



FOCUSED ULTRASOUND FOUNDATION

2019 SPRING REPORT

Highlights

- **First epilepsy patient treated with focused ultrasound**
- **First essential tremor patient receives bilateral treatment with focused ultrasound**
- **Foundation, MITA “fly-in” event on Capitol Hill educates Washington, DC policymakers**
- **The Tumor audiobook released; nearly one million print copies distributed**
- **Four new members join Foundation Council**
- **Foundation launches redesigned, modernized website**

Dear Friends,

In 2019 we are finding ourselves – at long last – at the inflection point of the adoption curve for focused ultrasound. We are also witnessing a sea change, as the field of focused ultrasound transitions from an environment that has been primarily research-oriented to one that is becoming much more focused on commercialization and patient treatment. Now is the most exciting time yet to be part of this field, which continues to gather momentum and grow at a rate that has vastly exceeded any of our expectations. Read on for important first-quarter updates on our programs, clinical trials, and other research milestones, as well as our aggressive awareness efforts, funding updates, and much more.

As always, thank you for your encouragement and support.

Be well,

Neal F. Kassell, MD



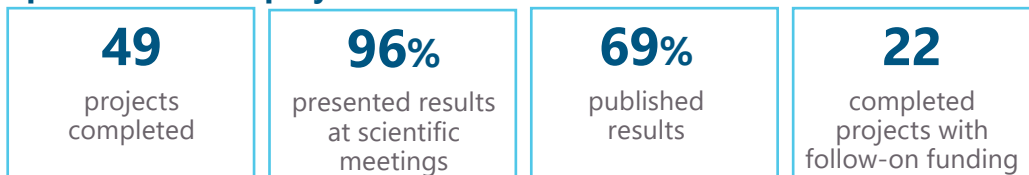


Creating Knowledge: Research Milestones

EXTERNAL RESEARCH AWARDS PROGRAM

To date, the Foundation has funded 67 external research projects totaling more than \$6.8 million; 49 of these projects have been completed, at a cost of \$4.8 million, and 96 percent have been presented at scientific meetings. Sixty-nine percent have been published in peer-reviewed journals, and 22 projects have achieved follow-on funding from the National Institutes of Health and other foundations, totaling \$36.7 million.

Completed external projects, cumulative



\$4.8M

Funding provided for completed projects



\$36.7M

Follow-on funding



x8

Factor by which the Foundation leverages donors' contributions

BRAIN PROGRAM

2019 has seen many “firsts” regarding focused ultrasound and the brain: the first patient has been treated with focused ultrasound (FUS) in an [epilepsy clinical trial](#), the [first bilateral treatment with focused ultrasound](#) performed has taken place in an essential tremor patient, and the next phase has begun in a groundbreaking Alzheimer’s disease study using FUS to target areas of the brain responsible for memory, cognition and learning. Important studies are also beginning or continuing in the areas of glioblastoma, neuropathic pain, Parkinson’s disease, and others.

Preclinical Laboratory Studies

A sonodynamic therapy study involving the activation of a cytotoxic drug with ultrasound has been completed. Researchers investigated whether sonodynamic therapy permitted the treatment of difficult-to-reach brain tumors by reducing the amount of ultrasound energy required for treatment. This internal project, conducted at the University of Virginia under the guidance of the Foundation’s Dr. Francesco Prada, tested the ability of low-powered focused ultrasound to activate fluorescein, an FDA-approved drug used to identify tumor boundaries during surgery. In a rat model of glioma, sonodynamic therapy with fluorescein and focused ultrasound was able to control tumor growth and induce large volumes of apoptosis (i.e., cell death) and necrosis (i.e., cell injury) within the treated tumors.

Clinical Trials

[Alzheimer’s Disease](#)

Researchers at Sunnybrook Health Sciences Centre in Toronto, Canada, have begun a [Phase 2 trial to temporarily open the blood-brain barrier](#) using MRI-guided focused ultrasound plus microbubbles in patients with Alzheimer’s disease. The team is targeting multiple areas of the brain that are critical for cognition, memory, and learning; two of 30 patients have been treated.



