Mechanisms of Action





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

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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



Ultrasound Applications and Biological Effects* Table

HISTOTRIPSY	HYPERTHERMIA	NONTHERMAL	NONTHERMAL, BBB OPENING	THERMAL ABLATION
biological effects	biological effects	29 biological effects	biological effects	biological effects
Alteration of tissue mechanics Amplification of cancer biomarkers Chemosensitization Clot lysis Immune cell trafficking Immunomodulation Liquid biopsy Radiosensitization Tissue destruction	Amplification of cancer biomarkers Chemosensitization Drug delivery Drug delivery, immunotherapeutic Drug delivery, vehicle Immune cell delivery Immune cell trafficking Immunomodulation Increased vascular permeability Liquid biopsy Radiosensitization Tissue destruction Vasodilation	Alteration of tissue mechanics Amplification of cancer biomarkers Angiogenesis BNB opening [†] BNB opening [†] drug delivery Cardiac pacing Chemosensitization Clot lysis Drug delivery Drug delivery, immunotherapeutic Drug delivery, vehicle Gene delivery Immune cell delivery 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	BBB opening Drug delivery Drug delivery, immunotherapeutic Drug delivery, vehicle Gene delivery Immune cell delivery Stem cell delivery	Alteration of tissue mechanics Amplification of cancer biomarkers Chemosensitization Hemostasis Immune cell trafficking Immunomodulation Liquid biopsy Neuromodulation Radiosensitization Tissue destruction

* 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



		Stages		Total ¹
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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

Histotripsy-Number of Sites for Biological Effects by Indications continued

		Stages		Total ¹
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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

² Protocols inclusive of more than one indication

Ultrasound Applications and Biological Effects

Graphic—Hyperthermia



Hyperthermia—Number of Sites for Biological Effects by Indications



		Stages		Total ¹
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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



		Stages		Total ¹
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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

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Ultrasound Applications and Biological Effects Graphic—Nonthermal



Nonthermal—Number of Sites for Biological Effects by Indications



		Stages		Total ¹
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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



		Stages		Total ¹
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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

		Stages		Total
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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

Nonthermal-Number of Sites for Biological Effects by Indications continued



		Stages		Total ¹
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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.

Nonthermal—Number of Sites for Biological Effects by Indications continued

		Stages		Total ¹
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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

Nonthermal-Number of Sites for Biological Effects by Indications continued



		Stages		Total ¹
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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

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Ultrasound Applications and Biological Effects Graphic—Nonthermal, BBB opening





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

		Stages		Total
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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

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

		Stages		Total
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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

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Ultrasound Applications and Biological Effects Graphic—Thermal ablation



Thermal ablation—Number of Sites for Biological Effects by Indications



		Stages		Total ¹
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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.

		Stages		Total ¹
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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



		Stages		Total ¹
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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



		Stages		Total
Ultrasound application Biological effects	Preclinical	Clinical	Commercial	
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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Thermal ablation-Number of Sites for Biological Effects by Indications continued

Total¹

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

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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