Highlights

- Treatment of prostate disease with focused ultrasound: US FDA approves first transurethral ultrasound device
- Treatment of brain tumors with focused ultrasound: US FDA approves new trial
- Foundation-hosted workshops explore focused ultrasound’s role in cancer immunotherapy and advanced imaging
- 2019 State of the Field Report published
- Biennial Foundation awareness event highlights latest focused ultrasound developments
- Reimbursement successes for focused ultrasound achieved in Japan, US
- Foundation honored for “Outstanding Contributions to Virginia Bioscience”

Dear Friends,

The work we do at the Foundation is in a league of its own. We believe that the highest purpose in life is to help other people. The Foundation provides us with a once-in-a-lifetime opportunity to improve the lives of millions of people by serving as the catalyst to create a revolution in therapy. Our mission is to accelerate the development and adoption of focused ultrasound as a mainstream standard of care. Through hard work, calculated risk-taking, and innovation, we are committed to ensuring that focused ultrasound is widely available for as many indications as possible in the shortest time possible. Saving time equals saving lives.

With the privilege of reducing the risk of death, disability, and suffering for countless people comes the daunting responsibility to get it right. Any errors in strategy or execution risk harm to patients by depriving them of the benefits of this game-changing technology. Accordingly, we are hyperfocused on activities that directly benefit patients and decrease time to adoption. Enclosed you will find important updates on such activities from May to August of this year – our programs and clinical trials, as well as funding and Council news, lives changed by focused ultrasound, and much more.

As always, we can’t thank you enough for your encouragement and support, and for sharing in this privilege with us. Be well,

Neal F. Kassell, MD
Creating Knowledge: Research Milestones

EXTERNAL RESEARCH AWARDS PROGRAM
Through August of this year, the Foundation has funded 69 external research projects, totaling more than $14.1 million; 52 of these projects have been completed, at a cost of $5.1 million, and 96 percent have been presented at scientific meetings. Sixty-nine percent have been published in peer-reviewed journals, and 28 projects have achieved follow-on funding from the National Institutes of Health and other foundations, totaling $42 million.

This summer, the Foundation funded two proposals for a total of $200,000: “The Needle-less Nerve Block: Targeted Non-Invasive Analgesia with Ultrasonic Uncaging of Local Anesthetics” at Stanford University in California, and “Development of Novel Porcine Models of Orthotopic Pancreatic Cancer for FUS and Histotripsy Tumor Ablation Applications” at Virginia Tech in Blacksburg.

Completed external projects, cumulative

| Completed projects | 52 | 96% results presented at scientific meetings | 69% published results | 28 completed projects with follow-on funding |

$5.1M Funding provided for completed projects
$42M Follow-on funding
8 Factor by which the Foundation leverages donors’ contributions

BRAIN PROGRAM
Brain projects currently include 10 technical projects, 23 preclinical laboratory studies, and 32 clinical trials. Important milestones this summer include the recent FDA approval of a new clinical trial to treat deadly brain tumors (glioblastomas) with focused ultrasound in the US. Studies are also beginning or continuing in the areas of Alzheimer’s, Parkinson’s, neuropathic pain, depression, essential tremor, and more.

Technical Research
A team at the University of Michigan in Ann Arbor recently completed a Foundation-funded project to develop a novel method for real-time 3D mapping of cavitation bubble clouds and the skull’s surface while applying histotripsy to the brain. This work provides the visualization that is necessary for ensuring that transcranial treatments are delivered safely and eliminates the need for MR-based treatment monitoring. Projects like this one are important for advancing the possibility of a nonthermal approach to treating various brain diseases and expanding the treatment envelope for focused ultrasound.

Ten focused ultrasound centers in the US are now actively using Kranion – the 3D planning and visualization software system for transcranial focused ultrasound developed by John Snell, PhD, Technical Director of the Foundation’s Brain Program – to assist in visualization and procedure preplanning.
BRAIN PROGRAM (CONT.)

Preclinical Laboratory Studies

Recognizing the need for consistency in comparing the effects of various focused ultrasound mechanisms, the Foundation funded a novel, multisite consortium project. Six labs across North America used the same experimental model of glioblastoma to evaluate the immune response to different forms of focused ultrasound. The results show intriguing differences in immune system interactions with focused ultrasound, and point to various ways in which immunotherapy drugs may be combined with focused ultrasound in the future. The published manuscript will be available in early 2020.

