Focused Ultrasound Foundation

Development of Novel Porcine Models of Orthotopic Pancreatic Cancer for FUS and Histotripsy Tumor Ablation Applications

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General Update (6/30/21)

We are pleased to report that we have completed all Milestones as of 6/29/21. Since the previous up-date (12/12/2020) we have worked to optimize imaging and treatment of animals without off-target effects. This includes the development of an effective dietary regime to minimize gas and maximize our optical window. We have also successfully generated pancreatic tumors in the pancreas and are now routinely conducting histotripsy studies using these models. Over the last 6 months, we have completed all proposed studies, including attempted histotripsy treatment of tumors implanted in our pigs, as proposed, and are now working to optimize treatments and conducting limitation testing. In total, we have utilized 31 pigs to complete the Milestones and Deliverables of this project.

MILESTONES AND PROGRESS:

1. Regulatory Progress:

Project Initiation: Completed

Institutional Animal Care and Use Committee (IACUC) Protocol Approval: Completed

Institutional Biosafety Committee (IBC) Protocol Approval: Completed

Virginia Board of Pharmacy License Renewal and Update: Completed

Drug Enforcement Agency Registration Update: Completed

2. Pig Usage:

1. February 2020: 5 Pigs
2. March 2020: 5 Pigs
3. April 2020: 5 Pigs
4. August 2020: 3 Pigs
5. September 2020: 3 Pigs
6. November 2020: 3 Pigs
7. March 2021: 4 Pigs
8. June 2021: 3 Pigs

Future Immunocompromised Pigs (post-award):

1. Litter due July 4th, 2021 (at least 5 piglets confirmed by ultrasound)

2. Litter due August 9th, 2021 (pregnancy confirmed, too early for ultrasound confirmation of piglet numbers)

As outlined in the proposal, we agreed to generate 12-18 pigs, with an additional 15 normal “wild type” pigs. As stated above, we have completed studies with 31 animals to date, including 16 immunocompromised pigs (with an additional 10-12 pigs anticipated in the immediate post-award period for future studies in July and August). As noted in the request for our proposal extension due to COVID-19, the generation of the immunocompromised pigs had been on-schedule up until a work-stop associated with COVID-19 and the suspension of new embryo transfers by the VT College of Agriculture and Life Sciences from March through mid-June 2020. There was an additional delay as the University and our animal care staff continued to navigate COVID-19 restrictions and cope with personnel shortages. This delayed the September implantation, which was rescheduled to run from December through March to ensure we generate enough genetically modified animals to complete the project. The pigs from these transfers are currently being used and will supply animals through the July and August post-award studies. We plan to continue using these animals to address the future studies discussed at the end of this report.

3. Optimize histotripsy ablation system and pulse sequences for use in the pig to target pancreas (Step 1 of 4): 100% Complete

Step 1: Utilize *ex vivo* pancreas tissue to define and optimize pulse parameters.

We have completed dose studies in a variety of tissues and tumors. These studies have provided us with sufficient data to guide the proposed *in vivo* studies. Some of our data was also generated following ablation of excised human pancreatic adenocarcinoma tissue. Tumor was excised from a patient at Carillon Hospital in Roanoke, VA and treated the same day. Treatments were applied using a custom built 500kHz system, 1-2 cycle pulses with peak negative pressures >30 MPa, and a PRF of 250Hz, allowing for histotripsy to be applied with high precision and accuracy. An automated ablation was done on 2 separate tests, covering a volume of 6x6x1.6mm. Ablation was monitored with real-time ultrasound guidance. These data complemented an *in vivo* study utilizing a Pan02 subcutaneous mouse model. The mouse data validation is necessary prior to progressing to the pig.

