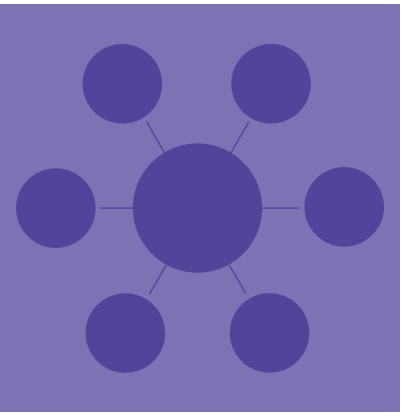
2023 Financial Landscape

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.

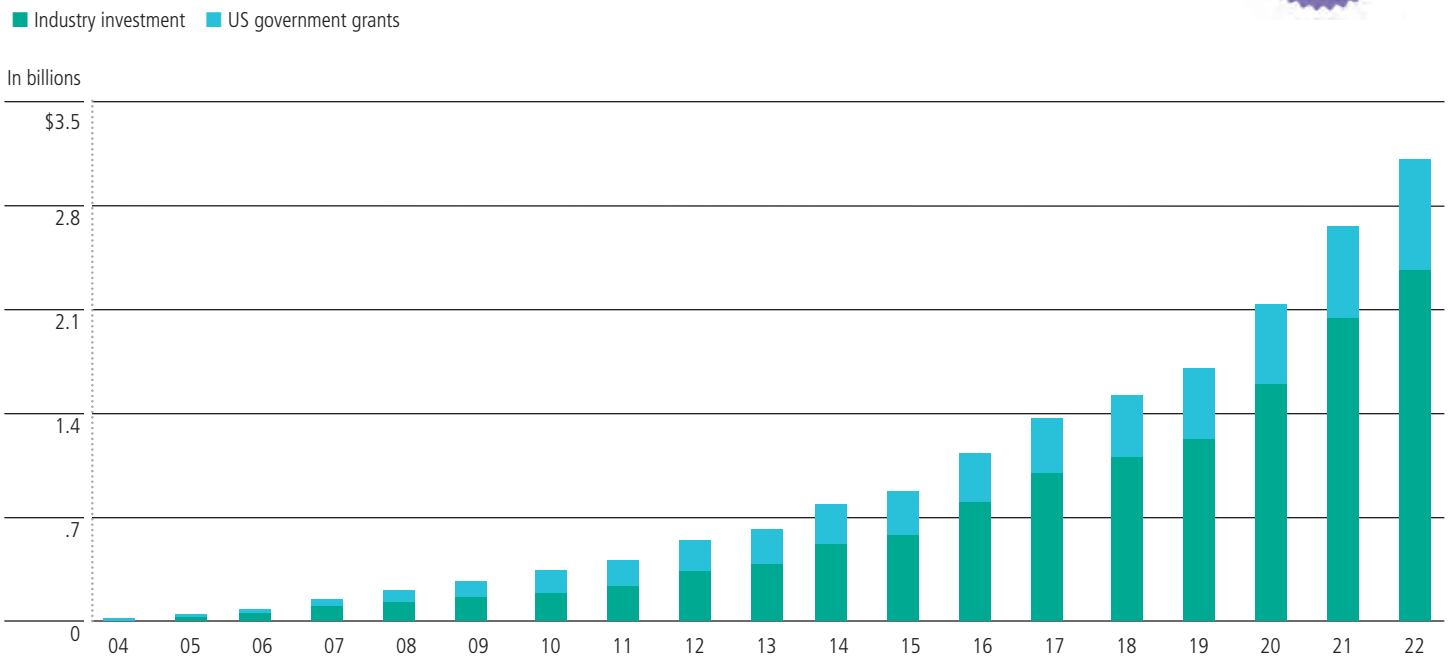
For the third year in a row, more than 300 million dollars was invested in focused ultrasound industry companies, bringing the three-year total of investments to more than one billion dollars. The cumulative amount of money invested in focused ultrasound research and the industry is over three billion.

