe	Asia	S. America	Oceania	Africa	Totals
Urological							
Benign prostatic hyperplasia	14	6	25	–	–	–	**45**
Kidney tumors	***1***	4	85	–	–	***1***	**91**
Prostate cancer	171	210	41	6	1	3	**432**

*Indications being performed off label in a region are shown in bold italic. A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary at the top.

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Commercial Treatment Sites by Indication and Region* continued

Indications	Regions: N. America	Europe	Asia	S. America	Oceania	Africa	Totals
Women's health							
Breast tumors, benign	–	10	3	–	–	–	**13**
Breast tumors, malignant	***1***	6	89	–	–	–	**96**
Cervicitis	–	***1***	–	–	–	–	**1**
Endometrial tumors	–	–	***1***	–	–	–	**1**
Endometriosis	–	***2***	–	–	–	–	**2**
Lichen sclerosis	–	–	1	–	–	–	**1**
Urinary incontinence, stress	–	***1***	–	–	–	–	**1**
Uterine adenomyosis	***3***	7	101	–	2	***2***	**115**
Uterine fibroids	11	32	270	–	2	***4***	**319**

*Indications being performed off label in a region are shown in bold italic. A site may perform treatments on more than one indication within the same body system. Because of this, the total number of sites within a body system in the table may not equal the values provided in the summary at the top.

For more information about specific commercial treatment sites and indications, please visit: www.fusfoundation.org/the-technology/treatment-sites. Use the "search by disease" dropdown menu and/or location.

2023 FUS Industry

Focused Ultrasound Foundation

Overview

Large medical device companies are continuing to show strong interest in partnering with start-up focused ultrasound companies, helping to move the commercial field forward. New in 2022 we saw investment from the pharmaceutical industry in companies working to advance focused ultrasound for drug delivery. We also saw a focused ultrasound company receive a 2022 Edison Award in the Science and Medical Outpatient Treatment category and we continue to see industry companies receive Breakthrough Device Designation from the FDA.

During 2022, 17 new focused ultrasound companies entered the ecosystem—ten manufacturers, five OEMs and two microbubble companies. From publicly available sources and industry reporting, we estimate the field employs nearly 3,000 individuals spread around the world. Just under half of the worldwide employee count is concentrated in the United States, Israel, and France. The median company size is 12 employees and 66 percent of companies have 20 or fewer employees. There are over 1,000 focused ultrasound devices in use for commercial treatment around the world; these are fairly evenly distributed between North America, Europe, and Asia.

VIII. FUS Industry

VIII. 2 Overview

Company Types, Employees, and Locations

VIII. 3 Geographic Distribution
VIII. 4 Companies
VIII. 5 Employees
VIII. 6 Employee Distribution
VIII. 7 Employee Locations by Country

Companies by Region

VIII. 8 North America
- VIII. 8 Timelines of Companies
- VIII. 9 Companies

VIII.11 Europe
- VIII.11 Timelines of Companies
- VIII.12 Companies

VIII.14 Asia
- VIII.14 Timelines of Companies
- VIII.15 Companies

Devices

VIII.18 In Use
VIII.19 In Use by Region
VIII.20 Distributors by Region
VIII.24 With Treatment and Planning Guidance
- VIII.24 North America
- VIII.26 Europe
- VIII.28 Asia

Geographic Distribution of Companies

2022

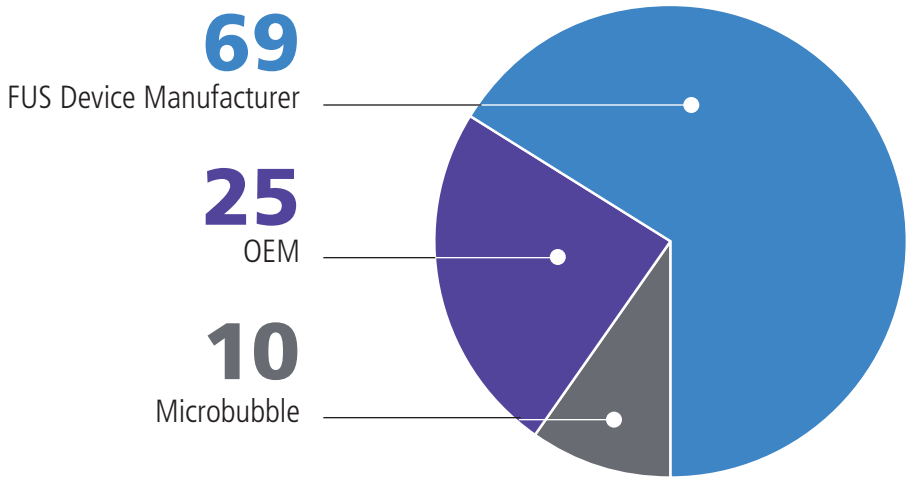
	North America	Europe	Asia
104 FUS companies	48	26	30
69 FUS device manufacturers	31	16	22
16 Companies with approvals	3	4	9

Companies

104

FUS companies*

Company distribution by type



* This analysis includes all FUS industry companies where employee information was available, including FUS device manufacturers, OEM, and microbubble companies.

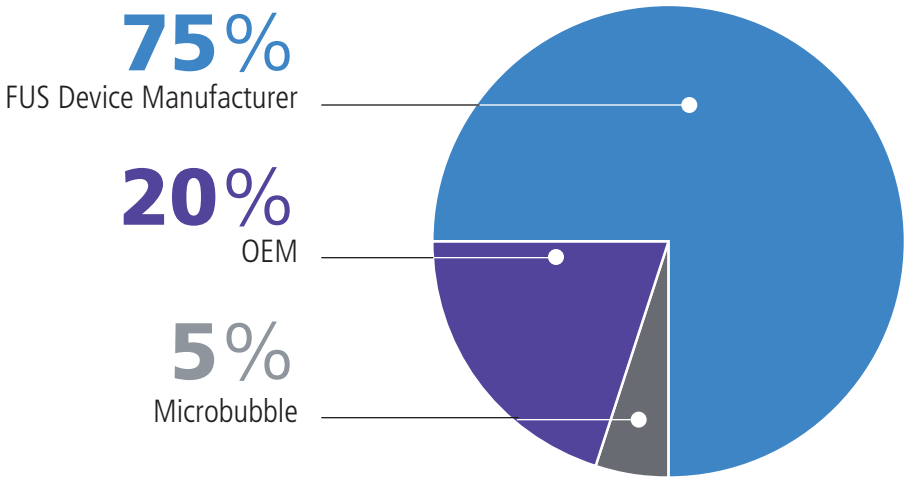
Just as a reminder, the company timelines include the year the company became involved in the focused ultrasound industry instead of the date of incorporation. For many early-stage focused ultrasound manufacturing companies, this date is one and the same; however, for the OEM and/or microbubble companies, it is often different.

Employees

2838

Employees*

Employee distribution



* Number of employees estimated from publicly available sources and directly reported by companies on our annual survey.

Most of the focused ultrasound industry employment is by focused ultrasound device manufacturers. Despite these companies being early stage and having small workforces, they are more numerous than OEM and microbubble companies. The largest geographic location of focused ultrasound employment is the United States, followed by Israel and France. These three countries comprise 50 percent of the labor pool with the remainder of the employees broadly distributed around the globe.

Employee Distribution*

12
employees
is the median company size

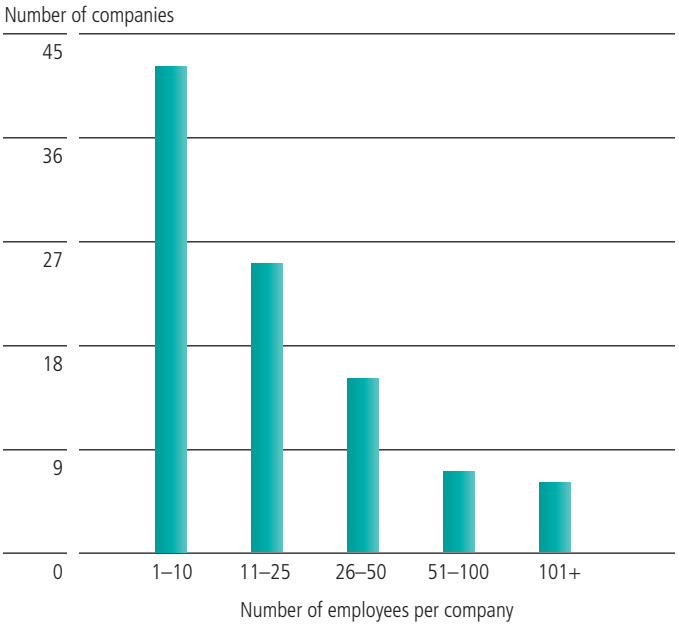
10%
of the total workforce is employed by the
52 smallest companies

66%
of companies have
20 or fewer employees

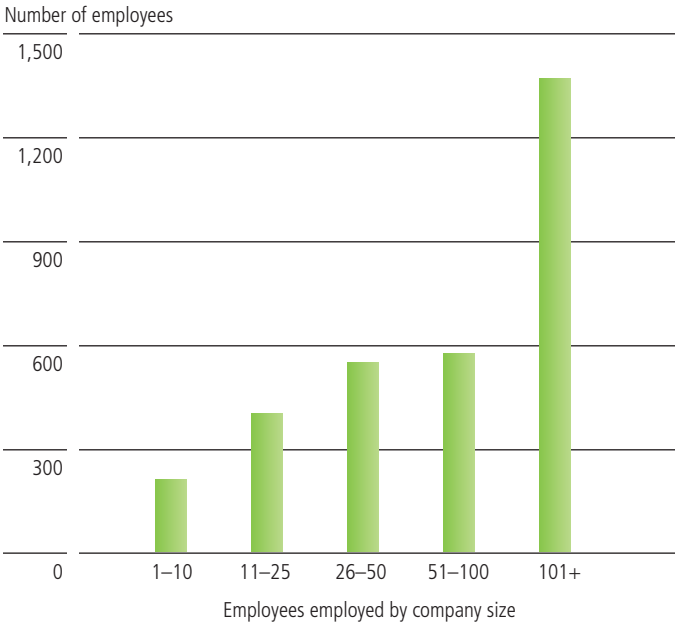
50%
of the total workforce is employed by the
8 largest companies

* This analysis includes device manufacturers, OEM, and microbubble companies.

Number of Companies



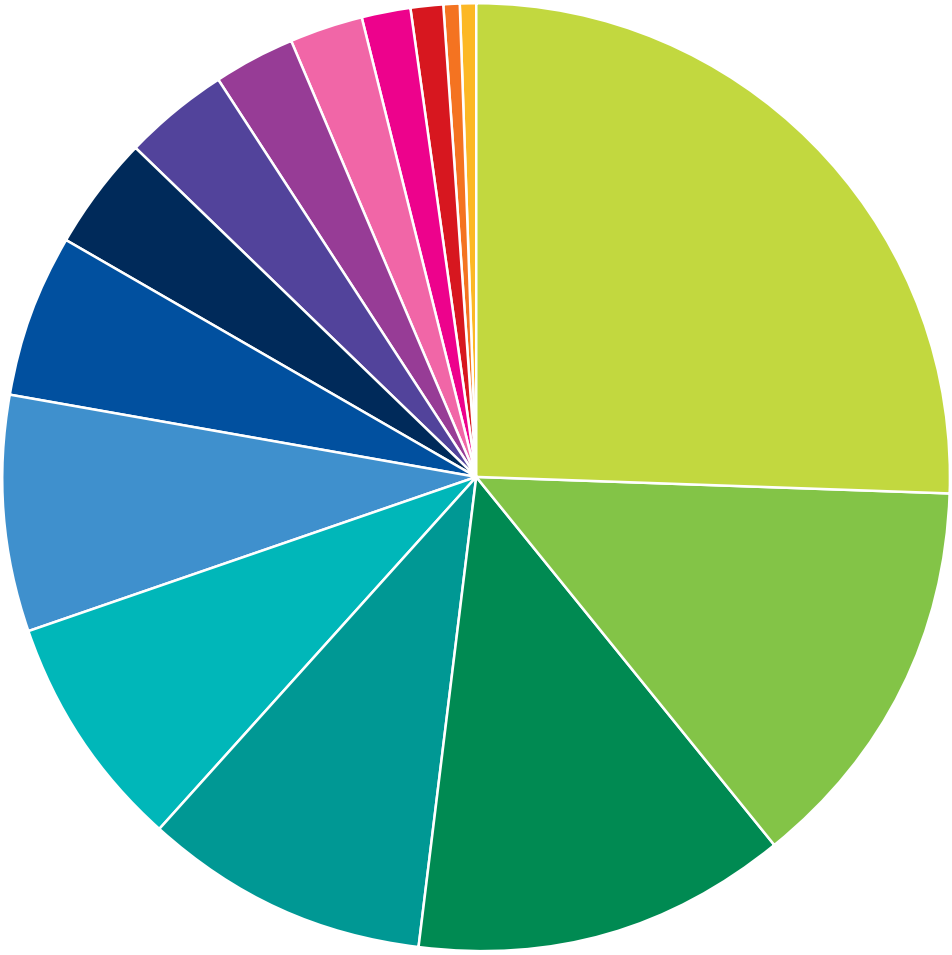
Number of Employees



FUS Employee Locations

2,019 employees*

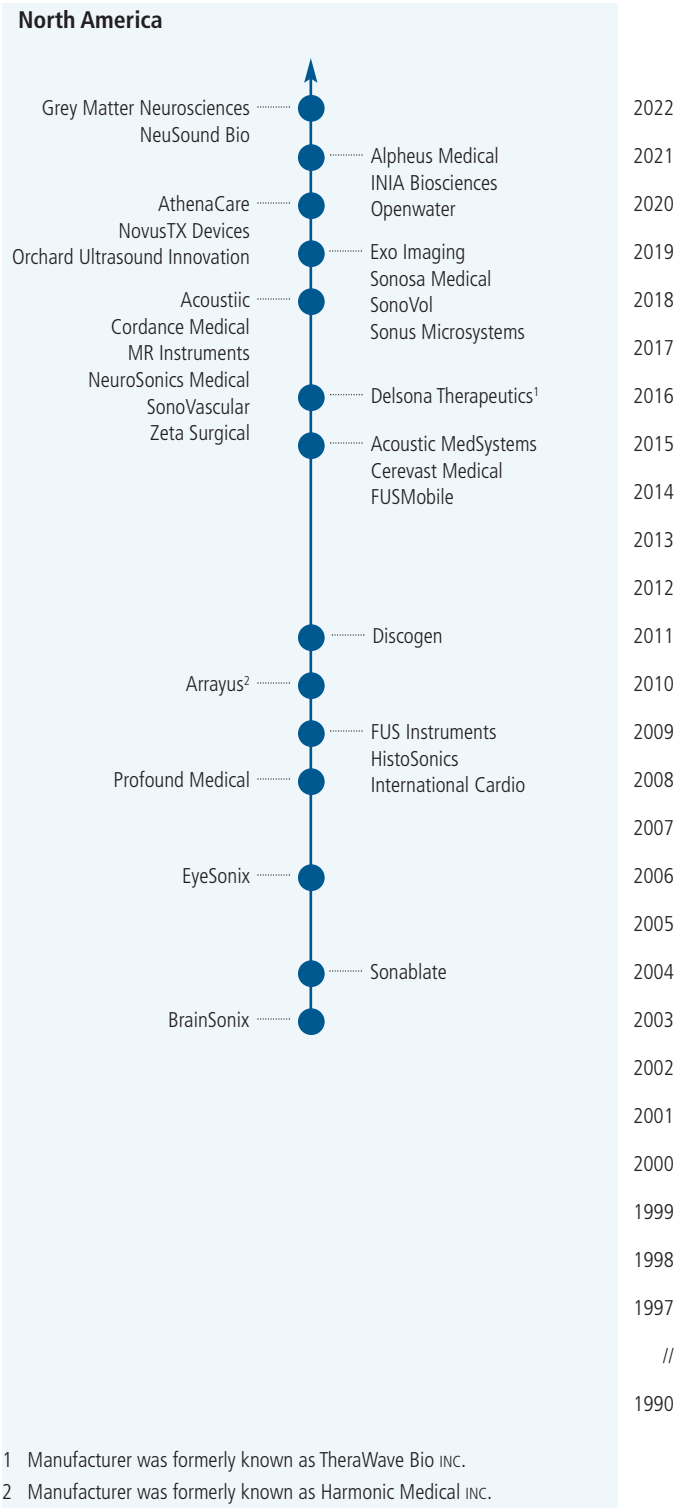
United States	516
Israel	272
France	259
South Korea	196
Canada	160
China	159
Japan	115
Germany	75
Taiwan	72
United Kingdom	59
Switzerland	50
Denmark	34
Finland	23
Norway	10
Malaysia	7
Columbia	5
Italy	3
United Arab Emirates	2
The Netherlands	1
Spain	1



*Number of employees directly reported by companies on our annual survey.

North America—Timelines of Companies

Clinical Device Manufacturers

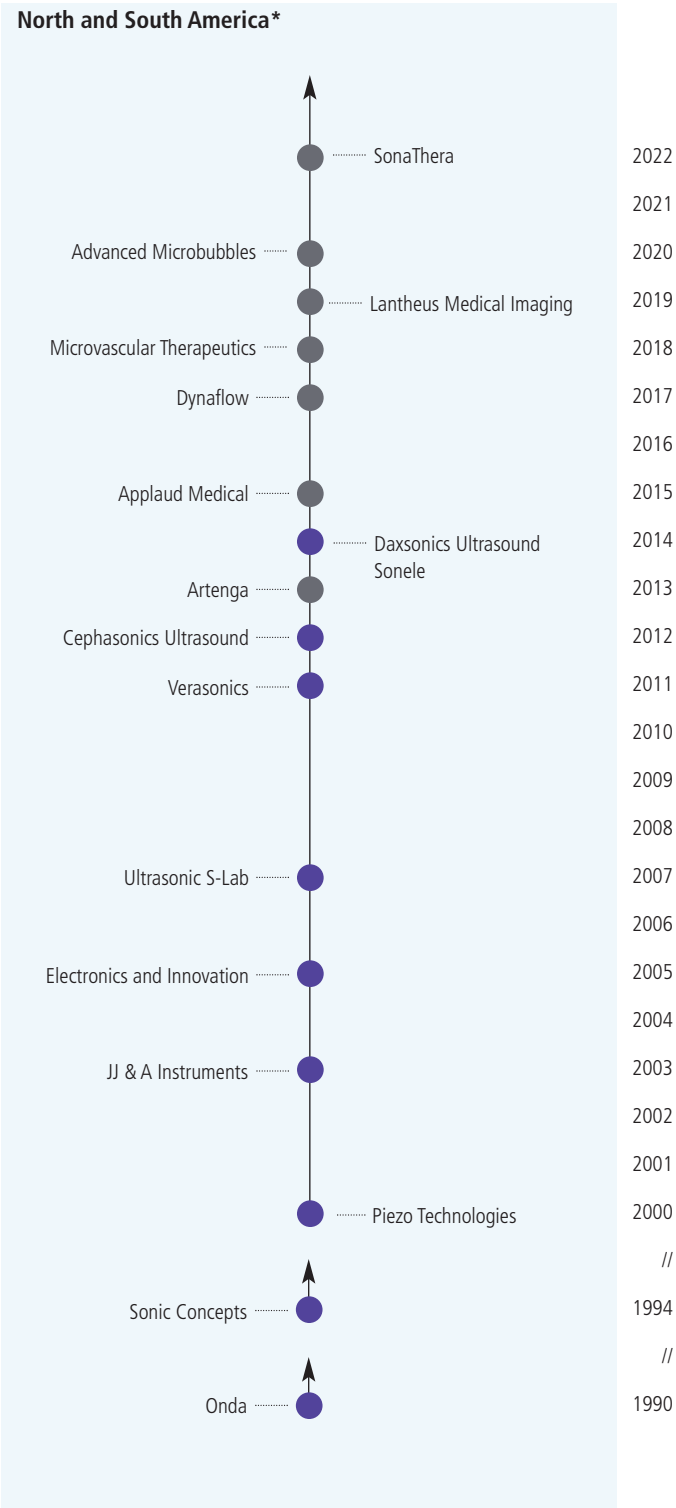


1 Manufacturer was formerly known as TheraWave Bio INC.

2 Manufacturer was formerly known as Harmonic Medical INC.

Other FUS Companies

Microbubble OEM



North America—Companies

North America

46

CLINICAL DEVICE MANUFACTURERS

✚ Acoustic MedSystems INC | Savoy, Illinois, United States, acousticmed.com

Acoustiic INC | Seattle, Washington, United States, acoustiic.com

Alpheus Medical INC | North Oakdale, Minnesota, United States, alpheusmedical.com

Arrayus Technologies INC[2] | Burlington, Ontario, Canada, arrayus.ca

AthenaCare LLC | Salt Lake City, Utah, United States

BrainSonix CORP | Sherman Oaks, California, United States, brainsonix.com

Cerevast Medical INC | Bothell, Washington, United States, cerevast.com

Cordance Medical INC | Mountain View, California, United States, cordancemedical.com

Delsona Therapeutics INC[1] | New York, New York, United States

Discogen | Weston, Florida, United States, discogen.com

Exo Imaging INC | Redwood City, California, United States, exo-imaging.com

EyeSonix | Long Beach, California, United Sates, eyesonix.com

FUS Instruments INC | Toronto, Ontario, Canada, fusinstruments.com

FUSMobile INC | Alpharetta, Georgia, United States, fusmobile.com

Grey Matter Neurosciences | Toronto, Ontario, Canada

HistoSonics INC | Ann Arbor, Michigan, United States, histosonics.com

INIA Biosciences INC | Boston, Massachusetts, United States, iniabiosciences.com

International Cardio CORP LLC | Edina, Minnesota, United States, hifu-rx.com

MR Instruments INC | Hopkins, Minnesota, United States, mrinstruments.com

NeuroSonics Medical INC | Baltimore, Maryland, United States, neurosonicsmedical.com

NeuSound Bio | California, United States

NovusTX Devices INC | Calgary, Alberta, Canada, novustx-devices.com

Openwater | San Francisco, California, United States, openwater.cc

Orchard Ultrasound Innovation | Sunnyvale, California, United States, orchardultrasound.com

✚ Profound Medical CORP | Mississauga, Ontario, Canada, profoundmedical.com

✚ Manufacturers with regulatory approvals. To see a detailed breakdown of regional and country approvals, see charts starting on p. IX.5.

1 Manufacturer was formerly known as TheraWave Bio INC.

2 Manufacturer was formerly known as Harmonic Medical INC.

North America—Companies continued

North America continued

CLINICAL DEVICE MANUFACTURERS continued

✚ Sonablate CORP | Charlotte, North Carolina, United States, sonablate.com

SonoVascular INC | Chapel Hill, North Carolina, United States, sonovascular.com

SonoVol INC | Durham, North Carolina, United States, sonovol.com

Sonus Microsystems | Vancouver, British Columbia, Canada, sonusmicrosystems.com

UltraNeuro | Cambridge, Massachusetts, United States, www.pivottheworld.com

Zeta Surgical INC | Boston, Massachusetts, United States, zetasurgical.com

MICROBUBBLE

Advanced Microbubbles INC | Newark, California, United States, advancedmicrobubbles.com

Applaud Medical INC | San Francisco, California, United States, applaudmedical.com

Artenga INC | Ottawa, Ontario, Canada, artenga.com

Dynaflow INC | Jessup, Maryland, United States, dynaflow-inc.com

Lantheus Medical Imaging INC | North Billerica, Massachusetts, United States, lantheus.com

Microvascular Therapeutics LLC | Tucson, Arizona, United States, mvtpharma.com

SonoThera INC | San Francisco, California, United States, sonothera.com

OEM

Cephasonics Ultrasound | San Jose, California, United States, www.cephasonics.com

Daxsonics Ultrasound INC | Halifax, Nova Scotia, Canada, daxsonics.com

Electronics and Innovation LTD | Rochester, New York, United States, eandiltd.com

JJ & A Instruments LLC | Rathdrum, Idaho, United States, jja-instruments.com

Onda CORP | Sunnyvale, California, United States, ondacorp.com

Piezo Technologies | Indianapolis, Indiana, United States, piezotechnologies.com

Sonele INC | Markham, Ontario, Canada, sonele.com

Sonic Concepts INC | Bothell, Washington, United States, sonicconcepts.com

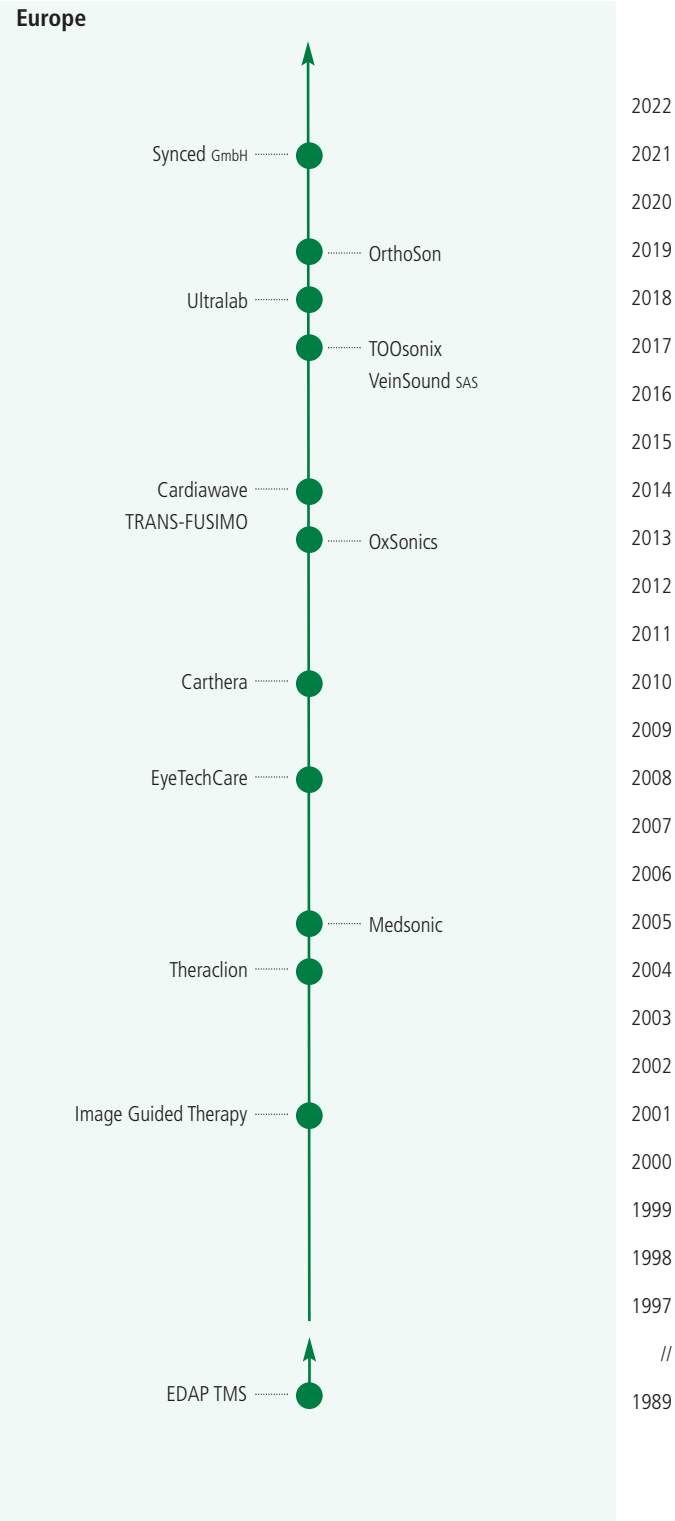
Ultrasonic S-Lab LLC | Concord, California, United States, ultrasonic-s-lab.com

Verasonics INC | Kirkland, Washington, United States, verasonics.com

✚ Manufacturers with regulatory approvals. To see a detailed breakdown of regional and country approvals, see charts starting on p. IX.5.

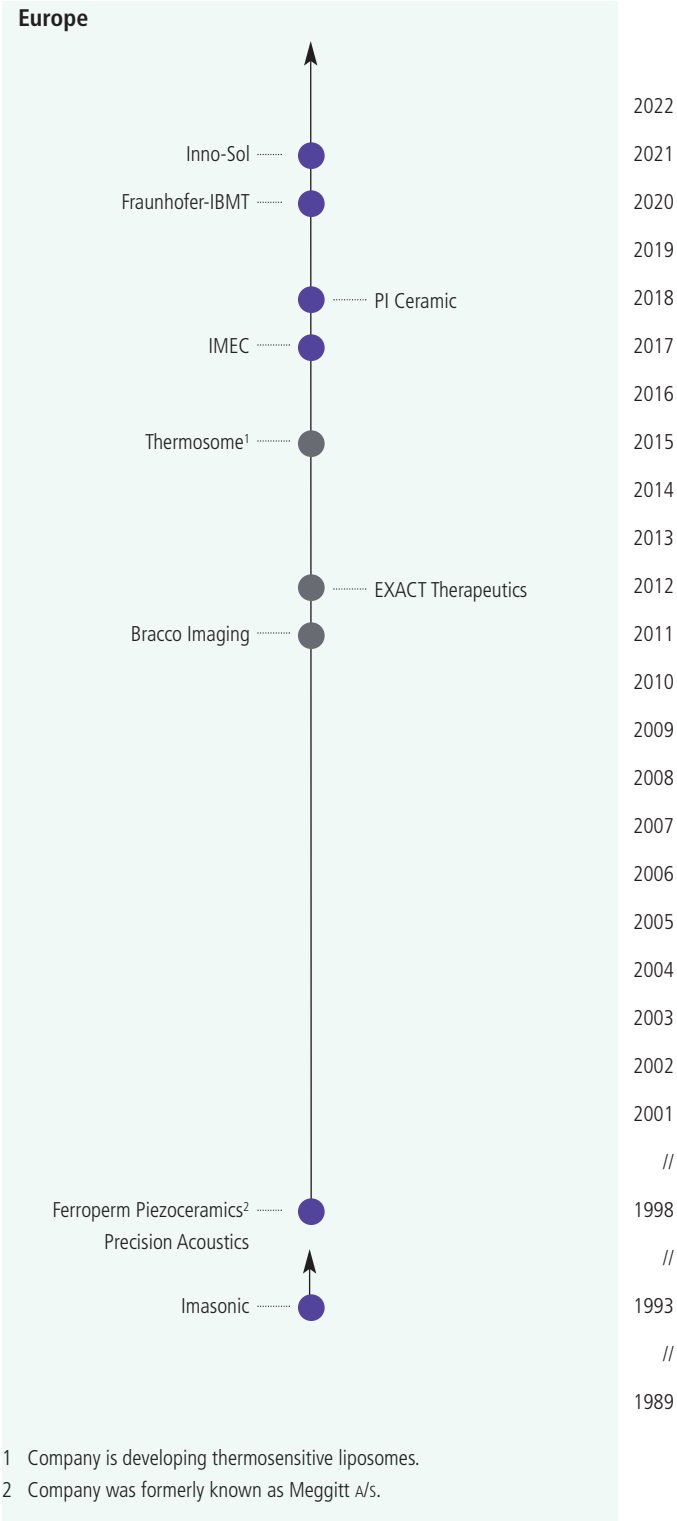
Europe—Timelines of Companies

Clinical Device Manufacturers



Other FUS Companies

Microbubble OEM



1 Company is developing thermosensitive liposomes.
2 Company was formerly known as Meggitt A/S.

Europe—Companies

Europe

25

CLINICAL DEVICE MANUFACTURERS

Cardiawave SA | Paris, France, cardiawave.com

Carthera SA | Paris, France, carthera.eu

✚ EDAP TMS SA | Vaulx-en-Velin, France, edap-tms.com

✚ EyeTechCare SA | Lyon, France, eyetechcare.com

Image Guided Therapy SA | Pessac, France, imageguidedtherapy.com

Medsonic LTD | Limassol, Cyprus, medsonic.com.cy

OrthoSon LTD | Oxford, England, United Kingdom, orthoson.com

OxSonics LTD | Oxford, England, United Kingdom, oxsonics.com

Qwanteus | France, qwanteus.com

Synced GmbH | Hamburg, Germany

✚ Theraclion SA | Malakoff, France, theraclion.fr

Therason | France

✚ TOOsonix A/S | Hørsholm, Denmark, toosonix.com

TRANS-FUSIMO | Bremen, Germany, trans-fusimo.eu

Ultralab LTD | Çankaya/Ankara, Turkey, ultralabltd.com

VeinSound SAS | Lyon, France, veinsound.com

✚ Manufacturers with regulatory approvals. To see a detailed breakdown of regional and country approvals, see charts starting on p. IX.5.

Europe—Companies continued

Europe continued

MICROBUBBLE*

Bracco Imaging SPA | Milano, Italy, braccoimaging.com

EXACT Therapeutics AS | Oslo, Norway, exact-tx.com

Thermosome GMBH[1] | Planegg/Martinsried, Germany, thermosome.com

OEM

Ferroperm Piezoceramics[2] | Kvistgaard, Denmark, meggittferroperm.com

Fraunhofer-Institut für Biomedizinische Technik | Sulzbach, Germany, ibmt.fraunhofer.de

Imasonic SA | Voray-sur-l'Ognon, France, imasonic.com

imec | Leuven, Belgium, imec-int.com

PI Ceramic GmbH | Lederhose, Germany, piceramic.com

Precision Acoustics LTD | Dorchester, England, United Kingdom, acoustics.co.uk

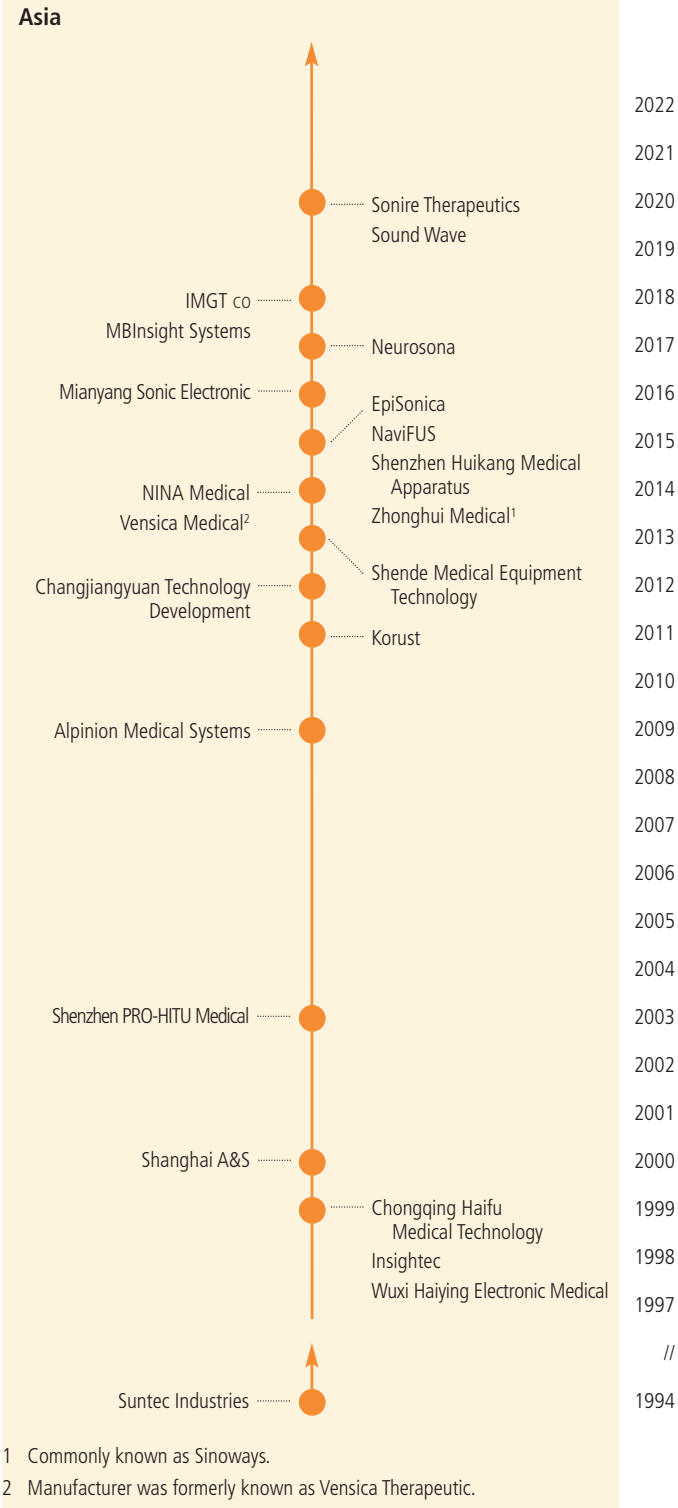
* Also includes thermosensitive liposomes.