Treatments were applied using a custom 1Mhz transducer, 1-2 cycle pulses with peak negative pressures >30 MPa and a PRF of 250Hz, allowing for histotripsy to be applied with high precision and accuracy. An automated treatment strategy was also developed to uniformly and completely ablate the entire tumor volume in the subcutaneous model. Briefly, 30 immunocompetent mice were injected with Pan02 cells (ATCC CRL-2947, 6 million cells in 100 μ L of Matrigel) in the subcutaneous flank. When the tumors reached ~0.5 cm (7 days after injection), histotripsy was applied to a central portion of the tumor in order to apply a partial ablation of the tumor to assess initial feasibility of this model. The targeted portion of the tumor was treated with histotripsy using real-time ultrasound imaging guidance (**Fig.1**) and an automated treatment method. An immediate group of mice were taken down within 10 minutes of

Figure 1. Pilot studies showing ablation zone in the subcutaneous Pan02 tumor following histotripsy.

treatment (n=3). Additional mice were recovered for 24 hours after treatment before take down (n=6 for treatment and control group). A third group of mice (n=7) was recovered and allowed to survive until the tumor reached the endpoint of ~1.6 cm in diameter. Results from the chronic group showed a partial tumor ablation with histotripsy decreased average tumor size and extended progression free and overall survival. While extensive mouse studies were not specifically undertaken as part of the proposed work, the results from these studies informed subsequent pig studies described below.

Step 2: Modify existing histotripsy ablation system for use targeting the pig pancreas.

We have designed a new transducer for the proposed pig studies based on pig size and ultrasound imaging data. We have also consulted with a veterinary radiologist to readily identify the pancreas. The transducer modeling data for the device has been completed and the system is currently in use. Based on the results from the optical window and healthy pig studies described in Milestone 4 below, our current system required a few modifications to improve targeting. Gas in the stomach and GI tract impacted targeting in our initial studies. Through additional literature and optimization studies, we have determined that this can be minimized by altering the diet of the animals prior to histotripsy (described below). As an alternative approach, we also considered cannulating the stomach to remove excess gas. However, this was not necessary in the current studies. We believe that gas can be further minimized through modifications to the histotripsy system to allow more pressure on the abdomen.

Figure 2: Histotripsy ablation system for use in large mammal pre-clinical and clinical studies in the veterinary clinic.

Step 3: Develop and modify software for pancreas treatment applications in the pig.

We have completed the optimization of our treatment software for pig pancreas applications proposed, including the completion of several triggering tests with the system. Indeed, the system is now being used to actually treat pigs, as well as, other veterinary species. The data were programmed into the treatment software by HistoSonics. The treatment system is currently housed in the Animal Surgical Suite within the Vivarium at the Virginia Maryland

College of Veterinary Medicine and has been used in the pig studies described here and in the clinical treatment of patients at the Veterinary Teaching Hospital.

4. Identify appropriate optical windows for imaging and treatment of the pancreas using histotripsy *in situ* (Step 2 of 4): 100% Complete

Step 1: Identify proper animal positioning, treatment techniques, and system design strategies to optimize the optical window for imaging and treating the pancreas.

Locating an appropriate optical window for treating the pancreas is challenging. However, following the completion of a series of positioning studies, dietary adjustments meant to minimize gas in the GI tract, and through consultations with our in-house veterinary radiologists, we have a set protocol for positioning, pancreas identification, and animal preparation. We utilized 10 animals for this phase of the study.

While we have been successful, we are routinely adjusting and optimizing our procedures to aid in future studies. This includes utilizing higher resolution ultrasound and imaging devices, conducting initial studies with potential contrasting agents to assist with imaging and treatment, and considering the utilization of a contrasting agent added to the Panc01/Matrigel to improve tumor targeting. These alternative approaches may be incorporated into future studies as they may prove necessary in human clinical applications.

