

# FOCUSED ULTRASOUND FOUNDATION

## 2015 YEAR IN REVIEW

### Highlights

- **Alzheimer's pre-clinical study in Australia confirms early findings that FUS may reduce plaques and improve memory; this serves as a predicate for early clinical studies.**
  - **The first US pediatric patients are treated as Children's National Medical Center begins its bone tumor study.**
  - **A pancreatic cancer study in Barcelona shows potential survival benefit.**
  - **Foundation's cancer immunotherapy program is established and working to develop a clinical trial.**
  - **The first depression patient is treated in a pilot trial in Korea.**
  - **Devices from two companies earn FDA approval to ablate prostate tissue.**
  - **Foundation-funded study opens the blood-brain barrier for the first time; researchers eyeing potential for uses in Alzheimer's and other applications.**
  - **John Grisham releases book about focused ultrasound; 250,000+ copies have been distributed.**
  - **Insightec applies to the FDA for approval to treat essential tremor.**
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# A MESSAGE FROM THE CHAIRMAN

## Dear Friends,

Focused ultrasound enjoyed a good year in 2015. We nonetheless have important challenges to deal with as we move forward.

First, our accomplishments: We have improved our understanding of the many biomechanisms by which focused ultrasound affects tissue. The number of treatable disorders has therefore grown. So have both the number of manufacturers in the field and the overall investment in focused ultrasound technology. The funds available for research continue to increase, and we have benefited from scientific articles and other media coverage. Patient treatments—one of our most important barometers—continue to climb in number, teaching us new things every day.

Despite this pattern of success, universal insurance reimbursement has not yet been granted for any of focused ultrasound's clinical indications. This is a reflection that this early-stage technology requires more long-term evidence of safety and efficacy, which should be forthcoming in the next several years.

Leaving aside one important gap in our organization—we have so far failed to recruit a medical director—the Foundation operates today with record levels of strength and efficiency, and we have gained invaluable new team members. Nora Seilheimer has become a Co-Director of Development. Alexandra de Olazarra, who interned with us while completing her Masters in Public Health, is now Senior Special Projects Officer. Kelsie Timbie, whose biomedical engineering PhD thesis is on focused ultrasound, has rounded out our scientific team.

Even though the Foundation is functioning very well and widely recognized as the catalyst for advancing the field, there is an indisputable need for us to improve. Clearly, focused ultrasound has grown more rapidly than we anticipated. We need to review our past successes and failures and reiterate our goal of sharpening our focus. At the same time, we must remain open to opportunities that unexpectedly arise in an environment that is rapidly evolving. If focused ultrasound can improve the lives of millions, one must accept the corollary that errors we make in strategy or execution will have negative and irreversible consequences for countless individuals.

We need to improve also by tapping into the focused ultrasound work in Asia, a goal that has been hampered by our lack of a physical presence and by cultural and language barriers. Currently, however, Dong-guk Paeng, PhD, professor of biomedical engineering at Jeju National University in Korea, is spending 18 months in Charlottesville as our Merkin Fellow. This summer, he will return to Korea and work part-time for the Foundation. He plans to visit Asian research sites and manufacturers with the intention of building personal and collaborative relationships for us.

In biomedical research and technology development, progress occurs exponentially. We believe focused ultrasound is at an inflection point, meaning that it is about to experience rapid advances. In this environment, we expect emphasis to shift from research and development to commercial success and to bring on the technology's widespread adoption as a standard of care. Seeing all of that in our future, we will use the tagline "Focused ultrasound at the tipping point" at our upcoming 5th International Symposium.

The Foundation's success is the result of our having brought together dedicated people—our donors, Board of Directors, Council, and team—who are driving focused ultrasound forward. None of what we have done would have been possible without the generosity of many of who have supported us with their minds as well as their money. Thank you, as we look ahead to a bright 2016.

Be well,



Neal F. Kassell, MD



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# Creating Knowledge: Research Milestones

The cornerstone of our activities is our research program, which consumes more than half of our expenditures and contributes materially to the rapidly expanding knowledge of focused ultrasound.