1 Company is developing thermosensitive liposomes

2 Company was formerly known as Meggitt A/S.

Asia—Timelines of Companies

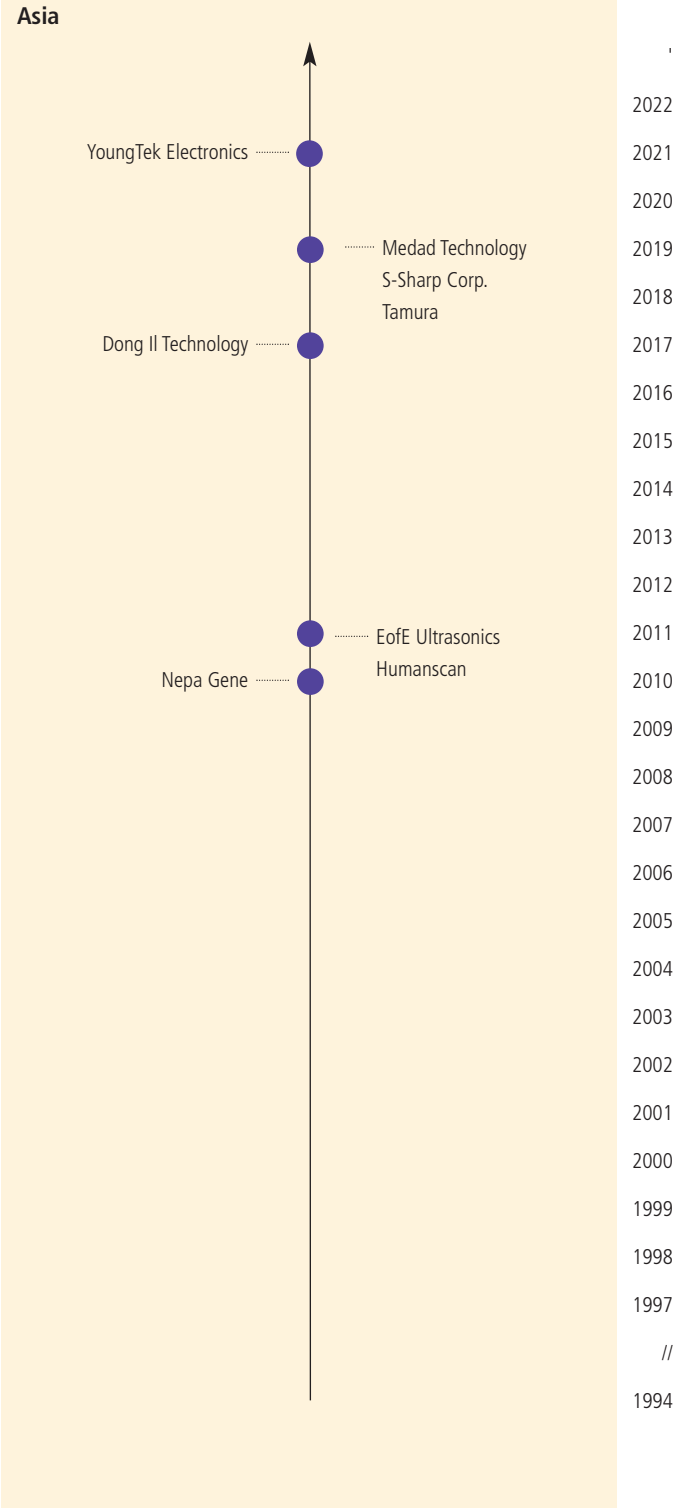
Clinical Device Manufacturers



1 Commonly known as Sinoways.
2 Manufacturer was formerly known as Vensica Therapeutic.

Other FUS Companies

Microbubble OEM



Asia—Companies

Asia

30

CLINICAL DEVICE MANUFACTURERS

- ✚ Alpinion Medical Systems CO LTD | Seoul, South Korea, alpinion.com
- ✚ Changjiangyuan Technology Development CO LTD | Beijing, China, cjykj.com
- ✚ Chongqing Haifu Medical Technology CO LTD | Chongqing, China, haifumedical.com
- ✚ EpiSonica CORP | Hsinchu, Taiwan, episonica.com
- IMGT CO LTD | Seongnam, South Korea, nanoimgt.com
- ✚ Insightec LTD | Tirat Carmel, Israel, insightec.com
- Korust CO LTD | Anyang, South Korea, korust.com
- MBInsight Systems INC | Taiwan
- Mianyang Sonic Electronic LTD | Mianyang City, China, ultrasound.cn
- NaviFUS CORP | New Taipei City, Taiwan, navi-fus.com
- Neurosona CO LTD | Seoul, South Korea, neurosona.com
- NINA Medical LTD | Nazareth, Israel, ninamed.com
- ✚ Shanghai A&S Science Technology Development CO LTD | Shanghai, China, aishen.com.cn
- ✚ Shende Medical Equipment Technology CO LTD | Shanghai, China, shendehc.com
- Shenzhen Huikang Medical Apparatus CO LTD | Shenzhen, China, eswl.cn
- ✚ Shenzhen PRO-HITU Medical Technology CO LTD | Shenzhen, China, pro-hifu.com
- SONIRE Therapeutics INC | Tokyo, Japan,sonire-therapeutics.com
- Sound Wave Innovation CO LTD | Tokyo, Japan, sw-innovation.com
- Suntec Industries CO LTD | Shanghai, China
- Vensica Therapeutics[2] | Misgav, Israel, vensica.com
- ✚ Wuxi Haiying Electronic Medical Systems CO LTD | Wuxi, China, haiyingmedical.com.cn
- Zhonghui Medical Technology CO LTD[1] | Shanghai, China, zhonghuimt.com

✚ Manufacturers with regulatory approvals. To see a detailed breakdown of regional and country approvals, see charts starting on p. IX.5.

1 Commonly known as Sinoways.

2 Manufacturer was formerly known as Vensica Therapeutic.

Asia—Companies continued

Asia continued

- OEM

Dong Il Technology LTD | Hwaseong, South Korea, dongiltech.co.kr

EofE Ultrasonics CO LTD | Seoul, South Korea, ultrasonics.co.kr

Humanscan CO LTD | Ansan, South Korea, humanscan.co.kr

Medad Technology | Dubai, United Arab Emirates, medadtechnology.com

Nepa Gene CO | Chiba, Japan, nepagene.jp

S-Sharp CORP | New Taipei City, Taiwan, s-sharp.com

Tamura CORP | Tokyo, Japan, tamuracorp.com

YoungTek Electronics | Hsinchu City, Taiwan, ytec.com.tw

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FUS Devices in Use

Number and Growth

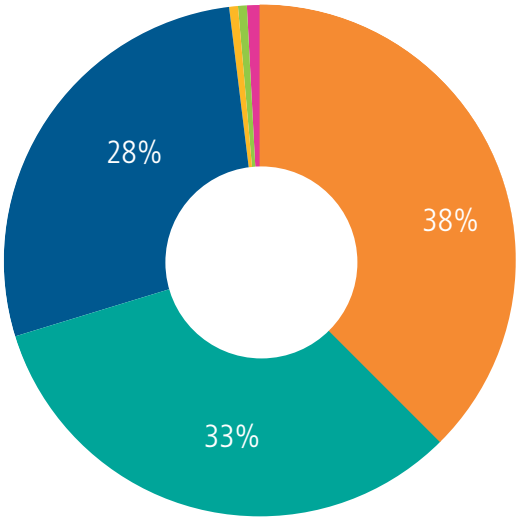
2022

1,265
FUS Devices

11%
Growth
2021 over 2020

Worldwide Distribution

2022



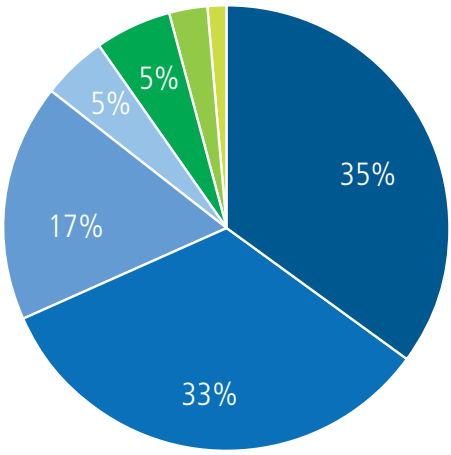
North America	28%
Europe	33%
Asia	38%
South America	>1%
Oceania	>1%
Africa	>1%

FUS Device Use by Region

North America

314

Devices



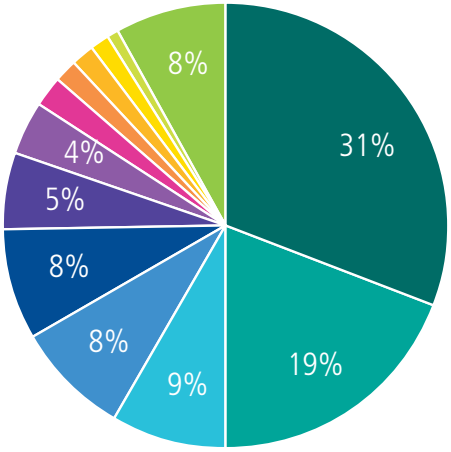
US, Central	35%
Eastern	33%
Pacific	17%
Mountain	5%
Canada	5%
Mexico	3%
Other*	1%

*Cayman Islands, Cuba, Dominica, and Dominican Republic

Europe

372

Devices



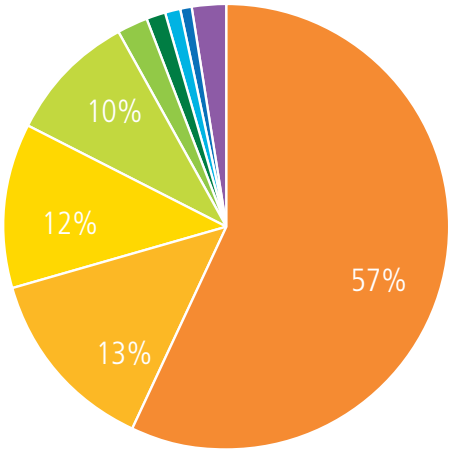
France	31%
Germany	19%
Italy	9%
Russian Federation	8%
United Kingdom	8%
Spain	6%
Switzerland	4%
The Netherlands	2%
Armenia	2%
Poland	2%
Norway	1%
Denmark	1%
Other*	8%

*Austria, Belgium, Bulgaria, Czech Republic, Finland, Georgia, Greece, Latvia, Monaco, Portugal, Romania, Serbia, Sweden, Turkey, and Ukraine

Asia

430

Devices



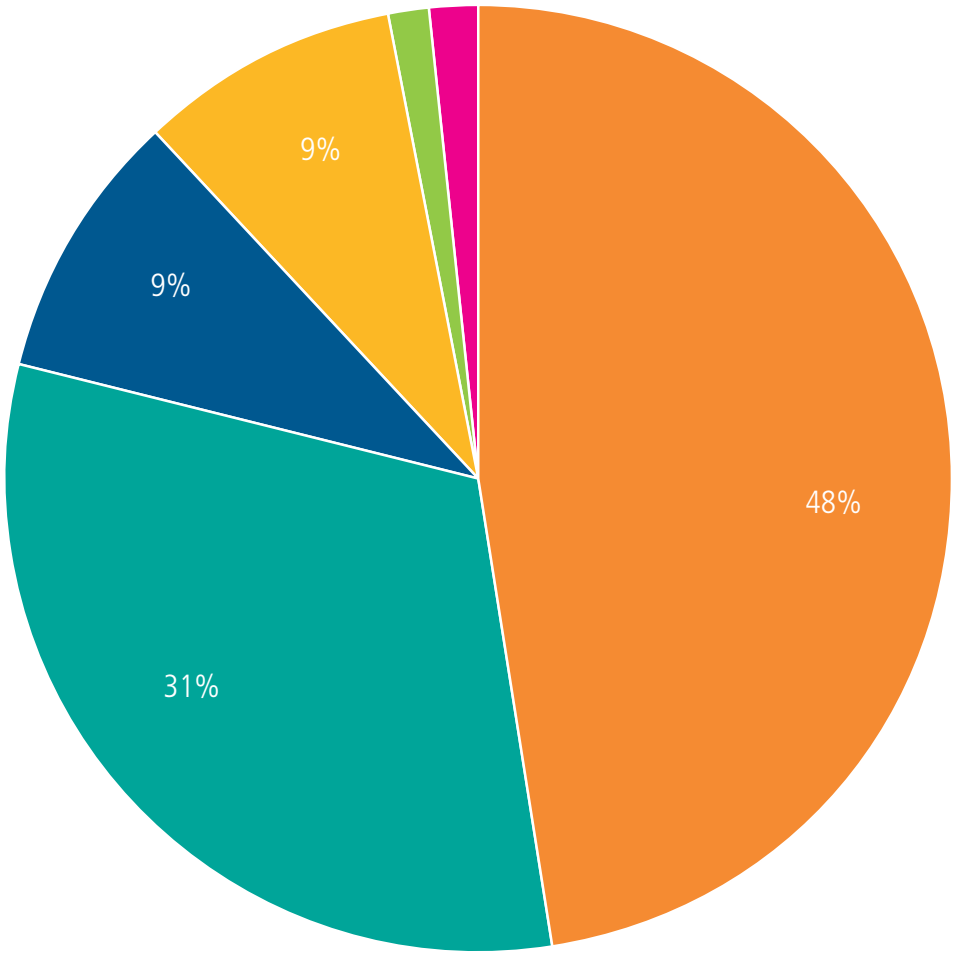
China	57%
South Korea	13%
Japan	12%
Taiwan	10%
India	2%
Israel	2%
Singapore	>1%
Thailand	>1%
Other*	3%

*Iran, Kazakhstan, Lebanon, Malaysia, Myanmar, Philippines, Uzbekistan, and Vietnam

Distributors by Region

67 distributors

North America	6	9%
Europe	21	31%
Asia	32	48%
South America	6	9%
Oceania	1	1.5%
Africa	1	1.5%



Distributors by Region continued

North America

- Agiliti Health INC
- American HIFU LLC
- Cyber Robotic Solutions SA de CV
- HIFU Prostate Services LLC
- Soluciones Medicas Avanzadas SAS
- Vituro Health LLC

Europe

- ab medica SPA
- ADS Elektronik Tıbbi Cihazlar AS
- Andromed Tıbbi Cihazlar ve Sağlık Hizmetleri
- Brainbox LTD
- Consultronix SA
- InnoMedicus AG
- Kungshusen Medicinska AB
- Levi Danismanlik ve Ticaret AS
- Medicina Analítica Consumibles SA
- Medistim Danmark APS
- Medkonsult SRO
- Palex Medical SA
- Promedica Bioelectronics SRL
- ProMedical OY
- Sigmacon UK LTD
- SofMedica
- Synektik Group
- Tema Sinergie SPA
- Timko SP ZOO
- Vingmed AS
- VIVAX Pharmaceuticals SRO

Distributors by Region continued

Asia

Allmed Solutions
Amed CO LTD
AMI Technologies LTD
Amos Gazit LTD
Beijing Beike Digital Medical Technology CO LTD
Beijing Ren De Sheng Technology
Best Digital CO LTD
Bravotac CORP LTD
CanAm Scientific
Century Scientific and Equipment CO WLL
Demakai CO LTD
Demed Solutions SDN BHD
Double Success CO LTD
DSS Imagetech PVT LTD
ECHO Healthcare INC
Ekpac China LTD
Hanyoung Trading CO LTD
Huons Medical
imedtac CO LTD
Medfocus CO LTD
Medical Imaging System PTE LTD
Nanomedix PVT LTD
Pro Chime Enterprise CORP
Rad Medical CORP
Sumo Corporations LTD
Takai Hospital Supply CO LTD
Tasly SonaCare Medical Engineering Technology CO LTD
Theraclion China LTD
Transmedic PTE LTD
Valor Health CO LTD
Varitron
Yangde Instrument CO LTD

South America

Cencomex SA
Imemed Bolivia
Medicinelaser SA
Protrauma SA
Sirex Médica SA
Strattner & Cia LTDA

Oceania

Getz Healthcare Australia

Africa

SARL Medimatec

Currently, 16 focused ultrasound device manufacturers have commercial products available. Please see Chapter 10 for further details on these companies and their products.

However, with an ecosystem of 70 manufacturers, that means 83 percent are in the R&D stage. The field is still very early stage.

What follows is a table with high-level information about the various devices around the world and what type of imaging is utilized for treatment and planning guidance.

FUS Devices with Treatment and Planning Guidance

Manufacturer	Device	Treatment guidance	Planning guidance	Approval
North America				
Research & Development				
Acoustic MedSystems	ACOUSTx	Ultrasound, CT-fluoroscopy, MRI, and 3D targeting	–	
	TheraVision	–	–	✚
Acoustiic	AgilitUS	MR guidance	MR guidance	
Alpheus Medical	CV01	–	–	
Arrayus[2]	Symphony	US & MR guidance	–	
AthenaCare	Muse MRgFUS System	MR guidance	MR guidance	
BrainSonix	BXPulsar 1001 LIFUP	MR guidance	MR guidance	
	BXPulsar 1002 LIFUP	MR guidance	MR guidance	
Cerevast Medical	Aureva Pulse	US guidance	–	
	Reflow RVO	US guidance	–	
Delsona Therapeutics[1]	Ultranav (prototype)	Image fusion	Neuronavigation	
Exo Imaging	Performance Ultrasound Platform	–	–	
EyeSonix	TUG - Therapeutic Ultrasound for Glaucoma	Unguided	Visual guidance	
FUS Instruments	DS-50	–	–	
	LP-100	MR guidance	–	
	RK-100	–	–	
	RK-20	Other guidance	–	
	RK-300	MR guidance	–	
	RK-50	Other guidance	–	
FUSMobile	Neurolyser	Other guidance	Not used	
HistoSonics	Edison	US guidance	US guidance	
International Cardio	HIFU Synthesizer	US guidance	US guidance	
MR Instruments	DuoFLEX ACCESS Coil	MR guidance	MR guidance	
	MR-guided TRUST (Transcranial Ultrasound Stimulation)	MR guidance	MR guidance	
NeuroSonics Medical	NeuroSonics (prototype)	US guidance	MR guidance	
Sonosa Medical	Sonosa Therapeutic	US guidance	Not used	

1 Manufacturer was formerly known as TheraWave.

2 Manufacturer was formerly known as Harmonic Medical INC.

FUS Devices with Treatment and Planning Guidance continued

Manufacturer	Device	Treatment guidance	Planning guidance	Approval
North America				
Commercial				
Profound Medical	Sonalleve	MR guidance	MR guidance	✚
	TULSA-PRO	MR guidance	MR guidance	✚
Sonablate Corp.	Sonablate	US guidance	MR/US fusion	✚
	Sonatherm	US guidance	US guidance	✚

FUS Devices with Treatment and Planning Guidance continued

Manufacturer	Device	Treatment guidance	Planning guidance	Approval
Europe				
Research & Development				
Cardiawave	Valvosoft	US guidance	US guidance	
CarThera	SonoCloud 1	Unguided	Not used	
	SonoCloud 9	Unguided	Not used	
EDAP TMS	EDAP (prototype)	US guidance	US guidance	
Image Guided Therapy	3Bop	Stereotactic frame	–	
	LabFUS	MR guidance	MR guidance	
	Rodent FUS System	MR guidance	MR guidance	
	TargetedFUS	MR guidance	MR guidance	
	UFOGUIDE	MR guidance	MR guidance	
Medsonic	Bone phantoms - Medsonic	MR guidance	–	
	MR-Compatible Transducers	MR guidance	–	
	Robotic Systems	MR guidance	–	
	Shinsei motor electronic system	MR guidance	–	
	Skull phantoms - Medsonic	MR guidance	–	
OxSonics	SonoTran System	US guidance	US guidance	
TOOsonix	System ONE-R	Image fusion	Visual guidance	
TRANS-FUSIMO	TransFUSIMO Treatment System	MR guidance	MR guidance	
VeinSound, SAS	PHEA1	US guidance	US guidance	

FUS Devices with Treatment and Planning Guidance continued

Manufacturer	Device	Treatment guidance	Planning guidance	Approval
Europe				
Commercial				
EDAP TMS	Ablatherm	Image fusion	US guidance	✚
	Focal One	Image fusion	MR & US guidance, Biopsies	✚
EyeTechCare	EyeOP1	Unguided	–	✚
Theraclion	Echopulse	US guidance	US guidance	✚
	SONOVEIN	US guidance	Not used	✚
TOOsonix	System ONE-M	Image fusion	Visual guidance	✚

FUS Devices with Treatment and Planning Guidance continued

Manufacturer	Device	Treatment guidance	Planning guidance	Approval
Asia				
Research & Development				
Alpinion Medical Systems	VIFU2000	US guidance	–	
Chongqing Haifu Medical Technology	CZG300	US guidance	–	
	JC200D	US guidance	–	
	JC300	US guidance	–	
	LCA200	Unguided	Not used	
IMGT	IMD10	US guidance	US guidance	
Korust CO LTD	Le Mette	Unguided	Not used	
	RHINOS	Other guidance	Other	
	UTIMS	Unguided	Not used	
Mianyang Sonic Electronic	CZ901	US guidance	–	
NaviFUS	NaviFUS System (Model 001)	Neuronavigation	MR/CT fusion	
	NaviFUS System (Model 101)	Other guidance	MR/CT fusion	
	NaviFUS System (Model 101-K)	Other guidance	MR/CT fusion	
Neurosona	NS-US100	Other guidance	MR/CT fusion	
	NS-US200	Other guidance	MR/CT fusion	
NINA Medical	LOTUS-1	US guidance	US guidance	
Shenzhen Huikang Medical Apparatus	HIFU 2001	US guidance	–	
Shenzhen PRO-HITU Medical	PRO3008	US guidance	US guidance	
	UT1000	Unguided	Not used	
Sonire Therapeutics	Suizenji	US guidance	CT guidance	
Suntec Industries	Suntec System	US guidance	–	
Vensica Medical[1]	The Vibe	–	–	
	Vensica (prototype)	US guidance	–	
Zhonghui Medical	SUA-I	US guidance	US guidance	
	SUV-I	US guidance	US guidance	

1 Manufacturer was formerly known as Vensica Therapeutics.

FUS Devices with Treatment and Planning Guidance continued

Manufacturer	Device	Treatment guidance	Planning guidance	Approval
Asia				
Commercial				
Alpinion Medical Systems	Alpius 900	US guidance	–	✚
Changjiangyuan Technology Development	NUTAS – Non-invasive Ultrasound Tumor Ablation System	US guidance	US guidance	✚
	SUPER Knife-Focused Beam Therapy System	MR & US guidance	–	✚
Chongqing Haifu Medical Technology	CZB	US guidance	–	✚
	CZF	US guidance	–	✚
	JC	US guidance	–	✚
	JC200	US guidance	–	✚
EpiSonica	ArcBLATE (ARC-100M)	MR guidance	MR guidance	✚
Insightec	Exablate Body[1]	MR guidance	MR guidance	✚
	Exablate Neuro	MR guidance	MR/CT fusion	✚
	Exablate Prostate	MR guidance	MR guidance	✚
Shanghai A&S	HIFUNIT9000	US guidance	MR guidance	✚
Shende Medical Equipment Technology	Aceso	MR guidance	–	✚
Shenzhen PRO-HITU Medical	PRO2008	US guidance	US guidance	✚
	PRO300	US guidance	US guidance	✚
	PRO5G	Other guidance	Visual guidance	✚
Wuxi Haiying Electronic Medical	HY2900	US guidance	–	✚

1 Device was formerly known as Exablate MrgFUS.

2023 Regulatory Approvals

Focused Ultrasound Foundation

Overview

Before a medical procedure can be considered for clinical use, the technology underlying that procedure—for instance, the focused ultrasound device—must first obtain regulatory approval from a governing body. Approval is based on clinical data demonstrating that the technology is safe and effective. Examples of regulatory approvals include the CE Mark for most countries in Europe and device approval from the US Food and Drug Administration (FDA).

Approvals are also disease-specific, meaning each device must go through the regulatory process for every different disease and/or condition it aims to treat.

Once a regulatory body clears a device for a select indication, physicians can begin treating patients on a commercial basis, but oftentimes on a cash-pay basis. For the treatment to be financially accessible by the greater patient population, it must obtain reimbursement.

Approvals may have changed or been updated since publication. For the most up-to-date information please visit: fusfoundation.org/the-foundation/programs/regulatory-approvals-search.

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Development Stage Advancements and New Indications

2022

13

New global regulatory approvals

China | NMPA

Benign prostatic hyperplasia

Macau | ISAF

Benign prostatic hyperplasia
Prostate tumors

United Arab Emirates | MOHAP

Essential tremor
Neuropathic pain
Parkinson's disease, tremor

Israel | AMAR

Prostate tumors

Taiwan | FDA

Parkinson's disease, tremor

United Kingdom | MHRA

Benign prostatic hyperplasia
Essential tremor
Neuropathic pain
Parkinson's disease, tremor
Prostate Tumors

FUS Regulatory Approvals by Indication and Region

Graphic

Global Landscape of Approved Indications and Manufacturers

Indication regional approvals	Indications	Manufacturers
	Cardiovascular	
🟢 🟠	Varicose veins	Theraclion
	Endocrine disorders	
🟢 🟠	Thyroid nodules	Theraclion
	Gastrointestinal	
🟢	Liver metastases	Chongqing Haifu Medical Technology
🟢 🟠	Liver tumors	Chongqing Haifu Medical Technology
🟠		Shanghai A&S
🟢 🟠	Pancreatic tumors	Chongqing Haifu Medical Technology
	Musculoskeletal	
🟢 🟠 🟡 🟢	Arthritis, facetogenic	Insightec
🟢 🟠 🟡 🟢	Bone cancer	Insightec
🔵 🟢 🟠 🟡 🟢	Bone metastases	Insightec
🟢 🟠 🟡 🟢		Profound Medical
🟠		Shanghai A&S
🟢 🟠 🟡 🟢	Bone tumors, benign	Insightec
🟢	Desmoid tumors	Profound Medical
🟢 🟠 🟡 🟢	Multiple myeloma	Insightec
🟢 🟠	Osteoid osteoma	Chongqing Haifu Medical Technology
🔵 🟢 🟠		Profound Medical
🟢 🟠	Soft tissue cancer	Chongqing Haifu Medical Technology
🟠		EpiSonica
🟠		Shanghai A&S
🟢 🟠	Soft tissue tumors, benign	Chongqing Haifu Medical Technology

Approval regions

- 🔵 **North America**
- 🟢 **Europe**
- 🟠 **Asia**
- 🟡 **South America**
- 🟢 **Oceania**
- 🟣 **Africa**

Global Landscape of Approved Indications and Manufacturers continued

Indication regional approvals	Indications	Manufacturers
	Neurological	
Asia	Depression	Insightec
North America, Europe, Asia, South America, Oceania	Essential tremor	Insightec
Europe, Asia, South America, Oceania	Neuropathic pain	Insightec
Asia	Obsessive-compulsive disorder	Insightec
North America, Europe, Asia	Parkinson's disease, dyskinesia	Insightec
North America, Europe, Asia, South America, Oceania	Parkinson's disease, tremor	Insightec
	Ophthalmological	
Europe, Asia	Glaucoma	EyeTechCare
	Pulmonary	
Europe, Asia	Rhinitis	Chongqing Haifu Medical Technology
	Urological	
North America	Benign prostatic hyperplasia	EDAP TMS
North America		Insightec
North America		Profound Medical
North America, Europe, Asia, South America, Oceania		Sonablate
Europe, Asia	Kidney tumors	Chongqing Haifu Medical Technology
North America, Europe, Asia, South America	Prostate cancer	EDAP TMS
North America, Europe, Asia, South America, Oceania		Insightec
North America, Europe, Asia		Profound Medical
North America, Europe, Asia, South America, Oceania, Africa		Sonablate
	Women's health	
Europe, Asia	Breast tumors, benign	Theraclion
Europe, Asia	Breast tumors, malignant	Chongqing Haifu Medical Technology
Asia		Shanghai A&S
Asia		Theraclion
Asia	Cervicitis	Chongqing Haifu Medical Technology

Approval regions

- North America
- Europe
- Asia
- South America
- Oceania
- Africa

Global Landscape of Approved Indications and Manufacturers continued

Indication regional approvals	Indications	Manufacturers
	Women's health continued	
🟠	Hyperplasia of the vulva	Shenzhen PRO-HITU Medical
🟠	Lichen sclerosis	Shenzhen PRO-HITU Medical
🟠	Uterine adenomyosis	Alpinion Medical Systems
🟢		Chongqing Haifu Medical Technology
🟢 🟠 🟡 🟢		Insightec
🟢 🟠 🟡 🟢		Profound Medical
🟠		Shenzhen PRO-HITU Medical
🟢 🟠	Uterine fibroids	Alpinion Medical Systems
🟢 🟠		Chongqing Haifu Medical Technology
🔵 🟢 🟠 🟡 🟢		Insightec
🔵 🟢 🟠 🟡 🟢		Profound Medical
🟢 🟠		Shanghai A&S
🟢 🟠		Shenzhen PRO-HITU Medical
🟠		Wuxi Haiying Electronic Medical

Approval regions

- 🔵 **North America**
- 🟢 **Europe**
- 🟠 **Asia**
- 🟡 **South America**
- 🟢 **Oceania**
- 🟣 **Africa**

FUS Regulatory Approvals by Region and Manufacturer

Indications	North America	Europe	Asia	South America	Oceania	Africa
Cardiovascular						
Varicose veins		▲	▲			
Endocrine						
Thyroid nodules		▲	▲			
Gastrointestinal						
Liver metastases		●				
Liver tumors		●	● ●			
Pancreatic tumors		●	●			
Musculoskeletal						
Arthritis, facetogenic		●	●	●	●	
Bone cancer		●	●	●	●	
Bone metastases	●	■ ●	■ ● ●	■ ●	■ ●	
Bone tumors, benign		●	●	●	●	
Desmoid tumors		■				
Multiple myeloma		●	●	●	●	
Osteoid osteoma	■	■ ●	■ ●			
Soft tissue cancer		●	● ● ●			
Soft tissue tumors, benign		●	●			

Manufacturers

North America
- ■ Profound Medical, *Canada*
- ■ Sonablate, *US*

Europe
- ▲ EDAP TMS, *France*
- ▲ EyeTechCare, *France*
- ▲ Theraclion, *France*

Asia
- ● Alpinion Medical Systems, *South Korea*
- ● Chongqing Haifu Medical Technology, *China*
- ● EpiSonica, *Taiwan*
- ● Insightec, *Israel*
- ● Shanghai A&S, *China*
- ● Shenzhen PRO-HITU Medical, *China*
- ● Wuxi Haiying Electronic Medical, *China*

FUS Regulatory Approvals by Region and Manufacturer continued

Indications	North America	Europe	Asia	South America	Oceania	Africa
Neurological						
Depression			●			
Essential tremor	●	●	●	●	●	
Neuropathic pain		●	●	●	●	
OCD			●			
Parkinson's dyskinesia	●	●	●			
Parkinson's tremor	●	●	●	●	●	
Ophthalmological						
Glaucoma		▲	▲			
Pulmonary						
Rhinitis		●	●			
Urological						
BPH	■ ■ ▲ ●	■	■	■	■	
Kidney tumors		●	●			
Prostate cancer	■ ■ ▲ ●	■ ■ ▲ ●	■ ■ ▲ ●	■ ▲ ●	■ ●	■
Women's health						
Breast tumors, benign		▲	▲			
Breast tumors, malignant		●	▲ ● ●			
Cervicitis			●			
Hyperplasia of the vulva			●			
Lichen sclerosis			●			
Uterine adenomyosis		■ ● ●	■ ● ● ●	■ ●	■ ●	
Uterine fibroids	■ ●	■ ● ● ● ● ●	■ ● ● ● ● ● ●	■ ●	■ ●	

Manufacturers

North America
- ■ Profound Medical, *Canada*
- ■ Sonablate, *US*

Europe
- ▲ EDAP TMS, *France*
- ▲ EyeTechCare, *France*
- ▲ Theraclion, *France*

Asia
- ● Alpinion Medical Systems, *South Korea*
- ● Chongqing Haifu Medical Technology, *China*
- ● EpiSonica, *Taiwan*
- ● Insightec, *Israel*
- ● Shanghai A&S, *China*
- ● Shenzhen PRO-HITU Medical, *China*
- ● Wuxi Haiying Electronic Medical, *China*

North America

FUS Regulatory Approvals by Country and Manufacturer

Indications	Bahamas Ministry of Health	Barbados Ministry of Health and Wellness	Canada Health Canada, Medical Devices Bureau	Costa Rica Ministerio de Salud	Dominican Republic MISPAS	US FDA, Center for Devices & Radiological Health
Musculoskeletal						
Bone metastases			●			●
Osteoid osteoma						■
Neurological						
Essential tremor			●			●
Parkinson's dyskinesia						●
Parkinson's tremor						●
Urological						
BPH			■	■	■	■ ■ ▲ ●
Prostate cancer	■	■	■ ■ ▲	■	■	■ ■ ▲ ●
Women's health						
Uterine fibroids			■ ●			●