Figure 3: Pancreas imaging and optical window identification

Step 2: Evaluate and optimize histotripsy parameters in vivo

Spherical treatment volumes of 1cm in diameter were generated in the pancreas by sweeping the focal point across the target region using the robotic micro-positioner and planning software. To validate the effectiveness of the selective ablation sequences, the ablation zones were generated in regions of the pancreas and regions directly adjacent to other organs (see Step 3 below). Vital signs (heart rate, blood pressure, temperature, ECG, SpO2) were monitored throughout the procedure to assess safety. Immediately after treatment, lesions were evaluated and the animals euthanized. Pancreas were harvested for histological evaluation (H&E stain) to characterize damage to pancreatic cells and critical structures in the ablation volume

Figure 4: Gas in the GI tract can cause issues with targeting

Step 3: Define the impact of histotripsy ablation in the healthy pancreas

We effectively targeted the pancreas with histotripsy as seen in the images below. While

multiple aspects of the procedure require optimization, in terms of proof-of-concept and impact on the healthy animal/pancreas, the studies proved successful. Intestinal gas and targeting through the stomach were the biggest challenges encountered. Further optimization indicates the following: 1) pig diet alterations 24 hours prior to treatment can significantly improve targeting; 2) removal of the gas following cannulation prior to histotripsy treatment can be used to ensure gas is not an issue; 3) we have identified several system changes that can improve our ability to shift the gas to enable improved targeting in the tumor carrying animals; and 4) a smaller transducer can be incorporated into our system to allow more flexibility in maneuvering the bubble cloud for improved targeting. As seen in the figures below, we were successful in generating lesions in the pancreas. However, off target effects were also observed, mostly in the bowel. Based on these data, gas reduction should improve imaging quality, pancreas targeting, and minimize these off-target effects.

Damage on pancreas noted by pathologist

Figure 5: Successful targeting of the pancreas and the generation of lesions via histotripsy. Several off-target effects were also noted, impacting the bowel.

Refinement of Protocols:

To decrease issues with gas, improve targeting and imaging, and minimize off-target treatment, we developed a dietary and pharmacological treatment regime to optimize histotripsy treatment in the pancreas. The pigs were fed 200mls of custard for 4 days prior to histotripsy. In addition to the custard, the animals were given 2 mL simethicone (GasX) daily for the full 4 days prior to histotripsy to reduce gas and 5 mg of bisacodyl (Dulcolax) as a laxative at least 30 mins prior to

treatment. Together, these changes significantly improved both imaging and treatment, minimizing off target effects. Animals were also allowed to survive and recover, with no negative effects following histotripsy ablation of the pancreas (**Figure 6**).

Figure 6: **A.** Successful targeting of the pancreas and the generation of 1.5 cm lesions via histotripsy near critical structures (splenic vein is the landmark and void in the image). **B.** Blood chemistry was routinely monitored over the course of 16 days with no significant changes observed in pancreas function or evidence of any detrimental effects of histotripsy (representative profile shown from subject 28-53, day 7 post treatment). **C.** Pigs were imaged via CT, with no off-target effects noted in the CT scans and no accumulation of fluid was observed around the treatment site. **D.** No evidence of off target effects were noted at necropsy following histotripsy.

5. Validate the utility of the immunocompromised pig model for histotripsy ablation (Step 3 of 4): 100% Complete

Step 1: Determine engraftment efficiency and tumor progression in the immunocompromised pig model (sub-cutaneous ear injection modeling)

The pancreatic cancer engraftment rate for Panc01 cells is 100% in our pigs. We completed 2 full studies using 9 pigs (as described) to evaluate engraftment, in addition to

Figure 7. Human xenograft in immunocompromised pigs. SCID pigs were generated using genome editing technology. **A)** Panc01 Cells (10^6 cells) were injected subcutaneously behind the ear and palpable tumors developed within the first 2 weeks of injection. **B)** Ultrasound imaging was utilized to monitor tumor progression. **C)** Subdermal tumor assessments were conducted at harvest. **D)** Each pig injected generated tumors between 1 and 1.6 cm in size. **E-F)** Histopathology assessments characterized each tumor at **(E)** low and **(F)** high magnification.

assessments of liver, colon, breast, and glioblastoma tumor cell lines for future studies and potential orthotopic models. To date, we have fully evaluated the Panc01 cells. Based on these data, we accurately modeled the orthotopic tumor engraftment and progression.