The Foundation continues to be the largest nongovernmental source of support for focused ultrasound research. Furthermore, we are encouraging NIH and disease-specific organizations to take a more active interest in focused ultrasound research and increase funding.

Numerous technical projects, pre-clinical studies and clinical trials are planned, but progress towards their completion has been frustratingly slow. Research efforts continue to be plagued by bureaucratic red tape and patient enrollment issues, creating a substantial backlog. We hope some of the major barriers will be overcome in 2016.

## FIRST-IN-HUMAN BRAIN BREAKTHROUGH

The [blood-brain barrier was non-invasively opened](#) in a patient for the first time in November. A team at Sunnybrook Health Sciences Centre in Toronto used focused ultrasound to enable temporary and targeted [opening of the blood-brain barrier](#), allowing more effective delivery of chemotherapy into a patient's malignant brain tumor. The Foundation supported this groundbreaking research.

*The blood-brain barrier has been a persistent impediment to delivering valuable therapies to treat tumors. We are encouraged that we were able to open this barrier... and we look forward to more opportunities to apply this revolutionary approach.*

-Dr. Todd Mainprize, Sunnybrook neurosurgeon and study principal investigator



## CANCER IMMUNOTHERAPY PROGRAM

This initiative explores where focused ultrasound may play a key role in [enhancing the body's immune response](#) to malignant tumors and augmenting the effectiveness of drugs.

A [2015 workshop](#), held in conjunction with the Cancer Research Institute, defined a roadmap of studies. To provide guidance for the program, an Advisory Board and working group have been created to coordinate activities and foster collaboration amongst research sites in academia and industry. Studies of metastatic melanoma to the brain, as well as cancer of the kidney, pancreas, breast and prostate are being organized. We have [partnered with other foundations](#), like the Cancer Research Institute and the Melanoma Research Alliance, to further advance the field.

This year, we'll collaborate with Quest Diagnostics to monitor immune biomarkers present after focused ultrasound treatment. We also plan to work with pharmaceutical companies to explore enhancing immunotherapy drugs with focused ultrasound.



Our staff celebrated Cancer Immunotherapy Awareness Month in June by participating in the White Out Cancer initiative.



# Creating Knowledge: Research Milestones

## BRAIN PROGRAM

### Technology Development

We have invested considerable effort into establishing more than 10 technical projects designed to make focused ultrasound brain treatments safer, faster and more effective.

### Pre-clinical Studies

Laboratory studies are being organized for [Alzheimer's](#) and [Parkinson's](#) diseases, [epilepsy](#), and [brain tumors](#). Approaches being studied include tissue destruction with [thermal](#) and [non-thermal](#) ablation, [sonodynamic therapy](#), [blood-brain barrier opening](#), and stimulating the brain's [immune response](#) to malignant tumor cells.

### Clinical Trials

#### ESSENTIAL TREMOR

Results of the essential tremor pivotal trial have been [submitted for publication and to the FDA](#). We hope FDA approval will be forthcoming this year, allowing US patients access to focused ultrasound for treatment.

#### PARKINSON'S DISEASE

The [Parkinson's tremor pilot trial](#) will be completed this spring, and results should be available for publication this year. Enrollment in the [Parkinson's dyskinesia trial](#) has begun and is also expected to be completed by the end of the year.

A pilot trial of a new target for treating Parkinson's tremor and dyskinesia - tractotomy - is being organized, and enrollment is expected to open this year.

#### BLOOD-BRAIN BARRIER OPENING

The [pilot trial](#) to open the blood-brain barrier for focal delivery of chemotherapy to treat glioblastomas began enrolling patients in late 2015.

#### DEPRESSION

The [first patient](#) in a [depression trial](#) was treated, and enrollment is anticipated to be completed in 2016.