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

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

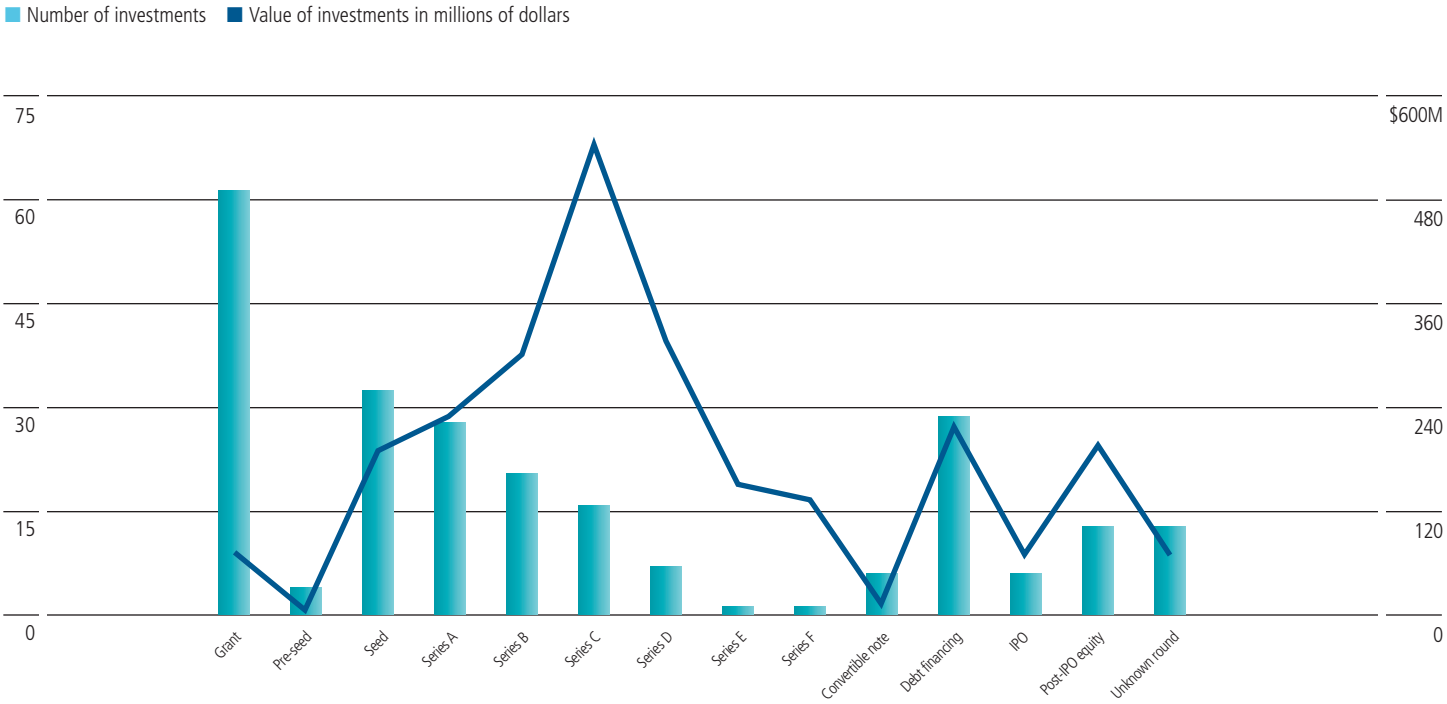
*Source: www.crunchbase.com and industry press releases