Step 2: Characterize tumor progression in the model to identify optimal histotripsy treatment timeframe

As mentioned above, tumor engraftment efficiency is 100% in our immunocompromised pigs. This is consistent with data from the PIs lab in NOD scid gamma (NSG) mice (mentioned in Milestone 2 above). Consistent with the prior human tissue transplant studies using the immunocompromised pigs, the tumors reached 1cm in size within 36 days post-injection. Based on these data, we will treat the tumors between Days 35 and 40 with histotripsy in Milestone 6.

Figure 8. Panc01 tumors demonstrated growth rates and progression similar to subcutaneous tumors and tumors implanted in other animal models (i.e. NOD scid gamma mice). Tumor implantation did not impact pig morbidity or mortality over the time course.

6. Define histotripsy parameters that are effective in the treatment of pancreatic cancer using a novel orthotopic pig model (Step 4 of 4): 100% Complete

Step 1: Using the optimized treatment parameters defined in the previous project phases, Step 4 will actively treat pancreatic tumors in situ.

We have designed and constructed a custom histotripsy system for *ex vivo* and *in vivo* pancreas ablation, adapted from our liver cancer system and our findings detailed in Milestone 3 (**Fig.2**). This system features 1) pancreas specific histotripsy transducers; 2) a specialized amplifier constructed in-house for intrinsic threshold histotripsy pulsing; 3) a co-axially aligned ultrasound imaging probe for real-time treatment guidance and feedback; 4) a robotic micro-positioner allowing for automated treatments; and 5) a control panel with software to integrate all components. The integrated system cart, imaging system, micro-positioner, and software were developed by HistoSonics. The system was modified to include three interchangeable histotripsy

transducers with frequencies of 500kHz, 700kHz, and 1MHz, each consisting of a 32-element array with identical geometries designed for targeted pancreatic tumors and a center hole for a co-axially aligned ultrasound-imaging probe for real-time imaging guidance and feedback. The transducers were constructed using rapid prototyping with associated driving systems to achieve the required acoustic outputs for “intrinsic threshold” histotripsy pulsing (i.e. single cycle pulses with $p > 30\text{MPa}$), which generate more precise and efficient ablation compared to conventional “shock-scattering” histotripsy methods that use multi-cycle pulses. The transducer geometry and frequencies were chosen based on modeling of the acoustic window available in our porcine models and the frequency range expected to be used in future human pancreatic studies, which based on our porcine studies we predict will range from ~500 kHz-1 MHz.

Figure 9. Surgery Optimization. Over the course of this proposal, we optimized our surgical techniques and continue to perfect our tumor implantation procedures. Pig pancreas prepared for implant (left); precision injection of pancreatic cancer cell lines with Matrigel (right)

Figure 10. CT Scan of pancreatic tumors (teal outline) in 2 different locations in the same pig. Masses were further imaged by ultrasound prior to histotripsy treatment (white outline).

Step 2: Characterize histotripsy ablation outcomes post-treatment

Histotripsy success depends on unobstructed optical windows. Gas and air disrupt ultrasound imaging and inhibit effective cavitation. Thus, the anatomical location of the pancreas in humans presents a significant challenge for this technology. Pigs effectively mimic multiple aspects of human pancreas anatomical features and positioning. As stated above, initial studies were successful in targeting specific regions of the pancreas (Fig. 5-6). However, off target effects, especially in the bowel, were a limiting factor (Fig. 5). Despite off-target effects, histopathology assessments confirmed effective pancreatic

