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.2 Focused Ultrasound Foundation | 2023 State of the Field
**EXECUTIVE SUMMARY**

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.

### Indication Development Pipeline

<table>
<thead>
<tr>
<th>New preclinical indications</th>
<th>New clinical indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>Neurological</td>
</tr>
<tr>
<td>Periodontal disease</td>
<td>Bipolar disorder</td>
</tr>
<tr>
<td>Neurological</td>
<td>Brain metastases, lung cancer</td>
</tr>
<tr>
<td>Autism</td>
<td>PTSD</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>Trema; orthostatic</td>
</tr>
</tbody>
</table>

For further details

Chapter 2: Indication Development Pipeline
EXECUTIVE SUMMARY

Clinical Trials with New MOAs

<table>
<thead>
<tr>
<th>No. of Trials</th>
<th>Biological Effect</th>
<th>Indication</th>
<th>Clinical Trial ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Histotripsy</td>
<td>Alteration of tissue mechanics</td>
<td>Heart valve calcifications</td>
</tr>
<tr>
<td>1</td>
<td>Hyperthermia</td>
<td>Radiosensitization</td>
<td>Bone metastases</td>
</tr>
<tr>
<td>18</td>
<td>Nonthermal</td>
<td>Liquid biopsy</td>
<td>Glioblastoma</td>
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<tr>
<td></td>
<td></td>
<td>Neuromodulation</td>
<td>Anxiety</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bipolar disorder</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dementia</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>Depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Essential tremor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Neuropathic pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Obsessive-compulsive disorder</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Parkinson’s disease, dyskinesia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Parkinson’s disease, tremor</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PTSD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Radiosensitization</td>
<td>Melanoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sonodynamic therapy</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td></td>
<td>Nonthermal, BBB opening</td>
<td>Drug delivery</td>
<td>Alzheimer’s disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Drug delivery</td>
<td>Immunotherapeutic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Brain metastases, lung cancer</td>
</tr>
</tbody>
</table>

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 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
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.

**FUS publications**
Top three topics: radiology, engineering, and neurological science

- **677** FUS publications
- Top three topics: radiology, engineering, and neurological science

**FUS abstracts presented**

<table>
<thead>
<tr>
<th>Increase at FUS meetings</th>
<th>Increase at other symposia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>72%</strong></td>
<td><strong>108%</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abstracts presented at FUS meetings</th>
<th>Abstracts presented at other symposia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>518</strong></td>
<td><strong>394</strong></td>
</tr>
</tbody>
</table>

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

- **North America**: 219 sites (25% growth from 2013–2022)
- **Europe**: 290 sites (4% growth from 2013–2022)
- **Asia**: 405 sites (12% growth from 2013–2022)
- **South America**: 7 sites (4% growth from 2013–2022)
- **Oceania**: 4 sites (19% growth from 2013–2022)
- **Africa**: 7 sites (15% growth from 2013–2022)

### 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
## Executive Summary

### FUS Industry

**104 Companies**

<table>
<thead>
<tr>
<th>Newly identified companies</th>
<th>Companies with approved devices</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>10 Clinical device manufacturers</td>
<td>3 North America</td>
</tr>
<tr>
<td>5 OEM</td>
<td>4 Europe</td>
</tr>
<tr>
<td>2 Microbubble</td>
<td>9 Asia</td>
</tr>
</tbody>
</table>

### 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
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
Executive Summary

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
EXECUTIVE SUMMARY

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
EXECUTIVE SUMMARY

Reimbursement

32
Indications with regulatory approvals
Worldwide

44%
have reimbursement
with varying levels in at least one country

63%
have reimbursement
5 indications are insured in some US states

8
Indications with US FDA approvals

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

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