Interdisciplinary Research (IDR) Origination Awards

Cover Page

Project Title

Accurate and efficient modeling for magnetic resonance-guided focused ultrasound treatment planning

Principal Investigator(s)

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| --- | --- | --- |
| **Name** | **Department** | **College** |
| Christopher R. Dillon (PI) | Mechanical Engineering | Engineering |
| Steven P. Allen | BYU MRI Facility | Family Home and Social Sciences |
| David B. Dahl | Statistics | Physical and Mathematical Sciences |
| Porter Jenkins | Computer Science | Physical and Mathematical Sciences |
| Britt Berrett | Healthcare Leadership Collaborative | Marriott School of Business |
| Allison Payne (Collaborator) | Radiology and Imaging Sciences | University of Utah School of Medicine |

Track

Track one

Abstract

Magnetic resonance-guided focused ultrasound (MRgFUS) is a minimally invasive alternative to conventional breast cancer therapies that promises effective treatment with reduced side effects. Though the field of MRgFUS is growing rapidly, it faces challenges of prolonged, expensive, and uncomfortable treatments. This proposal seeks to be develop model-based predictive tools of MRgFUS treatment progression to improve treatment times. Reducing the duration of treatments improves patient outcomes, reduces the cost of the procedure, and increases the diversity of patients who can benefit from MRgFUS.

Currently, the clinician’s experience and intuition inform most decisions affecting MRgFUS treatment progression. These decisions are made in a 24-to-48-hour treatment planning window. The clinician must balance treatment aggressiveness with potential damage to nearby healthy tissues. Impromptu changes during the treatment are universal, and unexpected events regularly prolong the treatment.

Our team hypothesizes that computational models can improve treatment planning by augmenting the information available to the clinician. The models would predict and, in turn, avoid problems that extend the treatment and negatively impact patient outcomes. We will test this hypothesis by building an accurate, rapid simulation framework that be executed by the clinical team during the treatment planning window.

Summary of Plans for External Funding

Our team will submit one internal and three external grant proposals during the award period. Each proposal will utilize results from our IDR study as preliminary data for submission. These grant proposals include:

* BYU MRI Facility seed grant. The proposal will request $8000 for MRI time that will enable an additional 40-60 subject volunteers be scanned.
* NIH National Institute of Biomedical Imaging and Bioengineering R21 Trailblazer. This opportunity allows direct costs up to $400,000 over 3 years.
* Focused Ultrasound Foundation pre-clinical award. This is a one-year award totaling approximately $100,000.
* NIH National Cancer Institute R15 Award. This three-year $300,000 award will pull together results from each of our IDR aims to reach our goal of developing a model-based treatment planning platform.

**Project Narrative**

1. **The need for alternative breast cancer treatments**

Breast cancer is the most common cancer among women worldwide and the second most common cancer overall. In the United States, it is projected that over 287,000 women will be diagnosed with new cases of invasive breast cancer in 2022, and an estimated 43,250 women in the United States will die from breast cancer [1]. While the 5-year relative survival rate for breast cancer is high (approximately 90%), breast cancer and its treatment can have a profound effect on a person's physical, emotional, and mental well-being [2–4].

Breast cancer treatment side effects strongly impact a patient’s quality of life. Chemotherapy may cause fatigue, nausea, vomiting, hair loss, and cognitive impairment, especially in the first few weeks of treatment [5,6]. Hormonal therapy drugs can cause menopausal symptoms [5,7,8]. Surgery and radiation therapy can cause pain and soreness, with skin changes including redness, itching, and dryness [9–11]. These treatments also cause physical changes to the body, such as scarring and loss of sensation, that lead to body image issues and low self-esteem [10,12]. Generally, patients may experience feelings of fear, sadness, anxiety, and depression that can be compounded by physical changes and stress associated with treatment [4,13].

Clearly, new, less-invasive treatments for breast cancer are needed, and many alternatives are being investigated and developed [14]. Magnetic resonance-guided focused ultrasound (MRgFUS) is one of these alternative therapies, with goals including both efficacious treatment and a reduction in the physical, mental, and emotional side effects associated with current standard treatments [15–18].