ablation (Fig. 5). Based on these proof-of-concept studies, we developed an effective, noninvasive, pre-treatment dietary regime (custard), supplemented with simethicone (anti-gas) and bisacodyl (laxative), based on human clinical trials with HIFU that significantly improves both imaging and histotripsy treatment of the pancreas (Fig. 6, 10, & 11). For example, Fig. 11 shows a representative histotripsy ablation of a 1.5cm region of the pancreas in close proximity to the splenic vein (Fig. 11A-B), animals were followed for 30 days and monitored for adverse effects, including pancreatitis (Fig. 11C). Histotripsy was applied using the custom 32-element 500kHz transducer using single cycle pulses applied at a PRF of 500Hz. A cavitation bubble cloud was generated by increasing the pressure at the focus until a robust bubble cloud was generated at the focus and visualized on ultrasound imaging. An automated treatment was then applied to uniformly treat a 1.5 cm spherical ablation volume at a treatment dose of 500 pulses/point. No adverse effects were observed, with all clinical and biochemical parameters within normal reference intervals (Fig. 11C).

Figure 11. Optimized histotripsy treatment in the pancreas with minimal off-target effects. A) bubble cloud in the pancreas; B) ablation zone in the pancreas; C) white blood cell, amylase, and lipase levels post-treatment are maintained well within porcine reference intervals for up to 30 days post-treatment (data shown from 14 day monitoring).

At this point, we have attempted to treat multiple pancreatic tumors in our pigs. However, we have not yet been successful in fully ablating an orthotopic pancreatic tumor in our pig models. We have been successful in visualizing the tumors, validating safety by following survival post-ablation, optimized treatment conditions, and defined limitations (i.e. tumors at a depth of 7-9 cm cannot be effectively targeted with our current system). We do feel that we are getting close and anticipate success in the upcoming studies currently planned in the post-award period using the pigs due to be delivered in July and August.

FUTURE STUDIES:

1. Histotripsy parameters still require further optimization and limit testing using the orthotopic pancreatic cancer pig models. Most tumors were located in the 4cm depth range. However, in larger pigs, tumor depth was an issue for our current device and we anticipate

this to also be an issue in human patients. Tumors in the 7-8 cm depth were challenging to effectively target. To circumvent this issue, we are currently negotiating with Histosonics to lease their newest generation system (our system is still a first-generation platform) that will allow for more efficient targeting of these deeper tumors within the pancreas. The advantage of this approach is that this system will be the one utilized in human clinical trials.

2. The immunocompromised pig models are effective, but difficult to work with. The requirement for germ free facilities and ultra-high levels of sterility during the surgical tumor implantation process is a significant limitation for the use of these animals beyond the unique facilities at Virginia Tech. Thus, to circumvent the difficulties associated with this model, we have recently begun utilizing an immunocompetent pig model and a porcine PDAC cell line. While we are still optimizing this model, we have thus far found this approach to be significantly faster and more cost-effective compared to the immunocompromised pig model. Likewise, because these pigs are not immunocompromised, we are able to evaluate immune system activation following histotripsy. The pig immune system is more similar to humans compared to mice and the larger orthotopic model is far superior to similar models in rodents. Thus, this is an exciting and emerging area of interest for our future studies.
3. No other common malignancy can match pancreatic cancer in terms of its rapid progression and near inevitable lethality. More than 75% of patients will present with borderline or unresectable disease (Stages II-IV). Chemotherapy and radiation treatment protocols result in limited response rates and are rarely curative. New therapeutic strategies and paradigms are direly needed. Over the last decade, a multitude of focal tumor ablation methods have emerged as potential treatment options for pancreatic cancer. Unfortunately, almost all of these modalities have high complication risks and many patients are not candidates for these focal ablation strategies due to tumor progression, tumor size, and location near critical structures. Currently, all clinically available ablation modalities with the exception of irreversible electroporation (IRE) are either ionizing or thermal-based, and have critical limitations, such as limited control in precision, inability to treat large (>3 cm diameter) or multiple tumor nodules, and incomplete ablation near major vessels. The risk of injury to critical structures near the ablation zone is also a major concern, particularly pancreatic duct injury, which can result in severe pancreatitis or even stenosis with resultant obstructive pancreatitis. Finally, the lack of real-time treatment feedback is an additional limitation to creating precise ablation zones. Our ultimate goal and future studies are to translate these proof-of-concept studies from pig-to-person and show that histotripsy is the first completely non-invasive, non-ionizing, non-thermal, and image-guided pancreatic cancer tumor ablation modality in human patients.

