Research Statement

Yamin Arefeen, Ph.D

Magnetic Resonance Imaging (MRI) enables critical assessment of patient health without ionizing radiation but is prohibitively expensive and inaccessible to many patients. My overall research goal is to make MRI the workhorse for noninvasive diagnostic imaging, treatment planning, and monitoring across the lifespan and beyond current economic barriers. Towards this end, I develop **computational AI methods for MRI through a holistic consideration of the diagnostic imaging pipeline**. My future lab will jointly use the available **hardware** at the scanner, **the interplay of biological tissue and MR physics to design acquisitions**, and novel **machine learning methods to reconstruct** images. To ensure clinical impact, my research group will actively **collaborate with clinicians** and industry partners. To realize this vision, I will pursue two thrusts in the first 5-10 years:

Project 1: *Accessible, Robust Early-Life Imaging Combining Foundation Models and Imaging Physics*

Significance: MRI enables brain assessment during the critical phase of early-life development. For example, Fetal MRI aids in diagnosis of intracranial haemorrhage and ischaemic brain injury [1,2], and MRI of infants inside the NICU improves decisions on surgical interventions compared to Ultrasound [3]. However, motion and long scan times precludes MRI access to many early-life patients [4], so there is a pressing need to develop modern computational MR methods [5] for the challenging setting of early life imaging. *Project 1 will combine MR Physics and advanced generative foundation modeling for robust of early life imaging in the presence of messy, real-world, and limited early-life MRI data.*

- *Aim 1.1: Generative models for motion robust in-NICU neonatal MRI with limited, noisy data*
- *Aim 1.2: Adapting pre-trained foundation models on public adult MRI data for in-NICU neonatal MRI*
- *Aim 1.3: Applying models for robust fetal MRI with an extended dataset and MR pulse sequence design*

Funding: [Public: NSF, NIHR01, NIHR21, ONR] [Industry: Aspect Imaging, Siemens, GE]

Collaborators: Texas Children's, UT Austin Dell Children's, Boston Children's, Aspect Imaging

Project 2: *Single-Scan, Fast, Comprehensive Abdominopelvic Cancer Imaging*

Significance: Varied images acquired with multi-parametric MRI (mpMRI) serves as a critical tool for assessment of many abdominopelvic cancers [6,7]. However, this entails lengthy scans that impart substantial monetary and physical burden on patients who are already distressed about their health. As a result, an opportunity exists to exploit the redundant information in mpMRI with computational AI to substantially reduce costs suffered by both patients and hospitals for abdominopelvic imaging. *Project 2 will develop a single scan for mpMRI of abdominopelvic cancer imaging that will replace the cumbersome standard acquisition through multi-modal self-supervised computational AI-based reconstruction methods.*

- *Aim 2.1: Multi-parametric prostate cancer MRI with self-supervised learning*
- *Aim 2.2: Efficient rectal cancer imaging with sharp, 3D volumetric MRI*
- *Aim 2.3: Developing a single, 3D MRI sequence sensitive to T_1 ,T_2 , and Diffusion for abdominopelvic cancer*

Funding: [Public: NIHR01, NIHR21, CPRIT, NIBIB] [Seed: UT Austin-MD Anderson JCCO]

Collaborators: MD Anderson (Body Radiologists: Dr. Gaiane Rauch, Dr. Tharakeswara Bathala)

My PhD and Postdoctoral experience in developing computational AI methods to address clinically impactful challenges in MRI holistically uniquely positions me to tackle the proposed research program. My previous research combined MR physics with AI for mpMRI [8-13], considered hardware, MR physics, and computation for accelerated Fetal MRI [13-16], and established methods to train generative models given messy, real-world clinical data for accelerated in-NICU neonatal and adult stroke imaging [17-20]. I actively **worked with clinicians** at Boston Children's Hospital, Dell Children's Hospital, Martinos Center, Harvard Medical School, and MD Anderson and **industrial partners** at Aspect Imaging, Siemens, and GE Healthcare towards translating these methods to clinical practice. I plan on receiving **funding for these projects** from governmental agencies including the NIH, CPRIT, NIBIB, NSF, and ONR and industrial collaborators including Siemens, GE, and Aspect Imaging. I will train **future students** to be experts in AI, signal processing, MRI physics, and clinical translation. Finally, I will continue my close relationship with **MD Anderson and Dell Children's**, and I will establish collaborations with other hospitals in Houston like **Texas Children's**. Long term, my goal is to **develop methods to make MRI as routine and accessible as X-ray and CT** so that cost, fear, and discomfort never precludes a patient from receiving the imaging care that they need.

