STATEMENT OF RESEARCH VISION

A. SIGNIFICANCE AND INNOVATION

Ultrasound is one of the safest, most accessible, and most widely used imaging tools in medicine, but today it primarily produces qualitative pictures. My research transforms ultrasound into a quantitative measurement technology that maps the mechanical properties of tissue with unprecedented accuracy and spatial resolution. Instead of simply showing echoes, my approach reconstructs intrinsic tissue properties such as stiffness and sound speed, enabling clinicians to distinguish healthy from diseased tissue in a way that approaches the level of detail typically associated with MRI but at a small fraction of the cost (**Fig. 1**)[1]. This advance is made possible by modeling full-wave physics through tissue and inverting that physics to recover the underlying structure—an approach fundamentally absent from conventional ultrasound imaging.

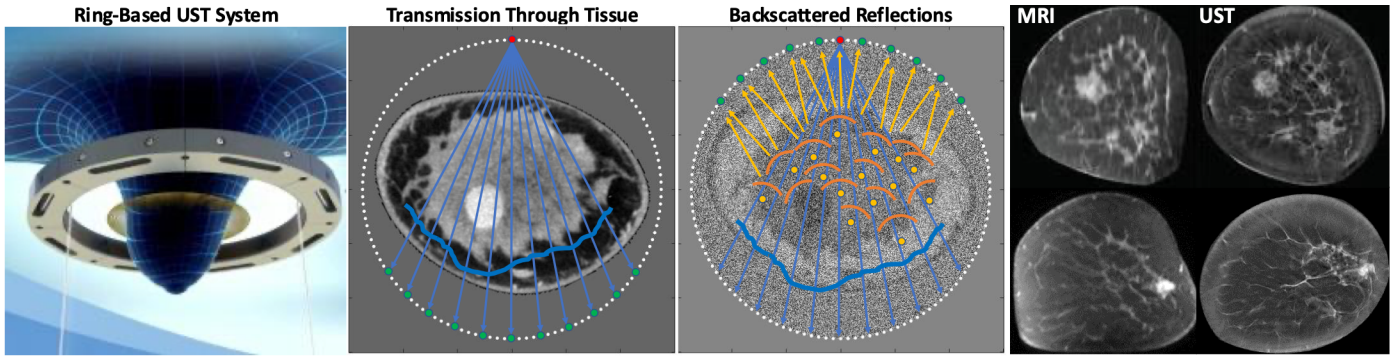

Fig. 1. Ring-based UST records transmissions through and reflections from tissue. *In-vivo* comparison of FWI-based UST to MRI for breast imaging.

In ultrasound tomography (UST), acoustic waves are transmitted through tissue and scattered fields are recorded (**Fig. 1**). The core challenge is recovering the material properties that generate these scattering patterns. My research advances UST by coupling wave physics, numerical optimization, and experimental data acquisition within a unified framework. I focus on full-waveform inversion (FWI) and related techniques that iteratively match simulated and measured waveforms to produce high-resolution maps of acoustic properties such as sound speed, attenuation, and density. By explicitly modeling wave propagation, UST becomes a quantitative imaging modality capable of revealing the structure and composition invisible to conventional pulse-echo ultrasound.

B. RESEARCH BACKGROUND AND ACCOMPLISHMENTS

My graduate research at Stanford University—funded by the NDSEG fellowship—focused on the inverse problem of reconstructing a spatially varying sound speed in tissue from aberrations in the pulse-echo ultrasound image and correcting the aberrations using the estimated sound speed. Collaborating with Dr. Biondo Biondi in the Department of Geophysics, I adapted tomographic imaging techniques from seismology, ultimately applying FWI to UST for high-resolution breast imaging under Dr. Neb Duric at the University of Rochester. I was previously funded by the Ruth L. Kirschstein Postdoctoral Individual National Research Service Award (NIH Grant F32-EB034589) and am ***currently funded by the K99/R00 Pathway to Independence Award (NIH Grant K99-EB037080)***, both from the National Institute of Biomedical Imaging and Bioengineering (NIBIB), to investigate new methods that extend the breast tissue characterization capabilities of transmission-based UST and handheld pulse-echo ultrasound. I have also worked with Dr. Duric's team to develop accurate, robust, and computationally efficient FWI techniques for emerging clinical applications such as transcranial whole-brain imaging. I view research as a collaborative enterprise and have promoted open, reproducible science by releasing major software and experimental datasets, now widely used by the ultrasound imaging community (see my **CV** for a complete **list of publications** and **open-source GitHub repositories** associated with each publication—**https://rehmanali1994.github.io/**).