Manufacturers

North America

- ■ Profound Medical, *Canada*
- ■ Sonablate, *US*

Europe

- ▲ EDAP TMS, *France*
- ▲ EyeTechCare, *France*
- ▲ Theraclion, *France*

Asia

- ● Alpinion Medical Systems, *South Korea*
- ● Chongqing Haifu Medical Technology, *China*
- ● EpiSonica, *Taiwan*
- ● Insightec, *Israel*
- ● Shanghai A&S, *China*
- ● Shenzhen PRO-HITU Medical, *China*
- ● Wuxi Haiying Electronic Medical, *China*

Europe
FUS Regulatory Approvals by Country and Manufacturer

Indications	Belarus MOH	Europe CE Marking	Russia Roszdravnadzor	Turkey TITUBB	United Kingdom MHRA
Cardiovascular					
Varicose veins		▲			
Endocrine					
Thyroid nodules		▲	▲		
Gastrointestinal					
Liver metastases		●			
Liver tumors		●	●		
Pancreatic tumors		●	●		
Musculoskeletal					
Arthritis, facetogenic		●	●	●	
Bone cancer		●	●	●	
Bone metastases	●	■ ●	●	●	
Bone tumors, benign		●	●	●	
Desmoid tumors		■			
Multiple myeloma		●	●	●	
Osteoid osteoma		■ ●	●		
Soft tissue cancer		●	●		
Soft tissue tumors, benign		●	●		

Manufacturers

North America
- ■ Profound Medical, *Canada*
- ■ Sonablate, *US*

Europe
- ▲ EDAP TMS, *France*
- ▲ EyeTechCare, *France*
- ▲ Theraclion, *France*

Asia
- ● Alpinion Medical Systems, *South Korea*
- ● Chongqing Haifu Medical Technology, *China*
- ● EpiSonica, *Taiwan*
- ● Insightec, *Israel*
- ● Shanghai A&S, *China*
- ● Shenzhen PRO-HITU Medical, *China*
- ● Wuxi Haiying Electronic Medical, *China*

Europe

FUS Regulatory Approvals by Country and Manufacturer continued

Indications	Belarus MOH	Europe CE Marking	Russia Roszdravnadzor	Turkey TITUBB	United Kingdom MHRA
Neurological					
Essential tremor		●	●	●	●
Neuropathic pain		●	●	●	●
Parkinson's dyskinesia			●		
Parkinson's tremor		●	●	●	●
Ophthalmological					
Glaucoma		▲			
Pulmonary					
Rhinitis		●			
Urological					
BPH		■	■		■
Kidney tumors		●	●		
Prostate cancer	●	■ ■ ▲ ●	■ ▲ ●	●	■
Women's health					
Breast tumors, benign		▲	▲		
Breast tumors, malignant		●	●		
Uterine adenomyosis		■ ● ●	●	●	
Uterine fibroids	●	■ ● ● ● ●	● ●	●	

Manufacturers

North America
- ■ Profound Medical, *Canada*
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Europe
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- ● EpiSonica, *Taiwan*
- ● Insightec, *Israel*
- ● Shanghai A&S, *China*
- ● Shenzhen PRO-HITU Medical, *China*
- ● Wuxi Haiying Electronic Medical, *China*

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Asia

FUS Regulatory Approvals by Country and Manufacturer

Indications	China (NMPA)	Hong Kong (MDD)	India (CDSCO)	Israel (AMAR)	Japan (MHLW)	Kazakhstan (NCEM)	Kuwait (MOH FDCD)	Macau (ISAF)	Malaysia (MDA)
Cardiovascular									
Varicose veins		▲							
Endocrine									
Thyroid nodules		▲							▲
Gastrointestinal									
Liver tumors	● ●								
Pancreatic tumors	●								
Musculoskeletal									
Arthritis, facetogenic		●				●			
Bone cancer		●		●		●			
Bone metastases	●	●				●	●		■
Bone tumors, benign		●				●			
Multiple myeloma		●				●			
Osteoid osteoma	●								
Soft tissue cancer	● ●								
Soft tissue tumors, benign	●								
Neurological									
Depression									
Essential tremor	●	●	●	●	●	●			
Neuropathic pain		●	●	●		●			
OCD									
Parkinson's dyskinesia					●				
Parkinson's tremor	●	●	●	●	●	●			

Manufacturers

North America
- ■ Profound Medical, *Canada*
- ■ Sonablate, *US*

Europe
- ▲ EDAP TMS, *France*
- ▲ EyeTechCare, *France*
- ▲ Theraclion, *France*

Asia
- ● Alpinion Medical Systems, *South Korea*
- ● Chongqing Haifu Medical Technology, *China*
- ● EpiSonica, *Taiwan*
- ● Insightec, *Israel*
- ● Shanghai A&S, *China*
- ● Shenzhen PRO-HITU Medical, *China*
- ● Wuxi Haiying Electronic Medical, *China*

Asia

FUS Regulatory Approvals by Country and Manufacturer continued

Indications	Pakistan DRAP	Philippines FDA	Saudi Arabia SFDA	Singapore HSA	South Korea MFDS	Taiwan FDA	Thailand FDA	UAE MOHAP	Vietnam DMEW
Cardiovascular									
Varicose veins				▲					
Endocrine									
Thyroid nodules				▲	▲	▲	▲		
Gastrointestinal									
Liver tumors					●				
Pancreatic tumors					●				
Musculoskeletal									
Arthritis, facetogenic					●		●		
Bone cancer							●		
Bone metastases			●	■	●		●		■
Bone tumors, benign							●		
Multiple myeloma							●		
Osteoid osteoma				■					
Soft tissue cancer						●			
Soft tissue tumors, benign									
Neurological									
Depression					●				
Essential tremor		●		●	●	●	●	●	
Neuropathic pain		●			●		●	●	
OCD					●				
Parkinson's dyskinesia					●				
Parkinson's tremor		●		●	●	●	●	●	

Manufacturers

North America
- ■ Profound Medical, *Canada*
- ■ Sonablate, *US*

Europe
- ▲ EDAP TMS, *France*
- ▲ EyeTechCare, *France*
- ▲ Theraclion, *France*

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- ● EpiSonica, *Taiwan*
- ● Insightec, *Israel*
- ● Shanghai A&S, *China*
- ● Shenzhen PRO-HITU Medical, *China*
- ● Wuxi Haiying Electronic Medical, *China*

Asia

FUS Regulatory Approvals by Country and Manufacturer

Indications	China (NMPA)	Hong Kong (MDD)	India (CDSCO)	Israel (AMAR)	Japan (MHLW)	Kazakhstan (NCEM)	Kuwait (MOH FDCD)	Macau (ISAF)	Malaysia (MDA)
Ophthalmological									
Glaucoma	▲								
Pulmonary									
Rhinitis	●								
Urological									
BPH	■	■	■	■	■			■	
Kidney tumors	●								
Prostate cancer	■	■ ●	■	■ ●		●		■	
Women's health									
Breast tumors, benign		▲							
Breast tumors, malignant	● ●								▲
Cervicitis	●								
Hyperplasia of the vulva	●								
Lichen sclerosis	●								
Uterine adenomyosis	●	●		●		●			■
Uterine fibroids	■ ● ● ● ● ●	●		●	●	●	●		■

Manufacturers

North America
- ■ Profound Medical, *Canada*
- ■ Sonablate, *US*

Europe
- ▲ EDAP TMS, *France*
- ▲ EyeTechCare, *France*
- ▲ Theraclion, *France*

Asia
- ● Alpinion Medical Systems, *South Korea*
- ● Chongqing Haifu Medical Technology, *China*
- ● EpiSonica, *Taiwan*
- ● Insightec, *Israel*
- ● Shanghai A&S, *China*
- ● Shenzhen PRO-HITU Medical, *China*
- ● Wuxi Haiying Electronic Medical, *China*

Asia

FUS Regulatory Approvals by Country and Manufacturer continued

Indications	Pakistan DRAP	Philippines FDA	Saudi Arabia SFDA	Singapore HSA	South Korea MFDS	Taiwan FDA	Thailand FDA	UAE MOHAP	Vietnam DMEW
Ophthalmological									
Glaucoma									
Pulmonary									
Rhinitis									
Urological									
BPH					■				■
Kidney tumors									
Prostate cancer	■			■	■ ▲	■	●		■
Women's health									
Breast tumors, benign				▲	▲	▲			
Breast tumors, malignant							▲		
Cervicitis									
Hyperplasia of the vulva									
Lichen sclerosis									
Uterine adenomyosis					● ●		●		■
Uterine fibroids			■ ●	■ ●	■ ● ● ● ●	● ●	● ●		■

Manufacturers

North America
- ■ Profound Medical, *Canada*
- ■ Sonablate, *US*

Europe
- ▲ EDAP TMS, *France*
- ▲ EyeTechCare, *France*
- ▲ Theraclion, *France*

Asia
- ● Alpinion Medical Systems, *South Korea*
- ● Chongqing Haifu Medical Technology, *China*
- ● EpiSonica, *Taiwan*
- ● Insightec, *Israel*
- ● Shanghai A&S, *China*
- ● Shenzhen PRO-HITU Medical, *China*
- ● Wuxi Haiying Electronic Medical, *China*

South America

FUS Regulatory Approvals by Country and Manufacturer

Indications	Argentina (ANMAT)	Brazil (ANVISA)	Chile (ANAMED)	Colombia (INVIMA)	Ecuador (ANRCVS)	Peru (DIGEMED)
Musculoskeletal						
Arthritis, facetogenic			●			
Bone cancer			●			
Bone metastases	■		●			
Bone tumors, benign			●			
Multiple myeloma			●			
Neurological						
Essential tremor	●	●	●	●		●
Neuropathic pain	●	●	●	●		●
Parkinson's tremor	●	●	●	●		●
Urological						
BPH	■			■	■	
Prostate cancer	■	▲	●	■	■	
Women's health						
Uterine adenomyosis	■		●			
Uterine fibroids	■		●			

Manufacturers

North America
- ■ Profound Medical, *Canada*
- ■ Sonablate, *US*

Europe
- ▲ EDAP TMS, *France*
- ▲ EyeTechCare, *France*
- ▲ Theraclion, *France*

Asia
- ● Alpinion Medical Systems, *South Korea*
- ● Chongqing Haifu Medical Technology, *China*
- ● EpiSonica, *Taiwan*
- ● Insightec, *Israel*
- ● Shanghai A&S, *China*
- ● Shenzhen PRO-HITU Medical, *China*
- ● Wuxi Haiying Electronic Medical, *China*

South America

FUS Regulatory Approvals by Country and Manufacturer continued

Indications	Trinidad and Tobago Ministry of Health
Musculoskeletal	
Arthritis, facetogenic	
Bone cancer	
Bone metastases	
Bone tumors, benign	
Multiple myeloma	
Neurological	
Essential tremor	
Neuropathic pain	
Parkinson's tremor	
Urological	
BPH	■
Prostate cancer	■
Women's health	
Uterine adenomyosis	
Uterine fibroids	

Manufacturers

North America
- ■ Profound Medical, *Canada*
- ■ Sonablate, *US*

Europe
- ▲ EDAP TMS, *France*
- ▲ EyeTechCare, *France*
- ▲ Theraclion, *France*

Asia
- ● Alpinion Medical Systems, *South Korea*
- ● Chongqing Haifu Medical Technology, *China*
- ● EpiSonica, *Taiwan*
- ● Insightec, *Israel*
- ● Shanghai A&S, *China*
- ● Shenzhen PRO-HITU Medical, *China*
- ● Wuxi Haiying Electronic Medical, *China*

Oceania

FUS Regulatory Approvals by Country and Manufacturer

Indications	Australia TGA	New Zealand MEDSAFE
Musculoskeletal		
Arthritis, facetogenic	●	●
Bone cancer	●	●
Bone metastases	■ ●	■ ●
Bone tumors, benign	●	●
Multiple myeloma	●	●
Neurological		
Essential tremor	●	
Neuropathic pain	●	
Parkinson's tremor	●	
Urological		
BPH	■	
Prostate cancer	■ ●	●
Women's health		
Uterine adenomyosis	■ ●	■ ●
Uterine fibroids	■ ●	■ ●

Manufacturers

North America
- ■ Profound Medical, *Canada*
- ■ Sonablate, *US*

Europe
- ▲ EDAP TMS, *France*
- ▲ EyeTechCare, *France*
- ▲ Theraclion, *France*

Asia
- ● Alpinion Medical Systems, *South Korea*
- ● Chongqing Haifu Medical Technology, *China*
- ● EpiSonica, *Taiwan*
- ● Insightec, *Israel*
- ● Shanghai A&S, *China*
- ● Shenzhen PRO-HITU Medical, *China*
- ● Wuxi Haiying Electronic Medical, *China*

Africa

FUS Regulatory Approvals by Country and Manufacturer

	South Africa					
Indications	MCC					
Urological						
Prostate cancer	■					

Manufacturers

North America
- ■ Profound Medical, *Canada*
- ■ Sonablate, *US*

Europe
- ▲ EDAP TMS, *France*
- ▲ EyeTechCare, *France*
- ▲ Theraclion, *France*

Asia
- ● Alpinion Medical Systems, *South Korea*
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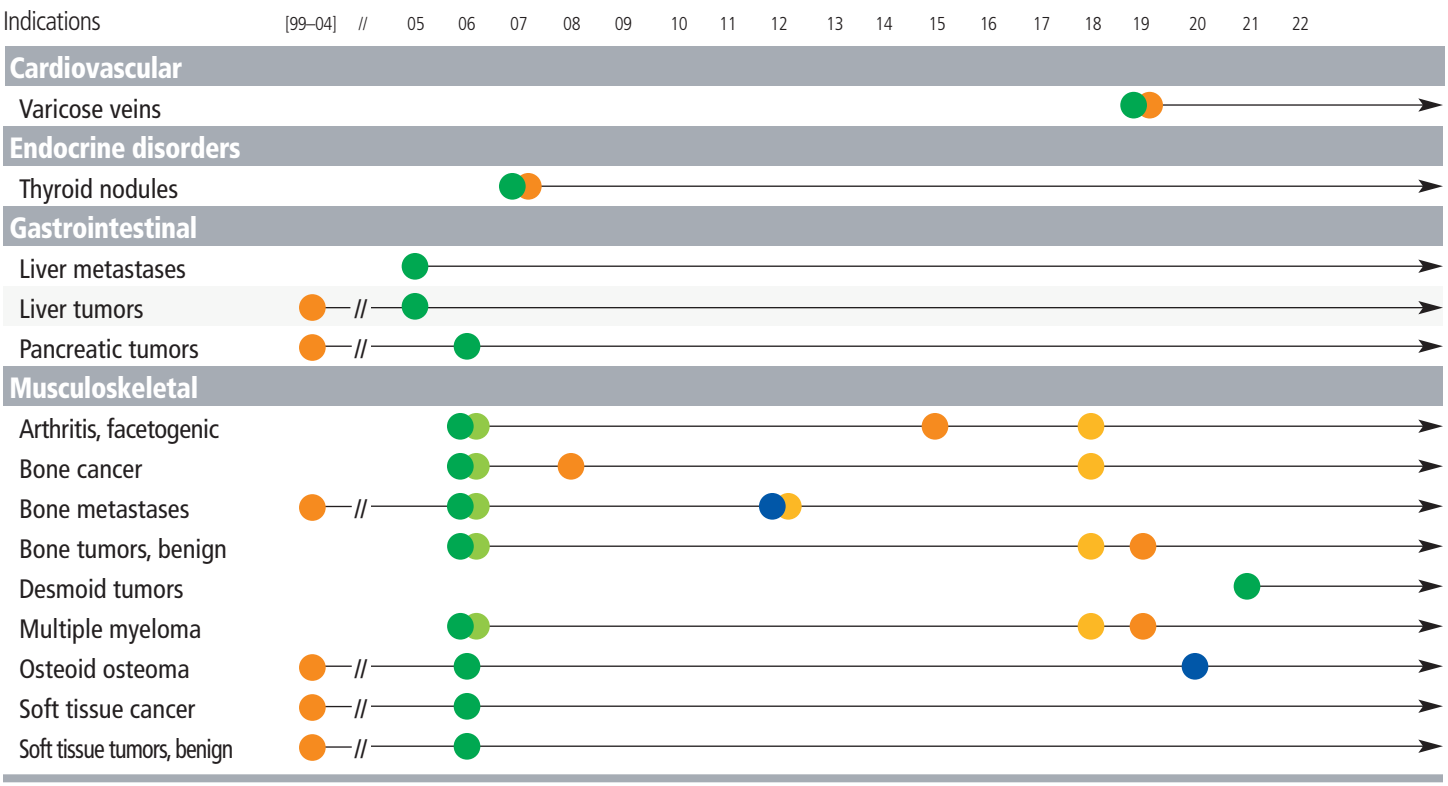
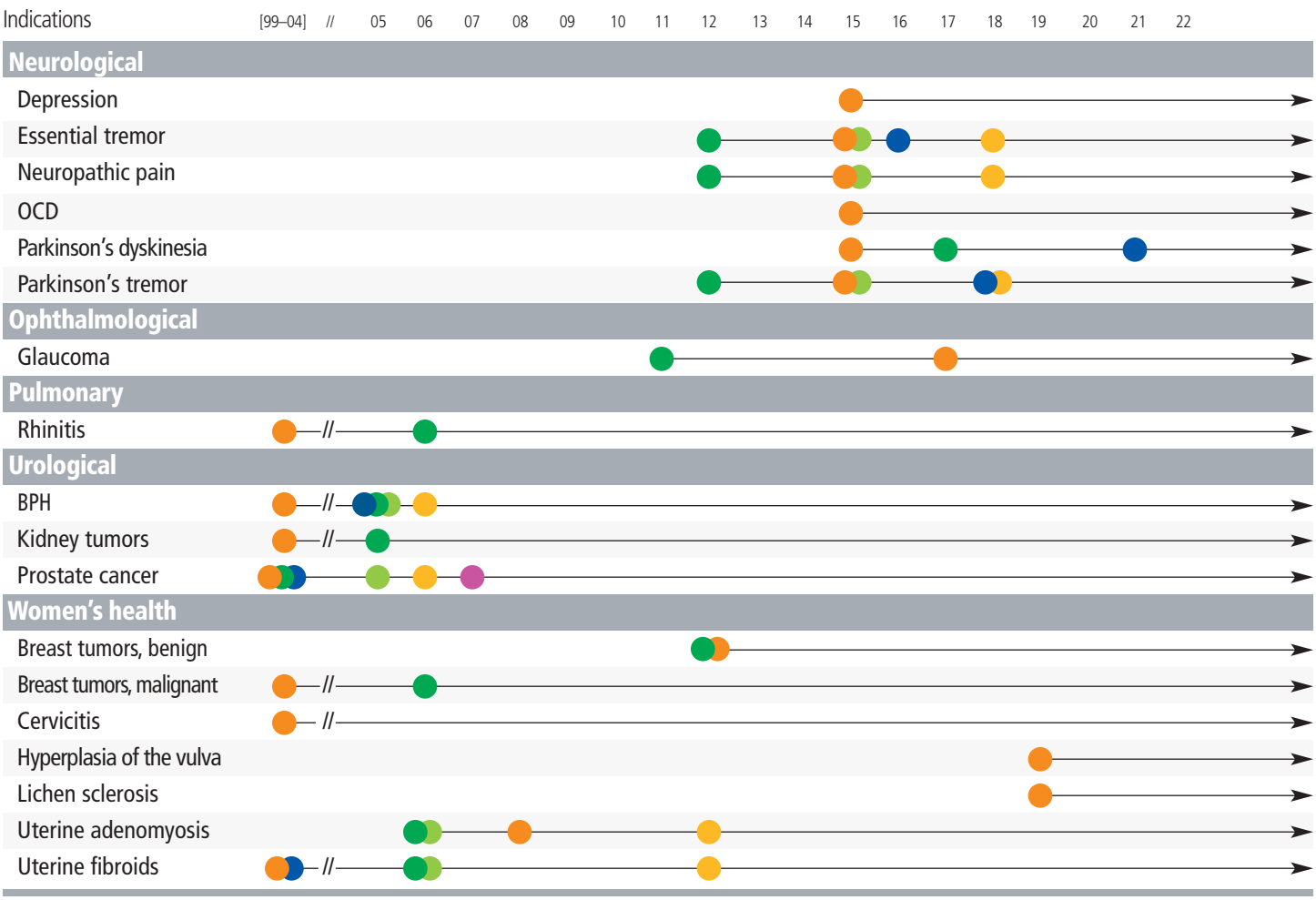
- ● Insightec, *Israel*
- ● Shanghai A&S, *China*
- ● Shenzhen PRO-HITU Medical, *China*
- ● Wuxi Haiying Electronic Medical, *China*

FUS Regulatory Approvals by Indication and Region



- North America
- Europe
- Asia
- South America
- Oceania
- Africa

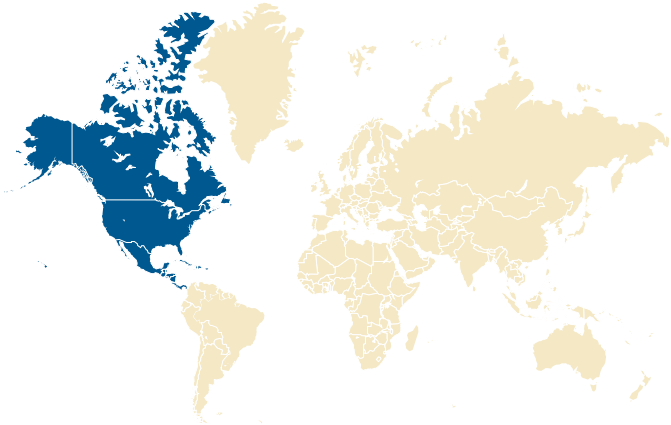
FUS Regulatory Approvals by Indication and Region continued

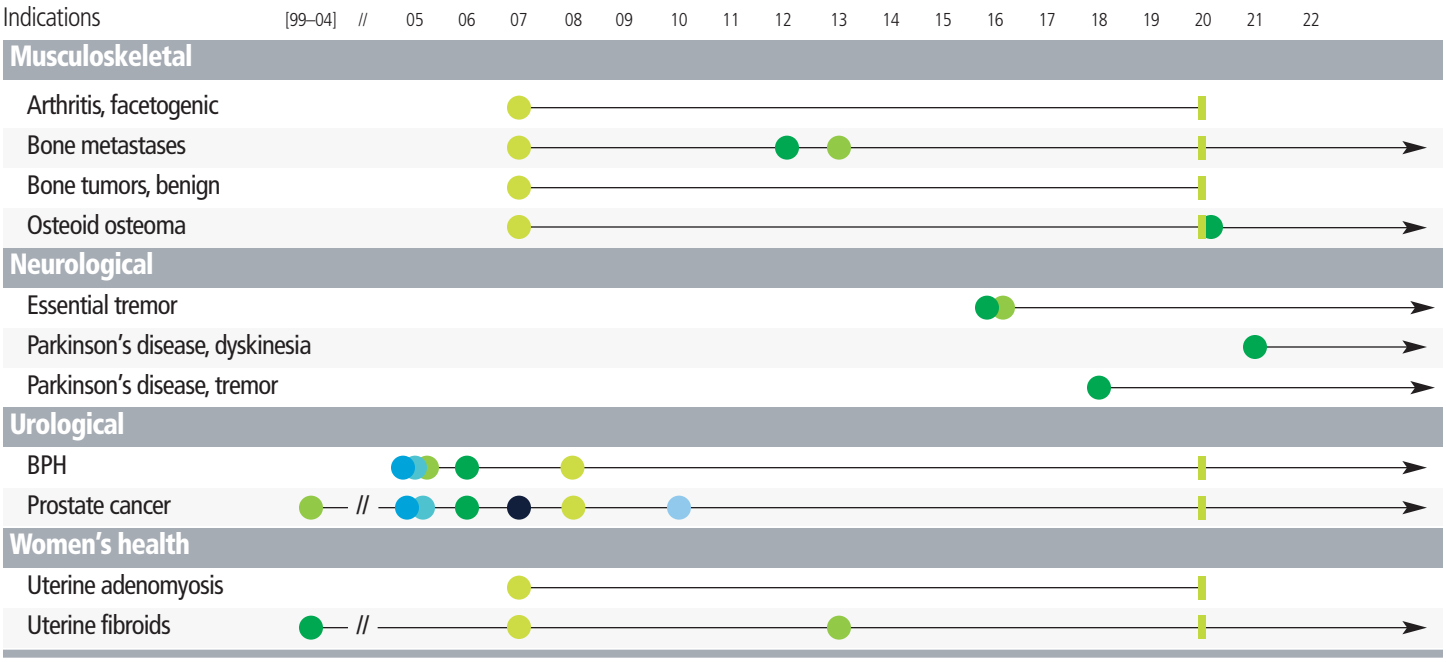


- North America
- Europe
- Asia
- South America
- Oceania
- Africa

North America
FUS Regulatory Approvals by Indication

8 Approvals



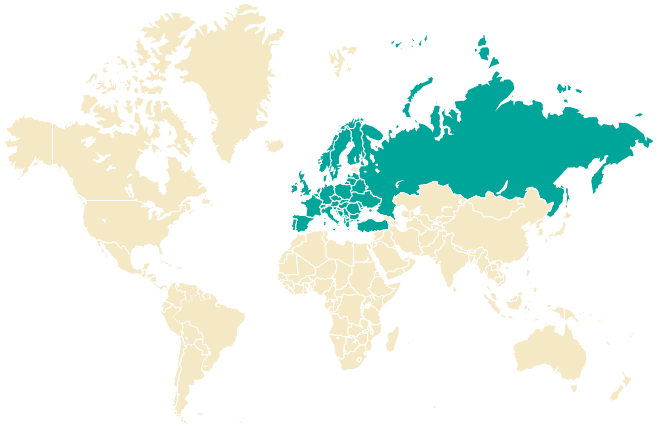


Approval
- Approval begin date
- Approval end date

North America
- Bahamas, *Ministry of Health*
- Barbados, *Ministry of Health and Wellness*
- Costa Rica, *Ministerio de Salud*
- Dominican Republic, *MISPAS*
- United States, *FDA, Center for Devices & Radiological Health*
- Canada, *Health Canada, Medical Devices Bureau*
- Mexico, *COFEPRIS*

Europe
FUS Regulatory Approvals by Indication

27 Approvals



Approval
- Approval begin date
- Approval end date

Europe
- Belarus, *MOH*
- Europe, *CE Marking*
- Russia, *Roszdravnadzor*
- Turkey, *TITUBB*
- United Kingdom, *MHRA*

Europe
FUS Regulatory Approvals by Indication continued

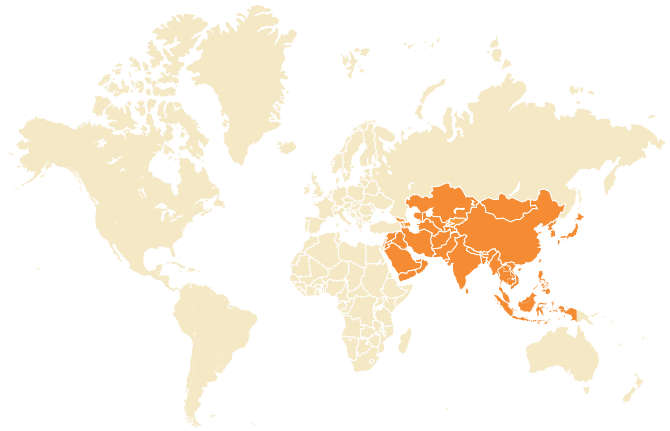
Approval
- Approval begin date
- Approval end date

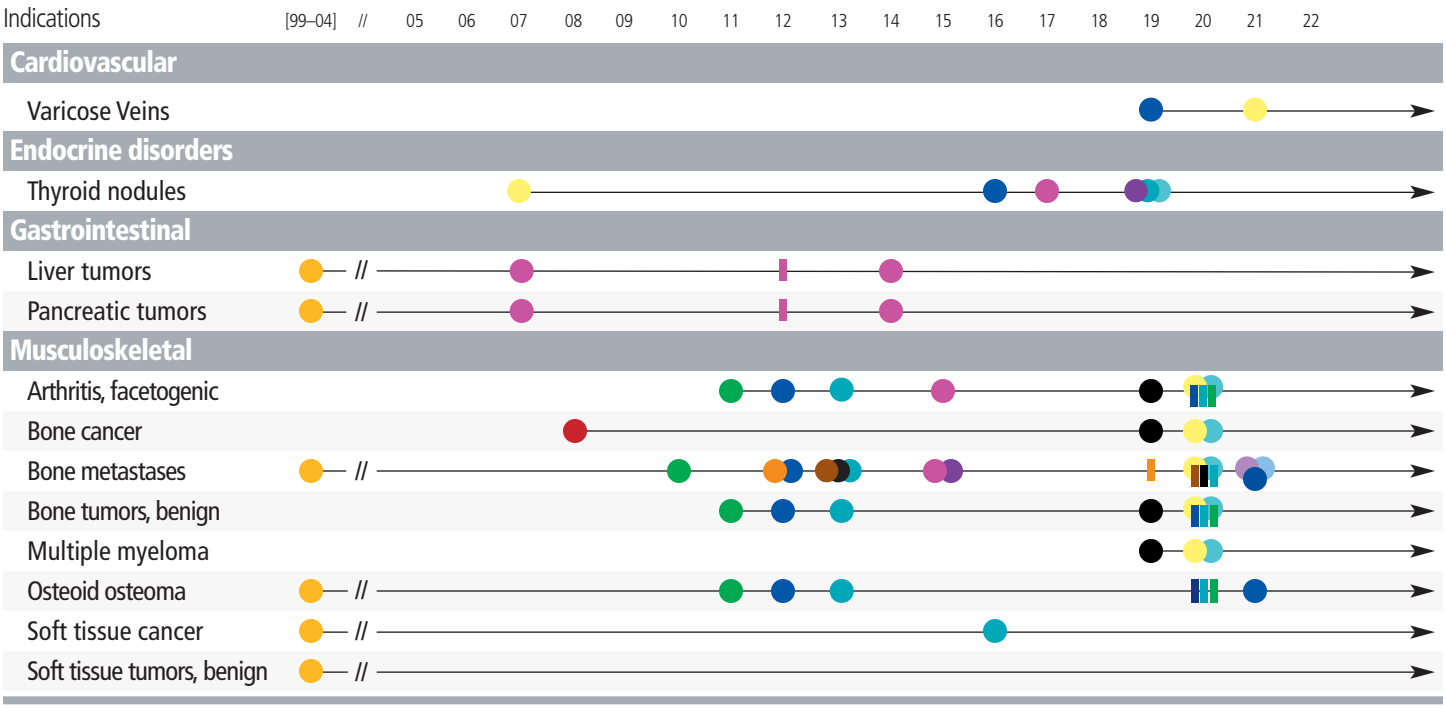
Europe
- Belarus, *MOH*
- Europe, *CE Marking*
- Russia, *Roszdravnadzor*
- Turkey, *TITUBB*
- United Kingdom, *MHRA*

Asia

FUS Regulatory Approvals by Indication

30 Approvals

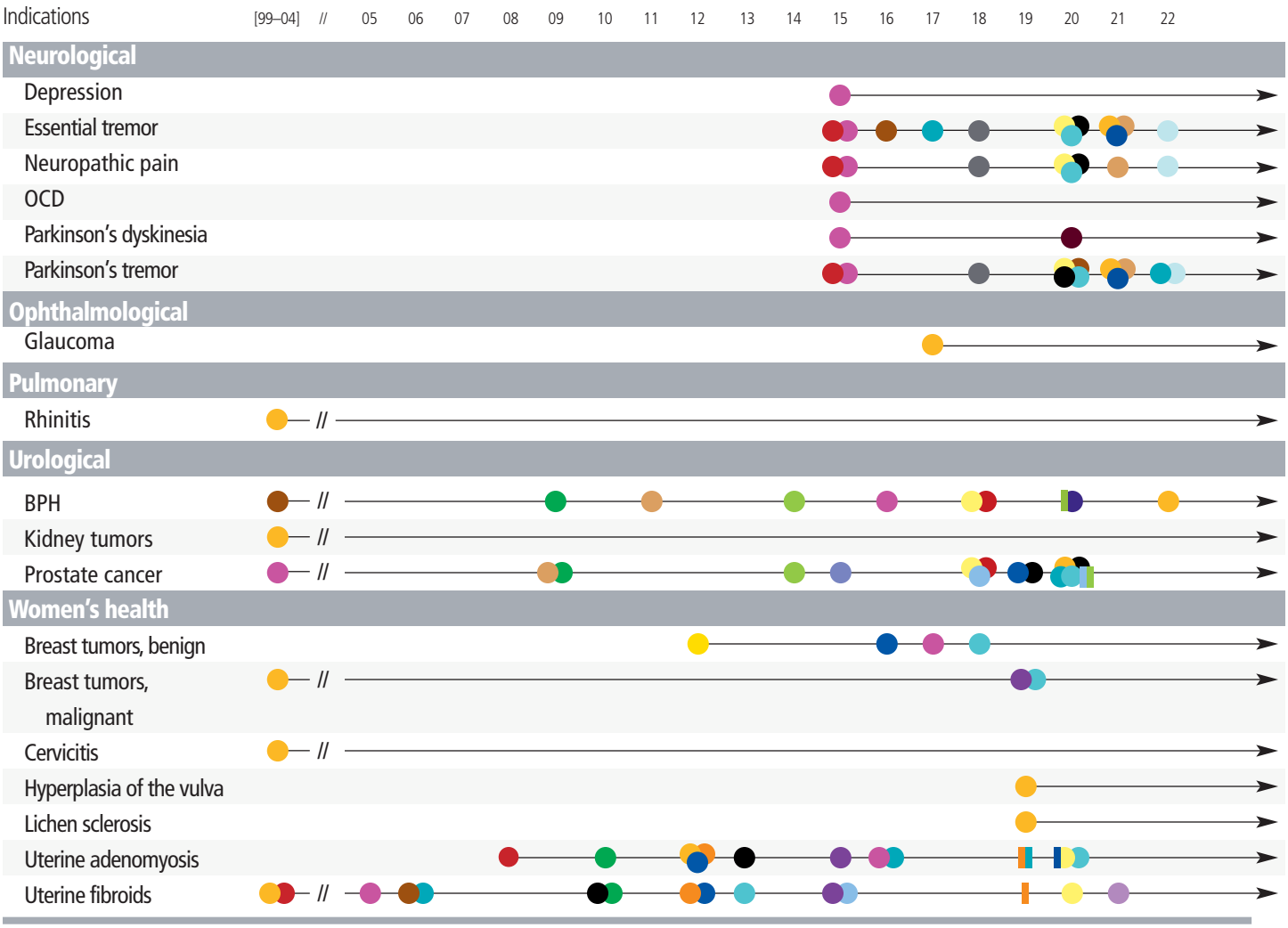




Approval
- Approval begin date
- Approval end date

Asia
- China, *NMPA*
- Hong Kong, *MDD*
- India, *CDSCO*
- Indonesia, *DGPMD*
- Israel, *AMAR*
- Japan, *MHLW*
- Kazakhstan, *NCEM*
- Kuwait, *MOH FDCD*
- Macau, *ISAF*
- Malaysia, *MDA*
- Pakistan, *DRAP*
- Philippines, *FDA*
- Saudi Arabia, *SFDA*
- Singapore, *HSA*
- South Korea, *MFDS*
- Taiwan, *FDA*
- Thailand, *FDA*
- United Arab Emirates, *MOHAP*
- Uzbekistan, *GDQC*
- Vietnam, *DMEW*