Researchers at Sunnybrook successfully open the BBB in a clinical trial



Creating Knowledge: Research Milestones

BRAIN PROGRAM/Clinical Trials (Cont.)

Parkinson's Disease, Globus Pallidus

Ten 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), bringing the total number of patients treated to 27 of 116. This pivotal 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 this common neurological condition. The study's target is the globus pallidus.

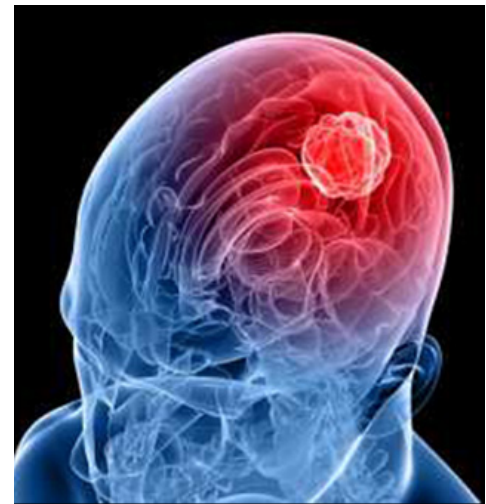
Parkinson's Disease, Subthalamic Nucleus

In another PD multicenter trial targeting a different area of the brain, the subthalamic nucleus (STN), seven additional patients have been treated with focused ultrasound, bringing the total number of patients treated to 38 of 40. This study is taking place at the University of Virginia Health System in the US and at Hospital Universitario HM Puerta del Sur in Madrid, Spain. The study's goal is to evaluate the benefits and risks of this treatment option; results will be compared to studies aimed at other targets and will help clinicians consider which approach yields the best risk-benefit ratio for patient treatment.

Glioblastoma

Additional patients with glioblastoma (GBM) have been treated or are in clinical trials using a variety of focused ultrasound protocols to open the blood-brain barrier (BBB).

The first trial used [CarThera's surgically implanted ultrasound device, SonoCloud-1](#), to perform repeated BBB disruption prior to chemotherapy. Two other trials are using [MR-guided focused ultrasound via Insightec's Exablate](#) device to disrupt the BBB prior to tumor removal or along with chemotherapy agents. Lastly, another approach in a separate trial is using the [NaviFUS optically guided neuronavigational technology](#) along with focused ultrasound to noninvasively treat GBM tumors.



Epilepsy

The [first patient has been treated in a clinical trial](#) investigating the use of focused ultrasound to control a specific type of epilepsy in adult patients. Up to 10 patients with medication-refractory lobe focal onset epilepsy will be enrolled in this Ohio State University College of Medicine study, which is funded by the Foundation. Patients will receive transcranial focused ultrasound therapy to ablate (i.e., destroy) a specific part of the brain involved in epilepsy.

Essential Tremor

The first of 30 patients has 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 is seeking to determine the safety and efficacy of treating both sides of the brain in patients with bilateral ET.



Creating Knowledge: Research Milestones

BRAIN PROGRAM/Clinical Trials (Cont.)

Neuropathic Pain

The first US trial of focused ultrasound to treat neuropathic pain has enrolled two additional patients in 2019, bringing the total treated to five of 10. The early-stage pilot trial at the University of Maryland, Baltimore aims to establish the safety of destroying a small target in the brain to treat chronic 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.

BODY PROGRAM

Facetogenic Back Pain

Enrollment is complete in a Canadian clinical trial assessing the safety, efficacy, and initial feasibility of using focused ultrasound to treat adult patients diagnosed with chronic lumbar facetogenic pain. The trial at McGill University's Alan Edwards Pain Management Centre in Montreal, Canada, has treated the final two of 10 patients using FUSMobile's inaugural device, the Neurolyser.

