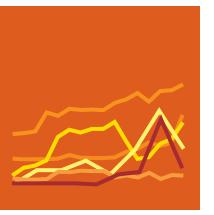
Research Sites







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 The United States superseded China as the top country with clinical research growth.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

IV	2	State of Research
ıv.	_	State of Nescardi

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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	
6 %	8%	Annual growth by reg	gion from 2013–2022 <u>—</u>	12%	_

Top Countries for Clinical ResearchNumber of sites

Top Countries with Clinical Research Growth

Sites added, cumulative 2017 to 2022

United States
China
France
Tie¹

0 6 12 18 24 30 36

Clinical research additional content

For more information about specific clinical research sites and indications, please visit:

www.fusfoundation.org/the-technology/research-sites

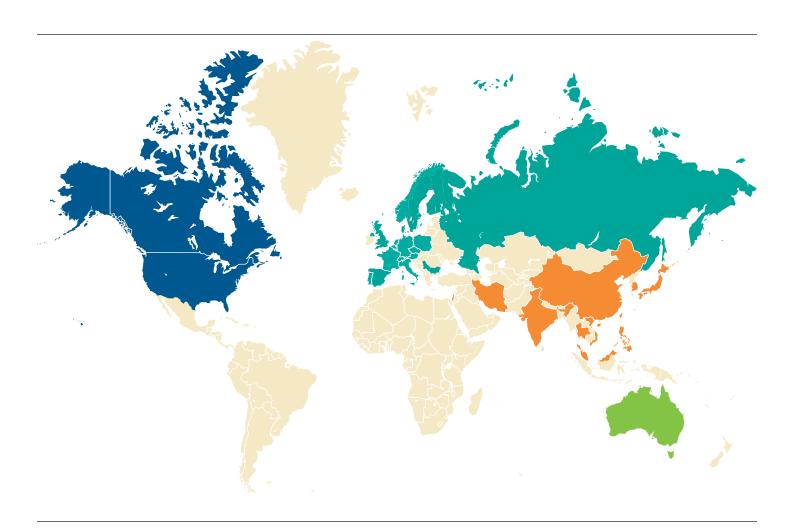
Use the "search by disease research" and/or "search by research stage" dropdown menu.

^{*} 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

- Serbia
- Spain 4
- 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
- Taiwan
- 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

63

Musculoskeletal sites
12 indications

83

Urological sites 6 indications

10

Endocrine disorders sites

2 indications

96

Neurological sites

37 indications

82

Women's health sites 12 indications **56**

Gastrointestinal sites 10 indications

7

Ophthalmological sites
1 indication

11

Miscellaneous sites 9 indications

2

Pulmonary sites 2 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.



		Regio	ns		Totals
ndications	■ N. America	■ Europe	Asia	Oceania	
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

		Regi	ons		Totals
Indications	■ N. America	Europe	Asia	Oceania	
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.



	Regions				Totals	
Indications	■ N. America	■ Europe	Asia	Oceania		
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	

		Regio	ns		Totals
Indications	■ N. America	■ Europe	Asia	Oceania	
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.



	Regions				
ndications	■ N. America	■ Europe	Asia	Oceania	
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.

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.



	Regions				
dications	■ N. America	■ Europe	Asia	Oceania	
leurological					
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

^{*} 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.



	Regions				
ndications	■ N. America	■ Europe	■ Asia	■ Oceania	3
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

^{*} 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.



		Regio	ns		Totals
Indications	■ N. America	■ Europe	Asia	Oceania	
Ophthalmological					
Glaucoma	1	5	1	_	7

		Regi	ons		Totals
Indications	■ N. America	■ Europe	Asia	Oceania	
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.



	Regions		Totals		
ndications	■ N. America	■ Europe	Asia	Oceania	
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.