Asia
FUS Regulatory Approvals by Indication continued



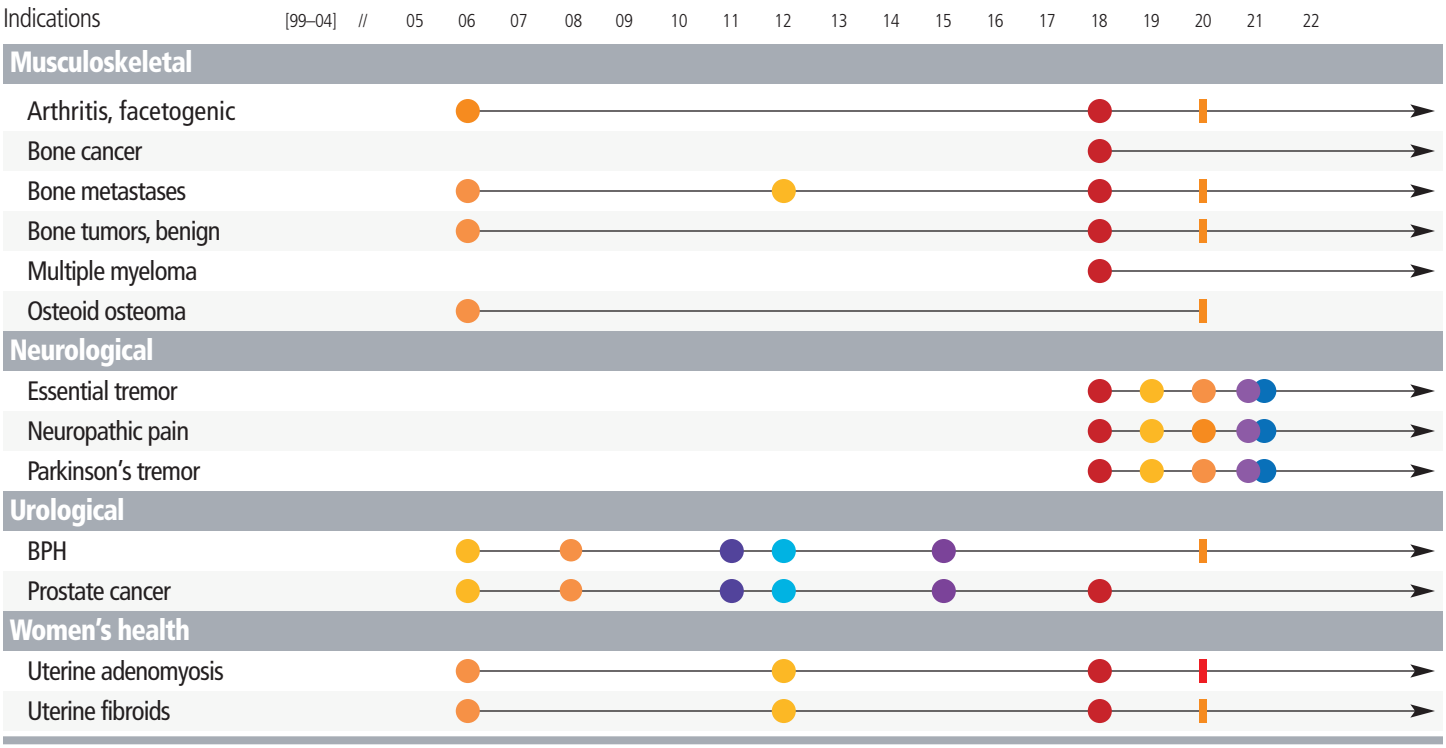
Approval
- Approval begin date
- Approval end date

Asia
- China, *NMPA*
- Hong Kong, *MDD*
- India, *CDSCO*
- Indonesia, *DGPMD*
- Israel, *AMAR*
- Japan, *MHLW*
- Kazakhstan, *NCEM*
- Kuwait, *MOH FDCD*
- Macau, *ISAF*
- Malaysia, *MDA*
- Pakistan, *DRAP*
- Philippines, *FDA*
- Saudi Arabia, *SFDA*
- Singapore, *HSA*
- South Korea, *MFDS*
- Taiwan, *FDA*
- Thailand, *FDA*
- United Arab Emirates, *MOHAP*
- Uzbekistan, *GDQC*
- Vietnam, *DMEW*

South America

FUS Regulatory Approvals by Indication

12
Approvals



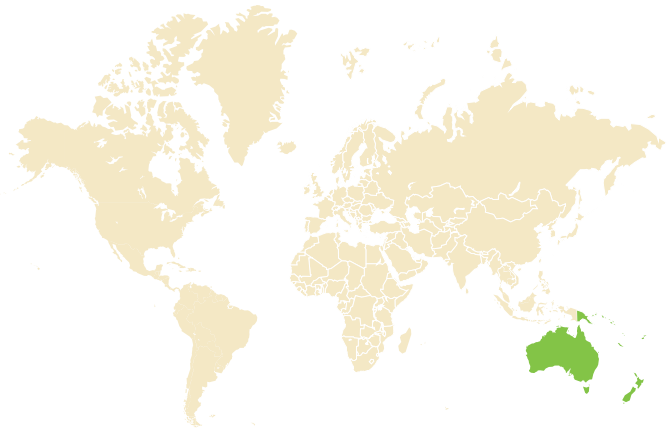
Approval
- Approval begin date
- Approval end date

South America
- Argentina, *ANMAT*
- Brazil, *ANVISA*
- Chile, *ANAMED*
- Colombia, *INVIMA*
- Ecuador, *ANRCVS*
- Peru, *DIGEMED*
- Trinidad and Tobago, *Ministry of Health*

Oceania

FUS Regulatory Approvals by Indication

12 Approvals



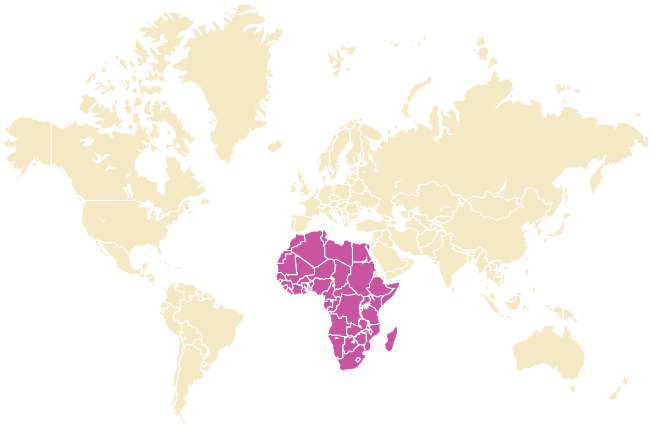
Approval
- Approval begin date
- Approval end date

Oceania
- Australia, *TGA*
- New Zealand, *MEDSAFE*

Africa

FUS Regulatory Approvals by Indication

1
Approval



Indications	[99–04] //	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22
Urological																			
Prostate cancer				●	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→

Approval
- Approval begin date
- Approval end date

Africa
- South Africa, *MCC*

2023 Commercial FUS Manufacturers

Focused Ultrasound Foundation

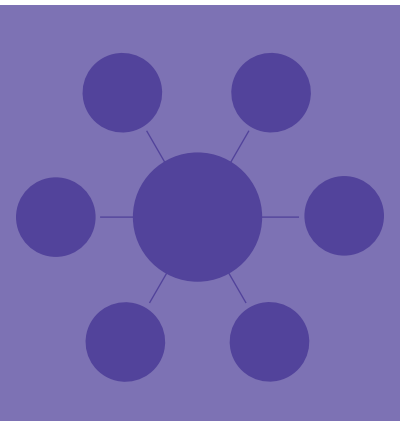
Overview

In the wake of exponential advancement, the industry has surpassed the inflection point, reflecting a shift in the mindset from "if" focused ultrasound will have a critical place in the therapeutic armamentarium to "when" it will be widely available as a mainstream standard of care.

Additionally, we are seeing increasing evidence that the field is transitioning from primarily a science-based research environment to commercialization with patient treatment spaces focused on marketing and sales. As this transition gains momentum, we want to keep pace with the data points and metrics needed to understand and evaluate this global commercialization, so that we may accurately analyze the information and disseminate our findings to all stakeholders. This chapter is a deep dive on the 16 companies that have commercial products available to treat 32 different indications. Information on companies that are still at the research and development stage can be found in Chapter 8 and/or on our website fusfoundation.org/for-industry.

A special thank you to all the industry partners in this space who, year after year, provide information on their companies so that we can collate the data in aggregate to better understand the field.

Approvals may have changed or been updated since publication. For the most up-to-date information please visit: fusfoundation.org/the-foundation/programs/regulatory-approvals-search.



X. Commercial FUS Manufacturers

X. 2 Overview

Approvals

X. 3 By Manufacturer
X. 3 Summary of Global Approvals
X. 4 Clinical Device Manufacturers
X. 5 For Companies by Region and Indication

Manufacturers

X. 6 Clinical Device Manufacturers with Regulatory Approvals
- X. 6 Acoustic MedSystems
- X. 7 Alpinion Medical Systems
- X. 9 Changjiangyuan Technology Development
- X.10 Chongqing Haifu Medical Technology
- X.14 EDAP TMS
- X.16 EpiSonica
- X.17 EyeTechCare
- X.18 Insightec
- X.28 Profound Medical
- X.32 Shanghai A&S Science Technology Development
- X.34 Shende Medical Equipment Technology
- X.36 Shenzhen PRO-HITU Medical Technology
- X.38 Sonablate
- X.41 Theraclion
- X.44 Theraclion Veterinary
- X.46 TOOsonix
- X.48 Wuxi Haiying Electronic Medical Systems

Photographs

X. 49 Approved Clinical Devices

Indication Approvals by Manufacturer

Manufacturer	North America	Europe	Asia	South America	Oceania	Africa
Acoustic MedSystems[1]	1	–	–	–	–	–
Alpinion Medical Systems	–	1	2	–	–	–
Changjiangyuan Technology Development	–	1	–	–	–	–
Chongqing Haifu Medical Technology	–	11	10	–	–	–
EDAP TMS	2	1	1	1	–	–
EpiSonica	–	–	1	–	–	–
EyeTechCare	–	1	1	–	–	–
Insightec	7	12	14	11	11	–
Profound Medical	4	6	5	3	3	–
Shanghai A&S Science Technology Development	–	1	5	–	–	–
Shende Medical Equipment Technology[3]	–	1	–	–	–	–
Shenzhen PRO-HITU Medical Technology	–	1	4	–	–	–
Sonablate	2	2	2	2	2	1
Theraclion	–	3	4	–	–	–
TOOsonix[4]	–	1	–	–	–	–
Wuxi Haiying Electronic Medical Systems	–	–	1	–	–	–

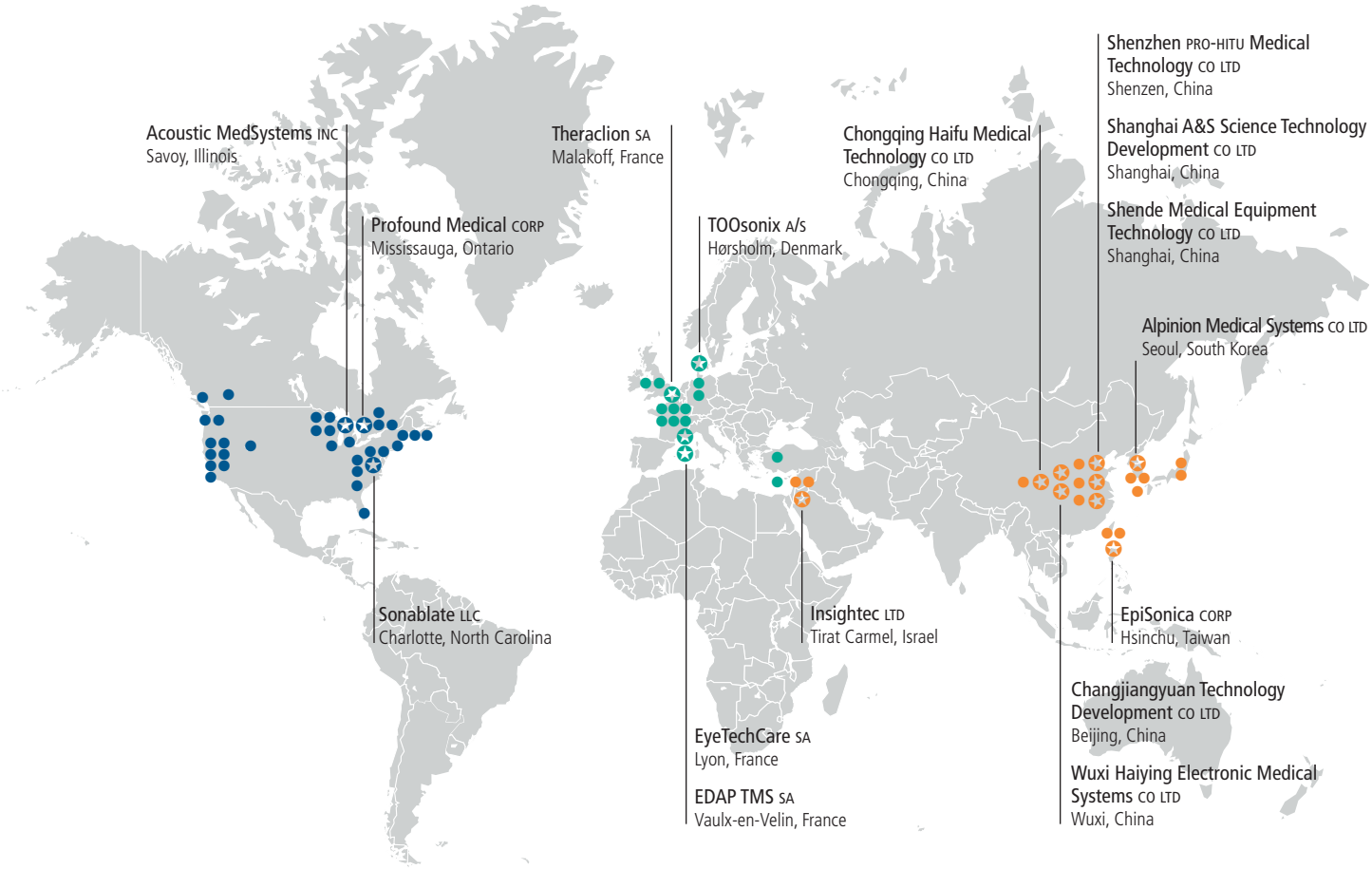
Summary of Global Approvals

39
Regulatory agencies

337
Approvals worldwide

1 Approval is for soft tissue ablation, excluding prostate.
2 Approval is for tumor ablation.
3 Approved indication(s) unknown
4 Approval are for aesthetic indications, which are not tracked by the Foundation.

Clinical Device Manufacturers with Regulatory Approvals



Clinical device manufacturers that have a device or devices with regulatory approvals by regional location.
Company listings of devices, approved indications, and regulatory agencies granting approvals are found on the subsequent pages.

Location of clinical device manufacturers without approved devices by region.

Regulatory Approvals for Companies by Region and Indication

North America

Acoustic MedSystems
Soft tissue ablation, excluding prostate

EDAP TMS
Benign prostatic hyperplasia
Prostate cancer

Insightec
Benign prostatic hyperplasia
Bone metastases
Essential tremor
Parkinson's disease, dyskinesia
Parkinson's disease, tremor
Prostate cancer
Uterine fibroids

Profound Medical
Benign prostatic hyperplasia
Osteoid osteoma
Prostate cancer
Uterine fibroids

Sonablate
Benign prostatic hyperplasia
Prostate cancer

Europe

Alpinion Medical Systems
Uterine fibroids

Changjiangyuan Technology Development
Tumor ablation

Chongqing Haifu Medical Technology
Breast tumors, malignant
Kidney tumors
Liver metastases
Liver tumors
Osteoid osteoma
Pancreatic tumors
Rhinitis
Soft tissue cancer
Soft tissue tumors, benign
Uterine adenomyosis
Uterine fibroids

EDAP TMS
Prostate cancer

EyeTechCare
Glaucoma

Insightec
Arthritis, facetogenic
Bone cancer
Bone metastases
Bone tumors, benign
Essential tremor
Multiple myeloma
Neuropathic pain
Parkinson's disease, dyskinesia
Parkinson's disease, tremor
Prostate cancer
Uterine adenomyosis
Uterine fibroids

Profound Medical
Bone metastases
Desmoid tumors
Osteoid osteoma
Prostate cancer
Uterine adenomyosis
Uterine fibroids

Shanghai A&S
Uterine fibroids

Shende Medical Equipment Technology
Indication(s) unknown

Shenzhen PRO-HITU Medical
Uterine fibroids

Sonablate
Benign prostatic hyperplasia
Prostate cancer

Theraclion
Breast tumors, benign
Thyroid nodules
Varicose veins

TOOsonix
Aesthetic indications

Asia

Alpinion Medical Systems
Uterine adenomyosis
Uterine fibroids

Chongqing Haifu Medical Technology
Breast tumors, malignant
Cervicitis
Kidney tumors
Liver tumors
Osteoid osteoma
Pancreatic tumors
Rhinitis
Soft tissue cancer
Soft tissue tumors, benign
Uterine fibroids

EDAP TMS
Prostate cancer

EpiSonica
Soft tissue cancer

EyeTechCare
Glaucoma

Insightec
Arthritis, facetogenic
Bone cancer
Bone metastases
Bone tumors, benign
Depression
Essential tremor
Multiple myeloma
Neuropathic pain
Obsessive-compulsive disorder
Parkinson's disease, dyskinesia
Parkinson's disease, tremor
Prostate cancer
Uterine adenomyosis
Uterine fibroids

Profound Medical
Bone metastases
Osteoid osteoma
Prostate cancer
Uterine adenomyosis
Uterine fibroids

Shanghai A&S
Bone metastases
Breast tumors, malignant
Liver tumors
Soft tissue cancer
Uterine fibroids

Shenzhen PRO-HITU Medical
Hyperplasia of the vulva
Lichen sclerosis
Uterine adenomyosis
Uterine fibroids

Sonablate
Benign prostatic hyperplasia
Prostate cancer

Theraclion
Breast tumors, benign
Breast tumors, malignant
Thyroid nodules
Varicose veins

Wuxi Haiying Electronic Medical
Uterine fibroids

South America

EDAP TMS
Prostate cancer

Insightec
Arthritis, facetogenic
Bone cancer
Bone metastases
Bone tumors, benign
Essential tremor
Multiple myeloma
Neuropathic pain
Parkinson's disease, tremor
Prostate cancer
Uterine adenomyosis
Uterine fibroids

Profound Medical
Bone metastases
Uterine adenomyosis
Uterine fibroids

Sonablate
Benign prostatic hyperplasia
Prostate cancer

Oceania

Insightec
Arthritis, facetogenic
Bone cancer
Bone metastases
Bone tumors, benign
Essential tremor
Multiple myeloma
Neuropathic pain
Parkinson's disease, tremor
Prostate cancer
Uterine adenomyosis
Uterine fibroids

Profound Medical
Bone metastases
Uterine adenomyosis
Uterine fibroids

Sonablate
Benign prostatic hyperplasia
Prostate cancer

Africa

Sonablate
Prostate cancer

Clinical Device Manufacturers with Regulatory Approvals

Acoustic MedSystems INC

Devices

2	1		
Total devices	Approved device		

Name	Status	Treatment guidance	Planning guidance
ACOUSTx	—	Ultrasound, CT-fluoroscopy, MRI and 3D targeting	—
TheraVision	✚	US guidance	—

Approvals

1	1	1	1
Approved indication	Region	Country	Total approvals*

Indication	Region	Country	Agency and date
—			
Soft tissue ablation, excluding prostate[1]	North America	United States	FDA, 2016

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

1 Approval language does not further delineate tissue type.

Clinical Device Manufacturers with Regulatory Approvals continued

Alpinion Medical Systems CO LTD

Devices

2	1		
Total devices	Approved device		

Name	Status	Treatment guidance	Planning guidance
Alpius 900	✚	US guidance	—
VIFU2000	—	US guidance	—

Approvals

2	2	2	3
Approved indications	Regions	Countries	Total approvals*

Indication	Region	Country	Agency and date
Women's health			
Uterine adenomyosis	Asia	South Korea	MFDS, 2018
Uterine fibroids	Europe Asia	Europe South Korea	CE Marking, 2016 MFDS, 2014

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

Clinical Device Manufacturers with Regulatory Approvals continued

Alpinion Medical Systems CO LTD continued

Clinical research

2 Indications	1 Region	1 Country	2 Sites

Indication	Region	Country	Site
Gastrointestinal			
Pancreatic tumors, malignant	1	1	1
Women's health			
Uterine fibroids	1	1	1

Clinical Device Manufacturers with Regulatory Approvals continued

Changjiangyuan Technology Development CO LTD

Devices

2	2		
Total devices	**Approved devices**		

Name	Status	Treatment guidance	Planning guidance
NUTAS - Non-invasive Ultrasound Tumor Ablation System	✚	US guidance	US guidance
SUPER Knife-Focused Beam Therapy System	✚	MR & US guidance	—

Approvals

1	1	1	1
Approved indication	**Region**	**Country**	**Total approvals***

Indication	Region	Country	Agency and date
—			
Tumor ablation[1]	Europe	Europe	CE Marking, 2012
Tumor ablation[1]	Europe	Europe	CE Marking, 2018

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

1 Approval language does not specify tumor type.

Clinical Device Manufacturers with Regulatory Approvals continued

Chongqing Haifu Medical Technology CO LTD

Devices

8	4		
Total devices	Approved devices		

Name	Status	Treatment guidance	Planning guidance
CZB	✚	US guidance	—
CZF	✚	US guidance	—
CZG300	—	US guidance	—
JC	✚	US guidance	—
JC200	✚	US guidance	—
JC200D	—	US guidance	—
JC300	—	US guidance	—
LCA200	—	Unguided	—

Approvals

12	2	4	33
Approved indications	Regions	Countries	Total approvals*

Indication	Region	Country	Agency and date
Gastrointestinal			
Liver metastases	Europe	Europe	CE Marking, 2005
Liver tumors	Europe	Europe	CE Marking, 2005
	Europe	Russia	Roszdravnadzor, 2011
	Asia	China	NMPA, 1999
	Asia	South Korea	MFDS, 2014

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

Clinical Device Manufacturers with Regulatory Approvals continued

Chongqing Haifu Medical Technology CO LTD continued

Approvals continued

Indication	Region	Country	Agency and date
Gastrointestinal continued			
Pancreatic tumors	Europe Europe Asia Asia	Europe Russia China South Korea	CE Marking, 2006 Roszdravnadzor, 2011 NMPA, 1999 MFDS, 2014
Musculoskeletal			
Osteoid osteoma	Europe Europe Asia	Europe Russia China	CE Marking, 2006 Roszdravnadzor, 2011 NMPA, 1999
Soft tissue cancer	Europe Europe Asia	Europe Russia China	CE Marking, 2006 Roszdravnadzor, 2011 NMPA, 1999
Soft tissue tumors, benign	Europe Europe Asia	Europe Russia China	CE Marking, 2006 Roszdravnadzor, 2011 NMPA, 1999
Pulmonary			
Rhinitis	Europe Asia	Europe China	CE Marking, 2006 NMPA, 1999
Urological			
Kidney tumors	Europe Europe Asia	Europe Russia China	CE Marking, 2005 Roszdravnadzor, 2011 NMPA, 1999
Women's health			
Breast tumors, malignant	Europe Europe Asia	Europe Russia China	CE Marking, 2006 Roszdravnadzor, 2011 NMPA, 1999
Cervicitis	Asia	China	NMPA, 1999
Uterine adenomyosis	Europe Europe	Europe Russia	CE Marking, 2006 Roszdravnadzor, 2011

Clinical Device Manufacturers with Regulatory Approvals continued

Chongqing Haifu Medical Technology CO LTD continued

Approvals continued

Indication	Region	Country	Agency and date
Women's health continued			
Uterine fibroids	Europe	Europe	CE Marking, 2006
	Europe	Russia	Roszdravnadzor, 2011
	Asia	China	NMPA, 1999
	Asia	South Korea	MFDS, 2014

Clinical research

17	2	7	17
Indications	**Regions**	**Countries**	**Sites**

Indication	Region	Country	Site
Gastrointestinal			
Liver tumors	1	3	4
Pancreatic tumors	1	1	1
Pancreatic tumors, malignant	1	4	5
Musculoskeletal			
Desmoid tumors	1	1	1
Osteoid osteoma	1	1	1
Sacral chordoma	1	1	1
Soft tissue cancer	1	1	2
Soft tissue tumors, benign	1	3	3
Neurological			
Neuropathic pain	1	1	1

Clinical Device Manufacturers with Regulatory Approvals continued

Chongqing Haifu Medical Technology CO LTD continued

Clinical research continued

Indication	Region	Country	Site
Pulmonary			
Rhinitis	1	1	1
Urological			
Kidney tumors	1	2	2
Prostate cancer	1	1	1
Women's health			
Breast tumors, malignant	1	3	4
Cervical tumors	1	1	1
Retained placenta	1	1	1
Uterine adenomyosis	1	2	3
Uterine fibroids	2	4	7

Clinical Device Manufacturers with Regulatory Approvals continued

EDAP TMS SA

Devices

3	2		
Total devices	Approved devices		

Name	Status	Treatment guidance	Planning guidance
Ablatherm	✚	Image fusion	US guidance
EDAP (Prototype)	—	US guidance	US guidance
Focal One	✚	Image fusion	MR guidance, US guidance, biopsies

Approvals

2	4	6	12
Approved indications	Regions	Countries	Total approvals*

Indication	Region	Country	Agency and date
Urological			
Benign prostatic hyperplasia	North America	United States	FDA, 2015
Prostate cancer	North America	Canada	Health Canada, 2003
	North America	United States	FDA, 2015
	Europe	Europe	CE Marking, 2013
	Europe	Russia	Roszdravnadzor, 2002
	Asia	South Korea	MFDS, 2002
	South America	Brazil	ANVISA, 2016

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

Clinical Device Manufacturers with Regulatory Approvals continued

EDAP TMS SA continued

Clinical research

3	2	6	28
Indications	Regions	Countries	Sites

Indication	Region	Country	Site
Urological			
Benign prostatic hyperplasia	1	1	1
Prostate cancer	2	6	26
Women's health			
Endometriosis	1	1	1

> **EDAP TMS** designs, produces, and markets medical equipment dedicated to minimally invasive therapies based on robotic therapeutic ultrasound. Our lead product, Focal One®, combines the latest technologies in imaging and treatment modalities."
>
> — EDAP TMS SA

Clinical Device Manufacturers with Regulatory Approvals continued

EpiSonica CORP

Devices

1 Total device	1 Approved device		
Name	Status	Treatment guidance	Planning guidance
ArcBLATE (ARC-100M)	✚	MR	MR

Approvals

1 Approved indication	1 Region	1 Country	1 Total approvals*
Indication	Region	Country	Agency and date
Musculoskeletal			
Soft tissue cancer	Asia	Taiwan	FDA, 2016

> **EpiSonica Corp** is a leading company that is focusing on development of a supine and prone MRgHIFU system. Our ArcBlate system provides treatment for uterine fibroids and uterine adenomyosis disease as well as the application of pain palliation for bone metastases."
>
> — EpiSonica CORP

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

Clinical Device Manufacturers with Regulatory Approvals continued

EyeTechCare SA

Devices

1 Total device	1 Approved device		
Name	Status	Treatment guidance	Planning guidance
EyeOP1	✚	Unguided	—

Approvals

1 Approved indication	2 Regions	2 Countries	2 Total approvals*
Indication	Region	Country	Agency and date
Ophthalmological			
Glaucoma	Europe	Europe	CE Marking, 2011
	Asia	China	NMPA, 2017

Clinical research

1 Indication	2 Regions	4 Countries	4 Sites
Indication	Region	Country	Site
Ophthalmological			
Glaucoma	2	4	4

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

Clinical Device Manufacturers with Regulatory Approvals continued

Insightec LTD

Devices

3	3		
Total devices	**Approved devices**		

Name	Status	Treatment guidance	Planning guidance
Exablate Body	✚	MR guidance	MR guidance
Exablate Neuro	✚	MR guidance	MR/CT guidance
Exablate Prostate	✚	MR guidance	MR guidance

Approvals

15	5	28	166
Approved indications	**Regions**	**Countries**	**Total approvals***

Indication	Region	Country	Agency and date
Musculoskeletal			
Arthritis, facetogenic	Europe	Europe	CE Marking, 2006
	Europe	Russia	Roszdravnadzor, 2017
	Europe	Turkey	TITUBB, 2017
	Asia	Hong Kong	MDD, 2020
	Asia	Kazakhstan	NCEM, 2019
	Asia	South Korea	MFDS, 2015
	Asia	Thailand	FDA, 2020
	South America	Chile	ANAMED, 2018
	Oceania	Australia	TGA, 2006
	Oceania	New Zealand	MEDSAFE, 2006

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

Clinical Device Manufacturers with Regulatory Approvals continued

Insightec LTD continued

Approvals continued

Indication	Region	Country	Agency and date
Musculoskeletal continued			
Bone cancer	Europe	Europe	CE Marking, 2006
	Europe	Russia	Roszdravnadzor, 2017
	Europe	Turkey	TITUBB, 2017
	Asia	Hong Kong	MDD, 2020
	Asia	Israel	AMAR, 2008
	Asia	Kazakhstan	NCEM, 2019
	Asia	Thailand	FDA, 2020
	South America	Chile	ANAMED, 2018
	Oceania	Australia	TGA, 2006
	Oceania	New Zealand	MEDSAFE, 2006
Bone metastases	North America	Canada	Health Canada, 2013
	North America	United States	FDA, 2012
	Europe	Belarus	MOH, 2021
	Europe	Europe	CE Marking, 2006
	Europe	Russia	Roszdravnadzor, 2017
	Europe	Turkey	TITUBB, 2017
	Asia	Hong Kong	MDD, 2020
	Asia	Kazakhstan	NCEM, 2019
	Asia	Kuwait	MOH FDCD, 2021
	Asia	Saudi Arabia	SFDA, 2021
	Asia	South Korea	MFDS, 2015
	Asia	Thailand	FDA, 2020
	South America	Chile	ANAMED, 2018
	Oceania	Australia	TGA, 2006
	Oceania	New Zealand	MEDSAFE, 2006

Clinical Device Manufacturers with Regulatory Approvals continued

Insightec LTD continued

Approvals continued

Indication	Region	Country	Agency and date
Musculoskeletal continued			
Bone tumors, benign	Europe	Europe	CE Marking, 2006
	Europe	Russia	Roszdravnadzor, 2017
	Europe	Turkey	TITUBB, 2017
	Asia	Hong Kong	MDD, 2020
	Asia	Kazakhstan	NCEM, 2019
	Asia	Thailand	FDA, 2020
	South America	Chile	ANAMED, 2018
	Oceania	Australia	TGA, 2006
	Oceania	New Zealand	MEDSAFE, 2006
Multiple myeloma	Europe	Europe	CE Marking, 2006
	Europe	Russia	Roszdravnadzor, 2017
	Europe	Turkey	TITUBB, 2017
	Asia	Hong Kong	MDD, 2020
	Asia	Kazakhstan	NCEM, 2019
	Asia	Thailand	FDA, 2020
	South America	Chile	ANAMED, 2018
	Oceania	Australia	TGA, 2006
	Oceania	New Zealand	MEDSAFE, 2006
Neurological			
Depression	Asia	South Korea	MFDS, 2015
Essential tremor	North America	Canada	Health Canada, 2016
	North America	United States	FDA, 2016
	Europe	Europe	CE Marking, 2012
	Europe	Russia	Roszdravnadzor, 2017
	Europe	Turkey	TITUBB, 2017
	Europe	United Kingdom	MHRA, 2022
	Asia	China	NMPA, 2021
	Asia	Hong Kong	MDD, 2020
	Asia	India	CDSCO, 2021
	Asia	Israel	AMAR, 2015
	Asia	Japan	MHLW, 20160

Clinical Device Manufacturers with Regulatory Approvals continued

Insightec LTD continued

Approvals continued

Indication	Region	Country	Agency and date
Neurological continued			
Essential tremor continued	Asia	Kazakhstan	NCEM, 2020
	Asia	Philippines	FDA, 2018
	Asia	Singapore	HSA, 2021
	Asia	South Korea	MFDS, 2015
	Asia	Taiwan	FDA, 2017
	Asia	Thailand	FDA, 2020
	Asia	United Arab Emirates	MOHAP, 2022
	South America	Argentina	ANMAT, 2019
	South America	Brazil	ANVISA, 2020
	South America	Chile	ANAMED, 2018
	South America	Colombia	INVIMA, 2021
	South America	Peru	DIGEMED, 2021
	Oceania	Australia	TGA, 2015
Neuropathic pain	Europe	Europe	CE Marking, 2012
	Europe	Russia	Roszdravnadzor, 2017
	Europe	Turkey	TITUBB, 2017
	Europe	United Kingdom	MHRA, 2022
	Asia	Hong Kong	MDD, 2020
	Asia	India	CDSCO, 2021
	Asia	Israel	AMAR, 2015
	Asia	Kazakhstan	NCEM, 2020
	Asia	Philippines	FDA, 2018
	Asia	South Korea	MFDS, 2015
	Asia	Thailand	FDA, 2020
	Asia	United Arab Emirates	MOHAP, 2022
	South America	Argentina	ANMAT, 2019
	South America	Brazil	ANVISA, 2020
	South America	Chile	ANAMED, 2018
	South America	Colombia	INVIMA, 2021
	South America	Peru	DIGEMED, 2021
	Oceania	Australia	TGA, 2015