#### AND OTHERS...

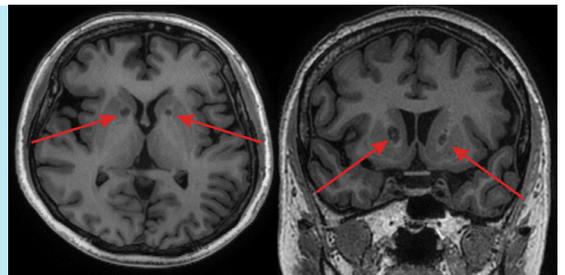
Early clinical trials for Alzheimer's disease, multiple sclerosis tremor, focal dystonia, epilepsy, metastatic brain cancer and brain tumors are being planned for 2016.

Once an avid biker, Kimberly's Parkinson's had made it impossible for her to balance safely. She was forced to turn to stationary bikes until she became the first patient treated at the University of Maryland. Now she's back on her bike and even running!  
[Read her story >](#)



#### MR Scans from First Depression Patient

The arrows show the ablated (or destroyed) brain tissue.





# Creating Knowledge: Research Milestones

## PEDIATRICS PROGRAM

The Foundation participated in a [Pediatric Workshop](#) last year where it was decided that [Osteoid Osteoma](#) - a benign but painful bone tumor - would be the lead pediatric focus. A paper defining treatment guidelines has been developed; a steering committee is in place for the study; and a worldwide registry has been established. A comparative study of focused ultrasound versus radiofrequency ablation is also being organized.

Jack was the first pediatric patient with a benign bone tumor treated with focused ultrasound in a Canadian clinical trial. He is now back to his active lifestyle and enjoys snowboarding and wakeboarding.

[Read more about Jack >](#)



## CENTERS OF EXCELLENCE PROGRAM

The Foundation's [Centers of Excellence Program](#) provides recognition and support for academic institutions that are luminary sites for collaboration in focused ultrasound patient care and research. In 2015, Brigham and Women's was named a Center of Excellence, and we hope to add more this year.



BRIGHAM AND WOMEN'S HOSPITAL

ICR The Institute of Cancer Research



## EXTERNAL RESEARCH AWARDS PROGRAM\*

In 2015, we funded five new investigator-initiated projects.

**33**

completed projects

**45**

projects presented at meetings

**37**

published projects

**14**

projects earned follow-on funding

This brings the total funded projects up to 52.

**\$3.3M**

Funding provided for completed projects

**\$22M**

Follow-on funding earned

**x7**

Factor by which the Foundation leverages donors' contributions

\*Unless specified, figures are since the Foundation's inception in 2006.

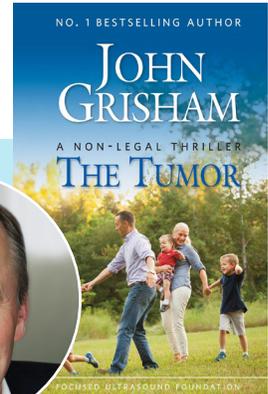


# Increasing Awareness

This year, major inroads were made in increasing awareness of the potential of focused ultrasound amongst all stakeholders. We hosted 17 awareness events, the largest of which counted over 1,000 attendees. These gatherings allow us to spread the word about the technology and our work.

## JOHN GRISHAM PUBLISHES FOCUSED ULTRASOUND BOOK

*The Tumor* is a short, fictional account of how this real medical technology could impact the future of medicine. The Kindle e-book is available for free on [Amazon](#), and we've distributed over 250,000 copies.



*"It's the most important book I've ever written. Everyone who is concerned about their health and loved ones should read The Tumor.... I have found no other cause, issue, or charity that can potentially save so many lives." -John Grisham*



## FOCUSED ULTRASOUND STUNS AT TEDx

Neal Kassell took the TEDx stage to discuss the potential of focused ultrasound to improve the lives of people with many serious medical disorders. Author, John Grisham related why he became involved in the Foundation and his role as a storyteller in helping to spread the word, introducing his new short book, *The Tumor*.

Kassell then showed a video of [Kimberly](#), a Parkinson's patient disabled by tremors. She stunned the audience by running on stage to share her experience as one of the first participants in a clinical trial using focused ultrasound to treat the symptoms of Parkinson's. The video has been watched over 10,000 times since November.