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1: Accessible and Robust Early-Life Imaging Combining Foundation Models and Imaging Physics

Aim 1.1: Generative models for motion-robust, in-NICU neonatal MRI with limited, noisy data

Motivation + Previous work: Neonatal MRI monitors brain abnormalities during development, but inability to remain still renders MRI inaccessible to many in-NICU patients. Adult MRI addresses motion by accelerating scans with computation and AI to reduce the likelihood of movement, but sparse training data precludes application of machine learning in the NICU. In response, I collaborated with UT Dell children's and Aspect Imaging to gather a novel in-NICU neonatal MRI dataset, proposed machine learning methods to train a generative model given messy, real-world clinical data, and performed a clinical validation study showing that images reconstructed from $1.5\times$ less scan time with the proposed generative model are non-inferior to the slower standard-of-care images [17-19]. Fig 1.A displays an example comparison.

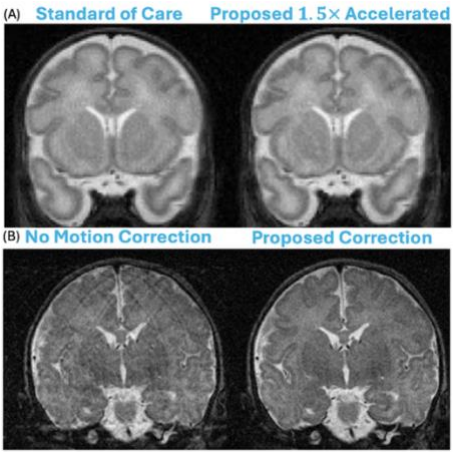

Fig 1: Proposed reconstructions for motion robust in-NICU MRI.

Future Goals: In addition to reducing scan times, motion artifacts in MRI can be mitigated by incorporating motion into the physical measurement model and reconstructing both a clean image and motion parameters. The previously described **generative model will be leveraged as a prior** to solve the physics-based MRI motion model as generative inverse problem solvers are measurement model agnostic. Preliminary results on 2D acquisitions in Fig 1.B Illustrates reduced motion artifacts with the proposed approach. We will **extend the algorithm to 3D acquisitions** and perform a **reader study with collaborators at UT Dell Children's** to verify the clinical utility of the motion-corrected images.

Aim 1.2: Adapting pre-trained foundation models on public adult MRI data for in-NICU neonatal MRI

Previous Work: The development of foundation models, like large language models, and corresponding scaling law indicate that model performance substantially improves with access to vast training data. Previously, in collaboration with **UT Austin Dell Medical,** I trained a generative foundation model on publicly available 3D MRI volumes from over 4000 adult subjects with varying MR contrasts [20]. The generative model was then fine-tuned on local data from just 20 stroke patients at UT Dell Medical. A clinical validation study demonstrated that the fine-tuned foundation model reduced scan time of stroke MRI by a factor of $2.5\times$ and maintained non-inferior image quality in comparison to the standard of care [20].

Future Goals: We suspect that performance of our generative model proposed in Aim1.1 will be bottle-necked by our limited training data. To address this, we will adapt the development strategy proposed for our stroke generative model to train a **new foundation model on wider range of public MRI data**, spanning a range of anatomies, contrasts, scanners, and magnetic field strengths. Then, the **model will be fine-tuned on our in-NICU dataset** with strategies like low-rank adaption and modified hyperparameter selection. While most public repositories contain data from adult subjects, we hypothesize that training on a large corpus of measurements will help the model learn a more general representation that efficiently adapts to in-NICU neonatal MRI when fine-tuned on our data in comparison to training from scratch with just our data. Experiments on accelerated MRI reconstruction and motion correction will characterize the benefit of pre-training, and we will collaborate with UT Dell Children's to evaluate the utility of our images.