¥		Regi	ons		Totals
ndications	■ N. America	■ Europe	Asia	Oceania	
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



Preclinical research sites worldwide*

North America	Europe	Asia	South America	Oceania	Africa
69	41	39	_	3	_
5 %	5 %	Annual growth by reg	ion from 2013–2021 <u>—</u>	5 %	_

Top Countries for Preclinical ResearchNumber of sites

13

0

United States

China
14

France
13

Taiwan
10

Tiel
7

26

39

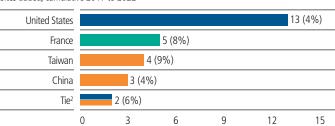
52

65

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.

Top Countries with Preclinical Research Growth

Sites added, cumulative 2017 to 2022



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.

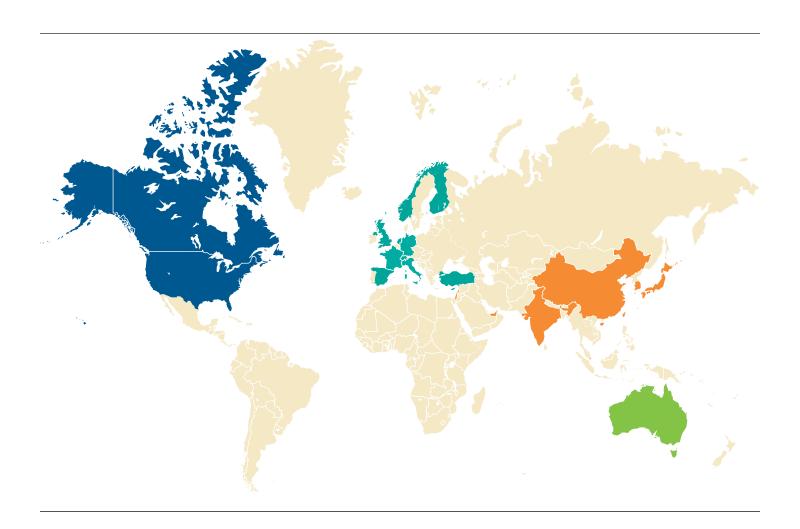
^{*} Preclinical research sites conduct nonhuman FUS research to collect data in support of the safety or feasibility of clinical applications.

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

31

Musculoskeletal sites 12 indications

Urological sites
9 indications

4

Endocrine disorders sites 3 indications

81

Neurological sites 32 indications

39

Women's health sites 8 indications 43

Gastrointestinal sites 8 indications

7

Ophthalmological sites 4 indications 24

Miscellaneous sites 9 indications

6

Pulmonary sites 2 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*

244

	Regions				Totals
ndications	■ N. America	■ Europe	Asia	Oceania	
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.



	Regions				
Indications	■ N. America	Europe	Asia	Oceania	
Endocrine disorders					
Diabetes	2	_	_	_	2
Thyroid cancer	2	-	-	-	2
Thyroid nodules	1	-	-	-	1

		Regi	ons		Totals
Indications	■ N. America	■ Europe	Asia	Oceania	
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.



		Regio	ns		Totals
Indications	■ N. America	■ Europe	Asia	Oceania	
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



		Regi	ons		Totals
Indications	■ N. America	■ Europe	Asia	Oceania	
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.



		Regio	ns		Totals
ndications	■ N. America	■ Europe	■ Asia	Oceania	
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.

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	Regions				Totals	
ndications	■ N. America	Europe	Asia	Oceania		
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.



	Regions				Totals
Indications	■ N. America	Europe	Asia	Oceania	
Ophthalmological					
Glaucoma	_	3	_	_	3
Macular degeneration	1	-	_	_	1
Presbyopia	_	1	1	_	2
Retinal injury	1	-	-	-	1

		Regi	ons		Totals
Indications	■ N. America	Europe	Asia	Oceania	
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.



	Regions				Totals	
Indications	■ N. America	Europe	Asia	Oceania		
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.