Clinical Trials

Alzheimer’s Disease

Three more patients have been treated in the first US study to open the blood-brain barrier (BBB) with focused ultrasound in Alzheimer’s patients. The multisite trial, at West Virginia University in Morgantown, Weill Cornell Medical College in New York City, and The Ohio State University in Columbus, has treated a total of five of 10 patients. The FDA is currently reviewing the first five patients before the remaining five will be treated.

One more patient with Alzheimer’s disease has been treated in a Phase 2 trial to temporarily open the blood-brain barrier using focused ultrasound plus microbubbles. The team at Sunnybrook Health Sciences Centre in Toronto, Canada, is targeting multiple areas of the brain that are critical for cognition, memory, and learning. Three of 30 patients have now been treated.

Depression

One more patient has been treated in a trial at Sunnybrook that aims to determine the safety, feasibility, and preliminary efficacy of using focused ultrasound to help patients with treatment-resistant major depression. In this first-in-North America trial, researchers are using focused ultrasound to disrupt a key circuit in the brain long associated with major depression by destroying a 5-mm structure known as the anterior limb of the internal capsule. Six of 12 patients have been treated.

Parkinson’s Disease, Globus Pallidus

Thirteen more patients have been treated in a global, multicenter pivotal trial using focused ultrasound to address the major motor symptoms of Parkinson’s disease (PD). This trial is a step toward US FDA regulatory approval and insurance reimbursement for the widespread use of focused ultrasound as a nonsurgical option to treat the symptoms of PD. The study’s target is the globus pallidus, and 40 of 116 patients have been treated.

Parkinson’s Disease, Subthalamic Nucleus

A PD multicenter trial targeting a different area of the brain, the subthalamic nucleus, is now complete after the final two patients were treated with focused ultrasound. This study took place at the University of Virginia Health System in the US and at Hospital Universitario HM Puerta del Sur in Madrid, Spain. Results of the 40-patient study will be compared to those of studies aimed at other targets in the brain, and will help clinicians consider which approach yields the best risk-benefit ratio for patient treatment. Results are expected to be published next year.
Creating Knowledge: Research Milestones

BRAIN PROGRAM/Clinical Trials (Cont.)

Glioblastoma

The US FDA has approved a new focused ultrasound trial to treat deadly brain tumors. French manufacturer CarThera recently announced that a US clinical trial of their SonoCloud-9 ultrasound device will begin in patients with recurrent glioblastoma (GBM). The trial will measure the safety, tolerance, and efficacy of repeatedly opening the BBB in 27 patients before infusion of the chemotherapy drug, carboplatin. Two French sites are already treating patients as part of this trial; MD Anderson Cancer Center in Houston, TX, and Northwestern Memorial Hospital in Chicago, IL, will soon begin enrollment.

Additional GBM studies are also aimed at opening the BBB. One trial is using Insightec’s MR-guided Exablate Neuro device to open the BBB prior to surgery, aiding intraoperative identification of the tumor boundary. Multiple sites in Canada, Korea, and the US are also using the Exablate Neuro to open the BBB for chemotherapy infusions after surgery. In addition, NaviFUS recently completed its neuronavigation-guided focused ultrasound treatment of six GBM patients and is preparing to couple this approach with chemotherapy infusion in a subsequent study.

Essential Tremor

Three more patients have been treated in a clinical trial using staged bilateral focused ultrasound to treat medication-refractory essential tremor (ET). This prospective, multisite, single-arm, open-label study at the Imperial College Healthcare NHS (National Health Service) Trust in London, UK, and HM CINAC (Centro Integral en Neurociencias) in Madrid, Spain, is seeking to determine the safety and efficacy of treating both sides of the brain in patients with bilateral ET. A total of four of 30 patients have been treated.

Neuropathic Pain

One additional patient has been treated in a clinical trial exploring focused ultrasound to treat chronic trigeminal neuropathic pain. The blinded, randomized trial at the University of Virginia Health System is assessing the safety and initial efficacy of using focused ultrasound to ablate a target in the brain implicated in transmitting craniofacial pain. Four of 10 patients have been treated.