Osteoid Osteoma

Four patients have been treated in a clinical trial investigating the use of focused ultrasound to treat osteoid osteoma in pediatric patients, bringing the total treated to 12 of 56. Taking place at the University of California, San Francisco and at Stanford University, this study is comparing CT-guided radiofrequency ablation with high-intensity focused ultrasound, assessing pain reduction between the two treatments along with procedural experience and quality of life during recovery.

CANCER IMMUNOTHERAPY PROGRAM

Prostate Cancer

Twelve patients out of 60 have been treated in a 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, FUS can trigger an enhanced immune response. This study is capturing blood samples to determine if focused ultrasound treatment produces a significant increase in the immune response of patients.

Pancreatic Cancer



Frédéric Padilla, PhD

A preclinical study at the University of Virginia Health System, led by the Foundation's Richard Merkin scholar, Frédéric Padilla, PhD, is investigating whether FUS combined with immunotherapies can control tumor growth in a mouse model of pancreatic cancer. A secondary objective of the study, titled "Focused ultrasound immunomodulation for pancreatic cancer," is to identify the mechanism of immune sensitization by focused ultrasound.



Creating Knowledge: Research Milestones

VETERINARY PROGRAM

A scientific advisory board has been created to help identify clinical needs and guide the scope and direction of the Foundation's new Veterinary Program. Thank you to those who have joined the Board including: Chairman Gregory Daniel, DVM; Craig Clifford, DVM, MS; Cynthia Cole, DVM, PhD; Richard Hawkins, DVM; Ashish Ranjan, PhD; and Ruth Rose, DVM.

Additionally, the Foundation has established a Veterinary Center of Excellence program, designed to identify and support veterinary centers with a proven interest in the use of focused ultrasound for veterinary applications. Each center must have a multi-disciplinary team dedicated to advancing the use and/or adoption of focused ultrasound for veterinary applications.

In funding news, [the Petco Foundation and Blue Buffalo have pledged](#) a portion of their \$2.6 million annual fundraising campaign to Oklahoma State University's Center of Veterinary Health Sciences Focused Ultrasound Treatment Program. Oklahoma State is one of several centers that participate in the Foundation's Veterinary Program to fund clinical trials that enroll pets. These types of programs ultimately benefit humans because the data gathered during the treatment of animals informs the knowledge base of how FUS can be used to treat a variety of conditions in humans.



Convening the Community

WORKSHOPS

In late February, the Foundation hosted a workshop to create a [clinical roadmap seeking to develop focused ultrasound for use in treating pancreatic cancer](#). A wide range of experts convened in Bethesda, Maryland, 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 workshop's diverse group of attendees included leaders in medical oncology, surgery, cancer immunotherapy, focused ultrasound ablation and histotripsy, government regulatory bodies, and industry, as well as scientific staff from the Cancer Research Institute and the Focused Ultrasound Foundation. A [meeting summary/white paper is available](#) on our website.

MEETINGS SPONSORED

The Foundation sponsored and/or exhibited at multiple scientific meetings this spring, including: Winter School on Therapeutic Ultrasound, Les Houches, France; Jane Neurosurgery Workshop, Seattle Science Foundation; Annual Brain Anatomy Residents & Fellows Course; Tom Tom Founders Festival, Charlottesville, Virginia; and The Society for Thermal Medicine 36th Annual Meeting, St. Pete Beach, Florida.

SYMPOSIUM UPDATE

[Presentation videos from the Foundation's 6th International Symposium](#) on Focused Ultrasound are now available on the Foundation website. Scientific presentations this year focused on the latest research in neurological indications including Alzheimer's disease, brain tumors, epilepsy, Parkinson's disease, and psychiatric disorders. Cancer immunotherapy, veterinary medicine, and applications for focused ultrasound in the liver, lung, and pancreas were also among the important topics discussed.