ADDITIONAL DELIVERABLES (DELIVERABLES 5 AND 6 POST-AWARD)

Publications:

1. Brock, R.M., Beitel-White, N., Coutermarsh-Ott, S., Grider, D.J., Lorenzo, M.F., Ringel-Scaia, V.M., Manuchehrabadi, N., Martin, R.C.G., Davalos, R.N., **Allen, I.C.** (2020). Patient derived xenografts expand human primary pancreatic tumor tissue availability for *ex vivo* ablation testing. *Frontiers in Oncology*. May 22;10:843. eCollection 2020. PMID: 32528898.

2. Hendricks-Wenger, A., Nagai-Singer, M.A., Uh, K., Vlaisavljevich, E., Lee, K., **Allen, I.C.** Employing Novel Porcine Models of Subcutaneous Pancreatic Cancer to Evaluate Tumor Ablation Strategies. Biosensors and Biodetection, 3rd edition. In *Methods in Molecular Biology*. Ed. Avraham Rasooly and Ben Prickril. Humana Press. 2020. Invited Book Chapter. (In Press).
3. Hendricks-Wenger, A., Aycock, K.N., Nagai-Singer, M.A., Coutermarsh-Ott, S., Lorenzo, M.F., Gannon, J., Uh, K., Farrell, K., Beitel-White, N., Brock, R.M. Simon, A., Morrison, H.A., Tuohy, J., Clark-Deener, S., Vlaisavljevich, E., Davalos, R.N., Lee, K., **Allen, I.C.** (2021). Establishing a SCID-Like Porcine Model of Human Cancer for Novel Therapy Development: A Pilot Study with Pancreatic Adenocarcinoma and Irreversible Electroporation. *Scientific Reports*. Apr 7;11(1):7584. doi: 10.1038/s41598-021-87228-5. PMID: 33828203.
4. Hendricks, A., Weber, P., Simon, A., Saunier, S., Coutermarsh-Ott, S., Grider, D., Jove, J.V., **Allen, I.C.**, Luyimbazi, D., Vlaisavljevich, E. Histotripsy for the Treatment of Cholangiocarcinoma Liver Tumors: In Vivo Feasibility and Ex Vivo Dosimetry Study. *IEEE Ultrasonics, Ferroelectrics, and Frequency Control*. Apr 15;PP. doi: 10.1109/TUFFC.2021.3073563. PMID: 33856990
5. Hendricks-Wenger, A., Hutchison, R., Vlaisavljevich, E., **Allen, I.C.** (2021). Immunological Effects of Histotripsy for Cancer Therapy. *Frontiers in Oncology*. May 31;11:681629. PMID: 34136405
6. Latifi, M., Hay, A., Carroll, J., Dervisis, N., Arnold, L., Coutermarsh-Ott, S., Kierski, K., **Allen, I.C.**, Vlaisavljevich, E., Tuohy, J. Focused Ultrasound Tumor Ablation in Small Animal Oncology. *Veterinary and Comparative Oncology*. May 31. doi: 10.1111/vco.12742. PMID: 34057278

Publications Currently Submitted/Under Review:

1. Hendricks-Wenger, A., Saunier, S., Simon, A., Grider, D., Luyimbazi, D., **Allen, I.C.***, Vlaisavljevich, E.* Histotripsy for the Treatment of Cholangiocarcinoma in a Patient-Derived Xenograft Mouse Model. *Ultrasound in Medicine and Biology*. (Submitted 5/15/2021). *Co-Corresponding Authors.
2. Hendricks-Wenger, A. Arnold, L., Gannon, J., Simon, A., Singh, N., Sheppard, H., Nagai-Singer, M.A., Imran, K.M., Lee, K., Clark-Deener, S., Byron, C., Larson, M.M., Rossmeisl, J.H., Coutermarsh-Ott, S.L., Dervisis, N., Klahn, S., Tuohy, J., **Allen, I.C.***, Vlaisavljevich, E.* Histotripsy Ablation in Preclinical Animal Models of Cancer and Spontaneous Tumors in Veterinary Patients. *IEEE Ultrasonics, Ferroelectrics, and Frequency Control*. (Revision Submitted June 2021). *Co-Corresponding Authors.