The University of Maryland in Baltimore has completed treatment of the first five neuropathic pain patients and has submitted the required materials for FDA review. Upon completion of the FDA process, they plan to treat an additional five patients, for a total of ten.
BODY PROGRAM

Osteoid Osteoma

Four more patients have been treated in a clinical trial investigating the use of focused ultrasound to treat osteoid osteoma in pediatric patients at the University of California, San Francisco, and Stanford University. This study is comparing CT-guided radiofrequency ablation with high-intensity focused ultrasound, assessing pain reduction, procedural experience, and quality of life during recovery. Of 56 patients, 16 have been treated.

Prostate Cancer

Eight more patients have been treated in an immunotherapy study at the Hospital Edouard Herriot in Lyon, France, investigating the use of focused ultrasound to treat prostate cancer. Prostate tumors can masquerade as normal tissue, limiting the immune response; however, focused ultrasound can potentially counter this by triggering an enhanced immune response. This study is capturing blood samples to determine whether focused ultrasound treatment produces a significant increase in the immune response of patients. Twenty of 60 patients have been treated.

CANCER IMMUNOTHERAPY PROGRAM

The Foundation’s Cancer Immunotherapy Program funded a new preclinical project led by Nelson Teng, MD, at Stanford University. The study aims to develop a new method for using a combination of focused ultrasound and immunotherapy to treat recurrent ovarian and cervical cancer. Titled “Activating Specific Cytotoxic T-cells by HIFU and Systemic Immunotherapy in Treatment of Recurrent Ovarian and Cervical Cancer in a Syngeneic Animal Model,” the idea is to combine focused ultrasound, checkpoint therapy, and a novel tumor-targeting antibody developed in the Teng Lab to expose the cancer to the natural immune system.

VETERINARY PROGRAM

Four more patients have been treated in a study at the Virginia-Maryland College of Veterinary Medicine (VMCVM) in Blacksburg, VA, using focused ultrasound to treat soft tissue tumors in canines, bringing the total number treated to 11 of 20. A second study at the Oklahoma State University Center of Veterinary Health Sciences, in Stillwater, has been initiated, which will use focused ultrasound to treat oral melanomas in canines. These types of studies will ultimately benefit humans because the data gathered during the treatment of animals informs the knowledge base of how focused ultrasound can be used to treat a variety of conditions in humans.

Convening the Community

2020 SYMPOSIUM UPDATE

Focused ultrasound pioneer Joan Vidal-Jové, MD, PhD, was recently selected to serve as honorary president at the Foundation’s 7th International Symposium on Focused Ultrasound in November 2020. Dr. Vidal-Jové, the Head of Focused Ultrasound Ablation Oncology at Barcelona University Hospital in Spain, has built his impressive career investigating focused ultrasound in the treatment of more than 200 cases of pancreatic cancer, liver tumors, soft tissue desmoid tumors, and lung cancer. The Symposium will take place November 8-12, 2020, at the Hilton McLean Tysons Corner in McLean, VA; registration will open later this year and more details will be forthcoming.
Convening the Community

MEETINGS SPONSORED

The Foundation sponsored and/or exhibited at five scientific meetings this summer, including: Virginia Bio – THRiVE biennial statewide conference in Richmond, VA; the Society for Image-Guided Neurointerventions (SIGN) 2019 meeting in Baltimore, MD; the 19th Annual International Society for Therapeutic Ultrasound (ISTU) joint meeting with the 5th Annual meeting of the European Union Focused Ultrasound Charitable Society (EUFUS) in Barcelona, Spain; the American Association of Physicists in Medicine (AAPM) Annual Meeting in San Antonio, TX; and the American Veterinary Medicine Association (AVMA) Convention in Washington, DC.

WORKSHOP OUTLINES FUTURE OF FOCUSED ULTRASOUND AND CANCER IMMUNOTHERAPY

In July the Foundation and the Cancer Research Institute (CRI) hosted a Focused Ultrasound and Cancer Immunotherapy Workshop in Arlington, VA, convening more than 50 of the world’s leading experts in the field of therapeutic ultrasound and cancer immunotherapy from 27 organizations across academia, industry, government, and advocacy. The ultimate goal of the Foundation’s Cancer Immunotherapy Program is to reduce the time it takes for focused ultrasound and immunotherapy combination treatments to reach clinical adoption; the workshop was another step toward accomplishing this goal, by critically evaluating the current body of evidence, assessing the value of ongoing work, and creating a roadmap of projects to address knowledge gaps and burning questions. A white paper summarizing the discussion and outputs of the workshop is now available.