1. Diagram, venn diagram

   Description automatically generated**Introduction to MRgFUS**

MRgFUS is a “knifeless” technology that heats and destroys diseased tissues deep within the body precisely and noninvasively [19]. During MRgFUS, high frequency sound waves propagate from an external transducer, pass through a coupling water bath and intervening healthy tissues without harm, and focus inside a tumor or other diseased tissue (see Figure 1). The energy from the focused ultrasound waves quickly increases the local tissue temperature, which induces protein coagulation and necrosis (i.e. cell death) in a region the size of a large grain of rice [20,21]. By moving the transducer or steering the ultrasound beam electronically, the entire tumor can be treated while minimizing damage to healthy tissues. To enable monitoring of the treatment, the focused ultrasound treatment is performed inside a magnetic resonance imaging (MRI) scanner. This guidance from the magnetic resonanceallows the clinician to observe the patient anatomy as well as the temperature changes being caused by the focused ultrasound in real-time [22–24].

Figure 1: Schematic of MRgFUS treatment. MRgFUS can noninvasively heat and destroy diseased tissues with high precision.

Focused ultrasound’s ability to non-invasively generate precise necrosis in deep tissues, with little impact on the surrounding structures, is unique. The severe side effects of chemo- and radiation therapy are not present with MRgFUS therapies. MRgFUS has no cumulative dose effects and can be repeated if necessary. The pain and recovery times for conventional surgery can last months, while patients treated with MRgFUS can return to regular life within a few days. For breast cancer patients, MRgFUS is an especially attractive alternative for those who desire breast conserving therapy, since it is completely non-invasive and could significantly improve cosmetic outcomes compared to surgery. Over the last two decades, the FDA has approved MRgFUS for the treatment of tremor-dominant Parkinson’s disease and essential tremor, uterine fibroids, benign and malignant prostate disease, bone metastases and osteoid osteomas [25]. Hundreds of other indications are currently under investigation at various stages of preclinical and clinical trials [25].

1. **MRgFUS treatment planning- current approach**

While MRgFUS promises to destroy tumors with fewer side effects than traditional interventions, many patients experience multi-hour MRgFUS treatments [26–28]. 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 costs, and increases the diversity of patients who can benefit from MRgFUS [28–31]. **This proposal seeks to address a major cause of prolonged MRgFUS treatment times: limited understanding of patient-specific treatment progression.**

The clinician uses a 24-to-48-hour pre-surgical treatment planning window to make decisions that have critical consequences for the patient. However, in current practice, the clinician relies almost entirely on previous experience and intuition to make these decisions. When the patient’s anatomy and pathology extend beyond the surgeon’s realm of experience, the treatment becomes suboptimal. For example, the position and orientation of the MRgFUS transducer relative to the patient’s anatomy plays a critical role in how quickly the diseased tumor reaches a lethal temperature. Bone, gas pockets, and even large packets of adipose tissue disrupt ultrasound transmission. For a complex tissue such as the breast, it is nearly impossible for a human to predict the complex ultrasound propagation patterns from the dozens to hundreds of possible applicator orientations. A misorientation, however, may introduce burns to the skin or other sensitive, healthy tissues or prevent full ablation of the target, diseased tissue .

A second critical decision is the determination of the treatment path, including where to start the treatment and how it should progress to fully destroy the tumor. Excessive time in one orientation can lead to slow but damaging thermal exposures to healthy tissues in the ultrasound beam path. However, reorienting the transducer or patient takes additional time with no guarantee of improved treatment outcomes. In short, the clinician must balance the aggressiveness of the treatment and the benefits of destroying the entire tumor against the harms of damaging nearby healthy tissues within a complex system with many variables and degrees of freedom. During the treatment planning phase, the clinician effectively draws on her previous experience and training to mentally simulate the course of the treatment. Regardless of the experience of the clinician, impromptu changes to the treatment plan are universal and unexpected events almost always prolong the treatment.

1. **Model-based treatment planning- a potential solution with challenges**

As an alternative to ad=hoc approach based on the clinician’s intuition, model-based treatment planning would use computational models of acoustic, temperature, and tissue-damage distributions to guide patient treatments. It would include optimization of the treatment path, heating duration and power-levels that will most effectively ablate the target tumor while sparing healthy tissues. However, before model-based treatment planning for MRgFUS become a reality, the acoustic and thermal models used for computational models require improvement and extensive validation. Additionally, given the 24-to-48-hour treatment planning window, the thousands of computational scenarios necessary for treatment optimization would require a faster, streamlined modeling process that can be completed in seconds or minutes.