C. SCIENTIFIC VISION AND CLINICAL APPLICATIONS

My goal is to establish a computational imaging program that advances UST from a promising technology into a versatile quantitative imaging platform. By integrating high-fidelity modeling, scalable optimization, and experimental validation, my research will yield quantitative biomarkers to improve disease diagnosis, monitoring, and treatment planning. Collaborations with clinicians will guide these developments toward practical applications in breast, brain,

musculoskeletal, and preclinical imaging. I aim to establish UST as a flexible, platform technology addressing diverse clinical and preclinical imaging needs:

1) 3D Breast Imaging for Cancer Screening, Diagnosis, and Treatment Monitoring (**Fig. 2**)[2]
2) Whole-Brain Transcranial Imaging through the Skull for Point-of-Care Stroke Triage (**Fig. 3**)
3) Neonatal Brain Imaging for Intraventricular Hemorrhage Detection and Diagnosis
4) Musculoskeletal Limb Imaging (Arthritis, Muscle Disorders, Postoperative Assessment of Implants)
5) Whole-Body Imaging (for a broader set of clinical applications)
6) Small Animal Imaging for Preclinical Testing of Drugs and Therapies

Ultimately, my scientific research vision is to establish a quantitative imaging paradigm that unites physics, computation, and experiment to reveal tissue structure and function.

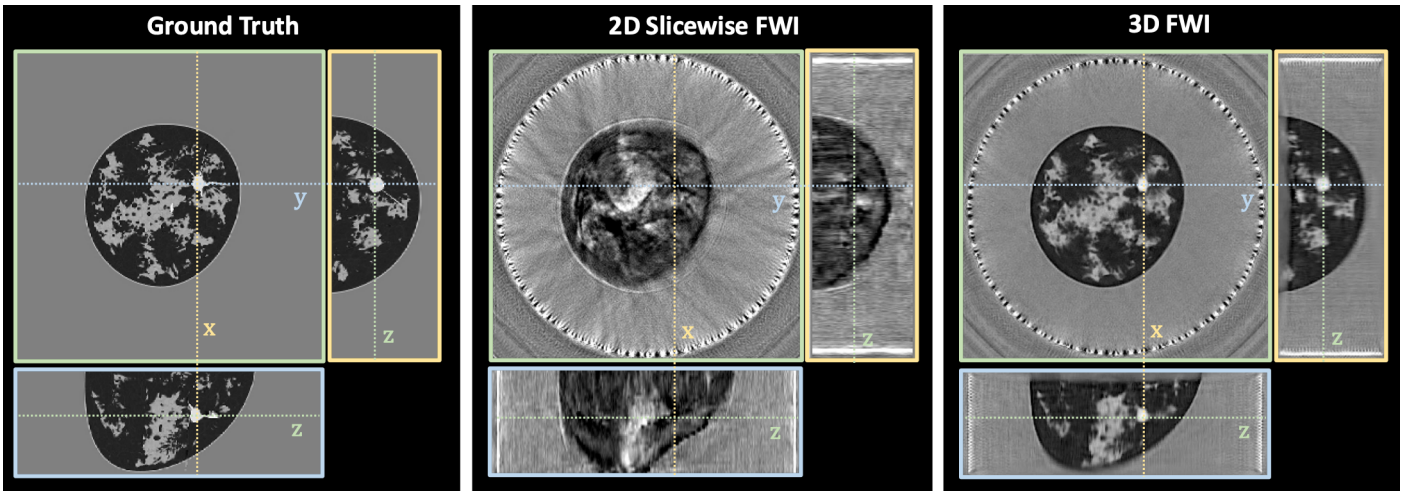

Fig. 2. Improvement from 2D Slice-Wise to 3D FWI[2]. Orthographic views of the reconstructed volume intersect at the simulated breast cancer.