WORKSHOP EXPLORES ADVANCED IMAGING FOR TARGETING THE BRAIN IN FOCUSED ULTRASOUND PROCEDURES

In August, a wide range of experts gathered at the University of Virginia’s Darden School of Business in Charlottesville for a Foundation-sponsored workshop to discuss the potential value of adding tractography as a targeting tool for transcranial focused ultrasound treatments. Tractography is a computational reconstruction method based on diffusion-weighted magnetic resonance imaging (MRI); it can be used to reveal the trajectory of neural pathways, or “tracts,” within the brain, which may improve the accuracy of targeting. The two-day summit, led by Vibhor Krishna, MD, MBBS, Professor of Neurological Surgery at The Ohio State University in Columbus, concluded that tractography is a tool that should be included in the transcranial focused ultrasound workflow. A white paper will be available in the near future.

ROADMAP NOW AVAILABLE FOR TREATING PANCREATIC CANCER WITH FOCUSED ULTRASOUND

As previously reported, the Foundation hosted a workshop in February to create a clinical roadmap seeking to develop focused ultrasound for use in treating pancreatic cancer. Experts convened in Bethesda, MD, to discuss the state of the technology, past studies, current challenges, and future preclinical and clinical research directions for using focused ultrasound to treat this devastating disease. The content of the workshop has been captured in a white paper available here.
PARTNERSHIPS

This summer marked the one-year anniversary of the formation of the Foundation’s partnership with the Medical Imaging & Technology Alliance (MITA), which aims to raise awareness of focused ultrasound technology among policymakers, payors, and medical specialty societies. The partnership has laid important groundwork to reducing barriers to commercialization and increasing patient access to focused ultrasound therapies: there have been more than 100,000 social media impressions of posts about focused ultrasound as well as 5,500-plus social media engagements, 30 Capitol Hill meetings, and five blog posts about focused ultrasound patients. This summer, MITA also submitted three public comments (to the US Department of Health and Human Services, the Office of Management and Budget, and the Centers for Medicare & Medicaid Services), and working group members presented about focused ultrasound at an HHS public hearing.

The Foundation has recently established a partnership with the Advanced Medical Technology Association (AdvaMed), which includes 11 focused ultrasound companies. The goal of the partnership is to address key issues that create roadblocks to commercialization and thus limit patient access to focused ultrasound therapies. AdvaMed is a trade association that leads the effort to achieve healthier lives and healthier economies around the world through the advancement of medical technology. It includes more than 400 members in more than 80 countries and acts as the common voice for companies producing medical devices, diagnostic products, and health information systems.

STATE OF THE FIELD

For the past five years, the Foundation has surveyed stakeholders to gain a global perspective on the focused ultrasound field. The newly released 2019 State of the Field Report includes the most up-to-date data on patient treatments, regulatory approvals, research and treatment sites, and much more. The report also highlights trends over time in commercialization, research priorities, and focused ultrasound in scientific literature. New this year are in-depth analyses of focused ultrasound for veterinary medicine, and investments in the field.

REGULATORY

New Ultrasound Device for Prostate Treatment Receives FDA Approval

Profound Medical announced this summer that its TULSA-PRO® device earned 510(k) clearance by the US FDA to ablate prostate tissue. This is the first transurethral ultrasound device approved in the US, and it allows physicians to predictably ablate whole-gland or partial prostate tissue using real-time MR guidance and temperature feedback control combined with radiation- and incision-free therapeutic ultrasound.

Exablate Neuro Approved for Use with SIGNA Premier MRI from GE Healthcare

Insightec’s Exablate Neuro device recently earned FDA approval and CE mark to be used with GE Healthcare’s most powerful wide-bore 3.0T device, the SIGNA® Premier MRI System. When coupled with MR imaging, Exablate Neuro delivers focused ultrasound therapy deep in the brain for pretreatment planning and real-time imaging guidance during treatment.
Overcoming Barriers

REIMBURSEMENT

This summer has seen success in reimbursement efforts for focused ultrasound treatment, including: 1) Insightec announced that their Exablate Neuro treatment for essential tremor will now be reimbursed in Japan, where nine medical centers are currently offering this option; 2) a new Current Procedural Terminology (CPT) code for EDAP’s high-intensity focused ultrasound (HIFU) Focal One prostate cancer treatment was established that will go into effect in January 2021; and 3) the University of Utah Health Plans, which has a patient base of more than 120,000 in the US, recently added MR-guided focused ultrasound treatment of essential tremor to their list of covered services.