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

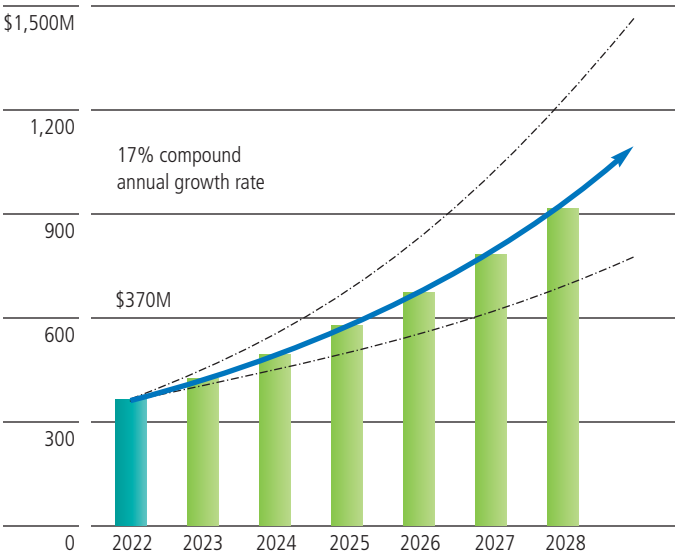
FUS Industry Investments by Stage



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

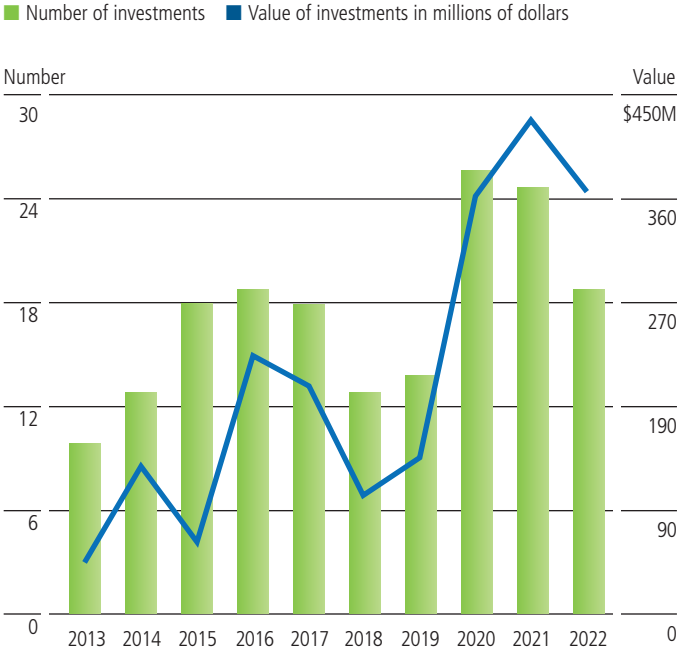
https://www.industrydataanalytics.com/reports/high-intensity-focused-ultrasound-hifu-market

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



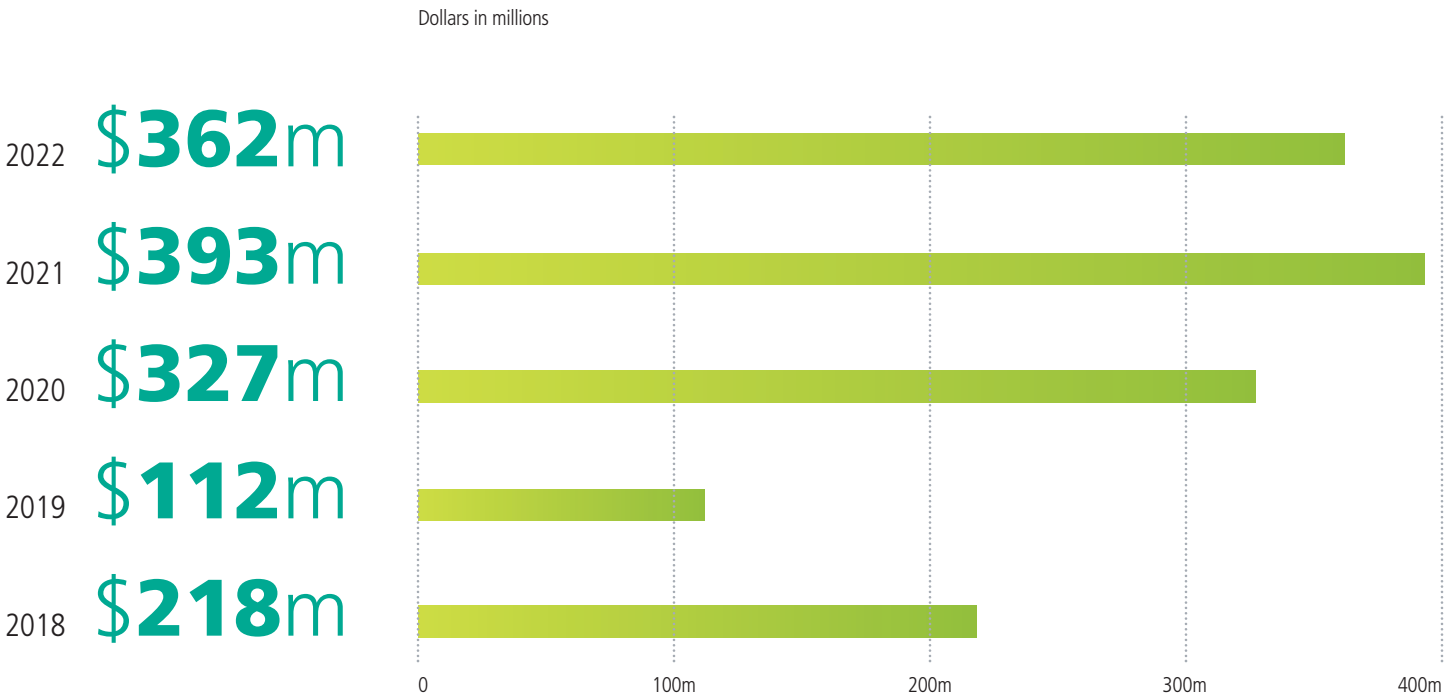
Source: www.crunchbase.com and industry press releases

