Machine Learning Temperature Prediction for Focused Ultrasound Treatment Targets in the Brain

and

Accessibility of Uterine Fibroid Treatments for Understanding Sociotechnical Setbacks for Focused Ultrasound

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On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

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Introduction

With emerging medical technologies, which have not yet become trusted and influential, ensuring equitable access to the technology often lags well behind the technology itself. One illustration is found in focused ultrasound treatments. Since focused ultrasound treatments are non-invasive, requiring no surgery, and targeted, causing almost no damage to surrounding tissue, access to the technology is life-altering. Current focused ultrasound technologies emphasize improvements in ultrasound transducer technology but fail to provide an accurate patient eligibility metric, which increases confidence in and therefore accelerates clinical use of the technology.

I propose the development of an improved treatment eligibility metric using a machine learning model to predict the temperature reached in the brain target region during focused ultrasound treatment. This metric will incorporate individualized skull density measurements from the standard treatment eligibility metric and additional anatomical and transducer for greater prediction accuracy. However, the creation of a treatment eligibility metric that ensures more beneficial access to treatments cannot be understood without considering the social environment of the technology. Focused ultrasound technology is young and must first evolve to fit patient and provider needs for the technology before it can become a widely accessible, non-invasive treatment option. To analyze the social needs focused ultrasound must facilitate to gain sociotechnical momentum, I will use the Science, Technology, and Society (STS) framework of technological momentum to consider reverse salients slowing further progress in the case study of uterine fibroid treatment accessibility (Freeman et al., 2021).

Below, I outline a technical project that aims to create an individualized, more accurate focused ultrasound treatment eligibility metric as compared to the clinical standard. I also

outline an STS project that analyzes the technical momentum of focused ultrasound treatment in a case study on the accessibility of focused ultrasound technology for uterine fibroids, which is underutilized, although application of the technology to uterine fibroids has been FDA-approved for nearly 20 years (FDA, 2004). The insights from the STS project into the social hurdles for focused ultrasound technology improvements will specifically inform the technical project by requiring the technical project to be open-source, well-documented, individualized, and easy to explain and understand to improve equitable access to focused ultrasound treatments.

Technical Project

Focused ultrasounds are gaining rapid technological acceptance as a non-invasive treatment method that allows targeted brain heating and ablation (ter Haar & Coussios, 2007). Applications of focused ultrasound are wide-ranging, spanning from neurological diseases such as Alzheimer's and Parkinson's to physical malignancies such as brain tumors (Meng et al., 2021). During treatment, multiple focused ultrasound beams are converged to a focal point on a pre-chosen target. The treatment is successful when the beams ablate the target. Physicians can determine whether ablation was successful using the peak average temperature reached in the target region during treatment and the known required ablation temperature. Treatment success is highly dependent on anatomical heterogeneity among patients, requiring an individualized patient eligibility metric. The greatest loss of ultrasound energy occurs within material interfaces in the porous bone of the skull; therefore, the current patient eligibility metric, the skull-density ratio (SDR), measures the ratio of the skull density between the skull's cancellous and cortical bones (Boutet et al., 2019).

The SDR is an imperfect indication of treatment success; in a Parkinson's trial, patients with a favorable SDR required more energy deposition than predicted (Sammartino et al., 2019).

The SDR lacks accuracy because it fails to account for key anatomical details such as skull thickness and key technological parameters such as sonication energy and duration. Should SDR continue to be used as the treatment eligibility metric for focused ultrasound clinical trials, many patients who can receive life-changing benefits from the treatment will be excluded from the trials; patients who cannot benefit will experience frustration and disappointment due to treatment failure; and the budding technology loses credibility and sociotechnical momentum.