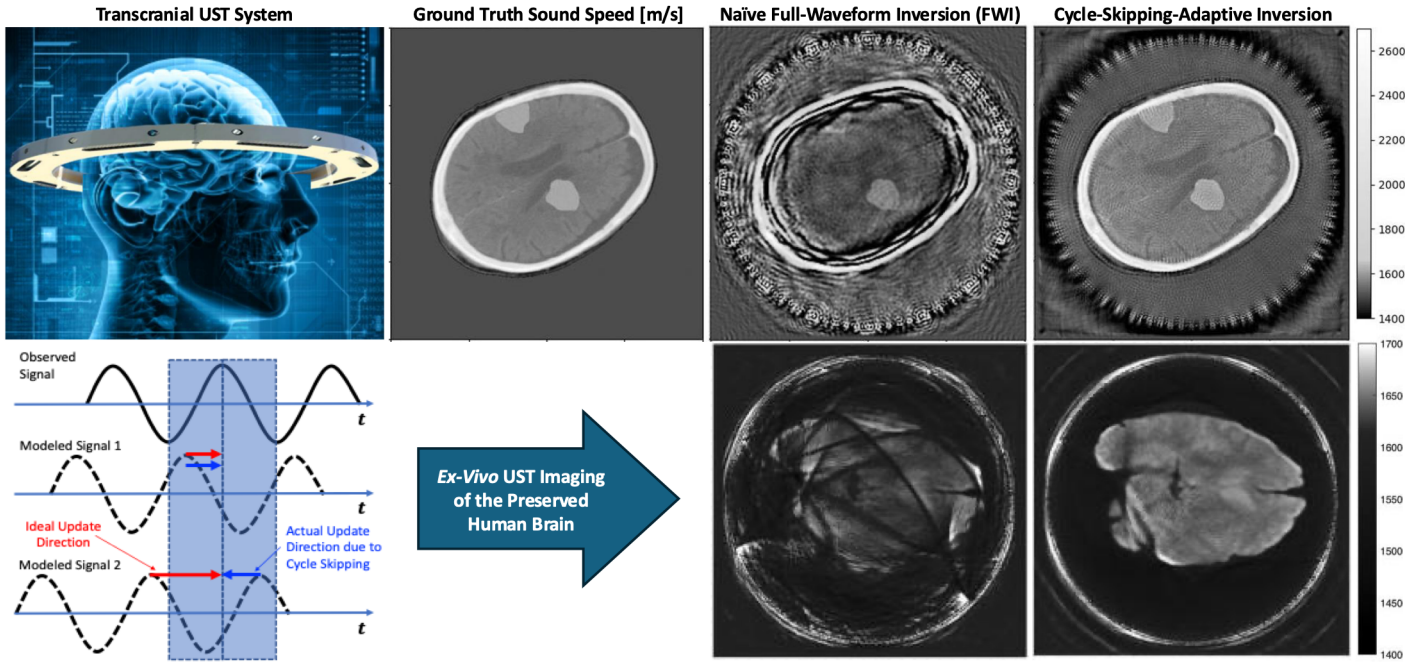

Fig. 3. Whole-brain transcranial UST enabled by adaptive Inversion algorithms[3,4] designed to overcome cycle skipping in conventional FWI.

D. FUTURE RESEARCH DIRECTIONS AND FUNDING STRATEGY

My research advances quantitative ultrasound imaging by developing robust, physics-based FWI algorithms for UST. In contrast with conventional pulse-echo ultrasound, which only has access to backscattered reflections, UST also captures transmitted (or forward-scattered) waves from all angles in a closed-ring geometry. FWI reconstructs spatial profiles of sound speed and attenuation by iteratively minimizing the difference between simulated and measured

waveforms. However, FWI can converge to false minima via *cycle skipping* when simulated waveforms lock onto the wrong cycles in the measured data (**Fig. 3**). My research addresses this challenge through 2 complementary strategies:

1) Low-Frequency Data Acquisition: Using lower-frequency ultrasound imaging hardware, we can expand the convex region around the true minimum, making it easier for the simulated waveform to reliably lock onto the correct cycle of the measured waveform over a broader range of initial sound speed guesses.
2) Forms of FWI Robust to Cycle Skipping: Alternative formulations of FWI[3,4] can mitigate or eliminate cycle skipping while maintaining sensitivity to the subtle diffraction patterns that encode structural information.

These advances establish a general computational imaging framework for making FWI reliable in complex biological media and enable the clinical applications described below.