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*

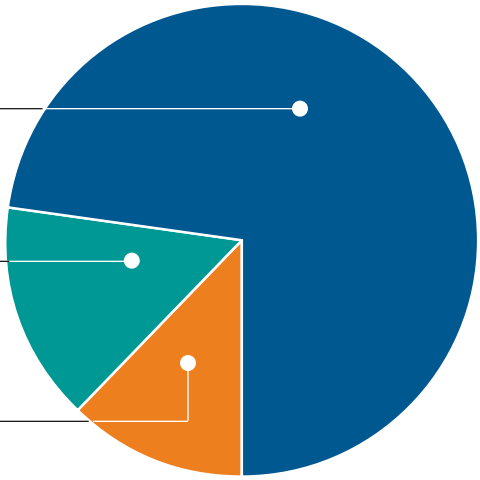
Investments by region[1]

Cumulative

$1,247m
North America

$257m
Europe

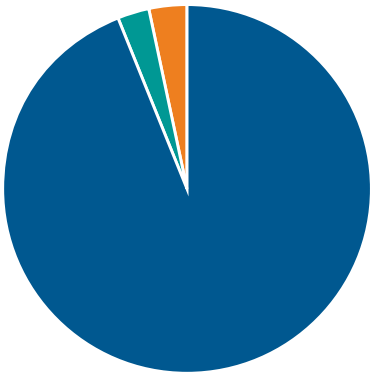
$208m
Asia



Disbursement to FUS Companies

Cumulative

$920m
North America



Source

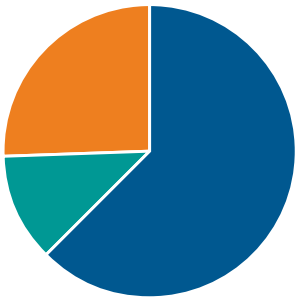
North America	$866.4m
Europe	$ 24.2m
Asia	$ 29.5m
Total	$920.1m