Increasing Awareness

LATEST DEVELOPMENTS IN FOCUSED ULTRASOUND HIGHLIGHTED AT BIENNIAL COMMUNITY EVENT

The Foundation held its biennial awareness event in May, which explored the latest breakthroughs in focused ultrasound and the technology’s potential to confront the most vexing challenges in medicine. Held in a packed ballroom in Charlottesville, VA, the event attracted an engaged audience of clinicians, patients, donors, community members, the Foundation’s Board of Directors and Council – and a Goldendoodle treated with focused ultrasound. Presentations included updates on the technology’s role in treating Parkinson’s and Alzheimer’s diseases, pain, and cancer, as well as recent successes in our Veterinary Program.

This awareness event is a unique opportunity for all sectors of the focused ultrasound community to converge and share with one another, which is especially exciting during a time when the technology is hitting its inflection point – becoming more widely commercialized and increasingly used as a mainstream therapeutic option.

FOUNDATION’S ASIA PROGRAM GATHERS MOMENTUM

With the support of Board and Council members – in particular, Syaru Shirley Lin, PhD, Jessica Che-yi Chao, and Bernice Szeto – the Foundation’s Asia Program continues to gather momentum, build connections, and foster collaboration throughout the global focused ultrasound community. Foundation staff recently visited Hong Kong and Taiwan where they participated in 22 meetings and engaged more than 60 stakeholders in discussions about the current and potential impact of focused ultrasound in Asia and around the world. The Foundation looks forward to having an official presence in Asia in the near future.
FOUNDATION HONORED AT THRIVE 2019 CONFERENCE

More than 400 members of the life science industry gathered in May in Richmond, VA, for the biennial conference of the Virginia Biotechnology Association, “THRiVE 2019: Creating the Future of Bioscience in Virginia.” Foundation Chairman Neal F. Kassell, MD, accepted an award on behalf of the Foundation for Outstanding Contributions to Virginia Bioscience, which recognized the organization for exemplifying the excellence, variety, and dynamism of the Virginia biosciences community. Attendees – including leaders from bioscience companies and health care systems, policymakers, and patient groups – were in attendance to discuss and drive forward research, development, and commercialization in Virginia.

PRESENTATIONS

This summer Foundation staff, along with former and current research fellows, attended 23 scientific meetings and presented at three of them. Highlights included the 19th International Symposium ISTU joint meeting with the 5th European Symposium of EUFUS in Barcelona, Spain (read the blog adapted from Dr. Neal Kassell’s ISTU speech here), and the Blood-Brain Barrier Drug Delivery (B3DD) meeting in Boston, MA.

MEDIA COVERAGE

Focused ultrasound technology has appeared in mainstream media outlets more than 170 times this summer. Highlights include Barron’s, the Philadelphia Tribune, the Cleveland Plain-Dealer, the Exponent Telegram/WVNews, the Houston Chronicle, the Daily Mail in the UK, and the Straits Times of Singapore. In addition, many scientific and medical outlets have provided coverage, such as WebMD, Physics World, Proto Magazine, Medical News Today, MedPage Today, the FDA, GE.com, and Phys.org. Favorable opinion pieces by industry insiders have been published in MassDevice and Fierce Healthcare. Finally, local television coverage of focused ultrasound has aired on CBSN New York, KSAT in San Antonio, and CBS 19 in Charlottesville.