Aim 1.3: Applying foundation models for robust fetal MRI with an extended dataset and MR pulse sequence design

Motivation + Previous Work: Fetal brain MRI enables evaluation of subtle brain abnormalities during the critical phase of fetal development, but frequent and unpredictable motion precludes widespread accessibility of fetal MRI. In response, I exploited MR physics to modify the T_2-weighted fetal MR pulse sequence, improving acquisition efficiency [14,15]. Fig 2. Shows initial experiments in

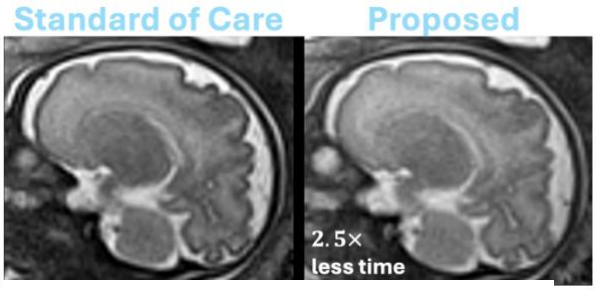

Fig 2: MR Physics for Rapid Fetal MRI

pregnancy, where the proposed approach maintains similar image quality with 2.5x less scan time. I also proposed a method that exploits external hardware to restrict the field-of-view to just the fetal brain, further improving scan efficiency [16]. Versions of this work [14] was amongst the top 5% of accepted submissions at ISMRM (the largest conference in the MRI field) and I wrote a successfully funded NIH R03 grant, titled "Rapid Fetal HASTE MR Imaging," and the Neuro-Training-Program Fellowship based on this work.

Future Goals: I will combine learned models with MR physics for robust fetal MRI. First, in collaboration with Texas Children's Hospital and Boston Children's hospital, I will collate a novel dataset of fetal MRI data to be used for model training. Then, we will take the foundation model trained from Aim 1.2 and fine-tune it to our fetal MRI data so that it can be used as a prior for accelerated MRI or motion correction inverse problems. This **learned model will then be combined with the previously proposed pulse sequence modifications** to produce a fetal protocol accelerated by both optimization of MR physics and learned priors. The strategy will be applied to clinical fetal MRI scans with the goal of substantially reducing scan time and increasing motion robustness, and images will be evaluated in close collaboration with pediatric radiologists.

2: Single-Scan, Fast, Comprehensive Abdominopelvic Cancer Imaging

Aim 2.1: *Multi-parametric prostate cancer MRI with self-supervised learning*

Motivation + Previous Work: MRI serves as a non-invasive replacement for TRUS biopsies when monitoring Prostate Cancer, but the multi-parametric Standard-of-care (SOC) exams incur substantial burden on both the hospital and patient to acquire, and infeasibility of acquiring fully sampled data in mpMRI precludes application of supervised machine learning to develop priors. To address this limitation, I utilized the MR Bloch equations to learn compact latent representation that serve as a temporal priors for signal dynamics [9] and combined this with self-supervised AI trained on just the acquired data [10,11]. I also optimized the acquisition with the Cramer-Rao-Bound by auto-differentiating through MR physics to improve SNR efficiency [13]. This work won the ISMRM magna cum laude award for being a top 15% submission.

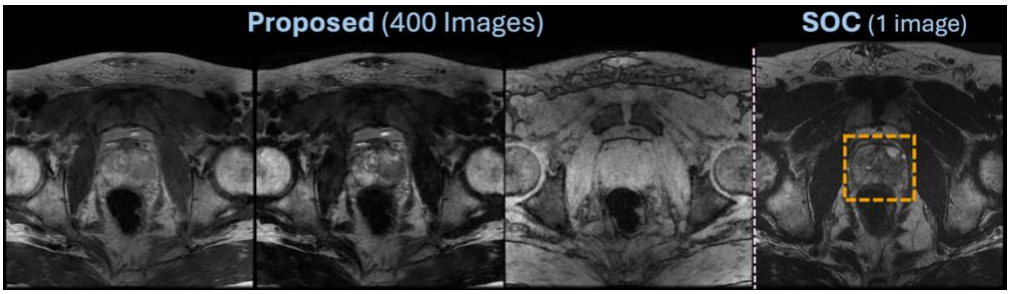

Fig 3: The proposed yields 400 images in one 6-minute scan.