[The Foundation's 7th International Symposium on Focused Ultrasound](#) will take place November 8-12, 2020, at the Hilton McLean Tysons Corner in McLean, Virginia. Please save the date and plan to join us for the latest in focused ultrasound research across the field.



Hilton McLean Tysons Corner

Fostering Collaboration

PARTNERSHIPS

In February, the Foundation partnered with the Medical Imaging & Technology Alliance (MITA) to plan and participate in a [“fly-in” event](#), in which patients and physicians met with policymakers and staff on Capitol Hill in Washington, DC, to educate them about focused ultrasound. The event largely focused on those indications that are already approved by the US FDA, including essential tremor, Parkinson’s disease, and prostate conditions. Patients representing these different disease categories shared their personal stories at more than 20 separate meetings, while a number of physicians and industry leaders were on hand to share why they are passionate about focused ultrasound. The “fly-in” is the latest product of a partnership between the Foundation and MITA; in April 2018, the two organizations formed a working group with the goal of raising awareness of focused ultrasound technology among policymakers, payors, and medical specialty societies.



Overcoming Barriers

REIMBURSEMENT

Health Plan Adds Coverage for Painful Bone Metastases

In its [newest policy document on the topic](#), Geisinger Health Plan added coverage for palliation of cancer pain in metastatic bone cancer patients. Metastatic bone cancer is thought to afflict at least 330,000, or approximately 1 in every 1,000, US patients. Geisinger Health Plan covers just over 600,000 patients in Delaware, Maine, New Jersey, Pennsylvania, and West Virginia. Other insurance companies that cover this indication include Amerigroup Healthcare, AmeriHealth, Blue Cross Blue Shield Plans in 40 states, CIGNA, HAP Health Alliance Plan, and Lifewise.

Insurance Coverage Expands for Essential Tremor

Device manufacturer Insightec announced in April that [coverage for Medicare patients with essential tremor has expanded](#) again, this time to include states covered by the Medicare Administrative Contractor (MAC) known as Noridian. Noridian insures patients in Alaska, Arizona, California, Hawaii, Idaho, Montana, Nevada, North Dakota, Oregon, South Dakota, Utah, Washington, and Wyoming. This brings the total Medicare coverage for essential tremor to 38 states, with combined coverage between Medicare MACs and the individual Blue Cross Blue Shield Plans in 47 states. Other companies providing coverage for essential tremor include AmeriHealth, Asuris Northwest Health, HAP Health Alliance Plan, Lifewise, and United Healthcare.

Additionally, Insightec announced that it has received national reimbursement from the Japanese Ministry of Health, Labour and Welfare for treating essential tremor. “This important milestone means patients in Japan will now have access to incisionless focused ultrasound as a treatment option,” said Yair Bauer, Country Manager, Insightec Japan.

REGULATORY

Theraclion Obtains CE Marking for Noninvasive Treatment of Varicose Veins

[Theraclion announced in April](#) that they had obtained the CE marking (European regulatory approval) for their Sonovein device to treat varicose veins, which are a problem for three out of 10 people around the world. According to Theraclion’s CEO, David Caumartin, this device has the competitive advantage, in that the procedure “can be performed almost anywhere, opening access to an ablative technique that can be performed by a whole new target group of doctors in private office settings without complex infrastructure.” This is in contrast to more invasive treatments that must be conducted in an operating room or other sterile environment.

Increasing Awareness

EVENTS & SPEAKING OPPORTUNITIES: SPREADING THE WORD ABOUT FUS

The Foundation has participated in several outreach opportunities this quarter in our ongoing commitment to educating new audiences about the technology. In addition to hosting an event at the Breakers in early February for our friends and donors who live in the Palm Beach, Florida, area, Foundation Chairman Neal F. Kassell, MD, traveled to Abu Dhabi in February to attend the 2019 MENA Conference, a medical education conference that convenes experts in a variety of disciplines to discuss new technologies, leading trends, and best practices in the medical industry. The venue provided an excellent opportunity to make valuable connections for the Foundation.