$211m
Europe

Source

North America	$ 17.0m
Europe	$162.2m
Asia	$ 31.6m
Total	$211.2m

$581m
Asia



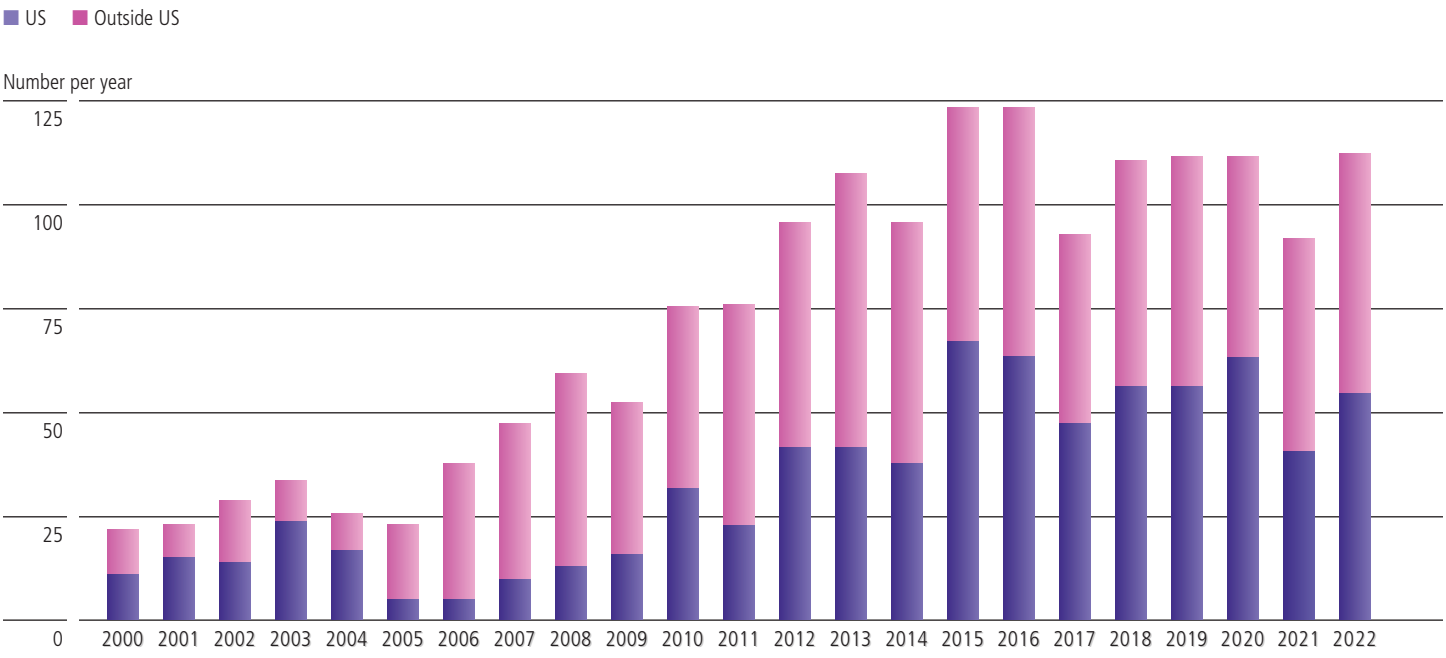
Source

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.

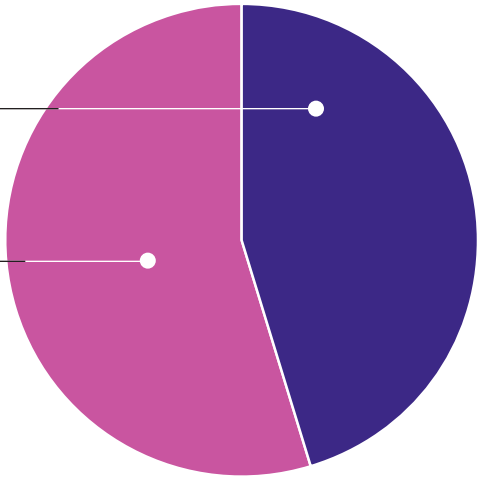
Specifically reviewing the data, not depicted graphically, for the last several years, we see most patents issued by the US Patent and Trademark Office, USPTO, were from US-based inventors or assignees, while 58 percent of WIPO patents had applicants based in the US. This is likely due to academic patent 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