Clinical Device Manufacturers with Regulatory Approvals continued

Insightec LTD continued

Approvals continued

Indication	Region	Country	Agency and date
Neurological continued			
Obsessive-compulsive disorder	Asia	South Korea	MFDS, 2015
Parkinson's disease, dyskinesia	North America	United States	FDA, 2021
	Europe	Russia	Roszdravnadzor, 2017
	Asia	Japan	MHLW, 2020
	Asia	South Korea	MFDS, 2015
Parkinson's disease, tremor	North America	United States	FDA, 2018
	Europe	Europe	CE Marking, 2012
	Europe	Russia	Roszdravnadzor, 2017
	Europe	Turkey	TITUBB, 2017
	Europe	United Kingdom	MHRA, 2022
	Asia	China	NMPA, 2021
	Asia	Hong Kong	MDD, 2020
	Asia	India	CDSCO, 2021
	Asia	Israel	AMAR, 2015
	Asia	Japan	MHLW, 2020
	Asia	Kazakhstan	NCEM, 2020
	Asia	Philippines	FDA, 2018
	Asia	Singapore	HSA, 2021
	Asia	South Korea	MFDS, 2015
	Asia	Taiwan	FDA, 2022
	Asia	Thailand	FDA, 2020
	Asia	United Arab Emirates	MOHAP, 2022
	South America	Argentina	ANMAT, 2019
	South America	Brazil	ANVISA, 2020
	South America	Chile	ANAMED, 2018
	South America	Colombia	INVIMA, 2021
	South America	Peru	DIGEMED, 2021
	Oceania	Australia	TGA, 2015

Clinical Device Manufacturers with Regulatory Approvals continued

Insightec LTD continued

Approvals continued

Indication	Region	Country	Agency and date
Urological			
Benign prostatic hyperplasia	North America	United States	FDA, 2021
Prostate cancer	North America	United States	FDA, 2021
	Europe	Belarus	MOH, 2021
	Europe	Europe	CE Marking, 2016
	Europe	Russia	Roszdravnadzor, 2017
	Europe	Turkey	TITUBB, 2017
	Asia	Hong Kong	MDD, 2020
	Asia	Israel	AMAR, 2022
	Asia	Kazakhstan	NCEM, 2019
	Asia	Thailand	FDA, 2020
	South America	Chile	ANAMED, 2018
	Oceania	Australia	TGA, 2016
	Oceania	New Zealand	MEDSAFE, 2016
Women's health			
Uterine adenomyosis	Europe	Europe	CE Marking, 2006
	Europe	Turkey	TITUBB, 2017
	Asia	Hong Kong	MDD, 2020
	Asia	Israel	AMAR, 2008
	Asia	Kazakhstan	NCEM, 2019
	Asia	Thailand	FDA, 2020
	South America	Chile	ANAMED, 2018
	Oceania	Australia	TGA, 2006
	Oceania	New Zealand	MEDSAFE, 2006

Clinical Device Manufacturers with Regulatory Approvals continued

Insightec LTD continued

Approvals continued

Indication	Region	Country	Agency and date
Women's health continued			
Uterine fibroids	North America	Canada	Health Canada, 2013
	North America	United States	FDA, 2004
	Europe	Belarus	MOH, 2021
	Europe	Europe	CE Marking, 2006
	Europe	Russia	Roszdravnadzor, 2006
	Europe	Turkey	TITUBB, 2017
	Asia	China	NMPA, 2013
	Asia	Hong Kong	MDD, 2020
	Asia	Israel	AMAR, 2003
	Asia	Japan	MHLW, 2006
	Asia	Kazakhstan	NCEM, 2019
	Asia	Kuwait	MOH FDCD, 2021
	Asia	Saudi Arabia	SFDA, 2021
	Asia	Singapore	HSA, 2012
	Asia	South Korea	MFDS, 2011
	Asia	Taiwan	FDA, 2006
	Asia	Thailand	FDA, 2020
	South America	Chile	ANAMED, 2018
	Oceania	Australia	TGA, 2006
	Oceania	New Zealand	MEDSAFE, 2006

> **Insightec** is a global healthcare company creating the next generation of patient care by realizing the therapeutic power of acoustic energy. Insightec is dedicated to the research and commercial application of focused ultrasound in multiple indications"
>
> — Insightec INC

Clinical Device Manufacturers with Regulatory Approvals continued

Insightec LTD continued

Clinical research

40 Indications	4 Regions	17 Countries	76 Sites

Indication	Region	Country	Site
Gastrointestinal			
Liver tumors	1	1	2
Pancreatic tumors, malignant	2	2	2
Miscellaneous			
Head & neck tumors	1	2	2
Musculoskeletal			
Arthritis, facetogenic	2	5	6
Arthritis, knee	1	1	1
Bone cancer	1	1	2
Bone metastases	3	7	12
Bone tumors, benign	1	1	1
Osteoid osteoma	2	3	5
Soft tissue cancer	2	2	2
Soft tissue tumors, benign	2	2	2
Neurological			
Alzheimer's disease	2	3	9
Amyotrophic lateral sclerosis	1	1	1
Astrocytoma	1	1	2
Brain metastases, breast cancer	1	1	1
Brain metastases, lung cancer	1	2	4
Brain metastases, melanoma	1	1	1
Brain tumors, general	1	2	2

Clinical Device Manufacturers with Regulatory Approvals continued

Insightec LTD continued

Clinical research continued

Indication	Region	Country	Site
Neurological continued			
Cancer pain	1	1	1
Depression	2	2	2
Dystonia	1	3	3
Dystonia, hand	1	1	1
Epilepsy	2	2	7
Essential tremor	3	10	17
Glioblastoma	3	6	16
Multiple sclerosis	1	1	1
Neurofibromatosis	1	1	1
Neuropathic pain	1	1	1
Obsessive-compulsive disorder	1	1	2
Painful amputation neuromas	1	1	1
Parkinson's disease, dyskinesia	3	4	14
Parkinson's disease, tremor	3	7	12
Parkinson's disease, underlying cause	1	1	1
Pontine glioma	1	2	4
Tremor, orthostatic	1	1	1
Trigeminal neuralgia	1	1	1
Urological			
Prostate cancer	2	2	6
Women's health			
Endometriosis	1	1	1
Uterine adenomyosis	3	4	5
Uterine fibroids	4	11	15

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Clinical Device Manufacturers with Regulatory Approvals continued

Profound Medical CORP

Devices

2	2		
Total devices	Approved devices		

Name	Status	Treatment guidance	Planning guidance
Sonalleve	✚	MR guidance	MR guidance
TULSA-PRO	✚	MR guidance	MR guidance

Approvals[1]

7	5	12	33
Approved indications	Regions	Countries	Total approvals*

Indication	Region	Country	Agency and date
Musculoskeletal			
Bone metastases	Europe	Europe	CE Marking, 2011
	Asia	Malaysia	MDA, 2015
	Asia	Singapore	HSA, 2021
	Asia	Vietnam	DMEW, 2010
	South America	Argentina	ANMAT, 2012
	Oceania	Australia	TGA, 2012
	Oceania	New Zealand	MEDSAFE, 2012
Desmoid tumors	Europe	Europe	CE Marking, 2021
Osteoid osteoma	North America	United States	FDA, 2020
	Europe	Europe	CE Marking, 2020
	Asia	Singapore	HSA, 2021

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

1 Approvals may have changed or been updated since publication. For the most up-to-date information please visit: fusfoundation.org/the-foundation/programs/regulatory-approvals-search.

Clinical Device Manufacturers with Regulatory Approvals continued

Profound Medical CORP continued

Approvals continued

Indication	Region	Country	Agency and date
Urological			
Benign prostatic hyperplasia	North America	United States	FDA, 2019
Prostate cancer	North America	Canada	Health Canada, 2019
	North America	United States	FDA, 2019
	Europe	Europe	CE Marking, 2016
	Asia	Singapore	HSA, 2019
Women's health			
Uterine adenomyosis	Europe	Europe	CE Marking, 2010
	Asia	Malaysia	MDA, 2015
	Asia	Vietnam	DMEW, 2010
	South America	Argentina	ANMAT, 2012
	Oceania	Australia	TGA, 2012
	Oceania	New Zealand	MEDSAFE, 2012
Uterine fibroids	North America	Canada	Health Canada, 2013
	Europe	Europe	CE Marking, 2009
	Asia	China	NMPA, 2018
	Asia	Malaysia	MDA, 2015
	Asia	Saudi Arabia	SFDA, 2015
	Asia	Singapore	HSA, 2021
	Asia	South Korea	MFDS, 2012
	Asia	Vietnam	DMEW, 2010
	South America	Argentina	ANMAT, 2012
	Oceania	Australia	TGA, 2012
	Oceania	New Zealand	MEDSAFE, 2012

Clinical Device Manufacturers with Regulatory Approvals continued

Profound Medical CORP continued

Clinical research

22 Indications	3 Regions	10 Countries	28 Sites

Indication	Region	Country	Site
Gastrointestinal			
Liver tumors	1	1	1
Pancreatic tumors, malignant	1	1	2
Miscellaneous			
Head & neck tumors	1	1	1
Multiple tumors[1]	1	1	1
Musculoskeletal			
Arthritis, facetogenic	1	1	1
Arthritis, sacroiliac	1	1	1
Bone cancer	1	2	4
Bone metastases	2	5	6
Bone tumors, benign	1	2	2
Desmoid tumors	2	5	6
Osteoid osteoma	2	2	3
Plantar fasciitis	1	1	1
Soft tissue cancer	1	2	2
Soft tissue tumors, benign	2	2	2
Neurological			
Neuroblastoma	1	1	1
Urological			
Benign prostatic hyperplasia	1	1	1
Prostate cancer	2	6	15

1 Protocols inclusive of more than one indication

Clinical Device Manufacturers with Regulatory Approvals continued

Profound Medical CORP continued

Clinical research continued

Indication	Region	Country	Site
Women's health			
Breast tumors, malignant	2	2	2
Uterine adenomyosis	2	3	3
Uterine fibroids	2	5	7
Vaginal tumors	1	1	1

> **Profound** develops customizable, incision-free ablative therapies which combine real-time MRI, thermal ultrasound, autonomous robotics, and closed-loop process control to change the standard of care for physicians and patients."
>
> — Profound Medical CORP

Clinical Device Manufacturers with Regulatory Approvals continued

Shanghai A&S Science Technology Development CO, LTD

Devices

1	1		
Total device	Approved device		

Name	Status	Treatment guidance	Planning guidance
HIFUNIT9000	✚	US guidance	MR guidance

Approvals

5	2	4	8
Approved indications	Regions	Countries	Total approvals*

Indication	Region	Country	Agency and date
Gastrointestinal			
Liver tumors	Asia	China	NMPA, 2002
Musculoskeletal			
Bone metastases	Asia	China	NMPA, 2002
Soft tissue cancer	Asia	China	NMPA, 2002
Women's health			
Breast tumors, malignant	Asia	China	NMPA, 2002
Uterine fibroids	Europe	Europe	CE Marking, 2008
	Asia	China	NMPA, 2002
	Asia	South Korea	MFDS, 2007
	Asia	Thailand	FDA, 2013

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

Clinical Device Manufacturers with Regulatory Approvals continued

Shanghai A&S Science Technology Development CO, LTD continued

Clinical research

1 Indication	1 Region	1 Country	1 Site

Indication	Region	Country	Site
Gastrointestinal			
Liver tumors	1	1	1

> **Shanghai A&S Science Technology Development** is a leading company focused on high intensity focused ultrasound for tumor ablation with ultrasound guidance. Based in Shanghai, A&S has expanded business in Asia with over 200 installations."
>
> — Shanghai A&S Science Technology Development CO LTD

Clinical Device Manufacturers with Regulatory Approvals continued

Shende Medical Equipment Technology CO LTD

Devices

1 Total device	1 Approved device		
Name	Status	Treatment guidance	Planning guidance
Aceso	✚	MR guidance	—

Approvals

1 Approved indication	1 Region	1 Country	1 Total approvals*
Indication	Region	Country	Agency and date
—			
—[1]	Europe	Europe	CE Marking, 2020

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

1 Indication(s) unknown

Clinical Device Manufacturers with Regulatory Approvals continued

Shende Medical Equipment Technology CO LTD continued

Clinical research

4 Indications	1 Region	1 Country	4 Sites

Indication	Region	Country	Site
Musculoskeletal			
Bone metastases	1	1	3
Women's health			
Breast tumors, benign	1	1	2
Uterine adenomyosis	1	1	3
Uterine fibroids	1	1	3

Clinical Device Manufacturers with Regulatory Approvals continued

Shenzhen PRO-HITU Medical Technology CO, LTD

Devices

5	3		
Total devices	Approved devices		

Name	Status	Treatment guidance	Planning guidance
PRO2008	✚	US guidance	US guidance
PRO300	✚	US guidance	US guidance
PRO3008	—	US guidance	US guidance
PRO5G	✚	Other guidance	Visual guidance
UT1000	—	Unguided	Not used

Approvals

4	2	4	10
Approved indications	Regions	Countries	Total approvals*

Indication	Region	Country	Agency and date
Women's health			
Hyperplasia of the vulva	Asia	China	NMPA, 2019
Lichen sclerosis	Asia	China	NMPA, 2019
Uterine adenomyosis	Asia Asia	China South Korea	NMPA, 2012 MFDS, 2016
Uterine fibroids	Europe Asia Asia	Europe China Taiwan	CE Marking, 2012 MDA, 2012 FDA, 2018

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

Clinical Device Manufacturers with Regulatory Approvals continued

Shenzhen PRO-HITU Medical Technology CO, LTD continued

Clinical research

2 Indications	1 Region	1 Country	4 Sites

Indication	Region	Country	Site
Women's health			
Uterine adenomyosis	1	1	3
Uterine fibroids	1	1	3

> **Shenzen PRO–HITU Medical Technology** was established in 2003, focusing on R&D of large ultrasonic treatment equipment. Vision: The pioneering of Non-Invasive Therapy. Mission: Respect Life in Therapy."
>
> — Shenzen PRO-HITU Medical CO, LTD

Clinical Device Manufacturers with Regulatory Approvals continued

Sonablate CORP

Devices

2	2		
Total devices	Approved devices		

Name	Status	Treatment guidance	Planning guidance
Sonablate	✚	US guidance	MR/US fusion
Sonatherm	✚	US guidance	US guidance

Approvals

2	6	25	46
Approved indications	Regions	Countries	Total approvals*

Indication	Region	Country	Agency and date
Urological			
Benign prostatic hyperplasia	North America	Canada	Health Canada, 2005
	North America	Costa Rica	Ministerio de Salud, 2005
	North America	Dominican Republic	MISPAS, 2005
	North America	United States	FDA, 2006
	Europe	Europe	CE Marking, 2006
	Europe	Russia	Roszdravnadzor, 2005
	Europe	United Kingdom	MHRA, 2019
	Asia	China	NMPA, 2022
	Asia	Hong Kong	MDD, 2018
	Asia	India	CDSCO, 2011
	Asia	Israel	AMAR, 2018
	Asia	Japan	MHLW, 2001
	Asia	Macau	ISAF, 2020
	Asia	South Korea	MFDS, 2016
	Asia	Vietnam	DMEW, 2009

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on pp. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

Clinical Device Manufacturers with Regulatory Approvals continued

Sonablate CORP continued

Approvals continued

Indication	Region	Country	Agency and date
Urological continued			
Benign prostatic hyperplasia con't.	South America	Argentina	ANMAT, 2006
	South America	Colombia	INVIMA, 2015
	South America	Ecuador	ANRCVS, 2011
	South America	Trinidad and Tobago	Ministry of Health, 2012
	Oceania	Australia	TGA, 2005
Prostate cancer	North America	Bahamas	Ministry of Health, 2007
	North America	Barbados	Ministry of Health and Wellness, 2010
	North America	Canada	Health Canada, 2005
	North America	Costa Rica	Ministerio de Salud, 2005
	North America	Dominican Republic	MISPAS, 2005
	North America	United States	FDA, 2006
	Europe	Europe	CE Marking, 2006
	Europe	Russia	Roszdravnadzor, 2005
	Europe	United Kingdom	MHRA, 2019
	Asia	China	NMPA, 2020
	Asia	Hong Kong	MDD, 2018
	Asia	India	CDSCO, 2011
	Asia	Israel	AMAR, 2018
	Asia	Macau	ISAF, 2020
	Asia	Pakistan	DRAP, 2015
	Asia	South Korea	MFDS, 2016
	Asia	Taiwan	FDA, 2020
	Asia	Vietnam	DMEW, 2009
	South America	Argentina	ANMAT, 2006
	South America	Colombia	INVIMA, 2015
	South America	Ecuador	ANRCVS, 2011
	South America	Trinidad and Tobago	Ministry of Health, 2012
	Oceania	Australia	TGA, 2005
	Africa	South Africa	MCC, 2007

Clinical Device Manufacturers with Regulatory Approvals continued

Sonablate CORP continued

Clinical research

6 Indications	3 Regions	5 Countries	15 Sites

Indication	Region	Country	Site
Gastrointestinal			
Colorectal tumors	1	1	2
Urological			
Prostate cancer	3	5	15
Women's health			
Cervical tumors	1	1	2
Endometrial tumors	1	1	1
Ovarian tumors	1	1	1
Vaginal tumors	1	1	1

> **Sonablate** is the leading innovator in minimally invasive ablation technology using high intensity focused ultrasound (HIFU). The Sonablate® prostate ablation system incorporates MRI/US image fusion for whole-gland, hemi, or focal procedures."
>
> — Sonablate CORP

Clinical Device Manufacturers with Regulatory Approvals continued

Theraclion SA

Devices

2	2		
Total devices	Approved devices		

Name	Status	Treatment guidance	Planning guidance
Echopulse	✚	US guidance	US guidance
SONOVEIN	✚	US guidance	Not used

Approvals

4	2	8	19
Approved indications	Regions	Countries	Total approvals*

Indication	Region	Country	Agency and date
Cardiovascular			
Varicose veins	Europe	Europe	CE Marking, 2019
	Asia	Hong Kong	MDD, 2021
	Asia	Singapore	HSA, 2019
Endocrine disorders			
Thyroid nodules	Europe	Europe	CE Marking, 2007
	Europe	Russia	Roszdravnadzor, 2017
	Asia	Hong Kong	MDD, 2007
	Asia	Malaysia	MDA, 2019
	Asia	South Korea	MFDS, 2017
	Asia	Singapore	HSA, 2016
	Asia	Taiwan	FDA, 2019
	Asia	Thailand	FDA, 2019

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

Clinical Device Manufacturers with Regulatory Approvals continued

Theraclion SA continued

Approvals continued

Indication	Region	Country	Agency and date
Women's health			
Breast tumors, benign	Europe	Europe	CE Marking, 2012
	Europe	Russia	Roszdravnadzor, 2017
	Asia	Hong Kong	MDD, 2012
	Asia	Malaysia	MDA, 2019
	Asia	Singapore	HSA, 2016
	Asia	South Korea	MFDS, 2017
	Asia	Taiwan	FDA, 2018
	Asia	Thailand	FDA, 2019

Clinical research

13	3	8	20
Indications	**Regions**	**Countries**	**Sites**

Indication	Region	Country	Site
Cardiovascular			
Varicose veins	3	4	4
Endocrine disorders			
Graves' disease	1	1	1
Thyroid nodules	1	3	9
Gastrointestinal			
Esophageal tumors	1	1	1
Gastric tumors	1	1	1

Clinical Device Manufacturers with Regulatory Approvals continued

Theraclion SA continued

Clinical research continued

Indication	Region	Country	Site
Miscellaneous			
Melanoma	1	1	1
Multiple tumors[1]	1	1	1
Pulmonary			
Lung cancer	1	1	1
Urological			
Acute tubular necrosis	1	1	1
Women's health			
Breast tumors, benign	2	2	5
Breast tumors, malignant	2	2	2
Cervical tumors	1	1	1
Ovarian tumors	1	1	1

> **Theraclion** believes that surgery, as we know it, is outdated. We replace it with a robotic treatment from outside the body using HIFU. Our leading-edge platforms are CE marked for varicose veins, breast fibroadenomas, and thyroid nodules."
>
> — Theraclion SA

1 Protocols inclusive of more than one indication

Clinical Device Manufacturers with Regulatory Approvals continued

Theraclion SA - Veterinary Medicine

Devices

1 Total device	1 Approved device		
Name	Status	Treatment guidance	Planning guidance
Echopulse	✚[1]	US guidance	US guidance

Clinical research

1 Indication	1 Region	1 Country	1 Site
Indication	Region	Country	Site
Feline			
Soft tissue cancer	1	1	1

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

1 Veterinary devices are not subject to regulatory review.

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Clinical Device Manufacturers with Regulatory Approvals continued

TOOsonix A/s

Devices

2	1		
Total devices	**Approved device**		

Name	Status	Treatment guidance	Planning guidance
System ONE-M	✚	Image fusion	Visual guidance
System ONE-R	—	Image fusion	Visual guidance

Approvals

0	1	1	0
Approved indications[1]	**Region**	**Country**	**Total approvals***[1]

Indication	Region	Country	Agency and date
—	Europe	Europe	CE Marking, 2020

✚ Devices with regulatory approvals.
Companies in this section can have approval for more than one indication from a given regulatory agency. To see a breakdown of the regional approvals, indications, and timelines, see charts starting on p. IX.22.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

1 This device is currently approved for aesthetic indications, which are not tracked by the Foundation.

Clinical Device Manufacturers with Regulatory Approvals continued

TOOsonix S/A continued

Clinical research

4 Indications	2 Regions	5 Countries	6 Sites

Indication	Region	Country	Site
Miscellaneous			
Actinic keratosis	1	2	2
Basal cell carcinoma	1	2	3
Kaposi's sarcoma	1	1	1
Neurological			
Neurofibromatosis	2	2	2

> **TOOsonix** is a Danish medical device company committed to the field of dermatology. Our CE marked 20 MHz HIFU systems deliver noninvasive ultrasound to target areas in the human skin, destroying target tissue, while surrounding tissue remains unharmed."
>
> — TOOsonix A/S

Clinical Device Manufacturers with Regulatory Approvals continued

Wuxi Haiying Electronic Medical Systems CO, LTD

Devices

1 Total device	1 Approved device		
Name	Status	Treatment guidance	Planning guidance
HY2900	✚	US guidance	—

Approvals

1 Approved indication	1 Region	1 Country	1 Total approval*
Indication	Region	Country	Agency and date
Women's health			
Uterine fibroids	Asia	China	NMPA, 2016

✚ Devices with regulatory approvals.

* The product of the number of approving agencies and the number of indications defined therein. More than one device may be approved for the same indication.

NEW

Approved Clinical Devices

Acoustic MedSystems

TheraVision	No image

Alpinion Medical Systems

Alpius 900	

As ambassadors for the technology to the wider public audience we often get asked what focused ultrasound medical devices look like. New in 2022, we are including a photographic index of focused ultrasound devices that are commercially available. The photos included were provided by the manufacturers. If there is no image, we were unable to secure a photo of the device by the publication date.

Approved Clinical Devices continued

Changjiangyuan Technology Development

NUTAS - Non-invasive Ultrasound Tumor Ablation System	No image
SUPER Knife - Focused Beam Therapy System	No image

Approved Clinical Devices continued

Chongqing Haifu Medical Technology

CZB	
CZF	No image

Approved Clinical Devices continued

Chongqing Haifu Medical Technology continued

JC	No image
JC200	

Approved Clinical Devices continued

EDAP TMS

Ablatherm

Focal One

Approved Clinical Devices continued

EpiSonica

ArcBLATE (ARC-100M)

EyeTechCare

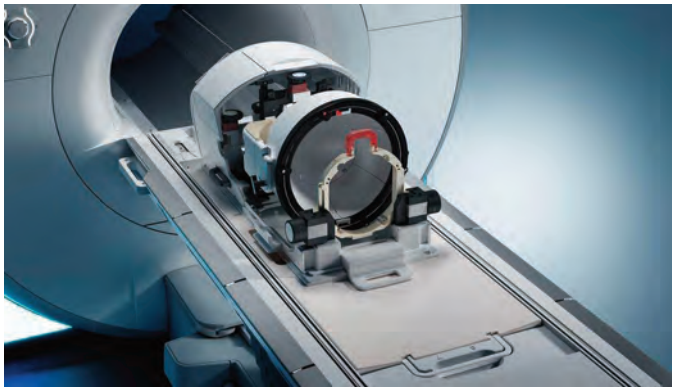
EyeOP1

Approved Clinical Devices continued

Insightec

Exablate Body

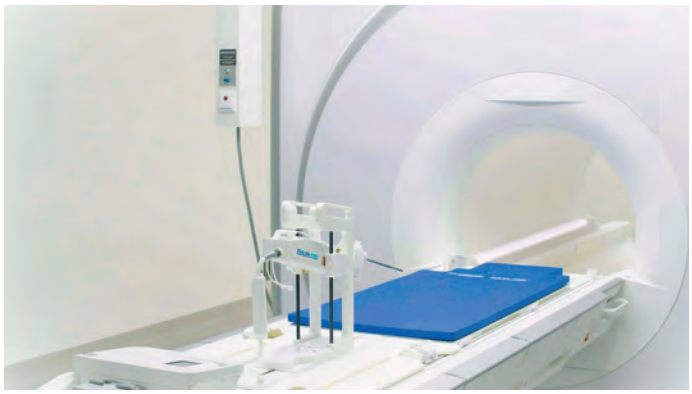
Exablate Neuro



Exablate Prostate

Approved Clinical Devices continued

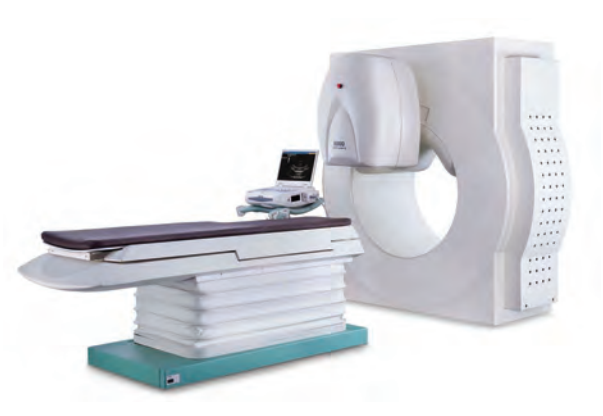
Profound Medical

Sonalleve	
TULSA-PRO	

Approved Clinical Devices continued

Shanghai A&S Science Technology Development

HIFUNIT9000



Shende Medical Equipment Technology

Aceso

Approved Clinical Devices continued

Shenzhen PRO-HITU Medical Technology

PRO2008

PRO300

PRO5G

Approved Clinical Devices continued

Sonablate

Sonablate	
Sonatherm	

Approved Clinical Devices continued

Theraclion

Echopulse	
SONOVEIN	

Approved Clinical Devices continued

TOOsonix

System ONE-M	

Wuxi Haiying Electronic Medical Systems

HY2900	No image

2023 Financial Landscape

Focused Ultrasound Foundation

Overview

Last year, for the first time, the US government invested more than one hundred million dollars in focused ultrasound research in a single year. These funds were spread over 21 different federal agencies.

For the third year in a row, more than 300 million dollars was invested in focused ultrasound industry companies, bringing the three-year total of investments to more than one billion dollars. The cumulative amount of money invested in focused ultrasound research and the industry is over three billion.

In 2022 we saw the first investment in focused ultrasound from a pharmaceutical company, Eli Lilly. Large publicly traded medical device companies with venture arms continue to invest in focused ultrasound as well. We saw the first investment from Boston Scientific in 2022 and a second investment from Johnson and Johnson Innovation. Additionally, 2022 included second investments from venture investors OrbiMed Advisors and the Yongjin Group.

XI. Financial Landscape

XI. 2 Overview

FUS Investments

XI. 3 Cumulative Funding
XI. 4 2022 Industry Investments
XI. 6 Industry Investments by Stage
XI . 7 Market Projection
XI . 7 Industry Investments Over Time
XI. 8 Annual
XI. 9 Flow of Investments

FUS Patents

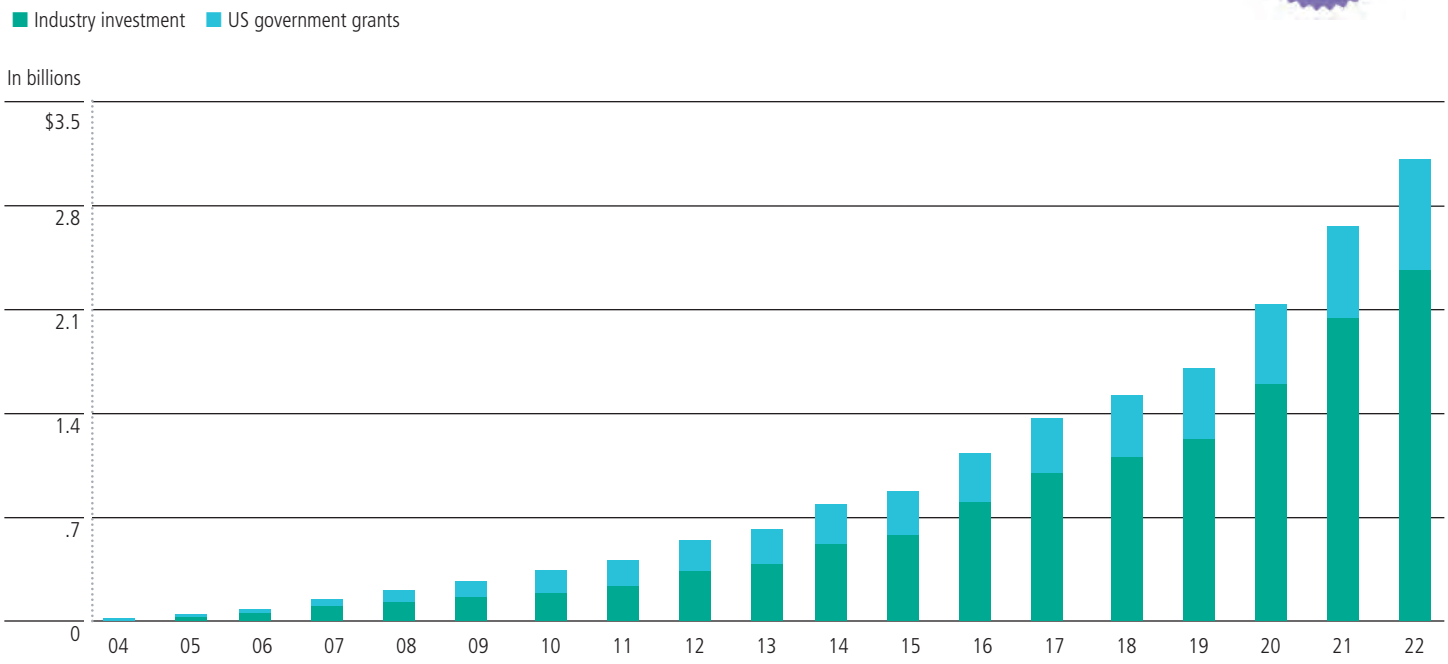
XI.10 Industry
XI.11 Cumulative
XI.11 Growth

US Government Funding of FUS

XI.12 Research—Top Funders
XI.13 2022 and Cumulative Totals
XI.15 Annual

NEW

Cumulative FUS Funding



$3.14B

Cumulative funding

2022 FUS Industry Investments*

Seed | Series A | Series B | Series D | Grant | Debt

Manufacturer	Funding type	Investors	Funding date	Money raised, millions $US
Insightec LTD				
	Debt	Perceptive Advisors The Community Fund	9.1.2022	$100.0M
HistoSonics INC				
	Series D	Johnson & Johnson Innovation Lumira Ventures State of Wisconsin Investment Board Venture Investors LLC Yonjin Venture	12.13.2022	$ 85.0M
	Debt	Signature Bank	12.13.2022	$ 15.0M
SonoThera INC				
	Series A	Alexandria Venture Investments ARCH Venture Partners Eli Lilly & CO Foothill Ventures Formic Ventures Illumina Ventures Johnson & Johnson Innovation Lifespan Investments Medical Excellence Capital LLC Wilson Sonsini Goodrich & Rosati	12.5.2022	$ 60.8M
Carthera SA				
	Series D	Boston Scientific Ventures European Innovation Council	11.21.2022	$ 34.2M
Sonire Therapeutics INC				
	Series B	Carbon Ventures CO LTD/QR Investment CO LTD Daiwa Corporate Investment CO LTD Fast Track Initiative INC FFG Venture Business Partners INC Higin Capital CO LTD JA Mitsui Leasing LTD Japan Growth Capital Investment CORP Mitsubishi UFJ Capital CO LTD Nissay Capital CO LTD Resona Capital CO LTD SBI Investment CO LTD	11.30.2022	$ 17.1M

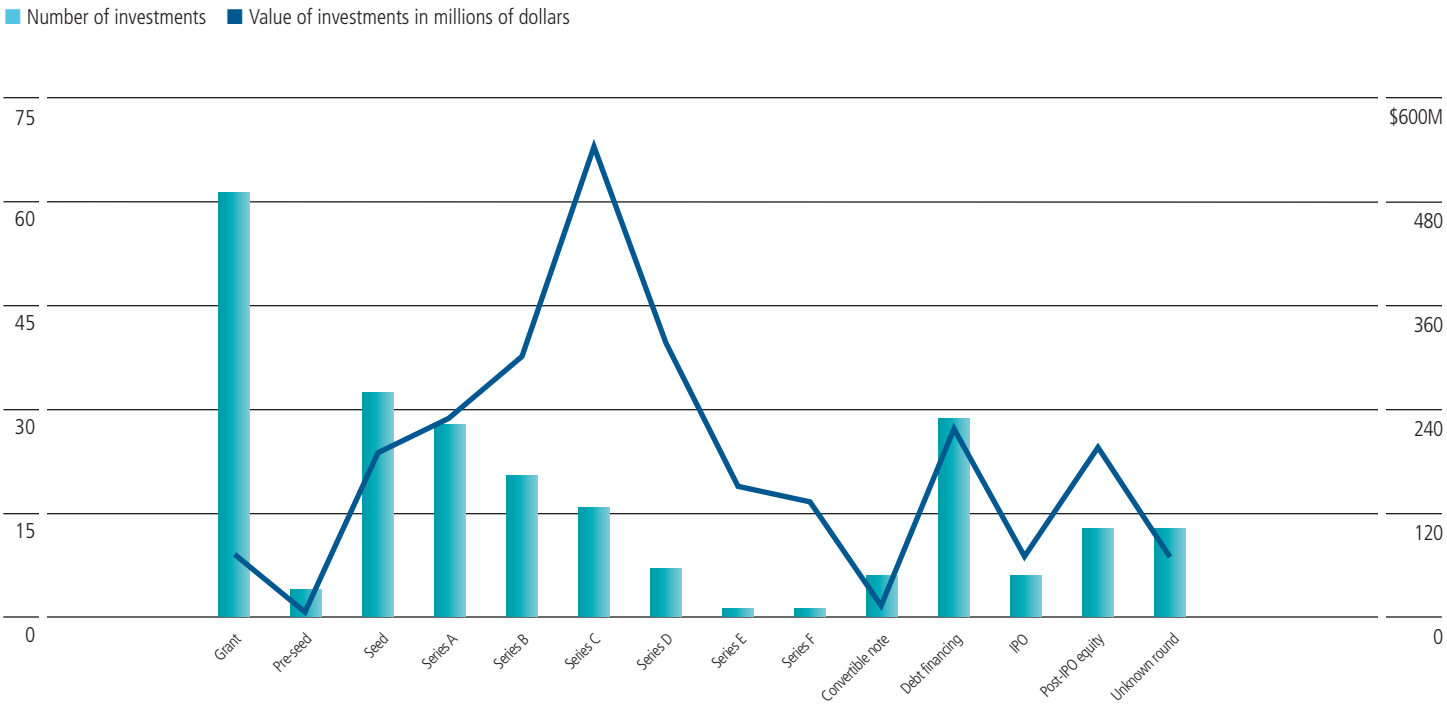
*Source: www.crunchbase.com and industry press releases