[WATCH THE TEDx VIDEO NOW >](#)

## WEB TRAFFIC AND OUTREACH HIT NEW HEIGHTS

John Grisham's new short book, *The Tumor*, placed a spotlight on focused ultrasound this winter. Due to this increased awareness, website visits doubled to 160,000, accompanied by an increase in social media activity.

Meanwhile, our [monthly newsletter](#) continues to be popular with a circulation of now more than 8,000 subscribers.

## MEDIA COVERAGE

Focused ultrasound earned more than 200 media placements in 2015, up 150% over the previous year.

Medscape



theguardian

VIRGINIA BUSINESS

THE WALL STREET JOURNAL

HUFFPOST LIVING

THE GLOBE AND MAIL



## Convening the Community

### LOOKING AHEAD TO SYMPOSIUM 2016

Our 5th International Symposium on Focused Ultrasound will be held August 28 to September 1, 2016 in Bethesda, Maryland. Jin Woo Chang, MD, PhD from Yonsei University College of Medicine in Seoul, Korea, has been named our [Honorary President](#).

The [symposium](#) is recognized as the leading forum for the latest translational and clinical advances in focused ultrasound and serves as a crucible to strengthen existing relationships and foster new collaborations. We will discuss applications in neurosurgery, oncology, pain management, women's health, and other emerging areas.



### FOUNDATION WORKSHOPS SPUR PROGRESS

Last year we held a number of small, invitation-only workshops where we convened clinicians, scientists, industry leaders, representatives from the FDA, and other experts to discuss ways to overcome roadblocks and advance progress for the technology. Topics included reimbursement hurdles for essential tremor and uterine fibroids, [brain treatment envelope and simulation](#), [immunotherapy](#), [Alzheimer's disease](#), and [brain tumors](#).



## Cultivating the Next Generation

### FOUNDATION FELLOW MAKES RESEARCH STRIDES

Dong-guk Paeng, PhD, our 2015 Merkin Fellow, has spent his time with the Foundation embarking on important technical research. He has initiated a study aimed at improving the safety and control of treatments and has completed a [histotripsy](#) study in conjunction with the University of Michigan, the University of Virginia, and Histosonics.



The Merkin Fellowship is made possible by the generous support of Richard Merkin, MD.



### FOUNDATION INTERNSHIP PROGRAM UPDATE

The local internships at the Foundation's Charlottesville, Virginia offices continue to enjoy success, attracting applicants ranging from high school level to MBA and medical students. This opportunity is supported in part by the Claude Moore Charitable Foundation, and in 2015, we welcomed 10 student interns.

The global intern program is now in its second year and pairs 20 students with mentors in focused ultrasound laboratories around the world for a summer session.

*"My internship was an important factor in encouraging me to apply for a PhD... I especially enjoyed the process of discussing ideas and benefitting from the experience of my supervisors, while being afforded the freedom to work independently." -Jemma Brown, global intern*



# Finances

## SPENDING

2015 TOTAL: \$5.5 MILLION

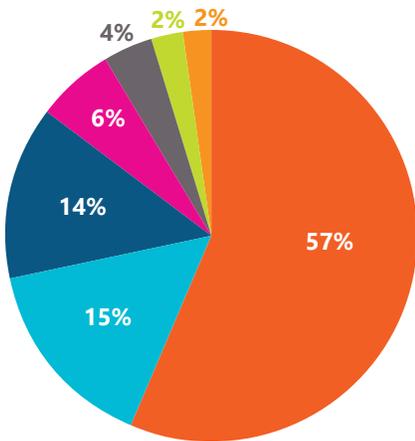
The Foundation spent just over \$5.5 million last year versus a budget of \$7.7 million. A difference was due in large part to slowness in initiation and completion of research projects and overall cost savings.

For 2016, spending is forecast to be \$8.7 million, with the increase mostly related to Symposium expenses.