Breast Cancer Screening: The long-term clinical goal is to provide quantitative maps of breast tissue properties that improve cancer detection and objective assessment of treatment response while addressing the limitations of conventional ultrasound and offering a low-cost ionizing-radiation-free alternative to MRI and CT. Building on my **NIH K99/R00 Pathway to Independence Award (K99-EB037080)**, I plan to pursue an **NIH R01** or **DoD Breast Cancer Research Program (BCRP)** proposal focused on translating 3D UST to breast cancer screening and monitoring. Under the K99/R00, I am developing cycle-skipping-robust formulations of FWI[3,4] (**Fig. 3**) that can recover high-resolution tissue properties in challenging cases. These robust FWI methods also establish the foundations for imaging in highly heterogeneous tissues beyond the breast, including tissues surrounding bone.

Transcranial UST Imaging: Rapid assessment of acute neurological disease, particularly stroke, can be limited by the availability, accessibility, and logistical constraints of CT and MRI. Reliable whole-brain UST imaging through the skull (**Fig. 3**) would enable portable, quantitative assessment of brain pathology at the point-of-care. The central scientific challenge is the strong contrast between skull and brain tissue—and the associated mode conversions between longitudinal and shear waves—that violate the assumptions of traditional acoustic models. I will address these challenges using finite-element and spectral-element solvers capable of capturing the full elastic wave equation in complex anisotropic media together with cycle-skipping-robust inversion strategies. These considerations make transcranial imaging an intellectually rich and technically engaging research direction. To pursue this line of inquiry, I am preparing an **NIH Trailblazer R21 application** focused on developing transcranial UST imaging systems that integrate advanced data acquisition and physics-driven reconstruction algorithms to compensate for skull-induced aberrations. Results from this project, together with ongoing work under the R00 phase of my award (3D FWI for multi-row ring-array UST[2]), will form the foundation for a **DP2 (NIH Director's New Innovator Award)** proposal to build the world's first 3D whole-brain UST system.

Quantitative Liver Imaging: The growing clinical burden of metabolic dysfunction-associated steatohepatitis (MASH) creates a need for accessible methods to quantify liver fat and support longitudinal monitoring without repeated biopsy or expensive imaging techniques such as MRI proton-density fat fraction. My research extends full-wave modeling and inversion to conventional handheld pulse-echo ultrasound systems[5], creating a path toward quantitative tissue characterization using hardware already widely deployed in clinical practice. Because sound speed decreases with fat content in tissue, I aim to pursue sound-speed estimation in pulse-echo ultrasound through a dedicated **NIH R01** grant focused on providing an ultrasound-based quantitative approach to liver fat fraction measurement.

Open-Source Tools for FWI: Finally, as early-career faculty, I plan to pursue an **NSF CAREER Award** through the **Directorate of Mathematical and Physical Sciences (MPS)** to develop open-source tools and educational resources for FWI-based imaging. These ***community-driven resources will promote open and reproducible science*** while expanding the use of FWI across diverse imaging domains—including optics, ultrasound, elastography, and photoacoustics. The broader impact will be to transform FWI from a specialized method into a reusable framework for quantitative imaging, lowering the barrier to adoption and accelerating translation to multiple imaging modalities.

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[1]Duric, Nebojsa, Peter Littrup, and C. Kuzmiak. "Breast Ultrasound Tomography." *Breast Imaging* 6 (2018).
[2]Ali, Rehman, Gaofei Jin, Melanie Singh, Trevor Mitcham, and Nebojsa Duric. "3D Frequency-Domain Full Waveform Inversion for Whole-Breast Imaging With a Multi-Row Ring Array." *IEEE Open Journal of Ultrasonics, Ferroelectrics, and Frequency Control* (2025).
[3]Warner, Michael, and Lluís Guasch. "Adaptive Waveform Inversion: Theory." *Geophysics* 81, no. 6 (2016): R429-R445.
[4]Ali, Rehman, Trevor Mitcham, Israel Owolabi, Sarah McConnell, and Nebojsa Duric. "Frequency-Differencing Strategy to Kickstart Full-Waveform Inversion Without Cycle Skipping." *JASA Express Letters* 5, no. 1 (2025).
[5]Ali, R., Mitcham, T. M., Doyley, M. M., Duric, N., & Dahl, J. J. (2026). Wave-Equation Migration Velocity Analysis for Multistatic Synthetic Aperture Ultrasound. arXiv preprint arXiv:2604.27428. [https://github.com/rehmanali1994/WEMVA]