2022 FUS Industry Investments* continued

Manufacturer	Funding type	Investors	Funding date	Money raised, millions $US
Alpheus Medical INC				
	Series A	Action Potential Venture Capital LTD BrightEdge OrbiMed Advisors LLC SV Health Investors	11.10.2022	$ 14.0M
OrthoSon LTD				
	Series B	Big Pi Capital Yongjin Group	6.1.2022	$ 9.0M
Theraclion SA				
	Post-IPO Equity	—	2.25.2022	$ 7.3M
Applaud Medical INC				
	Unknown Round	—	7.27.2022	$ 5.7M
Zeta Surgical INC				
	Seed	Trevor Fetter Innospark Ventures LLC Vishal Rao TSVC Y Combinator Management LLC	3.10.2022	$ 5.2M
Vensica Therapeutics				
	Unknown Round	Merz Pharmaceuticals LLC	2.7.2022	$ 3.0M
Exact Therapeutics AS				
	Grant	Research Council of Norway	6.23.2022	$ 1.8M
	Grant	Research Council of Norway	12.22.2022	$ 1.6M
SonoVascular INC				
	Debt	—	1.13.2022	$ 0.75M
Acoustiic INC				
	Grant	National Institutes of Health (SBIR)	9.15.2022	$ 0.40M
	Grant	National Institutes of Health (SBIR)	9.16.2022	$ 0.40M
Microvascular Therapeutics LLC				
	Grant	National Institutes of Health (SBIR)	9.19.2022	$ 0.40M
	Grant	National Institutes of Health (SBIR)	6.6.2022	$ 0.35M
	Grant	National Institutes of Health (SBIR)	4.1.2022	$ 0.29M
				$362.3 M USD Total

*Source: www.crunchbase.com and industry press releases

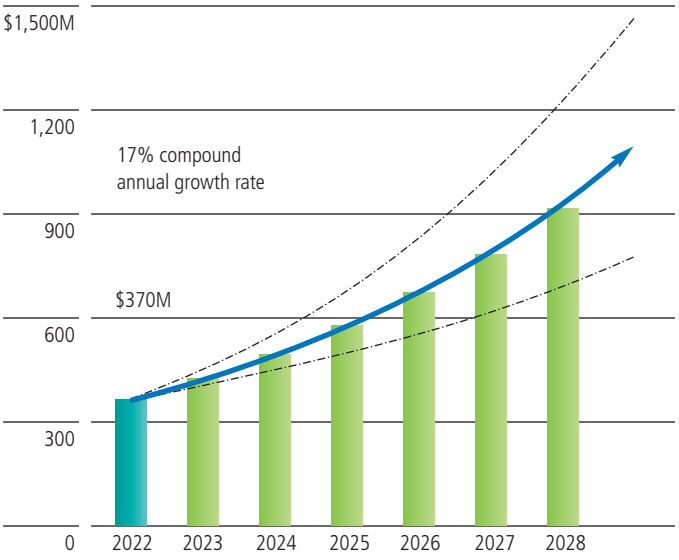
FUS Industry Investments by Stage



Source: www.crunchbase.com and industry press releases

FUS Market Projection

Revenue in millions of dollars



Market value and growth rate estimates were compiled from the following websites:

https://www.marketsandresearch.biz/report/256568/global-high-intensity-focused-ultrasound-system-market-2022-by-manufacturers-regions-type-and-application-forecast-to-2028

https://www.marketsandresearch.biz/report/229028/global-high-intensity-focused-ultrasound-hifu-market-growth-2022-2028

https://360researchreports.com/global-high-intensity-focused-ultrasound-system-market-19851546

https://www.grandresearchstore.com/life-sciences/global-highintensity-focused-ultrasound-equipment-2022-2028-905

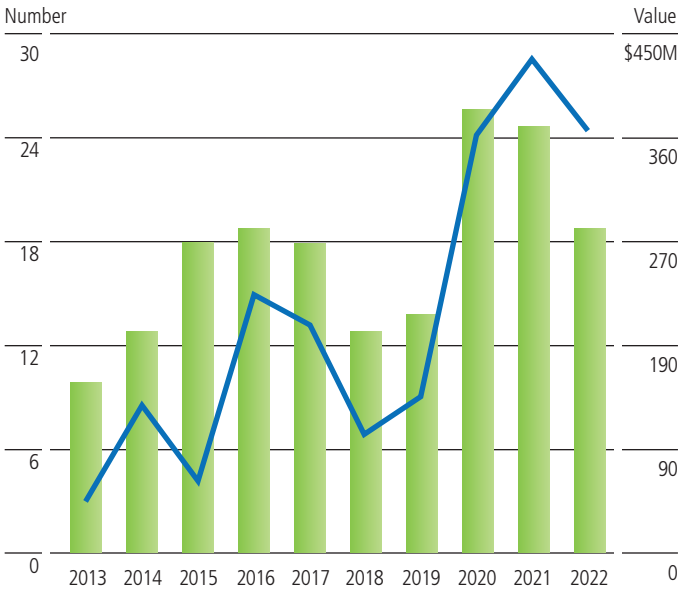
https://www.industrydataanalytics.com/reports/high-intensity-focused-ultrasound-hifu-market

https://www.qyresearch.com/index/detail/4940699/Global-High-Intensity-Focused-Ultrasound-HIFU-Market-Size-Manufacturers-Supply-Chain-Sales-Channel-and-Clients-2022-2028

https://www.marketresearchfuture.com/reports/high-intensity-focused-ultrasound-therapy-market-885

https://www.dhirtekbusinessresearch.com/market-report/High-Intensity-Focused-Ultrasound-HIFU-Market/report-description

FUS Industry Investments Over Time



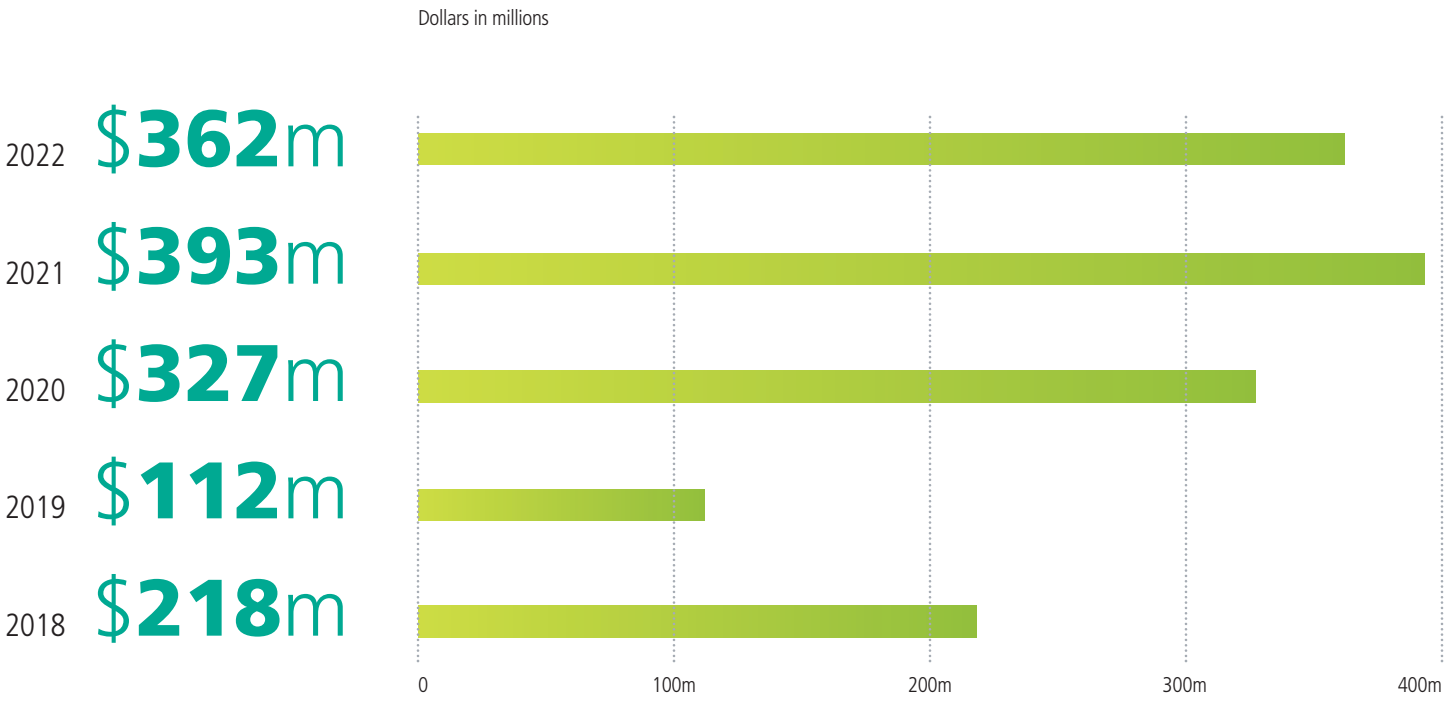
Source: www.crunchbase.com and industry press releases

Annual investments trends

Focused ultrasound investments were down slightly in 2022 as compared to the previous few years. This follows a trend of decreased healthcare investments in general as related to the state of the overall economy.

NEW

FUS Industry Investments
Annual



1B+ invested in the last 3 years

In looking at the graph above, it is easy to see the step change in the investments in focused ultrasound in the past three years. With a cumulative investment total of more than three billion, it is notable that over one-third of that money has been invested in the last three years alone. This is indicative of both the fact that the ecosystem is growing—there are more companies to invest in—and that the investment rounds are getting larger as the companies in the field mature.

Flow of Investments*

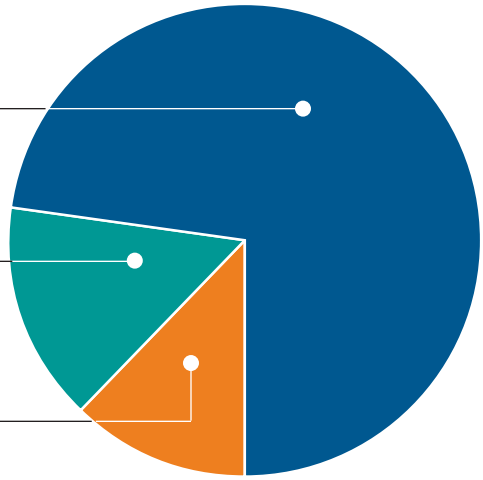
Investments by region[1]

Cumulative

$1,247m
North America

$257m
Europe

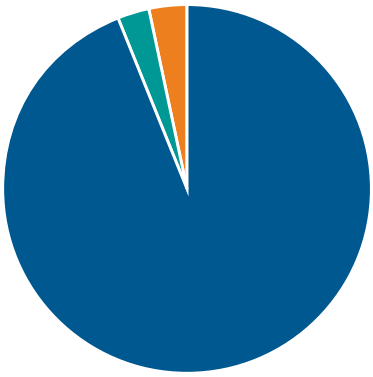
$208m
Asia



Disbursement to FUS Companies

Cumulative

$920m
North America



Source

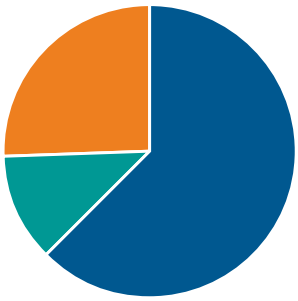
North America	$866.4m
Europe	$ 24.2m
Asia	$ 29.5m
Total	$920.1m

$211m
Europe

Source

North America	$ 17.0m
Europe	$162.2m
Asia	$ 31.6m
Total	$211.2m

$581m
Asia



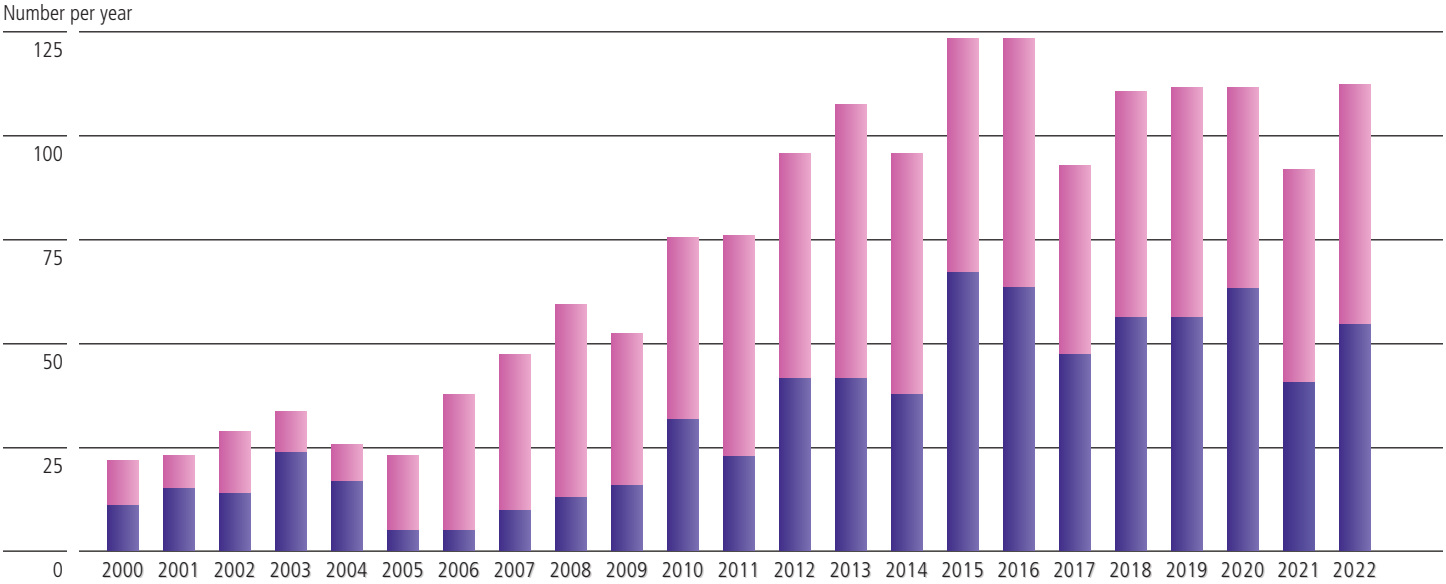
Source

North America	$363.4m
Europe	$ 70.7m
Asia	$ 147.3m
Total	$581.4m

* Source: www.crunchbase.com and industry press releases

1 Due to variable levels of data completeness, the value of total investments will not be the same as that on page XII.3.

Focused Ultrasound Industry Patents



Sources
https://ppubs.uspto.gov/pubwebapp/
https://patentscope.wipo.int/search/en/structuredSearch.jsf
Terms searched: "focused ultrasound", HIFU, MRgFUS, LIFU, "ultrasound ablation", LIPU

Patents issued through the World Intellectual Property Organization, WIPO, were mostly nationalized to all countries that recognize WIPO. Notably absent from WIPO countries is China, which is home to 10 of 69 focused ultrasound device manufacturers.

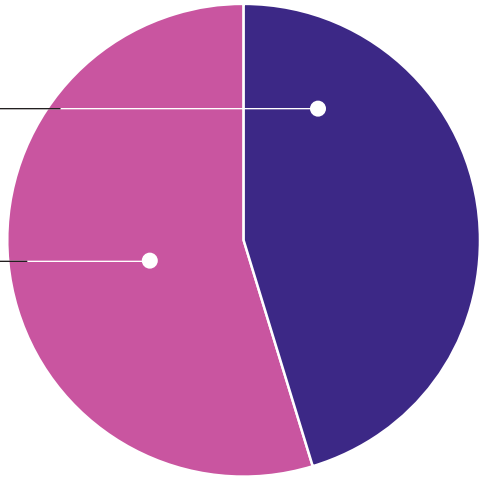
Specifically reviewing the data, not depicted graphically, for the last several years, we see most patents issued by the US Patent and Trademark Office, USPTO, were from US-based inventors or assignees, while 58 percent of WIPO patents had applicants based in the US. This is likely due to academic patent foundations in the US that are far more prolific than those of other countries.

Focused Ultrasound Industry Patents continued

Patents
Cumulative

784
United States

947
Outside United States



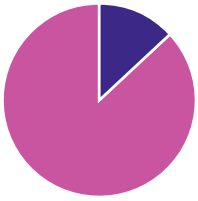
Snapshot of Growth in Patents
Number per year

5
1995

Source

US	4
Outside US	1
Total	5

38
2006*

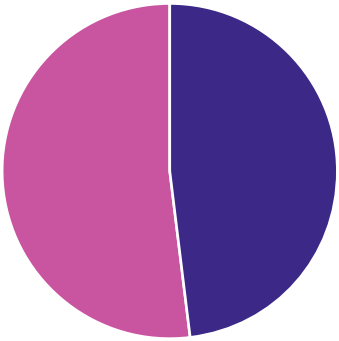


Source

US	5
Outside US	33
Total	38

*Focused Ultrasound Foundation founded

114
2022

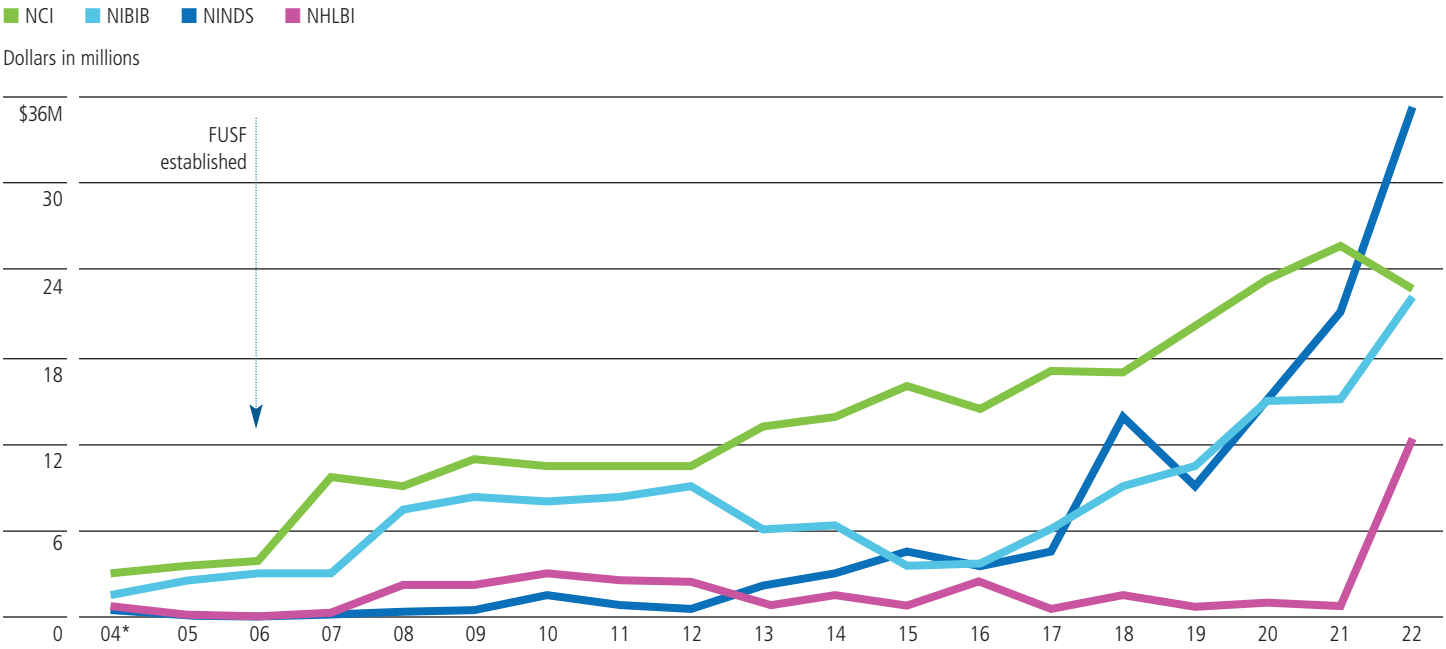


Source

US	55
Outside US	59
Total	114

Sources:https://ppubs.uspto.gov/pubwebapp/ and https://patentscope.wipo.int/search/en/structuredSearch.jsf

Research—United States Top Federal Government Funders



*The first record of funded focused ultrasound research by the United States Federal Government was in 2004.

Sources
https://projectreporter.nih.gov/reporter.cfm
https://www.usaspending.gov/search
Terms searched: "focused ultrasound", HIFU, LIFU, LIPU, MRgFUS, "ultrasound ablation"

United States federal government focused ultrasound grants

Encouragingly, there continues to be an increase in federal funding for focused ultrasound–related projects in the United States. Even though the National Institutes of Health, NIH, budget has been stagnant over the last 15 years, the portion of funding allocated to focused ultrasound research is growing. Funding increases of this nature are typical for medical innovations that have shown the most potential for improving patient health. 2022 funding totals are $37M higher than 2021 funding totals $13M increase in focused ultrasound spending by National Institute of Neurological Disorders and Stroke, NINDS over 2021 levels.

Total FUS Funding by United States Government Agencies

2022 FUS funding[1]	Total FUS funding[2] 2004–2022	Granting agency
$22,758,433	$263,805,286	**NCI** I National Cancer Institute
$22,595,070	$152,764,408	**NIBIB** I National Institute of Biomedical Imaging and Bioengineering
$34,786,085	$107,726,646	**NINDS** I National Institute of Neurological Disorders and Stroke
$12,343,551	$46,992,424	**NHLBI** I National Heart, Lung, and Blood Institute
—	$32,924,533	**NCRR**[3] I National Center for Research Resources
$4,667,333	$25,418,689	**NIMH** I National Institute of Mental Health
$2,013,843	$15,734,754	**OD** I Office of the Director, NIH
$4,640,121	$14,261,179	**NSF** I National Science Foundation
$5,047,165	$13,407,872	**NEI** I National Eye Institute
—	$11,593,232	**NIDDK** I National Institute of Diabetes and Digestive and Kidney Diseases
$4,410,972	$11,583,061	**NICHD** I Eunice Kennedy Shriver National Institute of Child Health and Human Development
$905,525	$11,261,396	**NIA** I National Institute on Aging
$2,084,213	$9,520,073	**CDMRP** I Congressionally Directed Medical Research Programs
$635,781	$7,703,166	**NIDA** I National Institute on Drug Abuse
—	$6,106,583	**NIGMS** I National Institute of General Medical Sciences
$968,750	$2,974,108	**FIC** I John E. Fogarty International Center
$913,858	$2,772,219	**CNRM** I Center For Neuroscience and Regenerative Medicine
$403,750	$2,193,730	**NIDCR** I National Institute of Dental and Craniofacial Research
$1,349,403	$1,926,163	**NIAMS** I National Institute of Arthritis and Musculoskeletal and Skin Diseases
$1,516,636	$1,516,636	**NINR** I National Institute of Nursing Research
—	$909,727	**NIDCD** I National Institute on Deafness and Other Communication Disorders

1 2021 funding for focused ultrasound was $85,244,178.
2 The first record of funding for focused ultrasound research by the US Federal Government was in 2004.
3 Agency dissolved in 2012.

Sources
https://projectreporter.nih.gov/reporter.cfm
https://www.usaspending.gov/search
Terms searched: "focused ultrasound", HIFU, LIFU, LIPU, MRgFUS, "ultrasound ablation"

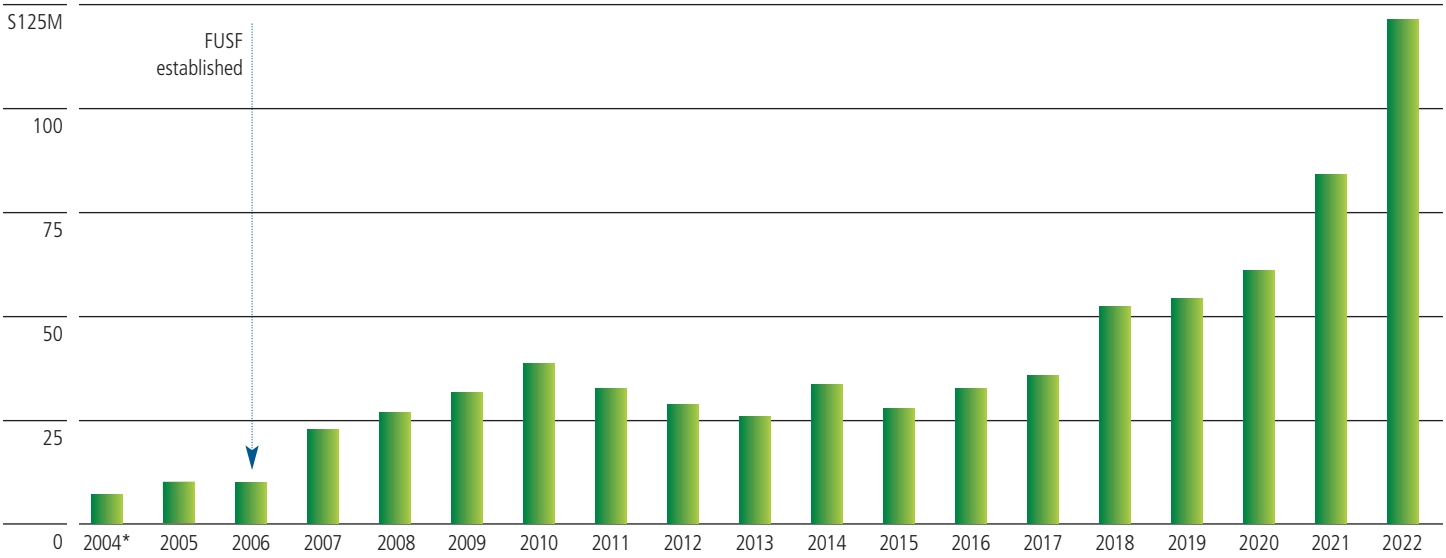
Total FUS Funding by United States Government Agencies continued

2022 FUS funding[1]	Total FUS funding[2] 2004–2022	Granting agency
$30,000	**$779,990**	**NCMHD** | National Institute on Minority Health and Health Disparities
$314,663	**$662,410**	**NIAAA** | National Institute on Alcohol Abuse and Alcoholism
$77,152	**$236,003**	**CLC** | Clinical Center
—	**$233,196**	**NHGRI** | National Human Genome Research Institute
$74,250	**$74,250**	**NCATS** | National Center for Advancing Translational Sciences
$122,536,554	**$745,071,734**	**TOTAL**

1 2021 funding for focused ultrasound was $85,244,178.
2 The first record of funding for focused ultrasound research by the US Federal Government was in 2004.

Sources
https://projectreporter.nih.gov/reporter.cfm
https://www.usaspending.gov/search
Terms searched: "focused ultrasound", HIFU, LIFU, LIPU, MRgFUS, "ultrasound ablation"

Annual US FUS Research Funding



*The first record of funding for focused ultrasound research by the US Federal Government was in 2004.

Sources
https://projectreporter.nih.gov/reporter.cfm
https://www.usaspending.gov/search
Terms searched: "focused ultrasound", HIFU, LIFU, LIPU, MRgFUS, "ultrasound ablation"

Clinical trails and MOA research fuel funding

As demonstrated by the graph above, NIH funding has steadily increased since 2016, with near exponential growth over the past three years. We believe this is due to plethora of research that has reached clinical trial stage along with the diversity of mechanisms of action being explored by the research community beyond thermal ablation.

2023 Reimbursement

Focused Ultrasound Foundation

Overview

Since very few patients have the capacity to pay out-of-pocket for their medical care, reimbursement of medical procedures by a government or private insurer is a critical element of the healthcare ecosystem and the adoption of new technologies like focused ultrasound. Despite its importance, the process of medical reimbursement is not as straightforward as simply sending a bill and receiving payment. As patients and physicians alike have experienced, the process of getting reimbursed for a medical procedure can be a complicated system that involves a labyrinth of policies and processes.

Because insurers often require preauthorization for procedures and because coverage is regional in some countries, we strongly recommend that patients confirm insurance coverage with their insurer prior to undergoing treatment. The good news is that, despite the complexities of reimbursement, the use of focused ultrasound to treat a wide range of diseases is available in many countries. Currently in the US, there is some level of insurance coverage of focused ultrasound to treat bone metastases, essential tremor, Parkinson's disease, uterine fibroids, and prostate cancer.

Europe, in its broadest geographical definition, comprises about 50 countries, each with its own legislation and healthcare system. Even within the biggest block of countries—the European Union with 27 member states—healthcare delivery and related funding is organized on a national level, and in some countries, even on a regional level. To assess the full scope of focused ultrasound-based procedure reimbursement in Europe, one must look at individual countries and their respective healthcare governance.

XII. Reimbursement

XII. 2 Overview
XII. 3 Global and US Reimbursement Levels

Global Insurance Coverage

XII. 4 By Region
XII. 6 By Country

US Insurance Coverage

XII. 8 Bone metastases
XII. 9 Essential tremor
XII.10 Prostate dancer
XII.11 Parkinson's disease, tremor
XII.12 Uterine fibroids

Global and US Reimbursement Levels

2022

Reimbursement

17

Countries offer varying levels of reimbursement

32

Indications worldwide have regulatory approvals

44%

have reimbursement

with varying levels in at least one country

8

Indications have US FDA approvals

63%

have reimbursement

5 indications are insured in some states

Insurance Coverage by Region*

Indications	North America	Europe	Asia	Oceania
Benign prostatic hyperplasia		France Germany	Saudi Arabia Singapore	Australia
Bone metastases	United States[1]	Germany Italy[3]	Israel Malaysia Saudi Arabia South Korea	Australia
Breast tumors, benign		Germany[4]		
Breast tumors, malignant		Germany[4]		
Desmoid tumors		Germany[4]		
Essential tremor	Canada[2] United States[1]	Denmark Germany Italy[3] Switzerland United Kingdom	Israel Japan	
Neuropathic pain		Germany Italy[3] Switzerland	Israel	
Osteoid osteoma		Germany Italy[3]		
Pancreatic tumors		Germany[4]		
Parkinson's disease, tremor	United States[1]	Germany Italy[3] Switzerland	Israel Japan	
Prostate cancer	United States[1]	France Germany United Kingdom	Japan Saudi Arabia Singapore South Korea	Australia

* All coverage decisions are conditional. The most current policy documents from the individual insurers should be referenced for a complete description.

1 A detailed analysis of government and private coverage status in individual US states is available on pages XII.8–XII.12 of this section.

2 In Canada, essential tremor and uterine fibroids are covered only in the province of Ontario.

3 In Italy: Essential tremor and TDPD are covered in Sicily, Abruzzo, and Lombardia. Neuropathic pain is covered in Milan. Bone metastases and osteoid osteoma are covered in Lombardia, Emilia Romagna, Lazio, and Abruzzo. Uterine fibroids are covered by all regions that provide "essential levels of assistance": Abruzzo, Basilicata, Emilia Romagna, Lazio, Lombardia, Marche, Tuscany, and Umbria.

4 Codes that are not specific to FUS procedures, but can be used to bill for them.

Insurance Coverage by Region* continued

Indications	North America	Europe	Asia	Oceania
Thyroid nodules		Germany[4]		
Uterine fibroids	Canada[2] United States[1]	Germany Italy[3]	China Israel Malaysia Saudi Arabia South Korea Vietnam	Australia
Varicose veins		Germany[4]		

Reimbursement

In medical care, reimbursement is the process of paying for healthcare services including office visits, labs/tests, imaging, and procedures, after an encounter has taken place. This is a significant difference between healthcare and other industries because the provider is not paid until after rendering a service.

After a physician or healthcare provider performs a procedure in a hospital or clinic as a treatment for a medical condition, they then send the bill to a payer. In a setting of many rules, the payer reimburses the physician, hospital/clinic, or patient for all or part of the fee for providing the treatment. Payers include private insurance companies, self-funded health plans, and government entities.

The process is not as simple as sending a bill and receiving payment. Payers collect and analyze data on patient outcomes and healthcare provider costs. They do not reimburse all procedures. Many procedures must have prior authorization to be considered for payment. Before payers will cover a new procedure or treatment, they require proof that, compared to the current standard of care, the new treatment is safe, is superior or equal in efficacy, and costs less in the short term or over an extended period of time.

* All coverage decisions are conditional. The most current policy documents from the individual insurers should be referenced for a complete description.

1 A detailed analysis of government and private coverage status in individual US states is available on pages XII.8–XII.12 of this section.

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4 Codes that are not specific to FUS procedures, but can be used to bill for them.

Insurance Coverage by Country*

	BPH	Bone metastases	Breast tumors, benign	Breast tumors, malignant	Desmoid tumors	Essential tremor	Neuropathic pain	Osteoid osteoma	Pancreatic tumors	Parkinson's tremor
North America										
Canada[2]						■				
United States[1]		■				■				■
Europe										
Denmark						■				
France	■									
Germany	■	■	■[4]	■[4]	■[4]	■	■	■	■[4]	■
Italy[3]		■				■	■	■		■
Switzerland						■	■			■
United Kingdom						■				
Asia										
China										
Israel		■				■	■			■
Japan						■				■
Malaysia		■								
Saudi Arabia	■	■								
Singapore	■									
South Korea		■								
Vietnam										
Oceania										
Australia	■	■								

* All coverage decisions are conditional. The most current policy documents from the individual insurers should be referenced for a complete description.

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4 Codes that are not specific to FUS procedures, but can be used to bill for them.

Insurance Coverage by Country* continued

	Prostate cancer	Thyroid nodules	Uterine fibroids	Varicose veins						
North America										
Canada[2]			■							
United States[1]	■		■							
Europe										
Denmark										
France	■									
Germany	■	■[4]	■	■[4]						
Italy[3]			■							
Switzerland										
United Kingdom	■									
Asia										
China			■							
Israel			■							
Japan	■									
Malaysia			■							
Saudi Arabia	■		■							
Singapore	■									
South Korea	■		■							
Vietnam			■							
Oceania										
Australia	■		■							

* All coverage decisions are conditional. The most current policy documents from the individual insurers should be referenced for a complete description.

1 A detailed analysis of government and private coverage status in individual US states is available on pages XII.8–XII.12 of this section.

