Magnetic resonance-guided focused ultrasound (MRgFUS) is a “knifeless” technology that uses sound waves to heat and destroy diseased tissues deep within the body precisely and noninvasively. While MRgFUS promises to destroy tumors with fewer side effects than standard surgical technologies, many patients experience multi-hour MRgFUS treatments. Long treatment times are not just inconvenient to the patient—they also correlate with adverse effects such as skin burns, incomplete tumor ablations, and unintended damage to surrounding healthy tissue. Reducing the duration of a given treatment improves patient outcomes, reduces the cost of the procedure, and increases the diversity of patients who can benefit from MRgFUS. This proposal seeks to address a major cause of prolonged MRgFUS treatment times: limited understanding of patient-specific treatment progression.

In current practice, the surgeon’s experience and intuition inform most decisions (such as device positioning, transmission power, and acoustic pathway) that affect treatment duration. These decisions are made in a 24–48-hour treatment planning window and are based on pre-surgical magnetic resonance imaging (MRI) scans. The surgeon must balance the aggressiveness of the treatment and the benefits of destroying the entire tumor against the harms of damaging nearby healthy tissues. During the treatment planning phase, the surgeon effectively draws on her previous experience and training to mentally simulate the course of the surgery. The accuracy and relevance of these simulations are limited by a host of patient-specific unknown factors. Regardless of the experience of the surgeon, impromptu changes to the treatment plan are universal and unexpected events almost always prolong the treatment.

As an alternative to this clinician-centric approach, model-based treatment planning would use computational models of acoustic, temperature, and tissue-damage distributions to guide patient treatments. It could include optimization of the treatment path, sonication duration and power-levels that will most effectively ablate the target tumor while sparing healthy tissues. Given the 24–48-hour treatment planning window, the thousands of computational scenarios necessary for treatment optimization would require either extensive computational resources and/or necessitate that simulations be completed in seconds to minutes. High fidelity full-physics simulations of the acoustic, thermal, and tissue-damage fields in heterogeneous tissues are not likely to be executable in such time frames.

Our team hypothesizes that model-based treatment planning can improve pre-surgical decision making by augmenting the extent and relevance of presurgical simulations. These models would predict and in turn avoid problems that would otherwise extend the course of treatment. We seek to test this hypothesis by building a MRgFUS simulation framework that can be executed by a member of the surgical team within a realistic time frame and with realistic accuracy. This work will involve three specific aims:

**Aim 1**: Improve model accuracy. Develop models that account for (a) temperature-dependent tissue properties, (b) water-content weighted property distributions, and/or (c) quantification of model output uncertainty based on uncertainty of model inputs. Comparison with actual treatment data would be ideal.

**Aim 2**: Reduce computational time and cost. This will be accomplished through (a) improved code efficiency and parallelization, (b) implementation of machine learning algorithms, and/or (c) the creation and use of rapid surrogate/reduced-order models.

**Aim 3**: Assess product-market fit. We will collect information from relevant stakeholders to identify the path of highest potential to clinical implementation of model-based treatment planning. Stakeholders include current clinicians performing treatments, companies developing hardware and software for MRgFUS, and staff engaged in the hospital workflow. We will identify data and visualization tools that will be most relevant and informative in developing treatments of highest efficacy and lowest cost.

Completion of these three aims will provide the team with preliminary data necessary for a successful NIH R01 application to develop a model-based MRgFUS treatment planning platform.

Initial ideas for how to use machine learning

* Automate/accelerate the tissue segmentation process (identifying tissue types based on MR images).
* Facilitate phase aberration correction (identifying timing delays of individual ultrasound elements that enable ultrasound waves to arrive at the target tissue synchronously and maximize heating).
* Tie machine learning to model predictions themselves (acoustic, thermal, and tissue damage models) in a physics-informed machine learning approach.