1. **Study Hypothesis**

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.

1. **Study Methodology**

An initial investigation of the study hypothesis presented above will be performed in three specific aims to 1) improve modeling accuracy for MRgFUS treatments, 2) reduce the computational time and cost of those models, and 3) assess the appropriate product-market fit for our proposed treatment planning platform within the US healthcare system. While these aims are insufficient to fully investigate the study hypothesis, they will provide crucial preliminary data and will be the catalyst for our planned external funding proposals, in which we will extensively explore model-based treatment planning’s challenges and opportunities.

**Aim 1:** Improve predictive model accuracy for breast cancer MRgFUS treatments. Develop models that include (a) temperature-dependent tissue properties, (b) water-content weighted property distributions, and (c) quantification of model output uncertainty based on uncertainty of model inputs. Comparison with actual treatment data from breast MRgFUS clinical trials at the University of Utah will provide evidence for model validation.

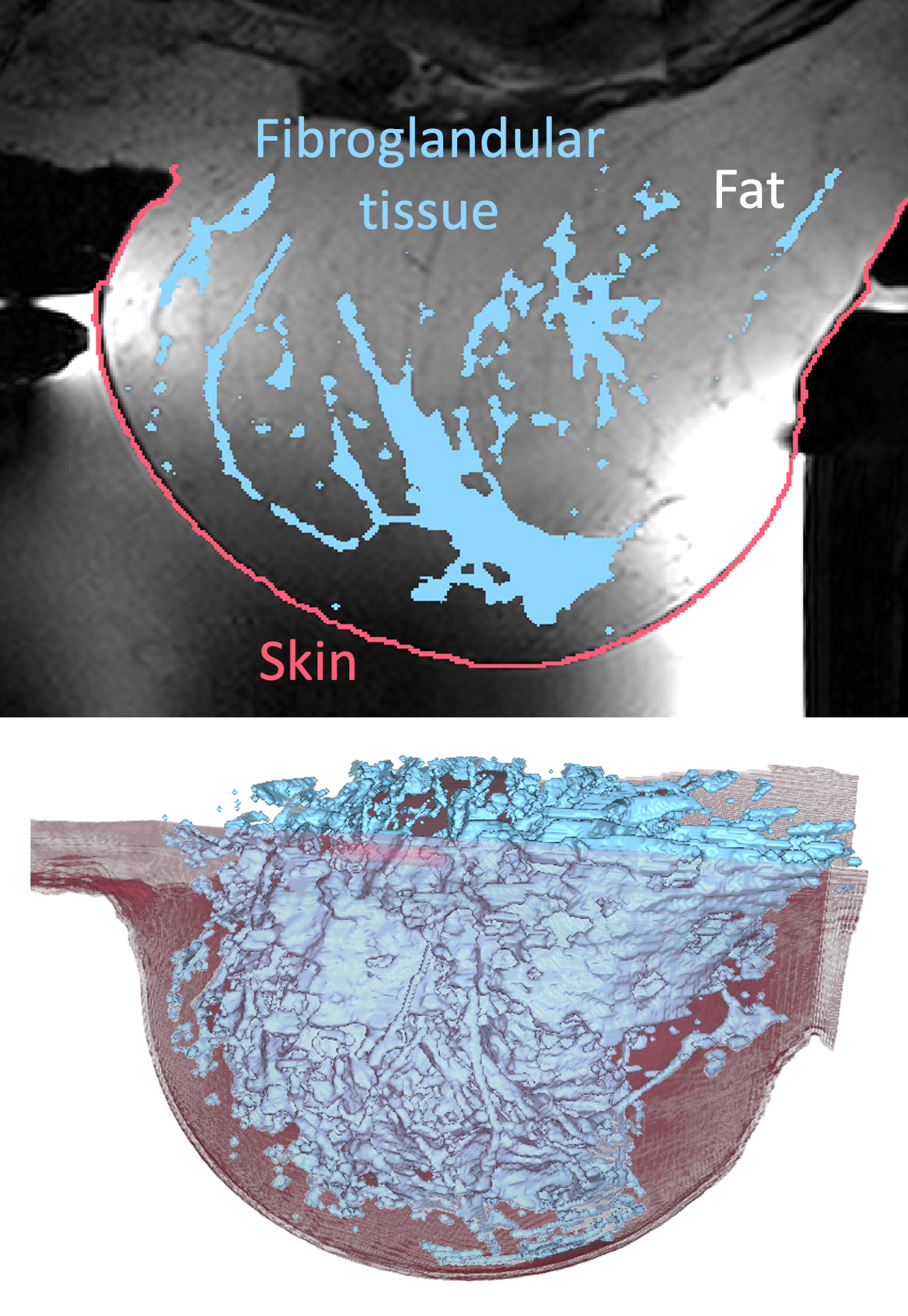
**Rationale:** Improved and clinically validated MRgFUS models are essential for the widespread adoption of model-based treatment planning. Most current MRgFUS models utilize the Pennes bioheat equation to predict how thermal energy from the focused ultrasound heats up the tissue and then dissipates through the tissues [35]. Unfortunately, those simulations consistently overpredict temperatures at the target tissue and regularly underpredict heating at other locations [36–38]. Without the ability to accurately predict temperature changes, confidence in the models is limited. For that reason, model-based treatment planning has not been widely used in the clinical setting.