Additionally, each semester Dr. Kassell is a guest lecturer for the Social Entrepreneurship and Innovation and Social Impact classes at the University of Virginia's Frank Batten School of Leadership and Public Policy. As a result of this year's lecture, four students have chosen the Foundation as the subject of their capstone project and are subsequently interning at the Foundation this summer.



Neal Kassell, MD gives keynote at Analyst & Investor Day

Dr. Kassell was also the [keynote speaker at Analyst & Investor Day](#) at the University Club of New York, New York, in April. Hosted by Profound Medical Corp., the event was a first-of-its-kind gathering in the field of focused ultrasound and included key researchers, clinicians, financial analysts, and institutional investors from around the world. Dr. Kassell spoke about the exponential growth of the focused ultrasound field, the technology's wide range of indications and mechanisms of action, and the global adoption of focused ultrasound as a therapeutic platform.

PRESENTATIONS

Foundation staff, along with former and current research fellows, have attended 12 scientific meetings and presented at four this year. Highlights include:

- JP Morgan Week (Jan 6 - 10, San Francisco, California)
- Colorado State University (Feb 25, Fort Collins, Colorado)
- European Congress of Radiology (Feb 27 - Mar 3, Vienna, Austria)
- Tata Memorial Hospital, Masterclass in Neurosurgical Oncology (Mar 8 - 10, Mumbai, India)
- Intraoperative Imaging Society Meeting (Mar 13 - 16, Houston, Texas)
- FDA-NBTS Public Workshop: Product Development for Central Nervous System Metastases (Mar 22, Silver Spring, Maryland)
- Society of Interventional Radiology Annual Meeting (Mar 23 - 28, Austin, Texas)
- The Society for Thermal Medicine 36th Annual Meeting (Apr 28 - May 2, St. Pete Beach, Florida)

NEWSLETTER

The Foundation newsletter is now being produced twice a month. It is distributed to more than 10,750 contacts and continues to receive an average open rate of over 22 percent. Popular stories this year have included our annual Symposium report, updates on brain indications (glioblastoma and essential tremor), [the Kranion system](#) (an open source, interactive transcranial focused ultrasound visualization system designed and produced by the Foundation's Brain Program Technical Director, John Snell, PhD), and the launch of *The Tumor* audiobook. Our newsletter is on pace to include more than 300 articles this year, many of which are promoted via our multiple social media channels, driving new audiences to our website to learn about focused ultrasound.

Increasing Awareness

MEDIA COVERAGE

Nearly [500 press placements](#) regarding focused ultrasound have appeared in the past 12 months (a 25 percent increase over the previous 12 months), including more than 20 unique placements in the first quarter alone. Recent worldwide print media coverage includes: Canada's *Globe and Mail*, *Psychology Today*, ABC News Australia, *Knowable*, *Fortune*, *Discover* magazine, *Scientific American*, *The Hill*, the *Chronicle of Higher Education*, *Los Angeles Times*, Hong Kong's *South China Morning Post*, *Brain & Life*, *Physics World*, West Virginia News, NBC29, WKYC, ABC Utah, *West Virginia Executive*, Healthcare IT News, GE Blog, Spain's *El Confidencial*, and *The Tennessean*. Additionally, the technology has recently been featured on popular mainstream broadcast programs – reaching millions of people – including *New Amsterdam* and *The Doctors*. If you have a story idea or connections with any media contacts, please let us know.

Read More Below:



SOCIAL MEDIA AND WEBSITE

Social media continues to be a critical platform for raising awareness of focused ultrasound among key audiences and driving traffic to our website. The Foundation has reached more than 75,000 users on Twitter and more than 25,000 via LinkedIn in the first quarter of 2019 alone. We have also engaged with almost 5,000 [Facebook](#) users and hundreds more via YouTube and Instagram. Please “like” and share our content!

