



## RESEARCH PROGRESS REPORT SUMMARY

**Grant 02773:** Histotripsy for Treatment of Canine Appendicular Osteosarcoma

**Principal Investigator:** Joanne Tuohy, DVM, PhD

**Research Institution:** Virginia-Maryland Regional College of Veterinary Medicine

**Grant Amount:** \$35,975

**Start Date:** 3/1/2020      **End Date:** 2/28/2022

**Progress Report:** Mid-Year 2

**Report Due:** 8/31/2021      **Report Received:** 8/25/2021

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*(The content of this report is not confidential and may be used in communications with your organization.)*

### Original Project Description:

Osteosarcoma (OS) is the most common bone cancer in dogs. Large and giant breeds such as Irish Wolfhound, Great Dane, Greyhound, Scottish Deerhound, Rottweiler, Boxer, Saint Bernard, and Irish Setter are most affected. OS is treated with a combination of surgical removal of the primary tumor and chemotherapy for metastatic disease. Surgical removal of the tumor usually involves limb amputation or limb salvage surgery, which can have high complication rates, and not all dogs are suitable for limb amputation. Even after surgical tumor removal and chemotherapy, the cancer often metastasizes and dogs usually die of metastatic disease within an average of 12 months after diagnosis. Survival times have not greatly improved over the last 30 years. Histotripsy is a precision non-thermal focused ultrasound method that mechanically breaks down tissues, can potentially induce immune activation towards an anti-OS immune response, and is an emerging modality for treating multiple cancers including liver and brain cancer. A non-surgical option for treatment of the primary tumor in OS will help patients preserve their limb and avoid complications of surgical limb-salvage. A therapy that stimulates an anti-tumor immune response may increase OS survival. This study aims to evaluate the efficacy of histotripsy to treat dogs with OS, to ultimately advance the development of histotripsy as a limb salvage treatment option for primary OS and an immunotherapy treatment against metastatic disease for OS.

### Publications:

(a) Our team has published a veterinary review paper on focused ultrasound ablation techniques including histotripsy for small animal oncology.



•Latifi M, Hay A, Carroll J, Dervis N, Arnold L, Coutermarsh-Ott SL, Kierski KR, Klahn S, Allen IC, Vlaisavljevich E, Tuohy J. Focused Ultrasound Tumor Ablation in Small Animal Oncology. *Veterinary and Comparative Oncology* 2021Sep;19(3):411-419;  
<https://onlinelibrary.wiley.com/doi/10.1111/vco.12742>

(b) Our team has also submitted a manuscript to describe the work performed for specific aim 1. This manuscript has been accepted for publication.

•Arnold, L., Hendricks-Wenger, A., Coutermarsh-Ott, S., Gannon, J., Hay, A. N., Dervis, N., Klahn, S., Allen, I. C., Tuohy, J., & Vlaisavljevich, E. (2021). Histotripsy Ablation of Bone Tumors: Feasibility Study in Excised Canine Osteosarcoma Tumors. *Ultrasound in Medicine & Biology*.  
<https://doi.org/10.1016/j.ultrasmedbio.2021.08.004>

(c) Our team is currently preparing a manuscript to describe a portion of the work performed for Specific Aim 2. This manuscript will be submitted to a special topic issue of BME Frontiers, and submission is planned for October 31, 2021.

#### **Presentations:**

The following abstracts have been presented or submitted as a result of this research.

•Abstract Title: Non-Invasive Focused Ultrasound Histotripsy Treatment of Canine Osteosarcoma: Ex Vivo Tumor Trials. This poster was presented at the Biomedical Engineering Society Annual Meeting in October 2020 (e-presentation format due to COVID-19 pandemic).

•Abstract Title: Evaluation of Histotripsy for Ablation of Primary Osteosarcoma: an Ex Vivo Feasibility Study. This oral abstract was presented at the annual symposium for the American College of Veterinary Surgeons in November 2020 (e-presentation format due to COVID-19 pandemic).

•Abstract Title: Histotripsy for the Treatment of Canine Osteosarcoma and Soft Tissue Sarcoma: In Vivo Feasibility Study. This oral abstract was presented at the International Society for Therapeutic Ultrasound Annual Conference in June 2021 (e-presentation format due to COVID-19 pandemic).

•Abstract Title: Investigating histotripsy as a novel treatment for canine osteosarcoma. This poster will be presented at the annual conference for the Veterinary Cancer Society in October 2021 (e-presentation format due to COVID-19 pandemic).

#### **Report to Grant Sponsor from Investigator:**

The study investigators have successfully designed and constructed a custom integrated histotripsy treatment system for canine patients with osteosarcoma. This system was utilized to carry out a clinical trial applying histotripsy therapy to the tumor in client-owned dogs with osteosarcoma. The investigators have successfully delivered histotripsy treatment to the tumor in all study dogs with osteosarcoma. Evaluations of the histotripsy-treated areas of tumor confirm effective tumor ablation. Preliminary observations of the evaluations on the immune response to histotripsy suggest a potential



activation of some immune cells after histotripsy treatment. These immune evaluations are still ongoing. This project has provided professional and educational training opportunities to multiple individuals, including graduate and undergraduate students, a post-doctoral research fellow, veterinary students and interns, and veterinary technicians. This study has also resulted in the submission and publication of manuscripts and successful presentation of abstracts.