# COVER PAGE

Title

Impact of Social Determinants on Atrial Fibrillation Symptom Burden and Management: A Rural Health Initiative

Principal Investigator

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# LAY ABSTRACT

Atrial fibrillation (AF) is a common heart rhythm problem that affects millions of Americans. It can significantly impact a person’s quality of life and increase their risk of stroke and heart failure. Doctors typically manage AF based on how much it bothers patients, but we don’t fully understand how a person’s social and economic circumstances affect their symptoms and treatment. Our research aims to fill this gap by studying how factors like where people live, their race or ethnicity, and their economic status influence their AF symptoms and the care they receive.

The proposal funding will support a study that will enroll participants from areas with limited access to care. We will use a mobile and web-based questionnaire to regularly check how AF is affecting participants’ quality of life. The AF quality of life reporting will be accompanied by monitoring the heart rhythm over the course of the study. We aim to identify what factors may be leading to disadvantages and advantages in the improvement of symptoms over time. We think that geographical factors, like living in a rural neighborhood, may affect how symptoms and quality of life are reported. We also think that patients from minority groups or with lower incomes might be less likely to receive certain advanced treatments, even when their symptoms are just as severe as other patients.

By understanding these patterns, we can develop better ways to care for all AF patients, regardless of their background. Our findings could lead to new policies and treatment approaches that ensure everyone with AF receives fair and effective care. Ultimately, this research could help reduce health disparities and improve the lives of many people living with this common heart condition.

# SPECIFIC AIMS

Atrial fibrillation (AF) is the most common cardiac arrhythmia, affecting millions of Americans and causing significant morbidity and mortality. Management of AF is primarily driven by patient-reported symptom burden, yet there are critical gaps in our understanding of how social determinants of health (SDoH) influence these symptoms and subsequent treatment decisions. Our preliminary work has demonstrated that SDoH, particularly neighborhood deprivation and race-ethnicity, significantly impact quality of life in AF patients over time. However, other factors such as access-to-care, environmental pollution, and educational levels may also play an important role in how quality of life is reported.

Our project aims to extend our previous work to include how regional and geographical aspects of SDoH affect the progression of AF symptom burden, and how these SDoH factors may mediate clinical decision-making. Our overall object is to elucidate the complex relationships between SDoH, AF symptom progression, and clinical management strategies to inform equitable, patient-centered care approaches. We propose to do so through the following aims:

**1. Implement a remote monitoring system for assessing patient reported symptom and arrhythmia burden in participants with AF in areas with limited access to care.**

**1. Determine the impact of social determinants on the progression of both arrhythmia and symptom burden of AF over time.**

We will utilize our current satellite sites to recruit and implement remote monitoring using the Atrial Fibrillation Effect on Quality-of-Life (AFEQT) questionnaire to assess Af symptom burden using mobile and web-based platforms, accompanied with long-term monitoring of AF burden. We will subsequently evaluate the trajectory of AF symptom burden, alongside EMR-based clinical data, to identify areas of health inequity based on management and outcomes.

Our research will provide crucial insights into the role of SDoH in AF symptom progression and management, addressing a significant gap in cardiovascular health disparities research. Our findings will inform the development of targeted interventions and policy recommendations to improve equity in AF care.

# DETAILED PROPOSAL

## Significance

Atrial fibrillation (AF) is the most common cardiac arrhythmia, significantly impacting cardiovascular morbidity and mortality (1). AF management is primarily driven by patient-reported symptom burden, which directly influences treatment decisions (2). Our preliminary work has demonstrated that social determinants of health (SDoH), particularly neighborhood deprivation and race-ethnicity, significantly impact quality of life in AF patients over time. However, critical gaps remain in understanding how geographical factors intersect with SDoH to influence AF symptom progression and management strategies. The geographical impact on SDoH and AF management represents a crucial area of investigation. While racial and ethnic disparities in AF outcomes have been documented (3), the specific role of geography in mediating these disparities remains poorly understood. This knowledge gap limits our ability to provide equitable care across diverse regions, particularly in areas with limited access to specialized AF management. Our proposed research aims to address this gap by implementing a remote monitoring system for assessing patient-reported symptoms and arrhythmia burden in participants with AF in areas with limited access to care. This novel approach has the potential to overcome geographical barriers to care, providing crucial data on AF progression and management in previously understudied populations. The insights gained may fundamentally change how we manage patients with AF, particularly those in rural or underserved regions, ultimately contributing to more equitable cardiovascular health outcomes.