Future Goals: Using my mpMRI work, I will **model the physics of structural prostate cancer acquisitions to produce a time-series of multi-contrast T_2-weighted images from a single scan**. Fig 3 shows preliminary data where the proposed approach produces multiple images with varying contrasts while the SOC yields a single image, given the same 6-minute scan time.

I will perform a reader study with collaborators at MD Anderson to determine if our multi-contrast approach adds diagnostic value. I will develop an implementation of the algorithm that runs in clinical times on the scanner. I have previously implemented clinical reconstruction algorithms for multi-contrast knee MRI at Stanford's Lucile Packard Children's Hospital, and I will use a similar approach for this project.

Aim 2.2: *Efficient rectal cancer imaging with sharp, 3D volumetric MRI*

Motivation: High-resolution MRI of rectal cancer helps clinicians decide whether to take patients directly to surgery or apply neoadjuvant chemoradiation to shrink the tumor first. Current standard of care rectal cancer imaging first uses a set of 2D, multi-planar MRI sequences to identify the lesion. Then, a clinician prescribes an imaging plane orthogonal to the lesion based on the 2D images, and second 2D MRI scan acquires images along this prescribed plane for best visualization of the tumor. This workflow requires real-time feedback from a clinician, and errors in the prescription necessitate multiple rounds of feedback, all while the patient waits on the MR Scanner table. This increases the duration of the uncomfortable scan, leading to motion artifacts and increased monetary costs for the patient.

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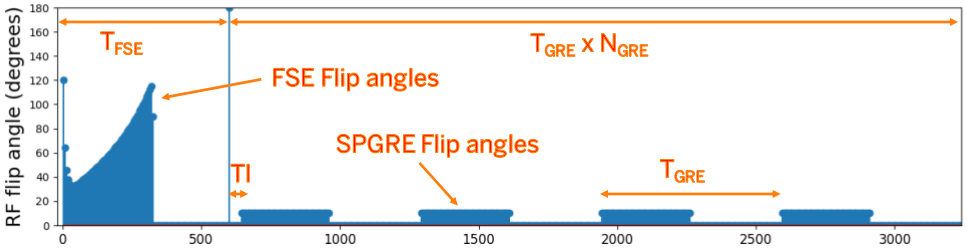

Fig 4: Sequence to adapt for high-resolution, 3D Rectal Cancer Imaging

Future Goals: High-resolution, isotropic 3D MRI obviates the need for two scans acquired with real-time feedback, as the single 3D scan can be retrospectively reformatted to view the optimal orthogonal plane. However, the standard-of-care persists because 0.6 mm^3 3D MRI either takes too long or suffers from significant blurring that precludes diagnostic utility. In response, **I will develop a 3D MRI sequence for Rectal Cancer that simultaneously achieves the desired resolution and yields sharp images**. Our preliminary work with prostate MRI developed a sequence, shown in Fig 4, that reconstructs multiple, time-resolved images from a single 5-minute scan with 3D reformat capability. Unlike standard 3D MRI, the technique models signal evolution, thus leading to substantially reduced image blur. To adapt this sequence to rectal cancer with higher resolution requirements, I will remove the gradient echo portions for lengthier echo trains and use shorter TRs for improved scan efficiency. In addition, I will combine our previously proposed self-supervised spatial prior learning with our knowledge of the physics to enable reconstruction from the ill-posed inverse problem. Fig 5 displays preliminary self-supervised AI for prostate cancer reconstruction. In collaboration with MD Anderson, a clinical validation study will analyze if standard 2D and proposed 3D provides the same diagnostic information and if time is saved by replacing the 2D protocol with a single scan.