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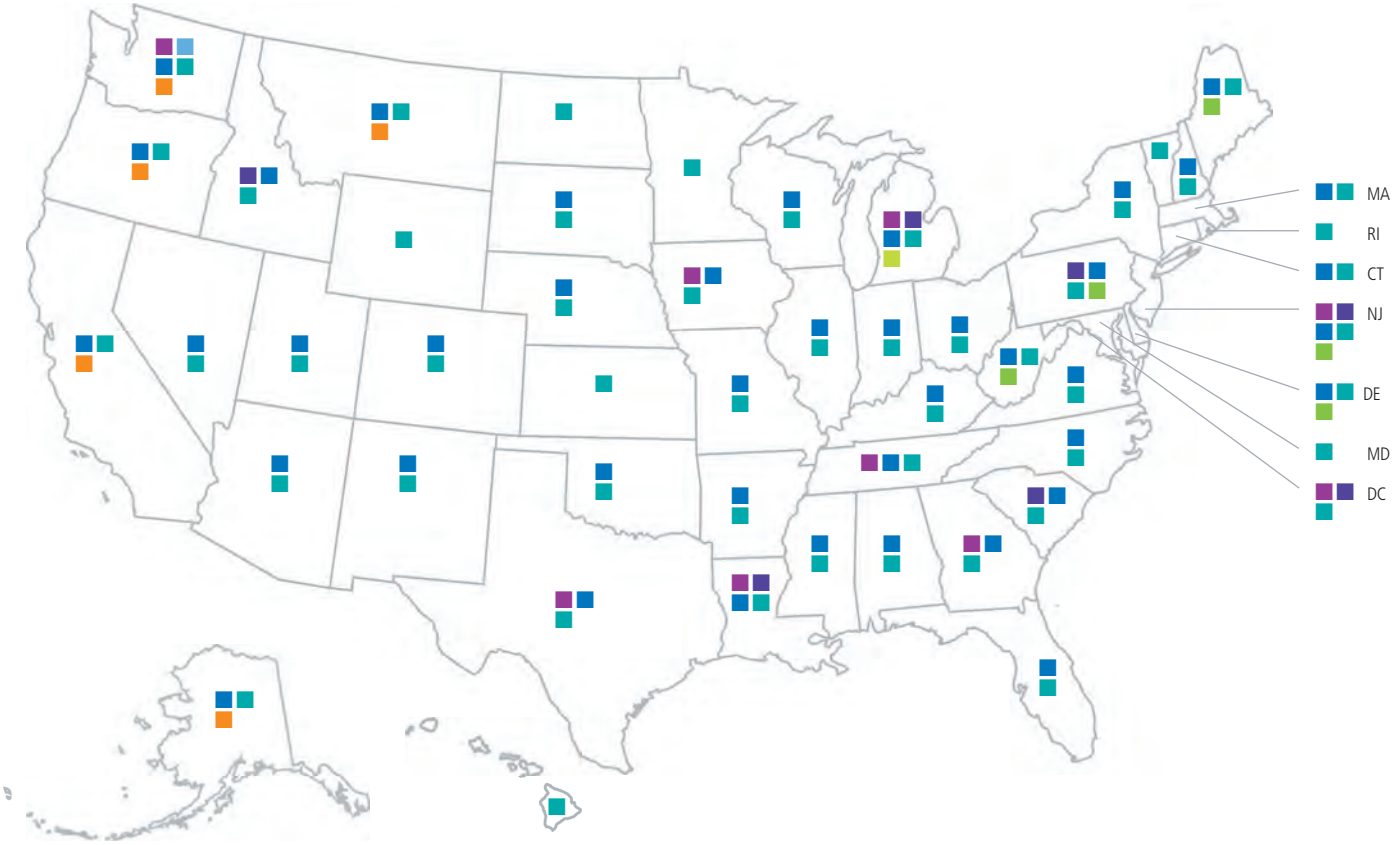
4 Codes that are not specific to FUS procedures, but can be used to bill for them.

Insurance Coverage in the United States*

Bone metastases | Pain palliation



Bone metastases | Pain palliation

Private carriers

- Amerigroup Healthcare
  DC, GA, IA, LA, MI, NJ, TN, TX, WA
- AmeriHealth
  DC, ID, LA, MI, NJ, PA, SC
- Asuris Northwest Health
  WA
- Blue Cross Blue Shield
  AK, AL, AR, AZ, CA, CO, CT, DE, FL, GA, IA, ID, IL, IN, KY, LA, MA, ME, MI, MO, MS, MT, NC, NE, NH, NJ, NM, NV, NY, OH, OK, OR, PA, SC, SD, TN, TX, UT, VA, WA, WI, WV
- CIGNA
  ALL STATES AND DC
- Geisinger Health Plan
  DE, ME, NJ, PA, WV
- HAP Health Alliance Plan
  MI
- Providence Health Plan
  AK, CA, MT, OR, WA

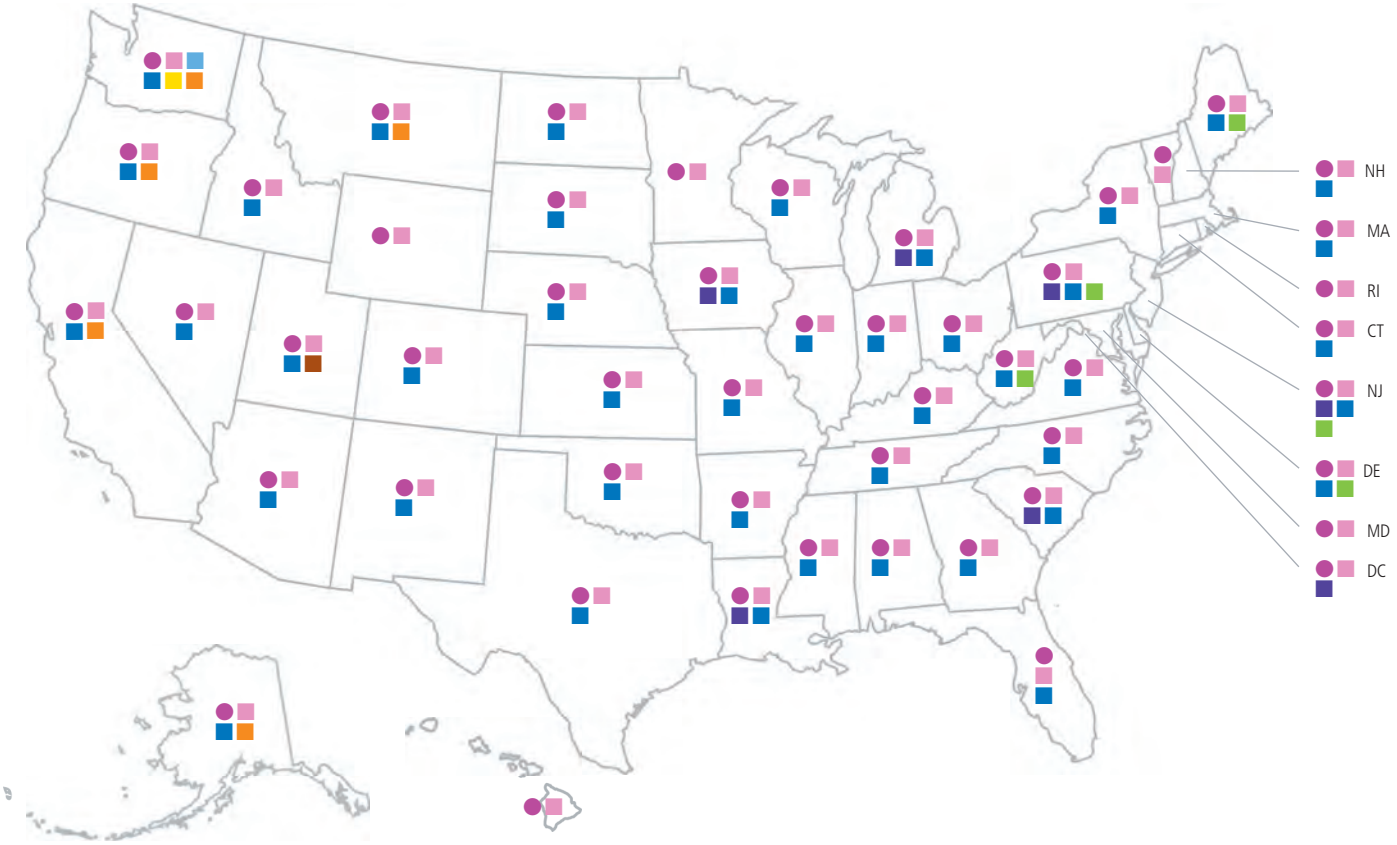
Covered lives

Medicare	—
Private	115.6
	115.6 million

* All coverage decisions are conditional. The most current policy documents from the individual insurers should be referenced for a complete description.

Insurance Coverage in the United States* continued

Essential tremor



Essential tremor

Public carrier

- Medicare
  ALL STATES AND DC

Private carriers

- Aetna
  ALL STATES AND DC
- AmeriHealth
  DC, IA, LA, MI, NJ, PA, SC
- Asuris Northwest Health
  WA
- Blue Cross Blue Shield
  AK, AL, AR, AZ, CA, CO, CT, DE, FL, GA, IA, ID, IL, IN, KS, KY, LA, MA, ME, MI, MO, MS, MT, NC, ND, NE, NH, NJ, NM, NV, NY, OH, OK, OR, PA, SC, SD, TN, TX, UT, VA, WA, WI, WV
- Geisinger Health Plan
  DE, ME, NJ, PA, WV
- Lifewise
  WA
- Providence Health Plan
  AK, CA, MT, OR, WA
- University of Utah Health Plans
  UT

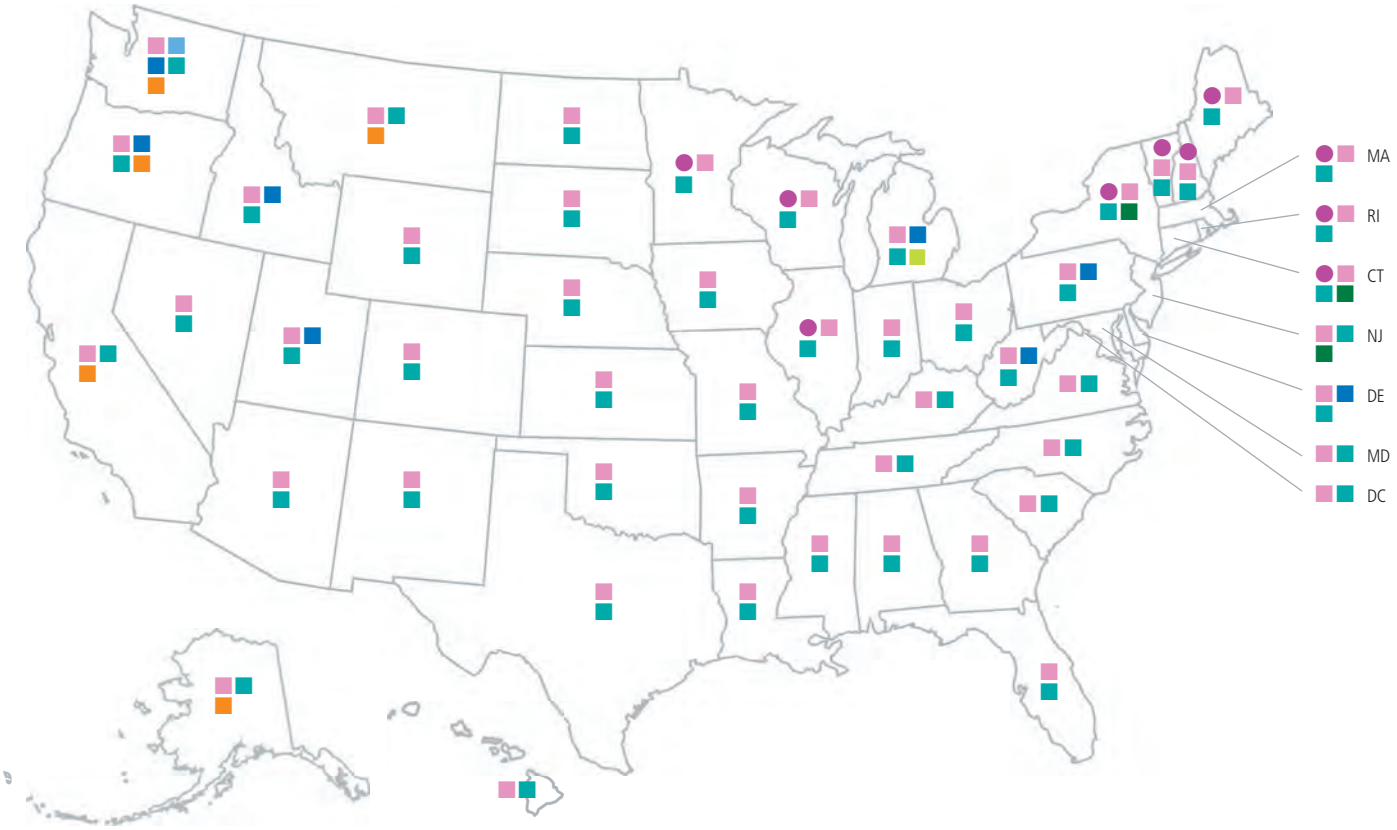
Covered lives

Medicare	63.0
Private	121.6
	184.6 million

* All coverage decisions are conditional. The most current policy documents from the individual insurers should be referenced for a complete description.

Insurance Coverage in the United States* continued

Prostate cancer | Salvage therapy[1]



Prostate cancer | Salvage therapy[1]

Public carrier

- Medicare
  CT, IL, MA, ME, MN, NH, NY, RI, VT, WI

Private carriers

- Aetna
  ALL STATES AND DC
- Asuris Northwest Health
  WA
- Blue Cross Blue Shield
  DE, ID, MI, OR, PA, RI, UT, WA, WV
- CIGNA
  ALL STATES AND DC
- Emblem Health
  CT, NJ, NY
- HAP Health Alliance Plan
  MI
- Providence Health Plan
  AK, CA, MT, OR, WA

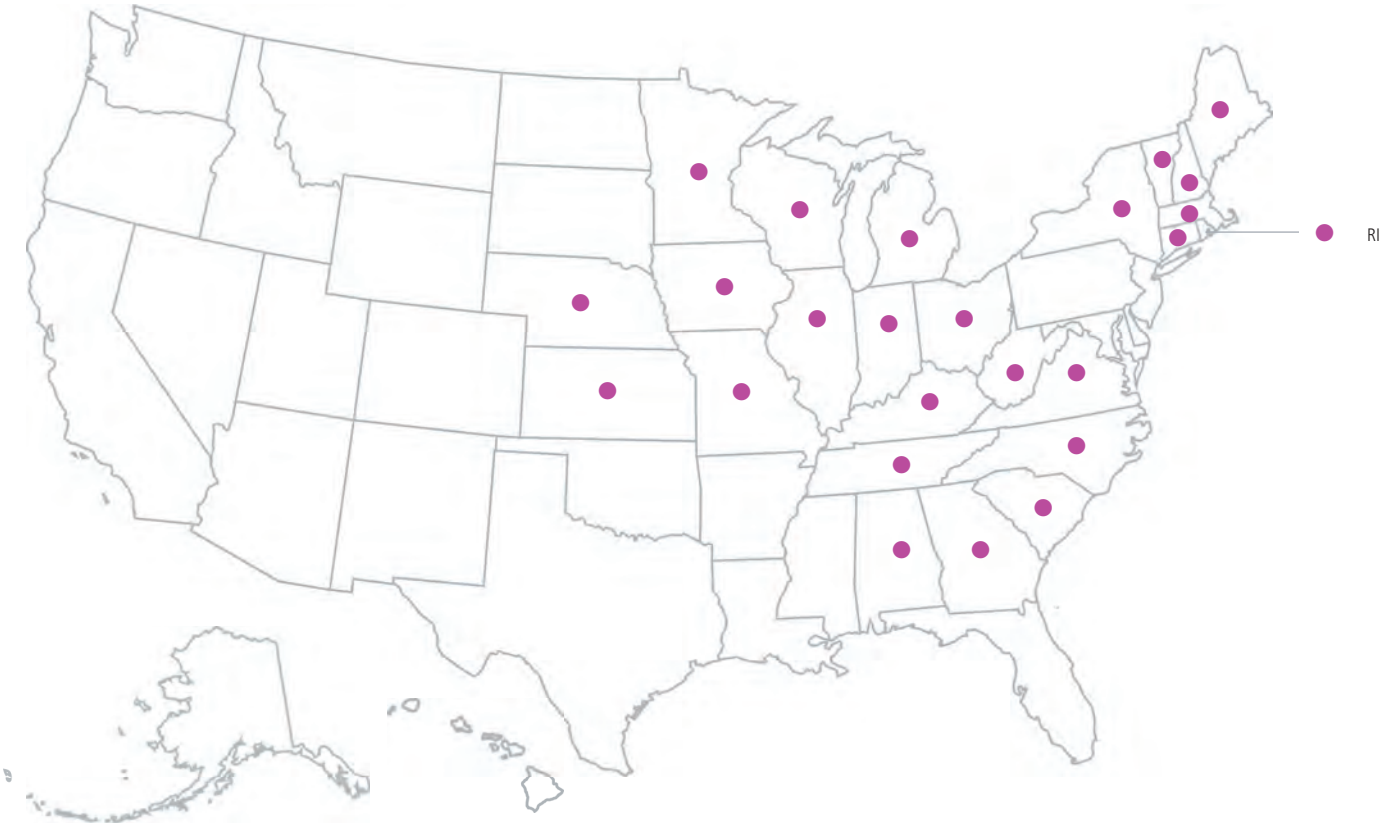
Covered lives

Medicare	11.5
Private	53.0
	64.5 million

* All coverage decisions are conditional. The most current policy documents from the individual insurers should be referenced for a complete description.
1 Local treatment for recurrent prostate cancer following radiation therapy

Insurance Coverage in the United States* continued

Parkinson's disease, tremor



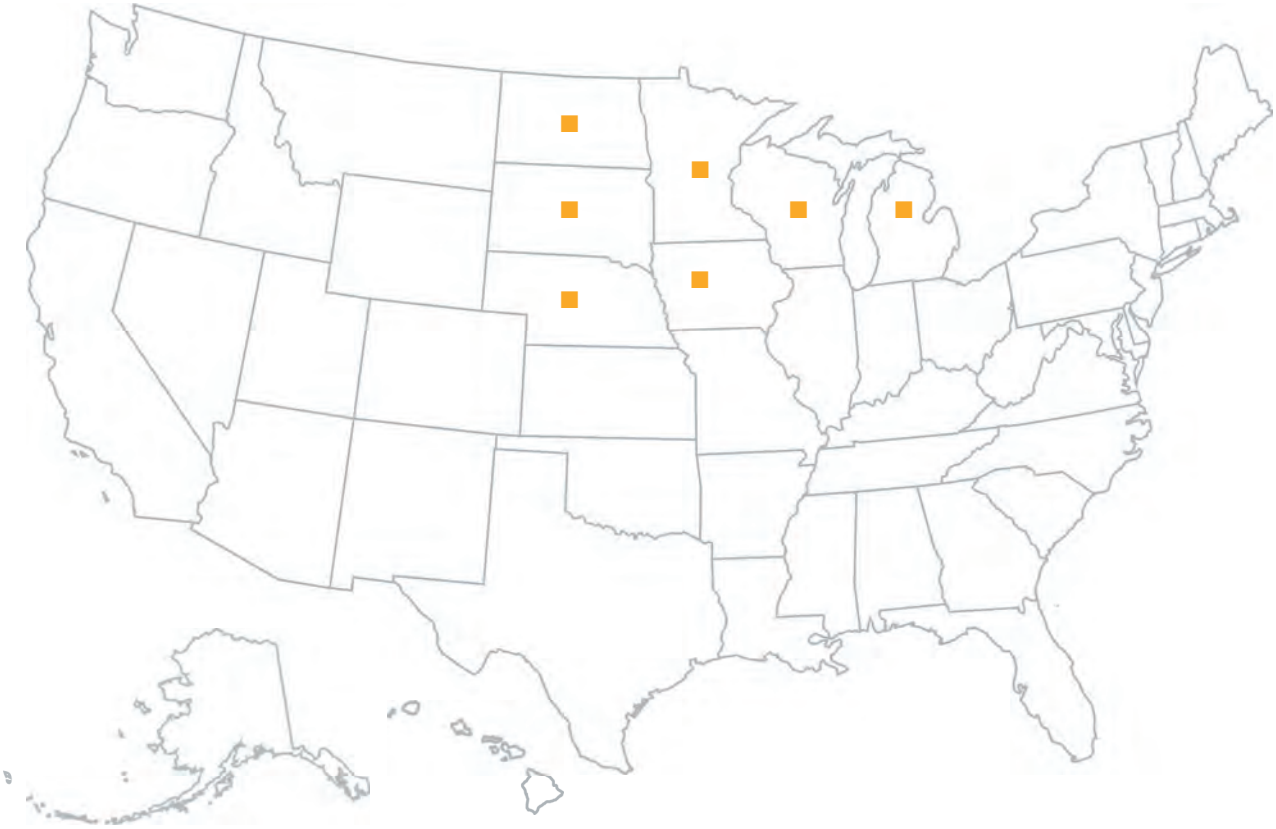
Parkinson's disease, tremor

Public carrier	● Medicare AL, CT, GA, IA, IL, IN, KS, KY, MA, ME, MI, MN, MO, NE, NC, NH, NY, OH, RI, SC, TN, VA, VT, WI, WV	
Covered lives	Medicare	30.7
	Private	—
		30.7 million

* All coverage decisions are conditional. The most current policy documents from the individual insurers should be referenced for a complete description.

Insurance Coverage in the United States* continued

Uterine fibroids



Uterine fibroids

Private carrier	■ Preferred One IA, MI, MN, NE, ND, SD, WI	
Covered lives	Medicare	—
	Private	0.37
		0.37 million

* All coverage decisions are conditional. The most current policy documents from the individual insurers should be referenced for a complete description.

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2023 Veterinary Medicine

Focused Ultrasound Foundation

Overview

FUS Veterinary Applications

Veterinary medicine offers a unique opportunity to expand research and commercial focused ultrasound applications into a market with reduced regulatory burdens, while also collecting data in naturally occurring disease models to support human clinical trials.

Focused ultrasound's ability to noninvasively treat tissue and enhance the efficacy of some therapies, thus reducing the length of hospital stays and total cost, is a crucial benefit for pet owners who pay out of pocket.

Currently, the most promising focused ultrasound applications in veterinary medicine are in oncology, particularly in indications where surgical approaches may significantly affect quality of life. Veterinary clinical trials have demonstrated that focused ultrasound is easily tolerated and effective in the treatment of soft tissue sarcoma, oral tumors, and osteosarcomas. Ongoing clinical work will investigate focused ultrasound's utility against other aggressive cancers, including bladder cancer, brain cancer, and liver cancer. Excitingly, focused ultrasound is now also in use in emergency veterinary medicine to treat feline uroliths.

XIII. Veterinary Medicine

XIII. 2 Overview

Applications and Markets

XIII. 3 Value Chain
XIII. 4 Potential Market
XIII. 5 Potential Market in the US

Research and Treatments

XIII. 6 State of Research by Indication and MOA
XIII. 8 Treated Patients by Indication
XIII. 9 Common Cancers in Popular US Dog Breeds

Case Study

XIII.10 Urinary Tract Stones

Sites and Publications

XIII.12 Veterinary Program Sites
XIII.13 Publications

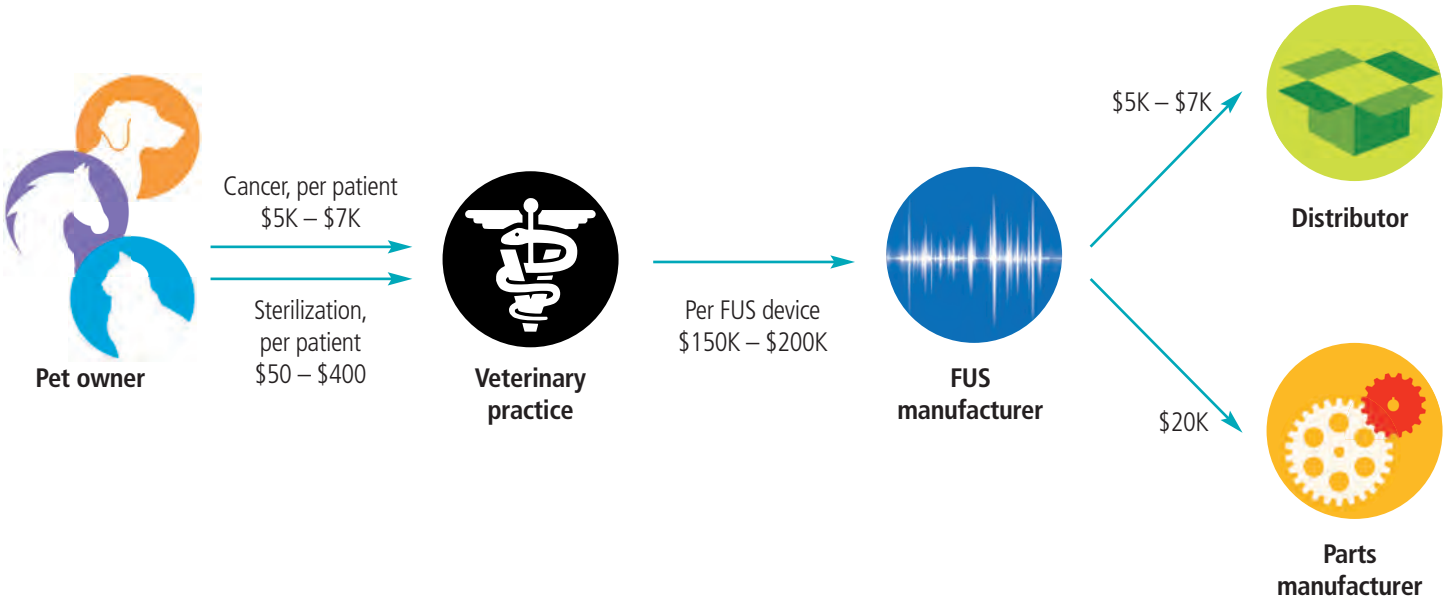
In recent years, the use of focused ultrasound in veterinary medicine has expanded beyond traditional thermally ablative procedures. Histotripsy, sonodynamic therapy, and drug and gene delivery are all currently being explored as alternative treatment approaches. These modalities may offer advantages due to their lower risk of damaging nearby structures such as skin, bone, and nerves. This is especially important in veterinary patients due to their smaller size and the prevalence of lesions on the limbs and body wall.

Focused ultrasound also shows great promise in the management of osteoarthritis, soft tissue injury, and elbow/hip dysplasia. Treatment can enhance blood flow to the damaged tissue, enhancing healing and reducing scar formation. Focused ultrasound can also be used to noninvasively ablate nerve tissue, relieving pain in advanced arthritis.

For more information

www.fusfoundation.org/for-researchers/high-priority-research-areas/veterinary-program.

Value Chain



Potential Market

Focused ultrasound can address many of the common diseases and conditions that affect our pets. For many of these indications, standard of care requires invasive surgery, which often carries significant post-treatment concerns including wound care, infection, pain management, and self-mutilation. The cost for focused ultrasound treatments is heavily dependent on the cost of the equipment. While we are currently projecting that these noninvasive treatments will cost more upfront than surgery, once the added costs and risks of an invasive procedure are accounted for, focused ultrasound may in fact be more cost effective.

This is especially true in oncology cases requiring chemotherapy and/or radiation in addition to surgery, which can add up to an additional $15,000. Factors that can aid in decreasing the cost of focused ultrasound include veterinary-specific device design, rapid large-volume treatment capabilities to decrease total treatment time, and flexible device design that will allow treatment of multiple indications with one unit.

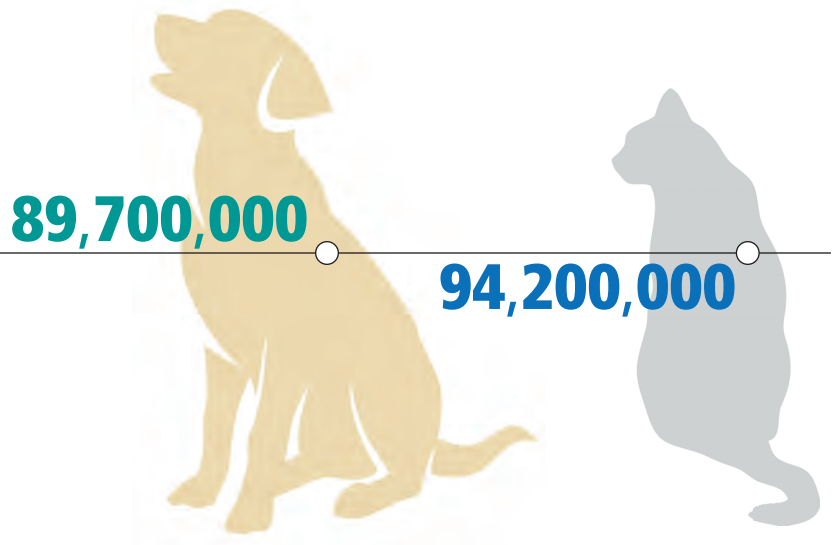
NEW

Potential Market in the US

Indication	Incidences per year US	Cost of Surgery	Cost of FUS estimated	Potential market value
Lipoma	269,100	$200 – $500	$1,000	$269,100,000
Urethral obstruction	264,514	$750 – $5,000	$1,000	$264,514,000
Mast cell tumor	112,125	$500 – $1,000	$1,000	$112,125,000
Soft tissue sarcoma	107,640	$500 – $2,000	$1,000	$107,640,000
Osteosarcoma	44,850	$800 – $1,000	$1,000	$ 44,850,000
Brain tumor	13,007	$5,000 – $7,000	$5,000	$ 65,035,000
		Additional costs		
Radiation, any cancer		$4,000 – $10,000		
Chemotherapy, any cancer		$300 – $5,000		

Sources
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3658424/figure/fig1/
https://www.animalsheltering.org/page/pets-by-the-numbers
https://www.embracepetinsurance.com/health/lipoma
https://www.embracepetinsurance.com/health/mast-cell-tumor
https://www.vet.cornell.edu/departments-centers-and-institutes/sprecher-institute-comparative-cancer-research/cancer-care-cuha/cancer-management-frequently-asked-questions
https://www.pawlicy.com/blog/urinary-blockage-in-cats/#cost
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6856054/
https://icatcare.org/advice/feline-lower-urinary-tract-disease-flutd/
https://onlinelibrary.wiley.com/doi/10.1111/jvim.16389
https://www.cbsnews.com/news/the-heartbreak-and-high-costs-of-pet-cancer/

US Canine and Feline Population



State of Research by Indication and MOA

Development stage: Proposed | Clinical trial | Clinical practice

MOAs: Histotripsy, Hyperthermia, Nonthermal, Thermal ablation

Oncology	Development stage	MOA
Soft tissue tumors*	2018	Thermal ablation - immunomodulation
	2021	Nonthermal - sonodynamic therapy
	2020	Histotripsy - immunomodulation
	2018	Nonthermal - drug delivery
Bladder cancer	2020	Thermal ablation - tissue destruction
Brain tumors	2021	Histotripsy - tissue destruction
Chronic wound	2018	Nonthermal - drug delivery
Glaucoma	2018	Thermal ablation - tissue destruction
Hepatocellular carcinoma	2019	Nonthermal - sonodynamic therapy
	2016	Nonthermal - gene delivery
	2021	Histotripsy - tissue destruction
Oral tumors**	2019	Thermal ablation -immunomodulation
	2020	Nonthermal - sonodynamic therapy
Osteosarcoma	2020	Histotripsy - immunomodulation
	2019	Nonthermal - sonodynamic therapy
Prostate tumors	2019	Nonthermal - sonodynamic therapy
Sarcomas	2021	Histotripsy - immunomodulation
Lipoma	2022	Histotripsy - immunomodulation
Lung cancer	2018	Thermal ablation - tissue destruction
Sarcoids	2018	Thermal ablation - tissue destruction

*Soft tissue tumors include soft tissue sarcoma and mast cell tumors.

**Oral tumors includes oral melanoma, plasmacytoma (of the gums/lips), ameloblastomas, salivary gland tumors, and squamous cell carcinoma (of the gums/lips).

State of Research by Indication and MOA continued

	Development stage (Proposed / Clinical trial / Clinical practice)	MOAs (Histotripsy, Hyperthermia, Nonthermal, Thermal ablation)
Pain		
Elbow/hip dysplasia	2018	Nonthermal - neuromodulation
Osteoarthritis	2018	Nonthermal - neuromodulation
Soft tissue injuries	2018	Nonthermal - neuromodulation
Miscellaneous		
Kidney stones	2022	Nonthermal - kidney stone fragmentation
Diabetes	2021	Nonthermal - neuromodulation
Epilepsy	2020	Thermal ablation - tissue destruction
Spay/neuter	2018	Thermal ablation - tissue destruction

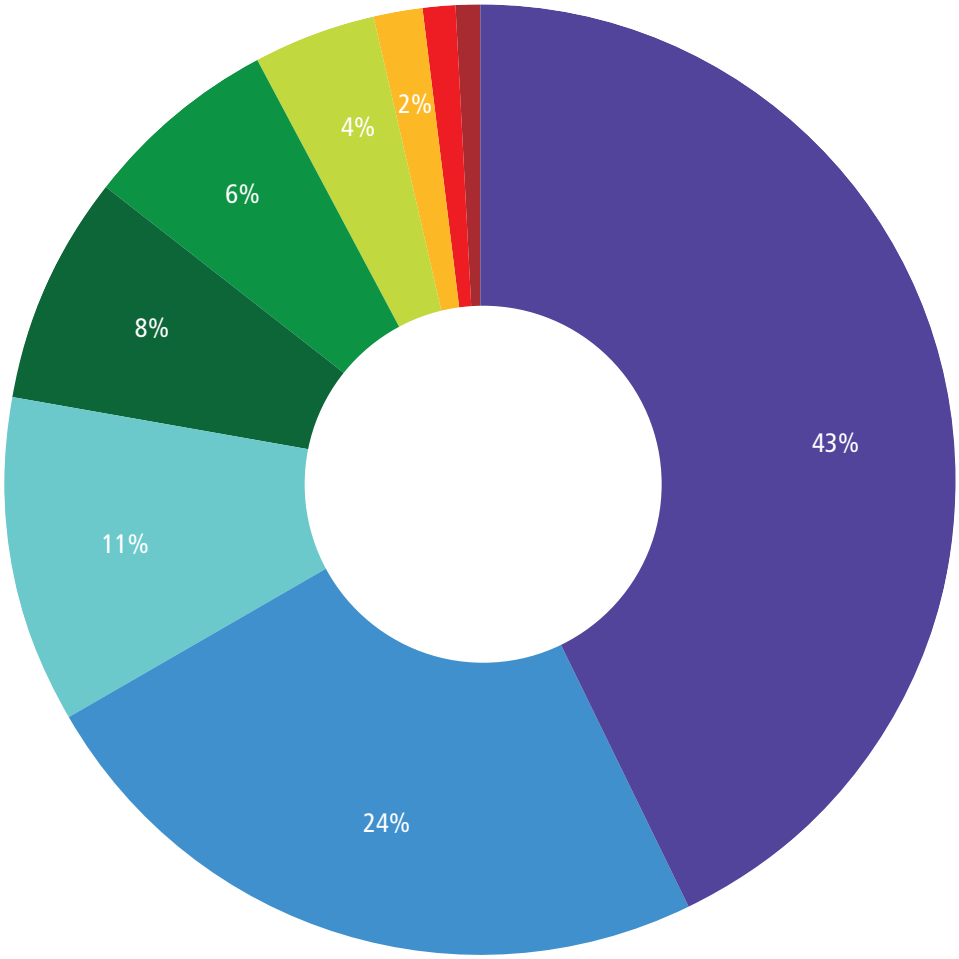
Veterinary advances

As the veterinary focused ultrasound field continues to mature, more technically demanding indications, such as glioblastoma and bladder cancer, are being explored. Focused ultrasound is also now in use for applications in emergency medicine (feline uroliths). Additional modes and bioeffects of focused ultrasound, including histotripsy, sonodynamic therapy, and drug and gene delivery, are now in use in the veterinary space and may offer advantages over more traditional thermally ablative procedures.