We hypothesize that 1) predicting temperature deposition in the target region, 2) using a multiple-regression machine learning model, and 3) taking into account additional anatomical heterogeneities and transducer parameters will create a more accurate treatment eligibility metric than the SDR. Our technological project aims to output the predicted maximum average temperature reached during treatment. Initially, this will take the form of a single number within a < 5 °C confidence interval. Ultimately, we aim to produce a predicted thermometry data spread (the temperature map in the brain during an ultrasound treatment) for a chosen patient, given their anatomical details and the planned treatment parameters. We will visualize the thermometry data to help our understanding, as seen in Figure 1, produced within Kranion software (Sammartino et al., 2019).

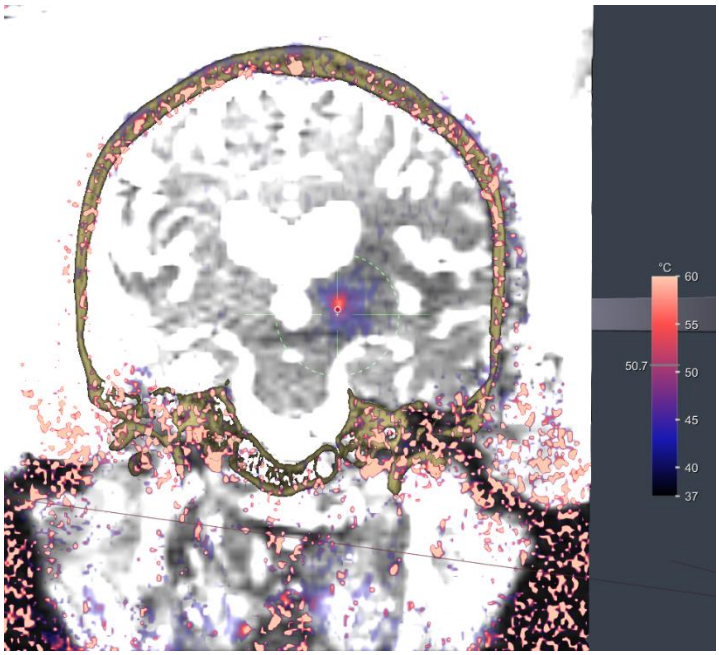

Figure 1. Ultrasound treatment data loaded into Kranion, showing thermometry data

Our advisors at the Focused Ultrasound Foundation (FUSF) have provided anonymized data from patients undergoing treatment at the UVA Focused Ultrasound Center. We will select variables deemed significant to include in the multiple regressor model based on a literature review and principal component analysis (PCA) of the provided-by-sonication treatment data. Kranion, an open-source focused ultrasound treatment planning software developed by FUSF, can load treatment exports as shown in Figure 1 (Sammartino et al., 2019). Kranion will help us visualize the effect of anatomical variance on HIFU treatment and the thermometry map. Although we will produce the temperature prediction model in the Python language due to its expanded machine learning capabilities, we hope to ultimately integrate the model with existing Graphical User Interface (GUI) displays in Groovy, Kranion's native language.

To evaluate project success, we will observe network model examples from scholarly articles on existing computational models for focused ultrasound target temperature prediction. These models rely on previously derived thermal dose equations, which will help us confirm our

model results in the future (Revathy & Sadasivam, 2016; Sassaroli et al., 2012). Our model will be trained and tested on anonymized patient data from the UVA Focused Ultrasound Center. Over 100 datasets are available to us, and we aim to use all of them to increase statistical rigor. At a minimum, we will add 20 datasets for each independent variable added to the multiple regression model to avoid overfitting. Since we are completing our work for the FUSF, a local nonprofit, success will also be measured in terms of project reusability, meaning we must keep detailed documentation throughout our project and publish all code as open-source.

STS Project

What do you do when a cure exists, but it sparkles just out of reach? For the up to 75% of women affected by uterine fibroids, this is a daily reality (Giuliani, E., 2020). Uterine fibroids are benign uterine tumors that can be accompanied by heavy bleeding and debilitating pain. Most patients are offered a choice among invasive surgeries that can damage or remove their uterus and their ability to conceive forever – despite the fact that noninvasive, targeted focused ultrasound treatments have been Food-and-Drug-Administration (FDA)-approved since 2004 (FDA, 2004) (FDA, 2015).