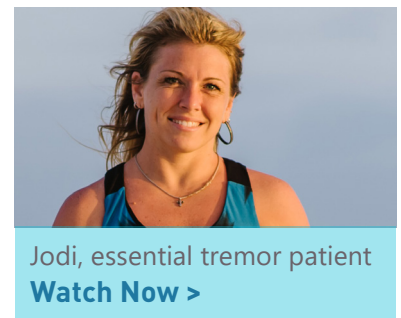


[The Foundation website](#) – which serves as the focused ultrasound encyclopedia for the field and in particular assists patients and potential patients in learning more about the technology – underwent a redesign earlier this year and now features a modernized look and feel, easier navigation, and more patient-friendly homepage content. The site is receiving an average of 80,000 new visitors per quarter – a 320 percent increase from just four years ago.

Increasing Awareness

JODI SHARES HER STORY NATIONWIDE

Jodi, Wisconsin mother of three, recently appeared on an episode of the popular US daytime talk show *The Doctors*, to discuss living with essential tremor and the impact focused ultrasound treatment has had on her life. [Her story](#) can be found on the Foundation website along with [other patient testimonials](#), which help amplify the human side of the story of this life-changing technology.



JOHN GRISHAM'S "THE TUMOR" NOW AVAILABLE AS AN AUDIOBOOK



[The Foundation launched an audiobook version](#) of bestselling author and Foundation board member John Grisham's short book *The Tumor*. Featuring an introduction read by the author himself, the audiobook has so far been downloaded more than 750 times. With nearly one million copies distributed since the book's launch in 2016, *The Tumor* continues to be a valuable tool for reaching consumers and other key audiences with the story of focused ultrasound.

BLOG UPDATE

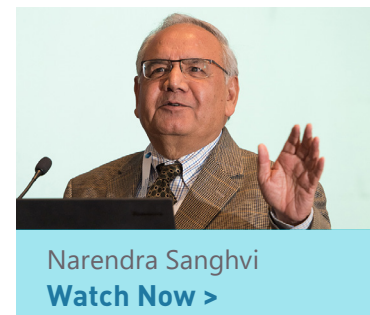
The [Foundation blog](#), which shares opinion pieces on topics related to focused ultrasound and medical technologies, can now be found on our website's newly redesigned homepage. Blog topics in 2019 have included: "Emerging Applications of Focused Ultrasound – Alzheimer's Disease," by West Virginia University neurosurgeon Ali Rezai, MD; "The Stigma of Negative Data ... and How Preprint Servers Can Help," by the Foundation's Scientific Program Manager Kelsie Timbie, PhD; "Modest Beginnings and Early Development of Focused Ultrasound," by SonaCare Medical's Narendra Sanghvi; and "Why Collaboration Is Critically Important to Propelling Focused Ultrasound Forward – And What the Foundation Is Doing About It," by Foundation Chairman Neal F. Kassell, MD. If you have an idea for a blog topic, please let us know.



Aggregating and Sharing Knowledge

WEBINAR SERIES

The Foundation continues to host [live webinars](#) on hot topics in the field of focused ultrasound, giving experts in the field an opportunity to present on areas of emerging interest or promising research. The talks are broadcast via webinar to help keep the broader community abreast of new advances. The Foundation recently hosted a webinar with Narendra Sanghvi of SonaCare Medical entitled, "[High Intensity Focused Ultrasound – Past and Present.](#)" which was broadcast via Facebook Live and can be accessed on our website.



MOOC AVAILABLE

[The Massive Online Open Course \(MOOC\)](#) dedicated to therapeutic ultrasound is available online via the Foundation website. The Laboratory of Therapeutic Applications of Ultrasound (LabTAU) in Lyon, France – in collaboration with the Foundation – launched the free online course to provide a flexible way to learn new skills or become familiar with a new topic. World-renowned experts in the field have provided unique presentations covering a variety of topics, such as technical explanations of various focused ultrasound applications and clinical case presentations.