Presentations:

1. “Employing Novel Porcine Model of Subcutaneous Pancreatic Cancer to Evaluate Tumor Ablation Strategies.” Alissa Hendricks, Sheryl Coutermarsh-Ott, Margaret Nagai-Singer, Jessica Gannon, Melvin F Lorenzo, Kenneth Aycock, Kyungjun Uh, Sherrie Clark-Deener, Joanne Tuohy, Eli Vlaisavljevich, Rafael Davalos, Kiho Lee, Irving C Allen. VCOM Research Day. Blacksburg, VA. April 2020.
2. “Determining Immunological Effects of Histotripsy on Cancer Cell Ablation In Vitro and Comparison to Other Common Ablation Modalities.” Jacqueline Sereno, Alissa Hendricks,

Allison Zheher, Eli Vlaisavljevich, Irving C. Allen. VCOM Research Day. Blacksburg, VA. April 2020.

3. "Investigating Changes in Immune Cell Populations in Pancreatic Tumors After Novel Treatments." Allison Zheher. Virtual Poster Presentation. Spring Graduate Research Symposium at Virginia Tech. Blacksburg, VA. April 20, 2020. *Third Place in Category.
4. "Non-Invasive Focused Ultrasound Histotripsy Treatment of Canine Osteosarcoma: *Ex Vivo* Tumor Trials." Arnold, L., Hendricks, A., Coutermarsh-Ott, S., Gannon, J., Dervisis, N., Klahn, S., Allen, I.C., Tuohy, J., Vlaisavljevich, E. Poster Presentation at the 2020 Biomedical Engineering Society Virtual Meeting. October 14-17th, 2020.
5. "Histotripsy Treatment of Primary Osteosarcoma Tumors: Feasibility Study in Excised Canine Tumors". Lauren Arnold, Joanne Tuohy, Sheryl Coutermarsh-Ott, Jessica Gannon, Alissa Hendricks, Nikolaos Dervisis, Shawna Klahn, Irving C. Allen, Eli Vlaisavljevich. Poster Presentation. International Society for Therapeutic Ultrasound (ISTU). June 13-15. (Virtual)
6. "Determining the mechanism of the immune response to histotripsy ablation of pancreatic cancer". Alissa Danielle Hendricks, Rebecca Michaela Brock, Jessica Gannon, Allison Zheher, Jacqueline Sereno, Eli Vlaisavljevich and Irving C Allen. Poster Presentation. Immunology 2020. Annual Meeting of the American Association of Immunology. Honolulu, HI (Abstract Published; Meeting Canceled Due to COVID-19)
7. "Feasibility Study Utilizing Patient Derived Xenograft Mice" Sofie Sauner. Poster Presentation. Biomedical Engineering Society 2020 Annual Meeting. San Diego, CA. October 14-17, 2020. (Virtual)

International Symposium on Focused Ultrasound Presentations

1. "Histotripsy is an effective pancreatic tumor ablation strategy that releases immunostimulatory molecules and promotes anti-tumor immunity". Hendricks, A. Oral Presentation. 7th International Symposium on Focused Ultrasound 2020. November 8-13, 2020.
2. "Establishing a SCID-Like Porcine Model of Human Cancer for Novel Therapy Development: A Pilot Study with Pancreatic Adenocarcinoma". Allen, I.C. Poster Presentation. 7th International Symposium on Focused Ultrasound 2020. November 8-13, 2020.