By developing models with fewer simplifying assumptions, the accuracy of model predictions should improve. Most models utilize a limited number of tissue types and constant, uniform properties within each tissue type. However, the reality of tissue distributions and property variations is much more complex. For example, many tissue properties vary with temperature and with the extent of treatment [39–41]. Mild heating will induce vasodilation and dynamically increased blood flow, which will carry away thermal energy. In many tissues, including the breast, the transition between tissue types (such as fat and fibroglandular tissue) is gradual rather than abrupt, so classifying tissue into coarse bins removes refinement in the model.

**Experimental Methods:** We propose to improve MRgFUS predictive models with two methods that reduce the number of simplifying assumptions and with one method that explicitly accounts for uncertainty in the model inputs. **Method 1**- We will extend current models of acoustic power deposition and the Pennes bioheat equation to account for temperature-dependent tissue properties found in the scientific literature. The acoustic properties will be updated periodically (based on time- or temperature-thresholds yet to be determined) for improved power deposition predictions. Thermal properties will be dynamically updated in a finite-difference time-domain solver as local tissue temperatures change. **Method 2**-Instead of applying the traditional modeling approach of segmenting tissue types into limited bins with constant, uniform properties, we propose to develop models with a spectrum of properties weighted by the MRI-quantified water content of the tissue. Tissue properties based on water content are available in the literature [42]. This method will capture the gradual transition between tissue types and potentially enable more accurate temperature prediction. **Method 3**-There are many uncertain model inputs introducing potential errors into MRgFUS predictions. This method seeks to quantify that model uncertainty rather than ignore it. Using the range and anticipated distribution of each property rather than a single point estimate, the full possibilities of MRgFUS model predictions can be explored and characterized statistically rather than relying on a single anticipated predictive scenario.

**Measures of Success:** To evaluate model improvement, the temperatures achieved during clinical MRgFUS treatments of breast cancer being performed by collaborator Dr. Allison Payne at the University of Utah [43] will be retrospectively predicted using each of the above methods in addition to the traditional modeling approach. Dr. Payne will provide de-identified MRI data from before, during, and after the treatment, as well as information including transducer positioning, ultrasound power and duration, time between heating, etc. We will develop a flexible Bayesian model for these data, which will allow us to fully propagate and quantify uncertainty. We will assess model accuracy using predictive accuracy based on leave-one-out cross validation. These validation efforts will demonstrate the accuracy of our methods and increase confidence in the usefulness of model-based treatment planning.

**Potential Problems and Alternative Strategies:** Property values and distributions in the scientific literature may not cover all desired tissue types. Dr Dillon’s research lab is developing the capability to measure temperature-dependent acoustic and thermal properties. If necessary, tissue samples of bovine or porcine skin, fat, muscle, or glandular tissue acquired from local slaughterhouses can be characterized and utilized in our models.

**Aim 2:** Reduce the computational time and cost to prepare and utilize predictive models for breast cancer MRgFUS treatments. This aim will address one of the most time-consuming portions of treatment modeling: the tissue segmentation process. We propose to reduce segmentation time by (a) developing a library of segmented breast models, (b) improving and confirming segmentation accuracy through iterative discussion and training with a clinical radiologist, and (c) using the library of segmented models to train a machine learning algorithm how to perform tissue segmentation.

