Final Report

"Metastable Perfluorocarbon Nanodroplets for Enhanced HIFU Ablation"

Research from this 1 year pilot project is best summarized in two published research articles, a third review article, and a fourth article which has been completed and is being submitted for review this week.

These four articles, which comprise this report are:

1. Puett C, Sheeran PS, Rojas JD, Dayton PA, "Pulse sequences for uniform perfluorocarbon droplet vaporization and ultrasound imaging.," *Ultrasonics*. 2014 Sep;54(7):2024-33

2. Doinikov A, Sheeran PS, Bouakaz A, Dayton PA, "Vaporization dynamics of volatile perfluorocarbon droplets: A theoretical model and in vitro validation," *Medical Physics*, 2014, 41, 102901:1-10.

3. Sheeran PS and Dayton PA, "Improving the Performance of Phase-Change Perfluorocarbon Droplets for Medical Ultrasonography: Current Progress, Challenges, and Prospects," *Scientifica*, 2014;2014:579684.

4. Moyer LC, Timbie KF, Sheeran PS, Price RJ, Miller GW, Dayton PA, "High Intensity Focused Ultrasound Ablation Enhancement In Vivo via Phase-shift Nanodroplets compared to Microbubbles," to be submitted to Journal of Therapeutic Ultrasound

Summary: Overall, this project has been very successful. We have shown that HIFU-mediated ablation can be significantly enhanced in-vivo with mixed perfluorocarbon nanodroplets compared to HIFU alone. Furthermore, data demonstrated that although microbubbles could also enhance HIFU ablation, they resulted in unintended prefocal thermal delivery and skin burns. These experiments highlight the benefit of our phase-change agent, which converts to a microbubble only at the acoustic focus, to enhance HIFU delivery. Furthermore, our data illustrated that an agent with an activation threshold tuned to match the delivered focal acoustic pressure can provide a mechanism for keeping thermal delivery enhancement to a spatially selected region of interest, as determined by the pressure field and vaporization threshold of the agent. Our conclusion is that phase change nanodroplets, such as our formulation, can potentially make MR-guided focused ultrasound surgery safer and shorten procedure times by enhancing ablation speed and volume. One point of note is that our formulation is made with identical excipients as FDA approved microbubble agents, and so the threshold for FDA approval of our nanodroplet formulation, which is condensed from precursor microbubbles, might be less than for a formulation not based on microbubbles.