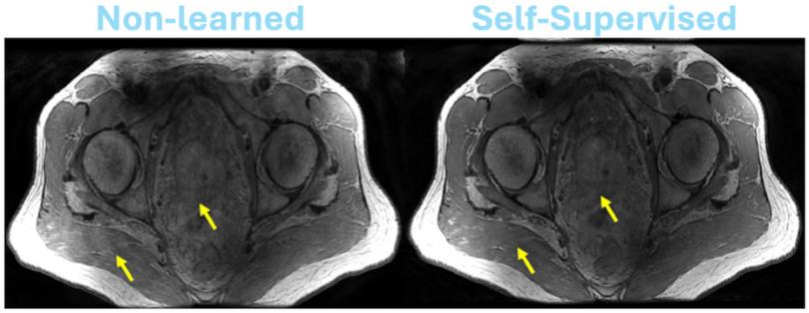

Fig 5: Initial self-supervised reconstructions on prostates.

Aim 2.3: *Developing a single, 3D MRI sequence sensitive to T_2 and diffusion for abdominopelvic cancer*

Motivation: Abdominopelvic cancer MRI relies heavily on three tissue parameters, T_2, T_1, and diffusion, requiring three separate acquisitions resulting in a lengthy 45-minute exam, shown in Fig 6.A. While each parameter highlights different tissue properties, redundant physics and structural information exists.

Future work: I will develop **a single MRI pulse sequence simultaneously sensitive to T_2, T_1, and diffusion**. The pulse sequence will be designed and optimized with the Bloch equations to achieve parameter sensitivity. The reconstruction inverse problem will exploit shared spatial and temporal information across the three parameters through the self-supervised mpMRI reconstruction techniques developed in Aims 2.1 and 2.2. As illustrated in Figure 6.B, by exploiting shared information, both in the MR physics and spatial image structure, I aim to develop a single scan that estimates relevant mpMRI for abdominopelvic cancer in substantially less time than the current standard of care, reducing cost and burden for both patients and hospitals.

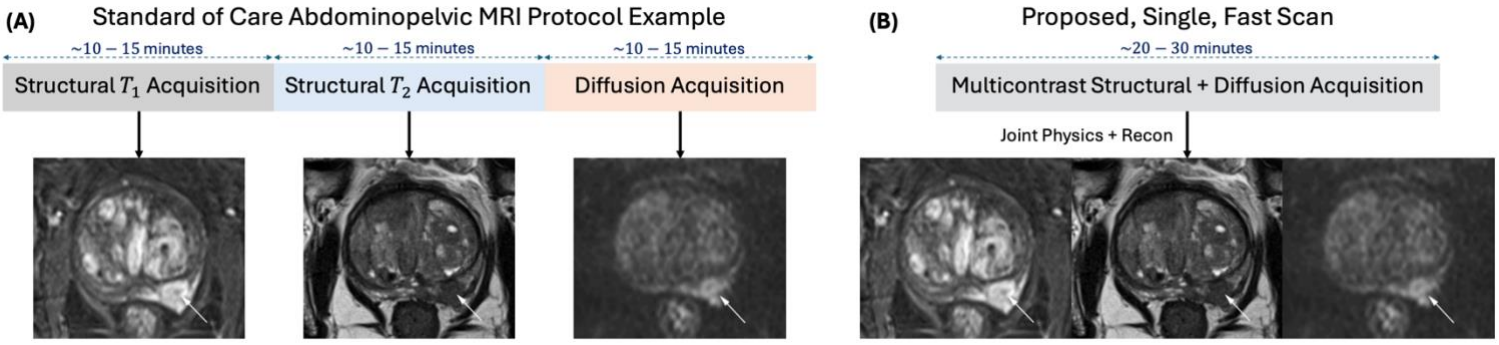

Fig 6: The standard-of-care abdominopelvic cancer examination requires three separate scans. The proposed method will estimate all mpMRI information through joint physics and reconstruction from a single scan.

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