**Rationale:** Given the 24-to-48-hour treatment planning window, the time required to perform MRgFUS treatment predictions must be reduced from hours to minutes. If such time reductions can be accomplished without sacrificing model prediction accuracy, thousands of unique treatment scenarios and plans could be evaluated to inform the surgeon of the most optimal treatment plan.

One of the most time-consuming aspects of treatment modeling is the tissue segmentation process, in which MR images are used to identify and differentiate the various tissue types required for acoustic and thermal simulations. This process of separating skin, fat, muscle, bone, tumor, etc. involves tedious often hand-determined analysis of each two-dimensional image in the three-dimensional MRI (an example of a segmented breast model is shown in Figure 2). While software exists that semi-automates portions of the segmentation process [44], cleanup of the segmented model is still required because multiple interrelated, case-specific imaging factors introduce variability and uncertainty. These imaging factors include, but are not limited to, MR image noise, physical proximity to the imaging coils, MR sequence sensitivity and contrast, and patient motion and respiration. The segmented breast model shown in Figure 2 required 40 hours for one BYU graduate student, although this timeframe is anticipated to shorten with further segmenting experience.

Figure 2: (Top) Single 2D slice of segmented breast model overlayed on MRI scan. (Bottom) 3D projection of the segmented breast model.

**Experimental Methods: Creating the library**-The clinical MRI data described for use in Aim 1 will form the foundation of our segmentation training library. Undergraduate students will be trained to interpret the MR anatomical images, in the use of segmentation software, and in model cleanup best practices. They will segment a model for each clinical patient that can be used for Aim 1 and Aim 2. The library will be expanded by enrolling female volunteers for anatomic breast imaging for segmentation at the BYU MRI Research Facility with IRB approval. The MRI parameters used for these scans will mimic those of clinical imaging protocols. Finally, students will search publicly available imaging databases for additional datasets to include in the segmentation library. **Evaluating the library**- After a set of five anatomic segmented models have been generated, a clinical radiologist at the University of Utah will be enlisted to evaluate the accuracy of the segmentation. Training and feedback from the radiologist will be used to correct segmentation errors and to prevent similar problems in future datasets. It is anticipated that a full library of 500-1,000 segmented models will be required to complete the segmentation training library. **Training the machine learning algorithm**- 80% of the MR imaging library and corresponding segmented models will be used to train a machine learning algorithm to perform segmentation. The remaining 20% of the data will be used to validate the accuracy of the machine learning-generated segmented models. We will study the effect of convolutional neural networks (CNN’s) and transformers on segmentation performance [REF]. We will evaluate our segmentation algorithm using mean intersection over union (mIoU), accuracy, precision, and recall, as is common in the literature [REF].

**Measures of Success:** Segmentation accuracy, of the library and machine learning results, will be evaluated by a clinical radiologist at the University of Utah. The development of the segmented models will be a valuable contribution, even without the machine-learning algorithm. The models will be used for retrospective analysis in Aim 1 and as part of treatment outcome studies for the University of Utah clinical trial. The development of a rapid segmentation protocol that uses machine learning will shorten the modeling timeline dramatically and will be foundational to our eventual goal of building a model-based treatment planning platform for MRgFUS thermal therapies.

**Potential Problems and Alternative Strategies:** Modern machine learning methods (i.e., deep learning), require a large amount of labelled data. If we determine that our student-produced segmented models lack sufficient accuracy or if we cannot collect sufficient patient and volunteer data for training, we will investigate 1) data augmentation techniques to increase dataset diversity, or 2) the use of unsupervised machine learning techniques for tissue segmentation [REF]. Reducing segmentation time will reduce MRgFUS predictive model computation times, but the challenge of slow acoustic and thermal models themselves will remain. Future efforts could include the use of physics-informed machine learning algorithms or reduced order models to accelerate predictive simulations.

**Aim 3:** Assess the product-market fit for our model-based treatment planning platform. 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, fiscal intermediaries for insurance reimbursement, 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 fiscal contribution.