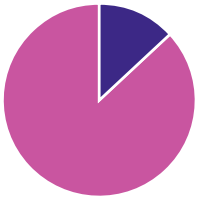


Snapshot of Growth in Patents
Number per year

5
1995

Source	
US	4
Outside US	1
Total	5

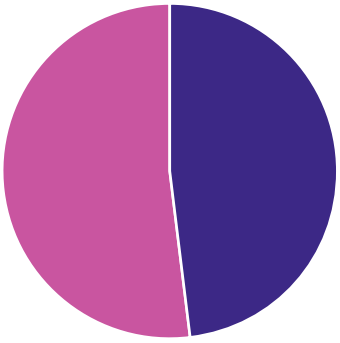
38
2006*



Source	
US	5
Outside US	33
Total	38

*Focused Ultrasound Foundation founded

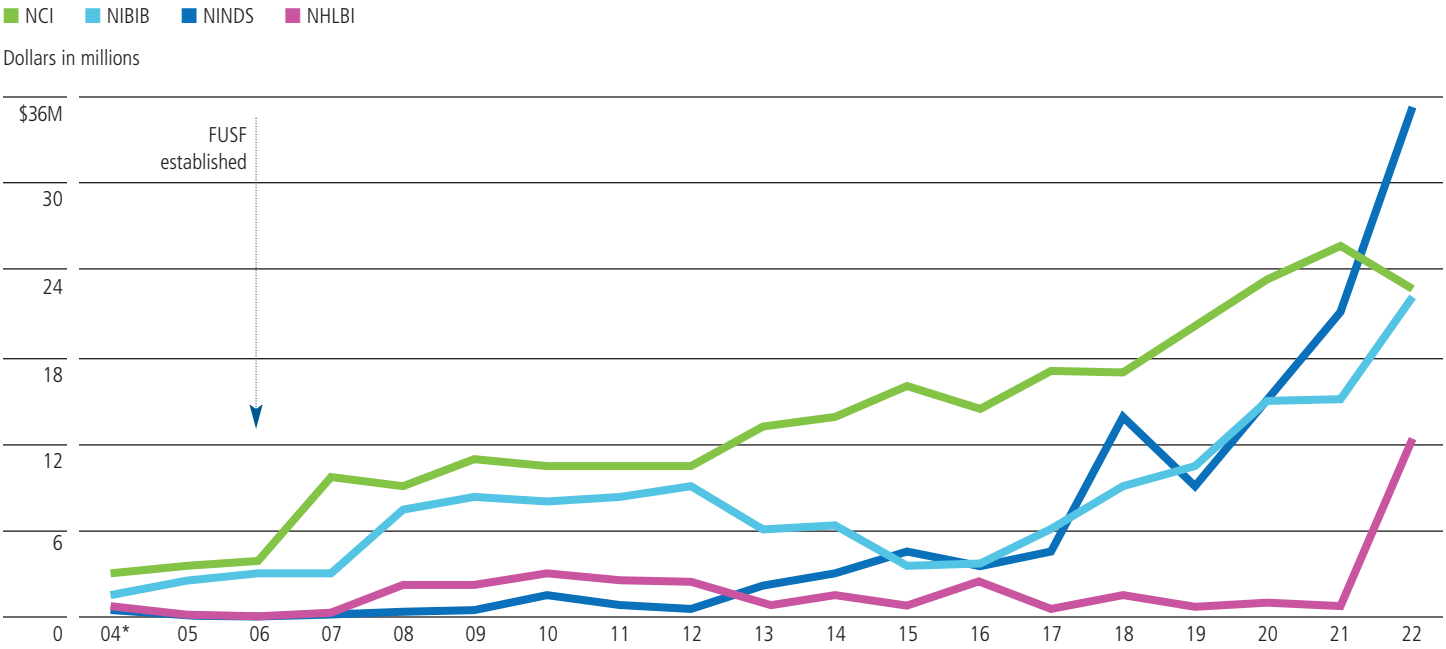
114
2022



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**	National Cancer Institute
$22,595,070	$152,764,408	**NIBIB**	National Institute of Biomedical Imaging and Bioengineering
$34,786,085	$107,726,646	**NINDS**	National Institute of Neurological Disorders and Stroke
$12,343,551	$46,992,424	**NHLBI**	National Heart, Lung, and Blood Institute
—	$32,924,533	**NCRR**[3]	National Center for Research Resources
$4,667,333	$25,418,689	**NIMH**	National Institute of Mental Health
$2,013,843	$15,734,754	**OD**	Office of the Director, NIH
$4,640,121	$14,261,179	**NSF**	National Science Foundation
$5,047,165	$13,407,872	**NEI**	National Eye Institute
—	$11,593,232	**NIDDK**	National Institute of Diabetes and Digestive and Kidney Diseases