Current attributions of the underutilization of focused ultrasound treatments for uterine fibroid patients often center on a lack of awareness of the technology itself or a lack of comprehensive post-operative outcome data (Behera et al., 2010). The newness of the technology does play a role in the lack of emphasis focused ultrasound receives as a treatment option for focused ultrasound; the technology truly began to be standardized for clinical use in the early 2000s with a 2006 protocol and has grown much more sophisticated since then (Boutet, A., 2019). There is also truth to the argument that the technology does not have large expansions of clinical trial testing evidence (FUSF, 2022). In addition to strict regulations that slow down

the clinical trial process, the current standard treatment eligibility metric is inaccurate (Sammartino et al., 2019). Inaccurate treatment eligibility screening excludes patients who could benefit from treatment and includes patients who cannot be successfully treated, causing losses in confidence in the technology and confusing clinical results that may seem to signal a lack of treatment efficacy.

However, these arguments can not be considered the only factors contributing to the underutilization of focused ultrasound treatments for uterine fibroid patients. For one, the awareness of the technology continues to grow as it gains rapid news coverage via organizations such as Charlottesville's local Focused Ultrasound Foundation, which has made CNN headlines. By the numbers, since 2000, focused ultrasound has been used to successfully treat 175,000 fibroid patients globally (FUSF, 2022). Furthermore, in addition to being FDA-approved for uterine fibroid treatment, the technology is popularly viewed as safe enough for continued use by patients: when 1,000 US women with fibroids were presented with treatment descriptions in a 2013 survey, 60% rated focused ultrasound as their top treatment choice (Borah, B. J. et al, 2013). The missing piece in the mystery of the underuse of focused ultrasound in uterine fibroid treatment is sadly to look no further beyond money, specifically, the dizzying labyrinth that is the medical insurance reimbursement process. If we continue to consider the underuse of focused ultrasound for uterine fibroid treatments as independent of medical profits, we fail to understand the reverse salient that renders even the best-designed, least invasive technology inaccessible for women. I argue that the underperformance of the focused ultrasound treatment system for uterine fibroid patients is largely due to the early life stage of focused ultrasound technology and the reverse salient of slow-rolled medical insurance reimbursement hindering patient access.

To frame my argument, I will draw on the STS concept of technological momentum. Technological momentum was developed by Thomas Hughes, a historian of technology who grew dissatisfied with both technological and social determinism theories of the role of technology (Freeman et al., 2021). Technological momentum combines the best of both theories and argues that when a technology, which is called a socio-technical system in this framework, is early in its development, society has the most power to shape it (Freeman et al., 2021). As the sociotechnical system grows and gains more social momentum, the system exerts more influence over society and is more resistant to change (Freeman et al., 2021). Importantly, the framework also includes the concepts of reverse salients: components in the system that fall behind others during complex change and cause the system to underperform (Freeman et al., 2021). To corroborate my argument, I will use scholarly articles on social and economic cost-benefit analyses of uterine fibroid treatment options, interviews on uterine fibroid patient stories in the popular press, and health system publications on the reimbursement process for focused ultrasound treatments.

Conclusion

The described technical project will deliver a focused ultrasound treatment eligibility metric that is more accurate by accounting for more anatomical and technological parameters. The described STS project will deliver an analysis of the accessibility of focused ultrasound treatment for uterine fibroid patients. From its analysis of the current technological momentum of focused ultrasound and the medical insurance reverse salient holding it back, the STS project will inform the technical project by influencing design choices to facilitate accelerated movement into eligibility for medical insurance reimbursement. Specifically, insights from the STS project will require the design to be explainable, reusable for research, easily usable by

clinicians, accurate, and precise. Together, the technical and STS projects contribute to a design for an improved treatment eligibility metric that is designed to both increase the accuracy of patient selection and work within the broader sociotechnical commercial medical system to accelerate focused ultrasound technology out of the lab and into the lives of patients in need.

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