**Rationale**: The introduction of new technology is complicated as interdisciplinary innovation requires participation by clinicians, researchers, vendors, facilities, and fiscal intermediaries. Currently, clinicians treat breast cancer with surgical intervention (lumpectomy, mastectomy), combined with chemotherapy, hormone therapy or radiation. Broad adoption of clinical innovations like MRgFUS combined with model-based treatment planning requires rigorous consideration by clinicians. It will therefore be critical to engage in discussions with current academic medical centers that offer MRgFUS in other clinical applications and evaluate their interest in enhanced treatment planning. Exploring current utilization of MRgFUS and the interest of clinicians to explore expanded treatment protocols will inform the magnitude and direction of the predictive tools we develop.

**Methods:** MRgFUS is a new and growing treatment protocol that is primarily provided in large academic medical centers. In year 2, we will determine current providers and scope of services for model-based treatment planning. We will interview clinicians and hospital staff regarding how our treatment planning results would integrate with their current workflow and prove most beneficial to them. By focusing specifically on breast cancer, we will identify facility Diagnosis Related Group codes (DRGs) and physician Current Procedural Terminology (CPTs) coding with their financial implications. Further, enhanced treatment planning will be explored and evaluated to determine improvements in processing time and enhanced clinical decision-making.

Obtaining insurance reimbursement for new therapies like MRgFUS is challenging. During year 2, we will also spend time engaging with fiscal intermediaries (Medicare, Medicaid and insurance entities) that develop comprehensive reimbursement models through facility DRG and clinician CPT coding. These efforts will improve the likelihood of our successful transition of our model-based treatment planning platform into the clinic.

**Measures of Success:** From these clinical discussions, interviews, and interactions, we will clearly identify what modeling data will be most useful to clinicians in the treatment planning process as well as the optimal presentation of those data. We will also be engaging early in the reimbursement process so that as we continue to develop our model-based treatment planning platform, we can maximize our likelihood of clinical success.

**Potential Problems and Alternative Strategies:** The most appropriate stakeholders to inform our study may be difficult to identify and have minimal time for academic discussion. A key to our success may be identifying one or more clinical champions to advance our model-based treatment planning platform. Actively networking at conferences, engaging with Dr. Allen’s and Dr. Dillon’s former and current collaborators at the University of Utah, University of Virginia, University of Michigan, Stanford University, and UCSF, and utilizing Dr. Berrett’s career’s worth of healthcare and hospital connections will help us realize this goal.

1. **Expected Project Outcomes**

**External funding proposals**: Completion of these three aims will provide the team with preliminary data to pursue external grants from the NIH/NIBIB (R21 Trailblazer, $400k over three years) and NIH/NCI (R15, $300k over three years) as well as from the Focused Ultrasound Foundation (one-year $100k).

**Conference presentations**: This work would enable graduate and undergraduate student presentations at the Society for Thermal Medicine Annual Meeting (2024, 2025), the Biomedical Engineering Society Annual Meeting (2024, 2025), 2024 Focused Ultrasound Symposium, ISMRM 2026, XXXXX, XXXX, XXXX. The work will also be presented by a statistics graduate student in the Joint Statistical Meetings in 2026.

**Scholarly articles** (Title, Journal, Lead Author): **1**. The impact of temperature-dependent properties on predicting MRgFUS clinical responses, International Journal of Hyperthermia, Dillon. **2**. Using water-content MRI to simplify predictive modeling for MRgFUS therapies, Medical Physics, Dillon. **3**. Statistical modeling to characterize uncertainty in MRgFUS heating profiles, Annals of Applied Statistics, Dahl. **4**. Breast segmentation time-reduction with a machine-learning algorithm, XXXXX, Jenkins. **5**. Translating simulation software for focused ultrasound treatment planning to the clinic, XXXXX, Berrett.

**Student mentoring**: The modeling improvements of Aim 1 will be performed by three graduate students in Dr. Dillon and Dr. Dahl’s lab with assistance from 3-4 undergraduate research assistants. Aim 2 will require ten undergraduate research assistants for recruiting, imaging, and segmenting MR data under the supervision of Dr. Allen and Dr. Jenkins, with the machine-learning algorithm developed by a graduate student in the Jenkins Lab. The market fit analysis will be performed by a graduate student under the guidance of Dr. Berrett. In total, **five graduate students and at least fifteen undergraduates** will receive mentoring and research opportunities from this project.