Foundation Organization

COUNCIL UPDATE

In January, the [Foundation welcomed four distinguished professionals to the Council](#): Jessica Chao, Rick Hamilton, Harry Lester, and Bernice Szeto.

Jessica Chao resides in Taipei and brings experience in the financial industry including banking, equity research, and strategic investment. Jessica is assisting the Foundation with the Asia Program.

Rick Hamilton is an expert in cloud, internet-of-things (IoT) technologies, and artificial intelligence, and has been known as the most prolific inventor in IBM history. Rick provides technology advice and has presented two webinars on behalf of the Foundation.

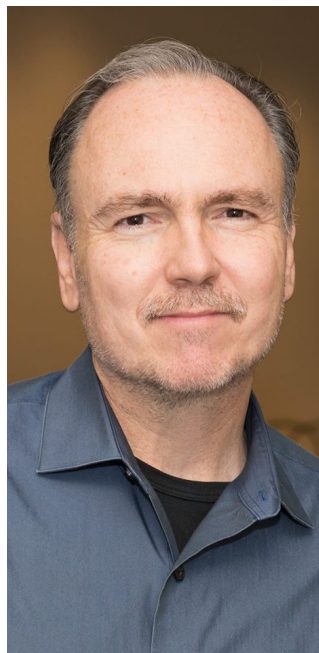
Harry Lester had a successful career in real estate business as well as deep-rooted community engagement in the Tidewater area of the US. Harry is a former naval officer and a cancer survivor currently assisting the Foundation with fundraising efforts and awareness.

Bernice Szeto has worked in the finance industry for 20 years in various capacities across family office, private equity and investment banking. Bernice currently resides in Hong Kong and is assisting the Foundation with the Asia Program.

“We are grateful to have Jessica, Rick, Harry and Bernice join our council. They bring a variety of experiences ranging from technology, finance, and real estate that are valuable to our organization,” said Foundation Chairman Neal F. Kassell, MD.



Jessica Che-yi Chao



Rick Hamilton



Harry Lester



Bernice Szeto

BOARD OF DIRECTORS/STAFF LUNCHEONS

At the suggestion of the [Board of Directors](#), the Foundation has initiated monthly staff luncheons with our Board members, to better connect names and faces, and to discuss our shared passion for making focused ultrasound available in the shortest time possible.

Foundation Organization

FUS PARTNERS

The Foundation's [FUS Partners](#) program is helping accelerate the pace of focused ultrasound adoption at a critical time for the field. By staying in close touch with FUS companies, the Foundation can

better understand their strategies and progress, including potential financing and partnering needs. One recent example involves manufacturer HistoSonics, which closed its financing round with additional investment from friends of the Foundation. The round solidly positioned HistoSonics for future growth. The company went on to close on a [venture capital funding round of \\$54 million](#) this quarter, notably led by two major health care companies – Varian Medical Systems and Johnson & Johnson Innovation LLC – giving “instant credibility to potential end users as it begins sales,” according to media coverage.



HistoSonics®

NEW TEAM MEMBERS

Four new employees have joined the Foundation this year: development officer Leslie Wenert, financial analyst Skyler Kitchen, medical writer Lauren Powlovich, and executive administrative assistant Michelle Majorin. Deborah Heishman also returned as Director of Salesforce Platforms after a short hiatus.



Leslie Wenert
Development officer



Skyler Kitchen
Financial analyst



Lauren Powlovich
Medical writer



Michelle Majorin
Administrative assistant

Finances

FUNDRAISING

The Foundation raised \$1.2 million in cash and \$1 million in pledges from January 1st to April 30th. This is a solid start to the year, as we work toward our goal of \$6 million in cash and \$5 million in pledges, to be paid in 2020.



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

Nora Seilheimer
nseilheimer@fusfoundation.org or (434) 326-9830

www.fusfoundation.org



1230 Cedars Court, Suite 206
Charlottesville, VA 22903
434.220.4993 www.fusfoundation.org