## ALLOCATION OF FUNDS

2015 TOTAL: \$5,543,357\*



	<u>ACTUAL</u>	<u>BUDGETED</u>
RESEARCH	\$3,132,080	\$5,059,005
FUNDRAISING	\$854,750	\$1,041,537
COMMUNICATIONS	\$784,672	\$814,046
SCHOLARS PROGRAM/ FELLOWSHIPS	\$331,538	\$239,301
EXTERNAL RELATIONS	\$217,701	\$228,158
REIMBURSEMENT/ FIBROID RELIEF	\$138,014	\$288,203
SYMPOSIA/MEETINGS	\$120,602	\$55,183

## FUNDRAISING

2016 GOAL: \$8 MILLION

The fundraising goal for 2016 is \$8 million - \$4 million in cash and \$4 million in multiyear pledges.

Our development efforts have been enormously facilitated by a generous multiyear \$1 million per year unrestricted pledge that must be matched on a 1:1 basis.



## TO OUR DONORS,

Your generosity enables us to fund groundbreaking research, convene the best minds in the field to overcome barriers, and spread the word about the immense potential of focused ultrasound. We thank you for your support and the important role you play in advancing this technology that could one day impact the lives of many.

**THANK YOU!**

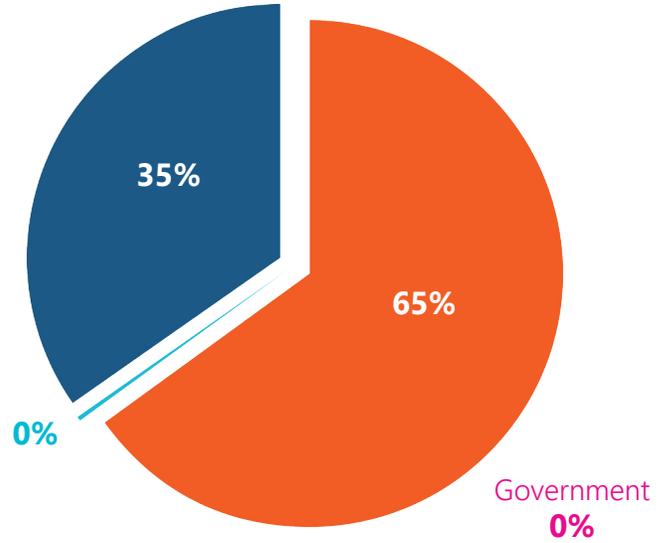
\*The Foundation's 2014 Audited Financial Reports are available on the website.



## FOUNDATION FUNDING SOURCES STATISTICS

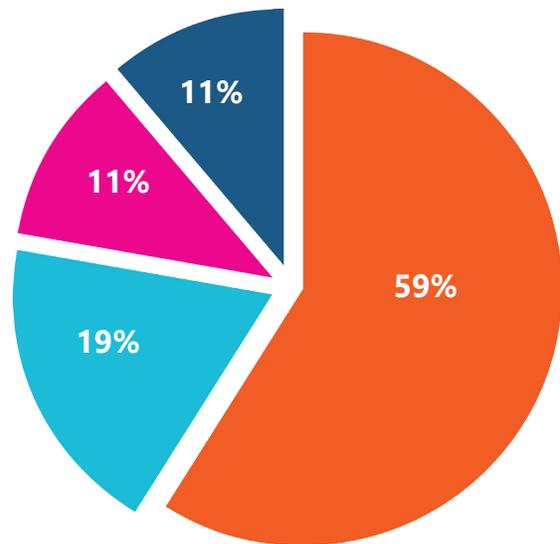
### 2015 DONATIONS

	<u>AMOUNT</u>	<u>NUMBER</u>
INDIVIDUAL	\$5,393,455	135
CORPORATE	\$7,500	1
GOVERNMENT	\$0	0
FOUNDATIONS	\$2,953,087	24
<b>TOTAL</b>	<b>\$8,354,042</b>	<b>160</b>



### ALL-TIME DONATIONS

	<u>AMOUNT</u>	<u>NUMBER</u>
INDIVIDUAL	\$39,025,622	553
CORPORATE	\$12,418,464	61
GOVERNMENT	\$7,019,000	4
FOUNDATIONS	\$7,546,439	53
<b>TOTAL</b>	<b>\$66,009,524</b>	<b>671</b>



If you would like additional information or want to discuss how you can support our mission, please contact:

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[www.fusfoundation.org](http://www.fusfoundation.org)