Read More Below:
Increasing Awareness

PATIENT STORIES

The Foundation shared multiple stories this summer about patients from around the world who have participated in focused ultrasound clinical trials to help advance the field and have benefitted from the treatment. Patient stories continue to be a useful tool for raising awareness of the technology among target audiences and provide a path for grateful patients to serve as focused ultrasound ambassadors. Recent patient highlights include: Kyle, who had struggled with ET symptoms since kindergarten and says focused ultrasound gave him his life back; Sally, an Alzheimer’s patient who recently became the first participant in a new focused ultrasound trial in Toronto, Canada; and Thomas, who was treated with focused ultrasound for prostate cancer and later flew to Washington, DC, to tell representatives about the treatment’s effectiveness. Read more inspiring patient stories below:

- Jodi, Alzheimer’s disease
- Hanna, Amyotrophic lateral sclerosis (ALS)
- Perry, Parkinson’s disease
- Victor, prostate cancer
- Sally, Alzheimer’s disease patient
- Thomas, prostate cancer patient

Aggregating and Sharing Knowledge

FOCUS FEATURE: FOUNDATION EDUCATES ON FOCUSED ULTRASOUND FOR CHRONIC PAIN CONDITIONS

Focused ultrasound is being investigated to address many types of chronic pain, which is a major public health concern with immense societal and economic impacts. Worldwide, more than 1.5 billion people suffer from some type of chronic pain. In the US alone, pain affects more than 50 million adults and costs society an estimated $560 to $635 billion, outranking heart disease, cancer, and diabetes combined. The Foundation recently compiled an overview of the current research landscape for pain including arthritis, bone pain, neuropathic pain, stump neuroma, and cancer pain. Read the full report here.

HISTORY AND FUTURE OF FOCUSED ULTRASOUND PRESENTED IN BLOG

The Foundation blog, which shares opinion pieces on important topics encompassing focused ultrasound and related medical technologies, can be found on our website’s homepage. Recent blog topics have included: “Focused Ultrasound for Lung Tumors: From Impossible to Possible,” by Foundation Medical Writer Lauren Powlovich, MD; “Low-Risk Prostate Cancer Diagnosis – Understanding the American Urological Association Recommendations,” by Foundation Chief Medical Officer Tim Meakem, MD; “Foundation Chairman on the Future of Focused Ultrasound,” by Neal F. Kassell, MD, in which he predicts that collaboration, commercialization, and competition will be the keys to driving the field forward; and “The Journey of MRI Guided Interventions and Focused Ultrasound,” adapted from a presentation by Morry Blumenfeld, PhD, at this year’s ISTU/EUFUS joint meeting, which pays tribute to the life of focused ultrasound pioneer Ferenc Jolesz, MD.
COUNCIL: FOUNDATION WELCOMES NEW MEMBERS.

The Foundation is pleased to announce that Allan C. Stam, PhD, and Deborah Caldwell have joined the Foundation’s Council, a dedicated group of goodwill ambassadors. Allan Stam, the former Dean of the Frank Batten School of Leadership and Public Policy at the University of Virginia in Charlottesville, said he considers joining the Council a great honor and is looking forward to participating in and supporting the work of the Foundation. Deborah Caldwell, Vice President of Content Marketing at Bank of America, previously held executive positions at Time Inc., CNBC, and Reader’s Digest Association. Deborah continues to stay involved in journalism, serving as a judge for Report for America, board member of Religion News Service, and member of the Institute for Nonprofit News.

FUS PARTNERS: PROGRAM GAINS MOMENTUM, PUBLISHES TOOL FOR FOCUSED ULTRASOUND ENTREPRENEURS

The success of the commercial sector is becoming more important in the focused ultrasound field as the technology progresses toward becoming a mainstream standard of care that can impact the lives of millions of people. The last several months have seen a strong uptick of interest in the Foundation’s FUS Partners program, launched in April 2018, which is continuing to help accelerate the adoption of focused ultrasound. Click here to read a program update from Chairman Neal F. Kassell, MD, and here to view a new list, compiled by the FUS Partners team, of important resources for entrepreneurs interested in the medical device and innovation fields. This list of books, blogs, podcasts, and more will be updated often.

Finances

FUNDRAISING

The Foundation raised $1.5 million in cash and $450,000 in pledges from May 1 to August 31, 2019.

Also of note, this summer an anonymous donor came forward with a challenge gift of $2 million a year over the next three years, to be matched 1-for-1. The Foundation needs your help in meeting this challenge. We hope you will consider a gift before year’s end, appreciating that its impact will be multiplied. Your support will help ensure we receive this generous $2 million matching gift for 2019.
If you would like additional information or want to discuss how you can support our mission, please contact:

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