¥	Regions				Totals
Indications	■ N. America	Europe	Asia	Oceania	
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

MOA research sites worldwide*

North America	Europe	Asia	South America	Oceania	Africa
80	42	55	_	3	_
7 %	9%	Annual growth by reg	ion from 2013–2021 —	20%	_

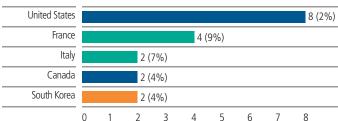
Top Countries for MOA Research Number of sites

United States China 20 France South Korea 10 Tie¹ 0 16 32 48 64 80

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.

Top Countries with MOA Research Growth

Sites added, cumulative 2017 to 2022



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

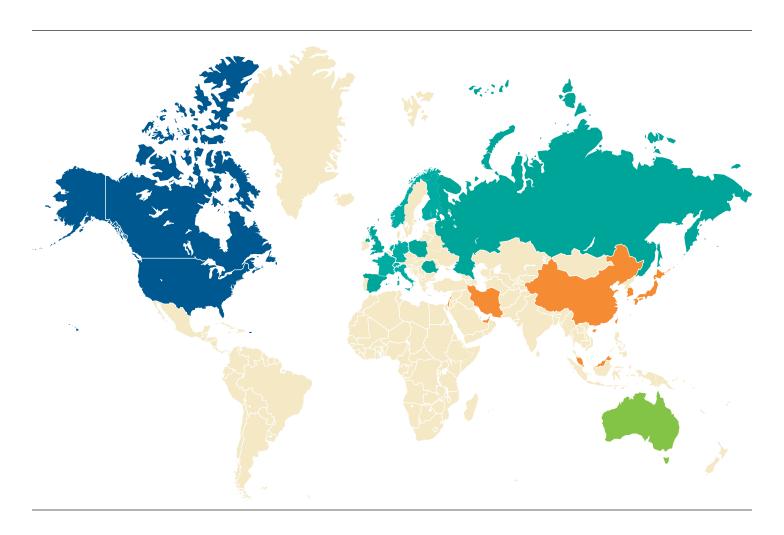
Use the "search by disease research" and/or "search by research stage" dropdown menu and choose "Bioeffect."

^{*} 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



	MOAs ¹		Sites		Total ²
Indications		■ Preclinical	Clinical	Commercial	
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.



	MOAs ¹		Sites	:	Total ²
ndications		Preclinical	Clinical	Commercial	
Endocrine disorders				·	
Diabetes	1	2	_	_	2
Graves' disease	1	-	1	-	1
Thyroid cancer	2	2	_	- !	2
Thyroid nodules	2	1	9	20	30



	MOAs ¹	Sites			Total ²
ndications		■ Preclinical	Clinical	Commercial	
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.



	MOAs ¹	Sites			Total ²
ndications		■ Preclinical	Clinical	Commercial	
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



	MOAs ¹	Sites			Total ²
ndications		■ Preclinical	Clinical	Commercial	
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.



(CKE	MOAs ¹		Sites		Total ²
Indications		■ Preclinical	Clinical	■ Commercial	
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.



The state of the s	MOAs ¹		Sites		Total
Indications		■ Preclinical	Clinical	Commercial	
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.



	MOAs ¹		Sites		Total ²
Indications		■ Preclinical	Clinical	Commercial	
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.



(C)	MOAs ¹		Sites		Total ²
Indications		■ Preclinical	Clinical	Commercial	
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.



	MOAs ¹	Sites			Total ²
ndications		■ Preclinical	Clinical	Clinical Commercial	
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.



\	MOAs ¹	Sites			Total ²	
Indications		Preclinical	Clinical	Commercial		
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.

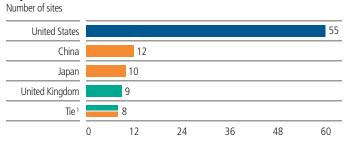


Technical Research Sites by Region

151 Technical research sites worldwide

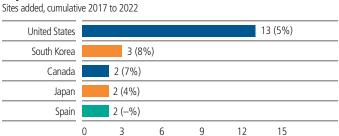
North America	Europe	Asia	Asia South America Oceania		Africa	
61	49	39	_	2	_	
5 %	10%	Annual growth by reg	gion from 2013–2022 <u>—</u>	15 %	_	

Top Countries for Technical Research



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.