**Scientific outcomes**: This study will enable the development and validation of more accurate predictive models for MRgFUS therapies. The pretreatment modeling process will be shortened by the machine learning-based segmentation algorithm we create. A clear path to clinical implementation of model-based treatment planning for MRgFUS therapies will be identified. In sum, these efforts will improve patient outcomes and quality of life through more time-efficient, safer, and efficacious MRgFUS treatments for breast cancer and other diseases.

1. **Study Schedule**

The study will be conducted according to the following schedule.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study Quarter** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | **Q6** | **Q7** | **Q8** |
| Aim 1 |  |  |  |  |  |  |  |  |
| Aim 2 |  |  |  |  |  |  |  |  |
| Aim 3 |  |  |  |  |  |  |  |  |
| Manuscript Preparation |  |  |  |  |  |  |  |  |
| Proposal Preparation |  |  |  |  |  |  |  |  |

1. **Study Team**

**Christopher R. Dillon** is a mechanical and biomedical engineer with a decade of experience in acoustic and biothermal modeling of MRgFUS therapies. He will oversee the project generally, coordinate between co-investigators at BYU and collaborators at the University of Utah, and mentor students for Aim 1. **Steven P. Allen** has a decade of experience using MRI to guide focused ultrasound surgeries, including MR sequence development, image acquisition, and image reconstruction. In this study, he will guide students in recruiting subjects and acquiring data at the BYU MRI Research Facility. **David B. Dahl** is a Bayesian statistician with extensive experience collaborating with scientists in the life sciences. He will be responsible for the statistical uncertainty modeling in Aim 1 and will also support the machine learning assessment in Aim 2 and quantitative analysis for Aim 3. **Porter Jenkins** is a computer scientist with expertise in 3D computer vision and machine learning. He will lead efforts to develop the library and machine learning algorithms for tissue segmentation described in Aim 2. **Britt Berrett** is a healthcare executive with 25+ years in academic, for-profit, not-for-profit and community-based hospitals and healthcare systems and experience introducing new clinical innovations into non-academic environments. He will oversee efforts to understand the product-market fit in Aim 3. **Allison Payne** and her team will provide de-identified MRI data for analysis from clinical breast cancer MRgFUS treatments at the University of Utah. They will provide feedback on how model-based treatment planning might be implemented clinically in Aim 3.

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**Study Budget**

|  |  |  |  |
| --- | --- | --- | --- |
| **Item** | **Year 1** | **Year 2** | **Total** |
| Undergraduate Student Support (10) | **12000** | **12000** | **24000** |
| Graduate Student Support (3.5) | **36000** | **46000** | **82000** |
| MRI Scanner Usage | **8000** | **0** | **8000** |
| Subject Compensation | **2000** | **0** | **2000** |
| Supplies | **2000** | **2000** | **4000** |
| **Total** | **60000** | **60000** | **120000** |

**Budget Narrative**

A total of **$120,000** is requested over the two-year period of this proposal. Of this amount, a total of **$82,000** is requested to support three graduate students (mentored by Drs. Dillon, Dahl, and Jenkins) who will perform, respectively, Aims 1.a - 1.b, 1.c, and 2. An additional $10,000 is budgeted in year 2 for part time support for an additional student under Dr. Berrett’s supervision to conduct the market study described in Aim 3. A total of **$24,000** is requested over both years to support up to 10 undergraduate students to undertake the laborious process of segmenting MR images acquired in Aim 2, conduct subject recruitment, and acquire MR images. A total of **$8,000** is requested to support 40 MRI scans of recruited subjects plus 8 pilot scans that will be used to ensure proper data collection. Our team will pursue an MRI Research Facility Seed Grant to fund an additional $8000 of scanning to supplement the study in year 2. A total of **$2,000** is requested for subject compensation. Finally, a total of **$4,000** is requested to purchase supplies, such as tissue samples, test equipment, supercomputer time, and purchasing market research as described in Aims 1-3.

**Plans for External Funding**

This interdisciplinary research award will jump start efforts and provide preliminary data for multiple internal and external funding proposals described below.

In December 2023, we will pursue a **BYU MRI Facility seed grant**. The proposal will request $8000 for MRI time that will enable an additional 40-60 subject volunteers be scanned during the 2-year study period to expand our imaging library for training and evaluating the tissue segmentation machine learning algorithm.