$4,410,972	$11,583,061	**NICHD**	Eunice Kennedy Shriver National Institute of Child Health and Human Development
$905,525	$11,261,396	**NIA**	National Institute on Aging
$2,084,213	$9,520,073	**CDMRP**	Congressionally Directed Medical Research Programs
$635,781	$7,703,166	**NIDA**	National Institute on Drug Abuse
—	$6,106,583	**NIGMS**	National Institute of General Medical Sciences
$968,750	$2,974,108	**FIC**	John E. Fogarty International Center
$913,858	$2,772,219	**CNRM**	Center For Neuroscience and Regenerative Medicine
$403,750	$2,193,730	**NIDCR**	National Institute of Dental and Craniofacial Research
$1,349,403	$1,926,163	**NIAMS**	National Institute of Arthritis and Musculoskeletal and Skin Diseases
$1,516,636	$1,516,636	**NINR**	National Institute of Nursing Research
—	$909,727	**NIDCD**	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"

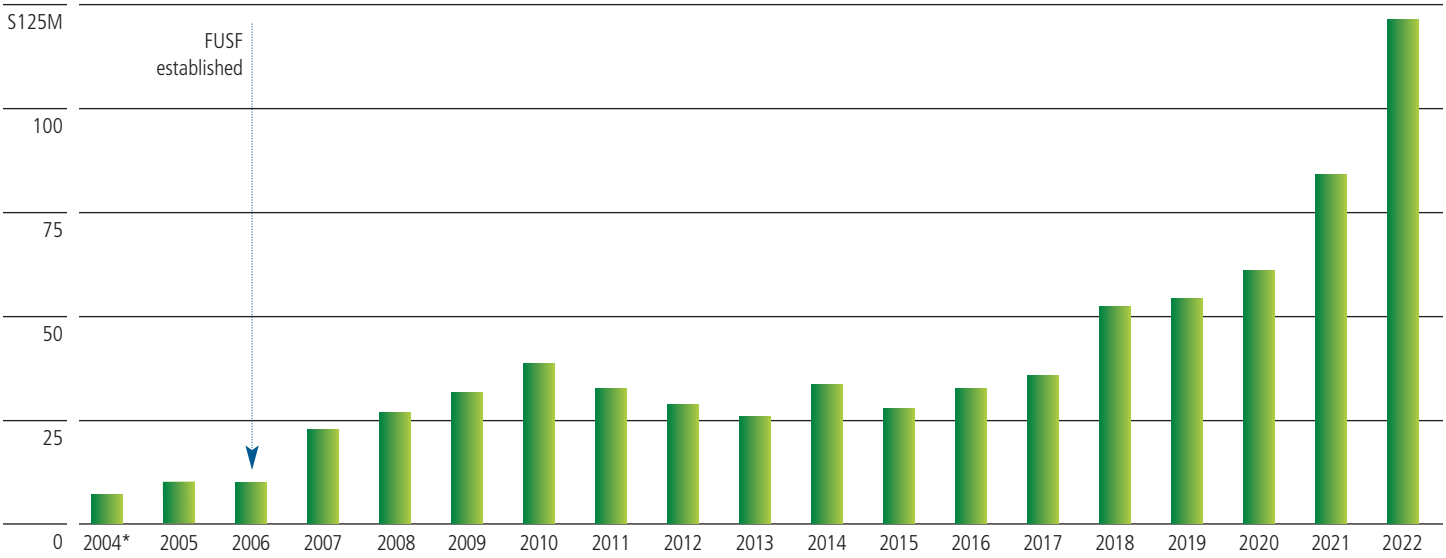
Total FUS Funding by United States Government Agencies continued

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.