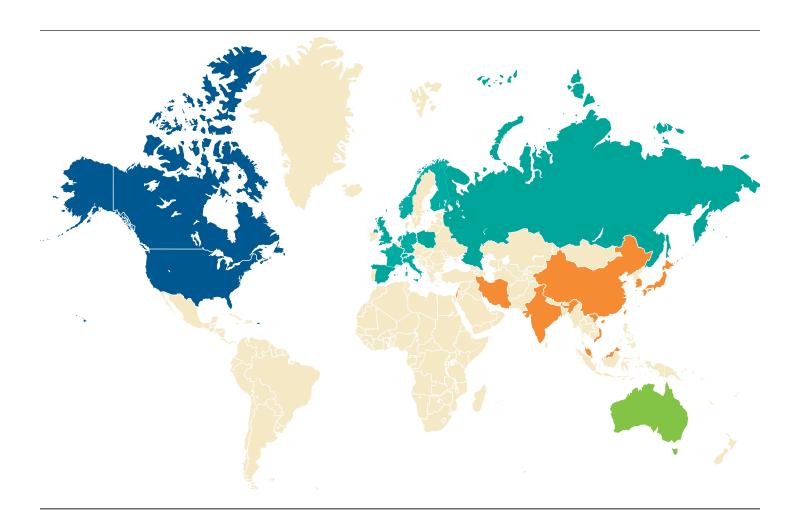
Top Countries with Technical Research Growth



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



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



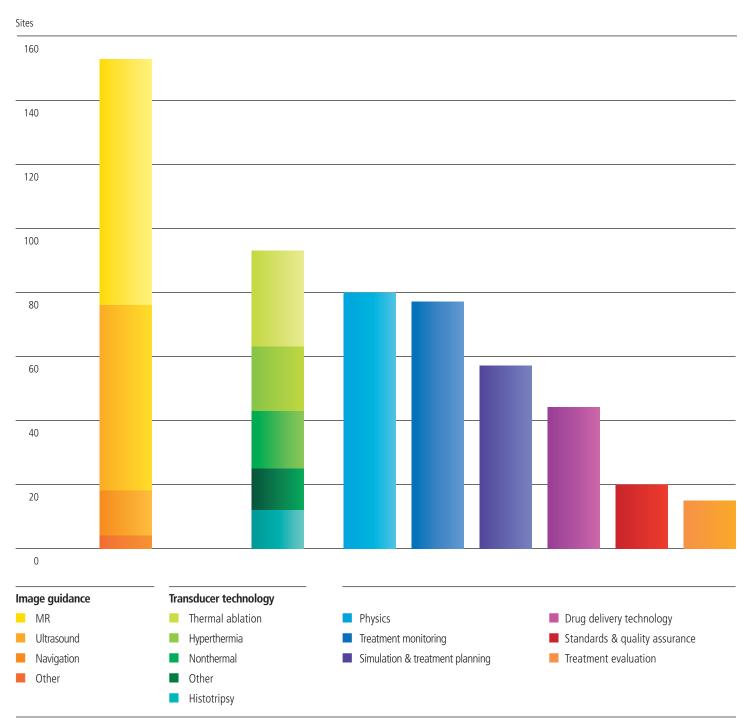
Technical Research Sites*

	Sites				Totals
Image guidance	North America	Europe	Asia	Oceania	153
MR	29	29	19	/ n-	F ' -
Ultrasound	31	18	9	4-3	
Navigation	4	8	2	- (1, 25)	
Other	1	1	2		
Transducer technology					93
Thermal ablation	11	12	7	-	
Hyperthermia	7	10	3	_	`~
Nonthermal	11	3	4	<u> </u>	
Other	8	4	-	1	
Histotripsy	7	3	2	4 -	<u></u>
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

 $[\]ensuremath{^{\star}}$ 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.