Treated Patients by Indication—Cumulative

168 total treatments

- 72 Soft tissue tumors[1]
- 40 Osteoarthritis
- 19 Osteosarcoma[2]
- 13 Hepatocellular carcinoma
- 11 Oral tumors[3]
- 7 Glaucoma
- 3 Chronic wound
- 2 Brain tumor
- 1 Thyroid carcinoma



1 Soft tissue tumors includes soft tissue sarcoma and mast cell tumors.
2 Osteosarcoma includes osteosarcoma and chondrosarcoma.
3 Oral tumors includes oral melanoma, plasmacytoma (of the gums/lips), ameloblastomas, salivary gland tumors, squamous cell carcinoma (of the gums/lips).

Common Cancers in Popular US Dog Breeds

Most popular breeds	Common cancers	Registered dogs per year	Cancer-caused mortality
Labrador Retriever	Lymphoma, Mast cell tumor, Melanoma, Osteosarcoma, Hemangiosarcoma	192,000	31%
German Shepherd	Hemangiosarcoma, Mast cell tumor, Melanoma, Lymphoma	129,000	20%
French Bulldog	Mast cell tumor, Brain tumor, Liver tumor	39, 000	38%
Golden Retriever	Mast cell tumor, Lymphoma, Oral melanoma, Brain tumor, Fibrosarcoma, Histiocytic tumors	93,000	39%
Poodle	Squamous cell carcinoma, Mast cell tumor, Lymphoma	119,000	30%

Mammary and testicular cancer are common in unaltered dogs of all breeds.

Several dog breeds routinely top popularity charts worldwide, notably Labrador and golden retrievers, German shepherd dogs, and poodles. These breeds are genetically predisposed to certain diseases and cancers and can heavily skew the prevalence of these conditions, even if they are rare in other breeds. When assessing clinical unmet needs, it is important to consider the effects of breed popularity and distribution.

NEW

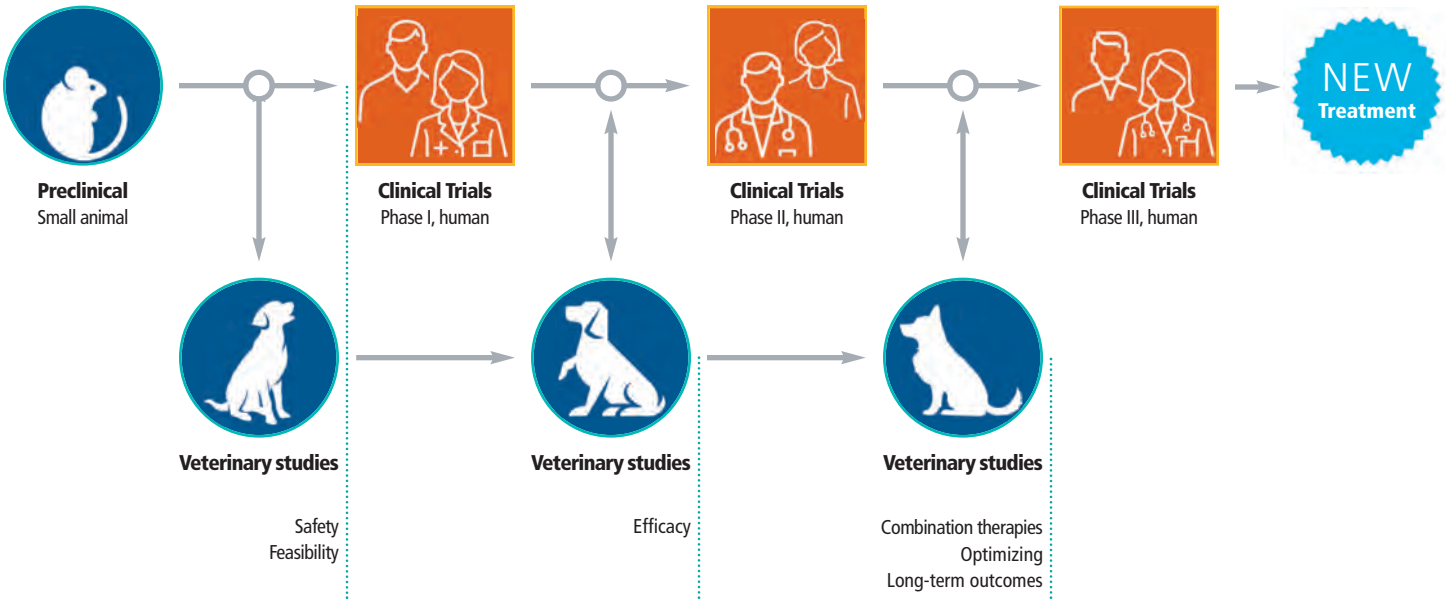
Case Study
Urinary Tract Stones

As with any medical device, regulatory agencies around the world require data from laboratory animal testing before approving focused ultrasound technology for use in humans. However, mouse or rat models often do not accurately represent human disease. Clinical focused ultrasound devices are seldom capable of treating small animals, which further complicates clinical translation. Large animal disease models, while more compatible with clinical focused ultrasound devices, are more expensive and less advanced.

Companion animals can offer the perfect solution to this conundrum. Client-owned animals are exposed to the same environments as their human owners and develop many of the same diseases. Unlike laboratory-induced diseases, these naturally occurring diseases in companion animals are remarkably similar to their human counterparts and respond similarly to therapy. Veterinary trials offer the ability to treat beloved pets while also collecting large-animal data that is more translatable than anything from a laboratory and can dramatically accelerate clinical development.

Bladder stones in pet cats are the only emergency medical condition currently treated using focused ultrasound. Urethral obstruction is one of the most common veterinary emergencies, representing 10% of all emergency cases with an incidence between 1.5 and 9%. Urethral obstruction can be fatal if left untreated, as it causes damage to the kidneys and severe electrolyte imbalances.

Comparative medicine
Integrated and comparative device development plan



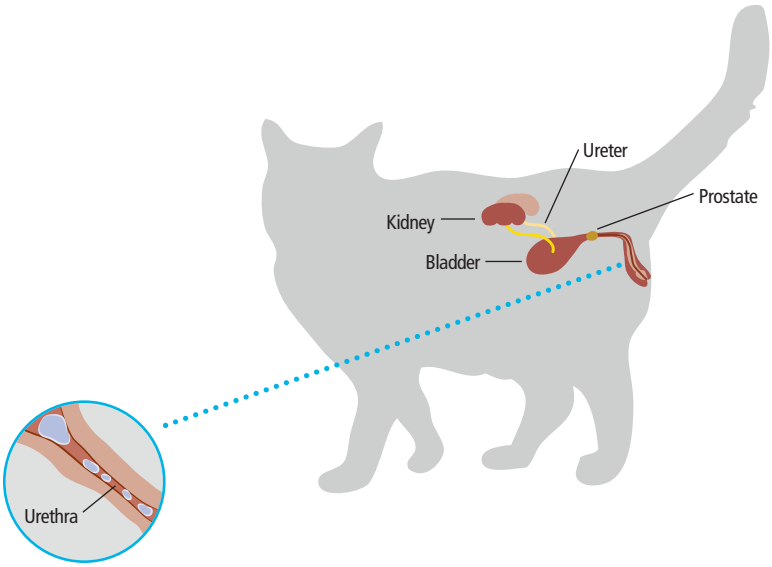
Case Study continued
Urinary Tract Stones

Current standard of care involves placing a catheter and administering supportive care while waiting for the bladder stones to pass. If this is not sufficient, invasive surgery is required to remove stones lodged in the urethra and bladder. Treatment typically requires a multi-day stay in the veterinary hospital and total costs range from $750 for a simple case to well over $5000 in complicated cases. Up to 43% of cats will have a recurrence, adding additional risk and cost.

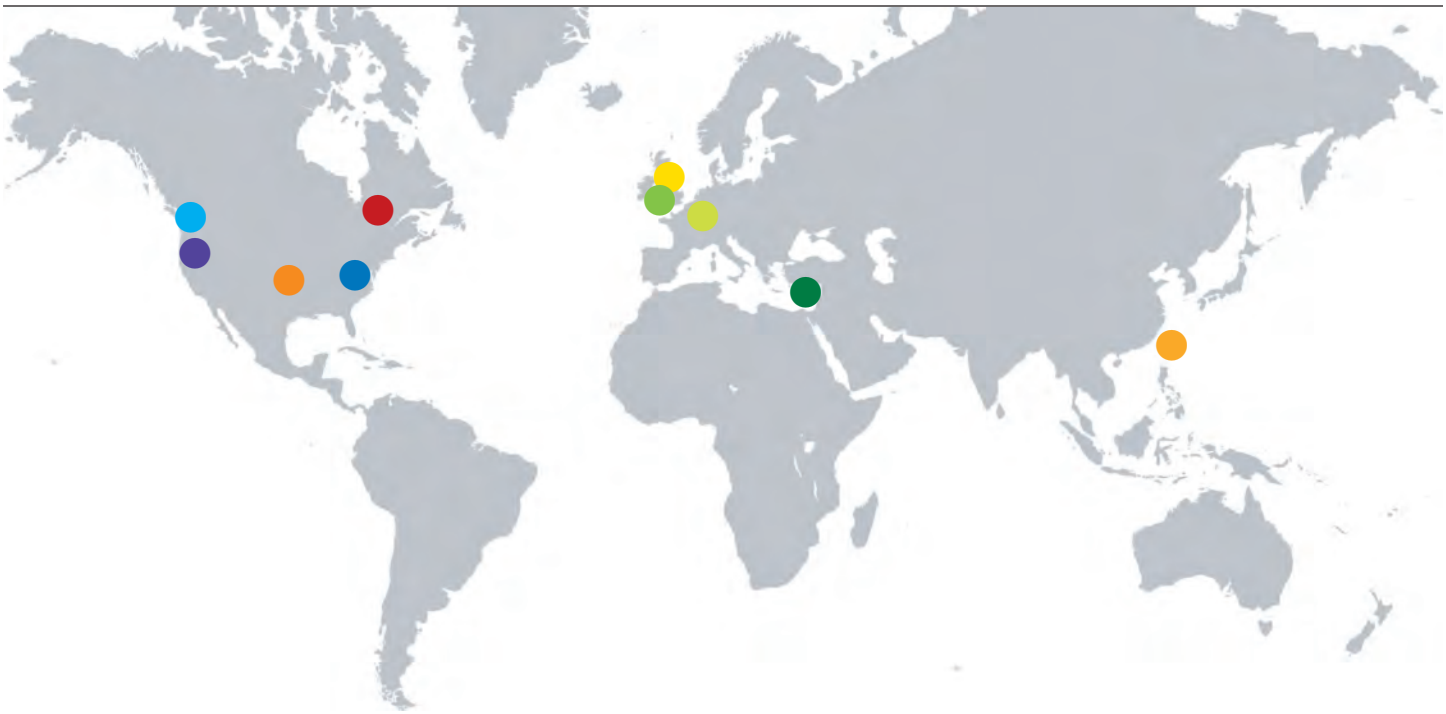
A type of focused ultrasound called lithotripsy may offer a safe, noninvasive, effective method to treat obstructing stones. This form of focused ultrasound produces high pressure mechanical forces that disintegrate bladder stones without the need for surgery. Once the stones have been broken down into smaller pieces, they can be passed to relieve the obstruction.

A veterinary clinical trial, led by Dr. Adam Maxwell of the University of Washington, is using lithotripsy to treat cats with obstructing bladder stones. In addition to developing a new treatment option for pet cats, this trial will provide additional safety and efficacy data for an ongoing human clinical trial testing the same technology. The system used in the human clinical trial was scaled down for veterinary use, and positive results from the veterinary trial will provide excellent supportive data for the use of this smaller device in the pediatric population.

Feline urinary system
Male



Veterinary Program Sites



North America

- Oklahoma State University
- Ontario Veterinary College*
- Stanford University
  In collaboration with University of California, Davis, School of Veterinary Medicine
- Virginia-Maryland College of Veterinary Medicine
- University of Washington*
  In collaboration with University of Minnesota Urolith Center

Europe

- Cyprus University of Technology*
- Institute of Cancer Research
- LabTAU
- Vet LIFU

Asia

- Taipei Animal Hospital*

*Newly identified site in 2022.

Publications

Veterinary publications—Cumulative as of 2022

Antoniou A, Evripidou N, Panayiotou S, Spanoudes K, Damianou C. Treatment of canine and feline sarcoma using MR-guided focused ultrasound system. J Ultrasound. 2022;25(4):895-904. doi:10.1007/s40477-022-00672-5

Arnold L, Hendricks-Wenger A, Coutermarsh-Ott S, et al. Histotripsy Ablation of Bone Tumors: Feasibility Study in Excised Canine Osteosarcoma Tumors. Ultrasound Med Biol. 2021;47(12):3435-3446. doi:10.1016/j.ultrasmedbio.2021.08.004

Carroll J, Coutermarsh-Ott S, Klahn SL, et al. High intensity focused ultrasound for the treatment of solid tumors: a pilot study in canine cancer patients. Int J Hyperthermia. 2022;39(1):855-864. doi:10.1080/02656736.2022.2097323

Foster RS, Bihrle R, Sanghvi N, et al. Production of prostatic lesions in canines using transrectally administered high-intensity focused ultrasound. European urology. 1993;23(2):330-336. http://www.ncbi.nlm.nih.gov/pubmed/7683997

Hendricks-Wenger A, Arnold L, Gannon J, et al. Histotripsy Ablation in Preclinical Animal Models of Cancer and Spontaneous Tumors in Veterinary Patients: A Review. IEEE Trans Ultrason Ferroelectr Freq Control. 2022;69(1):5-26. doi:10.1109/TUFFC.2021.3110083

Horise Y, Maeda M, Konishi Y, et al. Sonodynamic Therapy With Anticancer Micelles and High-Intensity Focused Ultrasound in Treatment of Canine Cancer. Front Pharmacol. 2019;10:545. doi:10.3389/fphar.2019.00545

Isard PF, Mentek M, Clément D, et al. High intensity focused ultrasound cyclocoagulation in dogs with primary glaucoma: a preliminary study. Open Veterinary Journal. 2018;8(3):305. doi:10.4314/ovj.v8i3.9

Kincaide LF, Sanghvi NT, Cummings O, et al. Noninvasive ultrasonic subtotal ablation of the prostate in dogs. American journal of veterinary research. 1996;57(8):1225-1227.

Kumar SU, Telichko AV, Wang H, et al. Acoustically Driven Microbubbles Enable Targeted Delivery of microRNA-Loaded Nanoparticles to Spontaneous Hepatocellular Neoplasia in Canines. Advanced Therapeutics. 2020;3(12):2000120. doi:10.1002/adtp.202000120

Latifi M, Hay A, Carroll J, et al. Focused ultrasound tumour ablation in small animal oncology. Vet Comp Oncol. 2021;19(3):411-419. doi:10.1111/vco.12742

Ranjan A, Kishore D, Ashar H, Neel T, Singh A, More S. Focused ultrasound ablation of a large canine oral tumor achieves efficient tumor remission: a case report. Int J Hyperthermia. 2021;38(1):552-560. doi:10.1080/02656736.2021.1903582

Roberts WW, Teofilovic D, Jahnke RC, Patri J, Risdahl JM, Bertolina JA. Histotripsy of the prostate using a commercial system in a canine model. The Journal of urology. 2014;191(3):860-865. doi:10.1016/j.juro.2013.08.077

Rong S, Woo K, Zhou Q, et al. Septal Ablation Induced by Transthoracic High-Intensity Focused Ultrasound in Canines. Journal of the American Society of Echocardiography. 2013;26(10):1228-1234. doi:10.1016/j.echo.2013.06.020

Ruger L, Yang E, Gannon J, et al. Mechanical High-Intensity Focused Ultrasound (Histotripsy) in Dogs with Spontaneously Occurring Soft Tissue Sarcomas. IEEE Trans Biomed Eng. 2022;PP. doi:10.1109/TBME.2022.3201709

Ruger LN, Hay AN, Gannon JM, et al. Histotripsy Ablation of Spontaneously Occurring Canine Bone Tumors In Vivo. IEEE Trans Biomed Eng. 2022;PP. doi:10.1109/TBME.2022.3191069

Ryu MO, Lee SH, Ahn JO, Song WJ, Li Q, Youn HY. Treatment of solid tumors in dogs using veterinary high-intensity focused ultrasound: A retrospective clinical study. Veterinary journal (London, England : 1997). 2018;234: 126-129. doi:10.1016/j.tvjl.2018.02.019

Seward MC, Daniel GB, Ruth JD, Dervisis N, Partanen A, Yarmolenko PS. Feasibility of targeting canine soft tissue sarcoma with MR-guided high-intensity focused ultrasound. International journal of hyperthermia: the official journal of European Society for Hyperthermic Oncology, North American Hyperthermia Group. 2019;35(1):205-215. doi:10.1080/02656736.2018.1489072

Spanoudes K, Evripidou N, Giannakou M, Drakos T, Menikou G, Damianou C. A High Intensity Focused Ultrasound System for Veterinary Oncology Applications. J Med Ultrasound. 2021;29(3):195-202. doi:10.4103/JMU.JMU_130_20

Yoo DH, Cho JY, Kwak C, Lee JY, Moon KC, Kim SH. Transabdominal high-intensity focused ultrasound therapy of the prostate and determination of the protective effect of rectal cooling: an experimental study using canine prostates. Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine. 2013;32(8):1419-1425. doi:10.7863/ultra.32.8.1419

Zheng M, Shentu W, Chen D, Sahn DJ, Zhou X. High-Intensity Focused Ultrasound Ablation of Myocardium In Vivo and Instantaneous Biological Response. Echocardiography. 2014;31(9):1146-1153. doi:10.1111/echo.12526

2023

Focused Ultrasound Foundation

Focused Ultrasound Foundation

Focused Ultrasound Foundation Overview

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.

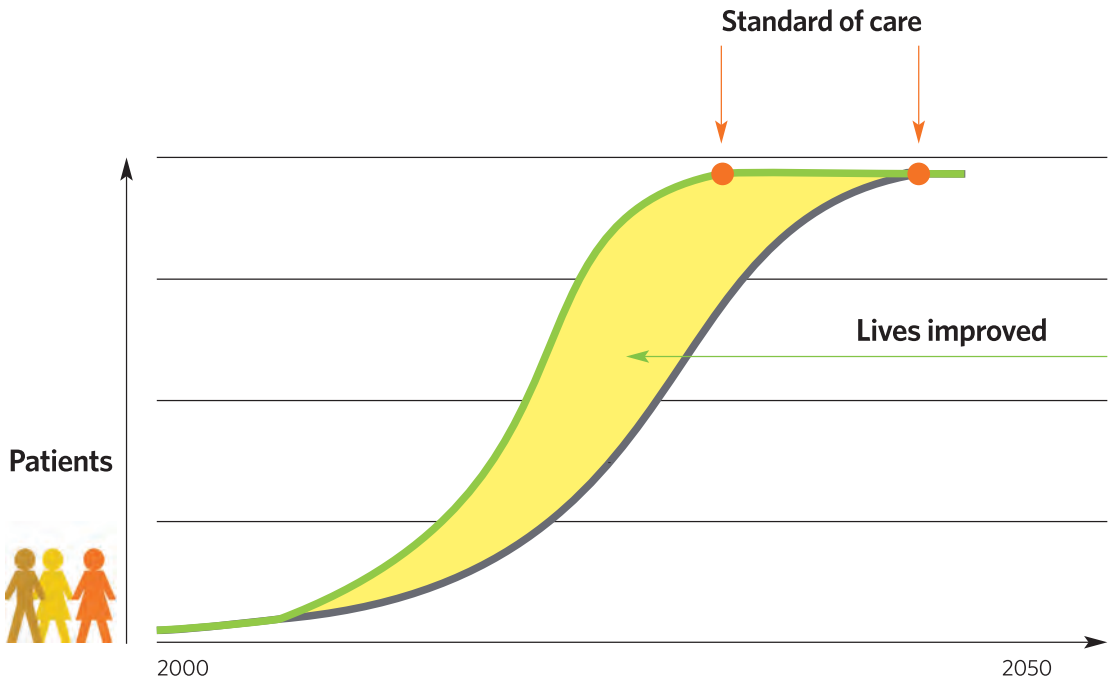
Major initiatives include

- 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 preclinical laboratory studies with an emphasis on brain disorders, oncology, and immunotherapy. It is the largest nongovernmental source of focused ultrasound research funding in the world.

Our mission is to accelerate the development and adoption of focused ultrasound as a mainstream standard of care. Through hard work, calculated risk-taking, and innovation, we are committed to ensuring that focused ultrasound is widely available in the shortest time possible.

fusfoundation.org



Saving time = Saving lives

FUS Partners Role in the Industry

To help accelerate the transition of the field from a primarily science-based research environment to a commercialization and patient treatment space focused on marketing and sales, the Foundation created FUS Partners in April of 2018. The FUS Partners program serves as a galvanizing force in facilitating rapid success of the commercial stakeholder segment of the focused ultrasound ecosystem, and thus helps speed the time from laboratory research to widespread adoption and utilization of the technology.

By virtue of its reputation as a trusted, independent, unbiased third party with an extensive network, FUS Partners is uniquely positioned to advance the field significantly and effectively by identifying commercial opportunities, making connections between stakeholders, and enhancing the flow of information between strategic and financial investors and focused ultrasound companies. The program has grown from two employees in 2016 to a team of five core team members.

Goals

- Produce a quantum change in the adoption rate of focused ultrasound as a mainstream standard of care
- Grow and rationalize the device manufacturers' segment of the focused ultrasound community by taking a holistic approach to the support of key stakeholders within the ecosystem

Activities

Regulatory & Reimbursement

- Engage with FDA, CMS, and commercial payers to inform them of the state of the field and obtain guidance for regulatory approvals and reimbursement
- Connect manufacturers with regulatory and reimbursement consultants
- Educate manufacturers on best practices and strategy for coverage, reimbursement, and coding and billing

Financial & Human Capital

- Connect institutional, strategic, and individual investors with manufacturers in need of financing and facilitate in due diligence and preparing investor relations materials
- Support focused ultrasound companies in attracting and hiring talent

Strategic Partnerships & Technology Transfer

- Connect manufacturers with academic research laboratories, strategic sponsors, and other manufacturers of focused ultrasound and related equipment and components

Advocacy

- Inform regulatory agencies, payers, and MedTech advocacy organizations about focused ultrasound
- Monitor clinical trials and potentially decrease cost of care while improving quality
- Connect and engage focused ultrasound manufacturers with advocacy organizations

Intellectual Property

- Educate academic researchers and focused ultrasound companies about why, what, and how to patent
- Connect researchers and focused ultrasound companies with intellectual property consultants

If you would like to talk with someone from the FUS Partners Team, please contact:

Emily White
Managing Director, FUS Partners
ewhite@fusfoundation.org

The Focused Ultrasound Foundation wishes to thank its exceptional Board of Directors and Council for their steadfast dedication to helping make focused ultrasound a clinical reality and improving the lives of millions of patients.

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Date 9.5.2023

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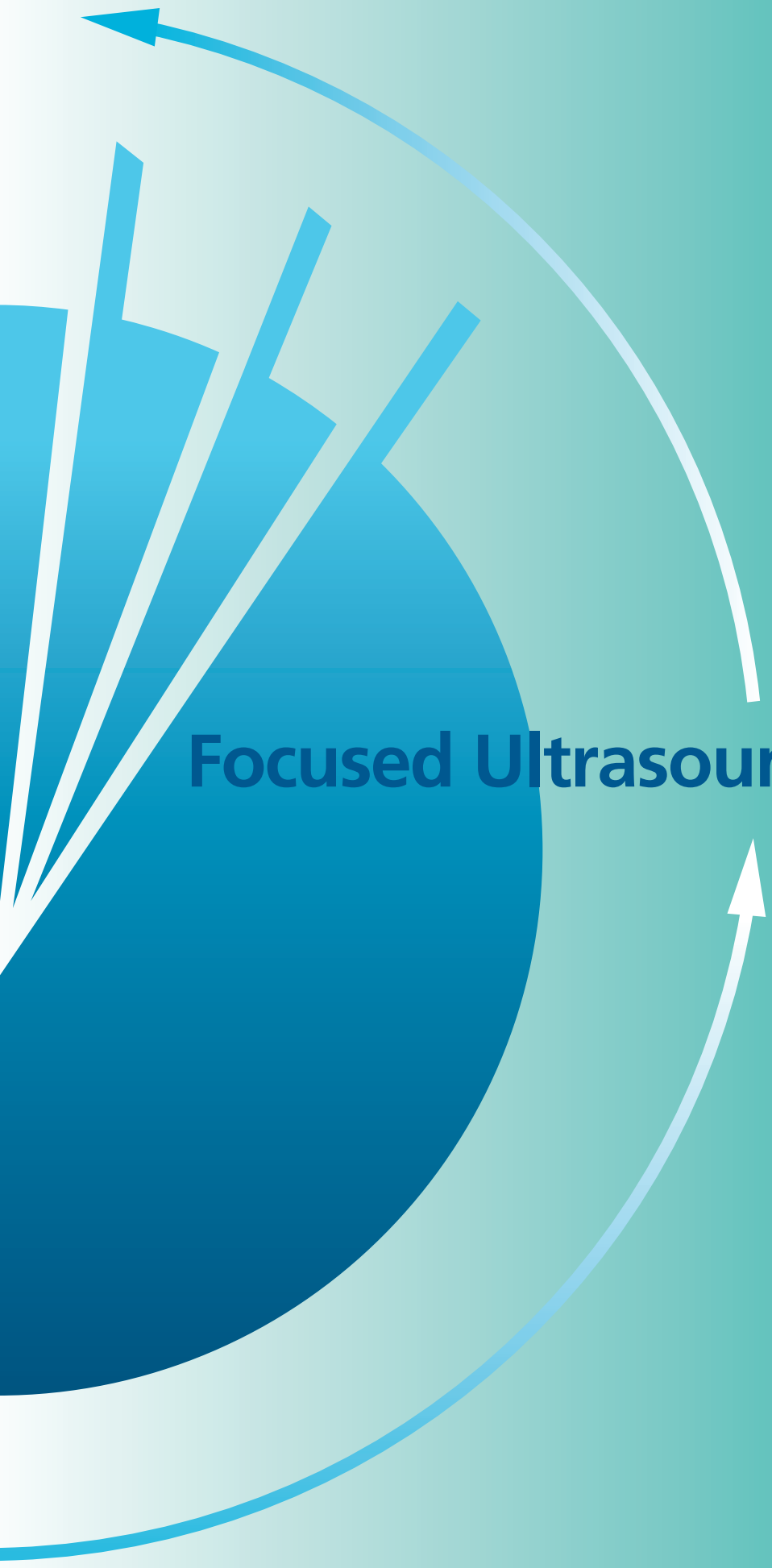

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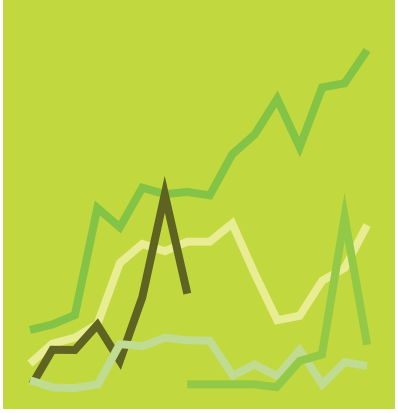
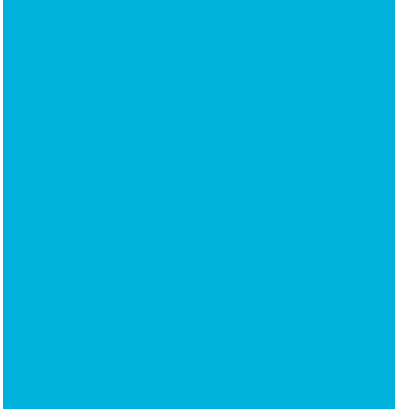
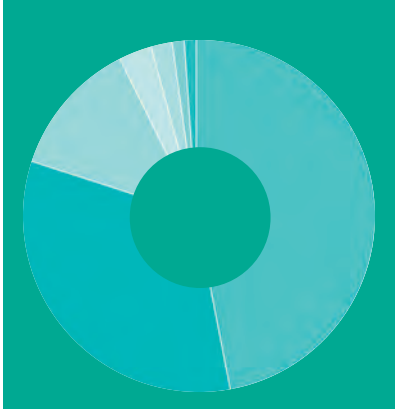
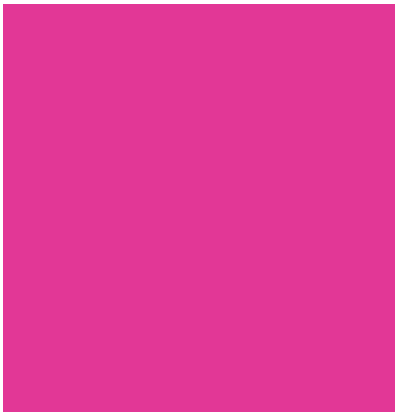
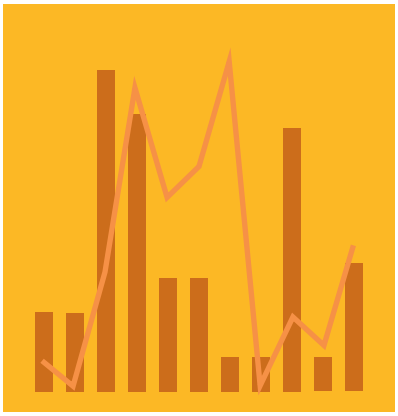
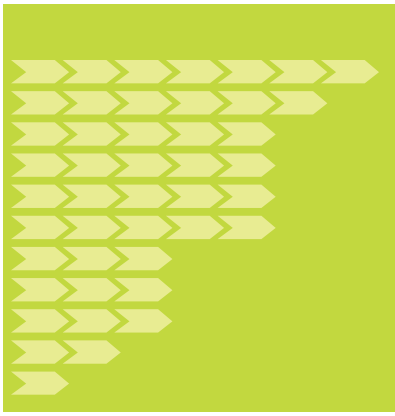

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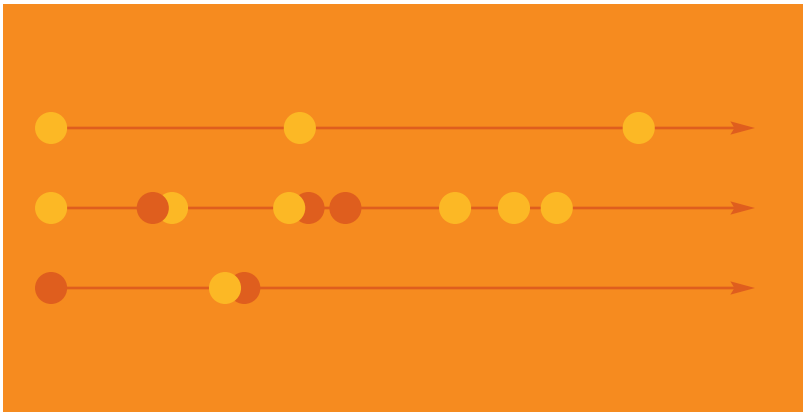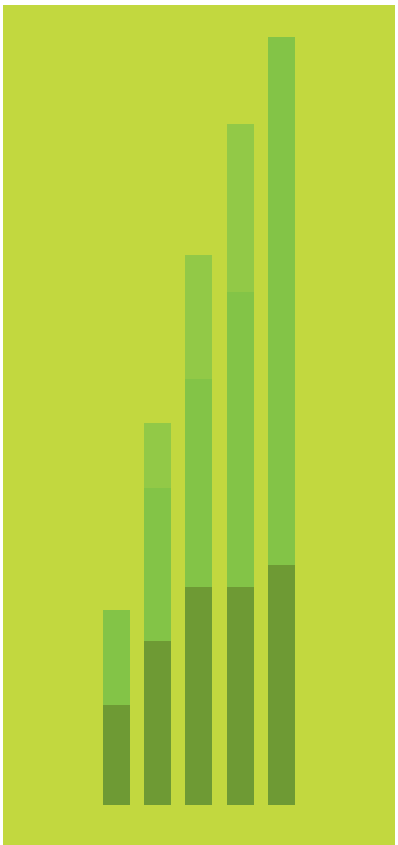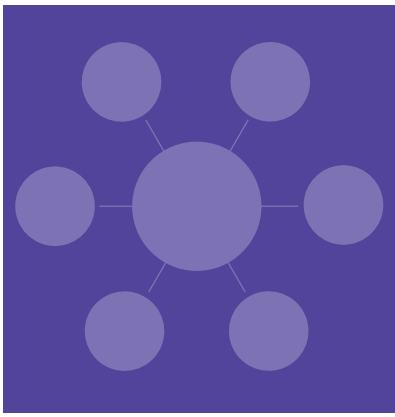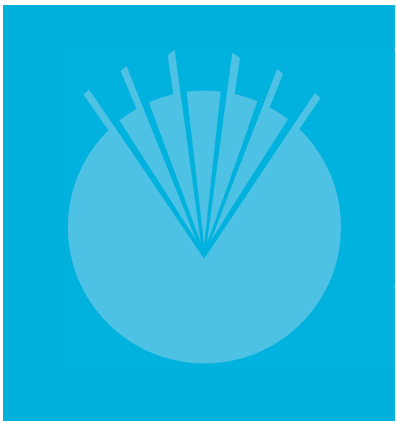
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