In February of 2025, we will submit a **R21 Trailblazer proposal to the National Institute of Biomedical Imaging and Bioengineering (NIBIB) at the NIH**. This opportunity is limited to New and Early Stage Investigators (Dr Dillon and Dr Jenkins qualify) and allows direct costs up to $400,000 over 3 years. This proposal would expand upon results from our IDR study to investigate other applications of machine learning in MRgFUS therapy treatment planning.

The team will submit a **Focused Ultrasound Foundation pre-clinical award** proposal in the Summer of 2025. This is a one-year award totaling approximately $100,000. These funds will be used to translate our machine-learning algorithm into a clinically relevant tool for segmenting breast MRI data for MRgFUS patients.

In June of 2025, we will use the preliminary data from our IDR efforts to support a **Research Enhancement Award (R15) proposal to the National Cancer Institute (NCI) at the NIH**. This three-year $300,000 award will help us pull together results from each of our IDR aims to create a model-based treatment planning platform that can be utilized for improved MRgFUS treatment planning for breast cancer. We will also work to extend the platform to other types of cancer and other diseases.

Submission of these grant proposals will follow the schedule below.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study Quarter** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | **Q6** | **Q7** | **Q8** |
| BYU MRI Facility |  |  |  |  |  |  |  |  |
| NIH/NIBIB R21 |  |  |  |  |  |  |  |  |
| FUS Foundation |  |  |  |  |  |  |  |  |
| NIH/NCI R01 |  |  |  |  |  |  |  |  |

**Biographical sketches & Current and Pending Support**

**Biosketch: Dillon (2 pg limit)**

**Current and Pending Support**

Christopher R. Dillon

**Project/Proposal Title:** BYU/SNL Reduced Order Methods Collaboration

**Status of Support:** Active

**Proposal Award Number:** PO 2363288

**Source of Support:** Sandia National Laboratories

**Primary Place of Performance:** Brigham Young University

**Start Date:** 04/2022

**End Date:** 12/2023

**Total Award Amount:** $64,993 (Includes indirect costs)

**Time commitment (Person Months):** 0.75 months

**Project/Proposal Title:** Using imaging to understand Achilles tendon adaptation and injury in female athletes

**Status of Support:** Active

**Source of Support:** BYU Interdisciplinary Research Award

**Primary Place of Performance:** Brigham Young University

**Start Date:** 06/2022

**End Date:** 05/2024

**Total Award Amount:** $120,000 (~$4,000 for ME EN student support)

**Time commitment (Person Months):** 0.25 months

**In Kind Contribution:** New Faculty Start-up Funds

**Status of Support:** Active

**Source of Support:** Brigham Young University

**Primary Place of Performance:** Brigham Young University

**Start Date:** 11/2021

**End Date:** 12/2024

**Summary:** Student Wages $60,000; $20,000/year for three years

Capital Equipment: $180,000

PhD Stipend: $8,000

Tuition: $18,000; $6,000/year for three years

**Total Award Amount:** $266,000

**Project/Proposal Title:** Investigating the impact of subcutaneous fat properties on focused ultrasound thermal therapy outcomes

**Status of Support:** Pending

**Source of Support:** NIH/NIBIB

**Primary Place of Performance:** Brigham Young University

**Start Date:** 06/2023

**End Date:** 05/2026

**Total Award Amount:** $ 593,198 (Includes indirect costs)

**Time commitment (Person Months):** 3.00 months per year

**Biosketch: Allen (2 pg limit)**

**Current and Pending Support: Allen**

**Biosketch: Dahl (2 pg limit)**

**Current and Pending Support**

David Dahl

Dr. Dahl has no current research support to report for this IDR proposal. Pending support is listed below.

**Project/Proposal Title:** Investigating the impact of subcutaneous fat properties on focused ultrasound thermal therapy outcomes

**Status of Support:** Pending

**Source of Support:** NIH/NIBIB

**Primary Place of Performance:** Brigham Young University

**Start Date:** 06/2023

**End Date:** 05/2026

**Total Award Amount:** $ 593,198 (Includes indirect costs)

**Time commitment (Person Months):** 0.25 months per year

**Biosketch: Jenkins (2 pg limit)**

**Current and Pending Support: Jenkins**

**Biosketch: Berrett (2 pg limit)**

**Current and Pending Support**

Britt Berrett

Dr. Berrett has no current and pending research support to report for this IDR proposal.