## Innovation

Our study attempts to tackle the complex interplay between social determinants of health (SDoH), geographical factors, and AF symptoms, while also evaluating the relationship between electrical burden of atrial fibrillation and the patient-reported symptom burden. By assessing the impact of overcoming geographical barriers in AF care by implementing a remote monitoring system for rural participants, we are able to evaluate the impact of SDoH and management strategies on AF progression in underserved populations. Rural populations are in particularly vulnerable to health disparities, as they are often excluded from clinical studies and have limited access to specialized care (4). By utilizing our approach of integrating patient-reported outcomes with arrhythmia data, we are able to assess multiple facets of AF burden and progression simultaneously. Our integrated symptom burden represents an advance over traditional assessment methods (2, 5), providing an approach may lead to more nuanced and individualized management strategies (6). By creating a longitudinal data collection system that combines monthly AFEQT assessments with repeat ECG monitoring, we are able to track both symptom and arrhythmia progression over time. Having both subjective and objective data will also allow us to create novel phenotypes of AF progression and trajectory. This approach challenges the current paradigm of AF management, which often relies on infrequent in-person visits. Our method has the potential to transform understanding and management of AF in underserved areas, addressing critical gaps in cardiovascular health disparities research (7).

## Approach

Our study will employ a mixed-methods approach to address the complex interplay between social determinants of health (SDoH), geographical factors, and atrial fibrillation (AF) symptoms. We will focus on implementing a remote monitoring system for assessing patient-reported symptoms and arrhythmia burden in participants with AF in areas with limited access to care. Our project builds off of preliminary work, seen in [Figure 1](#fig-afeqt), that demonstrates the impact of neighborhood deprivation on AF symptom burden over time. We found that increased levels of deprivation, which factor in income, education, household composition, and employment, were associated with worse AF symptom burden over time in a dose-dependent manner.

|  |
| --- |
| Figure 1: We evaluated AFEQT scores over a 12-month period, and stratified the changes in score by the National Deprivation Index (NDI). Participants in areas with worse or more deprivation showed minimal to no improvement in AFEQT scores regardless of treatment or intervention. This population is approximately 800 individuals from an urban area, seen at an academic hospital |

**Aim 1: Implement a remote monitoring system for assessing patient reported symptom and arrhythmia burden in participants with AF in areas with limited access to care.**

We will work with our information technology team to develop a mobile/web-based interface for monthly completion of the Atrial Fibrillation Effect on Quality-of-Life (AFEQT) questionnaire (5). The AFEQT questionnaire is a validated tool for assessing AF symptom burden and quality of life (5), and can be repeated in monthly (or greater) intervals. This questionnaire will be integrated with AF arrhythmia burden data from mobile cardiac telemetry devices, creating a comprehensive tracking system for patient symptom burden. Participant recruitment will leverage existing outreach programs in rural areas, including clinics in Vernal and Blanding, UT and Rock Springs, WY. Additional recruitment will focus on individuals that have rural addresses attending clinics at the University of Utah. Research coordinators will play a crucial role in enrolling participants and providing training on the mobile/web interface. Clinical data will be extracted from the electronic medical record, including mobile cardiac telemetry data, to provide a comprehensive view of AF management and outcomes.

*Remote Monitoring System Implementation:*

1. AFEQT Questionnaire: We will administer the validated Atrial Fibrillation Effect on Quality-of-Life (AFEQT) questionnaire (5) monthly via a secure web-based platform or mobile application. This frequent assessment will provide granular data on symptom progression.
2. ECG Monitoring: Participants, when clinically indicated, will receive short-term and long-term ECG recordings that can be used to assess the burden of arrhythmia. Telemetry will include both wearable and implantable devices if available.
3. Data Integration: We will develop a secure, HIPAA-compliant system to integrate AFEQT scores and ECG data, providing a comprehensive view of both subjective and objective AF burden.

To ensure efficacy and engagement, our research coordinators will routinely track and evaluate the remote monitoring system, providing feedback directly to participants on how to utilize the system. We will implement automatic reminders for AFEQT completion, with routine check-ins to address any technical issues or concerns. If technical issues arise, we will plan to obtain AFEQT scores through phone interviews or in-person visits, ensuring data continuity and quality.

**Aim 2: Determine the impact of social determinants on the progression of both arrhythmia and symptom burden of AF over time.**

To address this aim, we will collect comprehensive demographic and socioeconomic data during enrollment and utilize geospatial data to assess neighborhood-level SDoH factors. Additionally, we will incorporate geospatial techniques to map AF burden in relation to local SDoH factors, analyzing the relationship between geographical barriers to care and AF outcomes. We will obtain detailed clinical histories, including comorbidities such as hypertension, diabetes, obesity, heart failure, sleep apnea, as well as lab and imaging data, such as echocardiography. We will utilize data from clinic visits and encounters with arrhythmia specialists to determine management strategies, from non-invasive interventions, such as anti-arrhythmic drug therapy, to invasive procedures such as electrical cardioversion or arrhythmia ablation. Our longitudinal outcome analysis will focus on trends in AFEQT scores, examining overall and domain-specific changes (8), while also quantifying AF episodes, duration, and frequency from ECG data. We will employ mixed-effects models to evaluate the influence of geographical and socioeconomic factors on AF progression, building upon our previous work (9).

*Team Roles and Investigator Synergy:*

Our team is multidisciplinary, combining expertise in epidemiology and electrophysiology to address the complex interplay between social determinants of health and AF progression. The principal investigator, who is a currently a fellow in training in cardiac electrophysiology, Dr. Anish S. Shah, is an well-trained cardiovascular epidemiologist with experience in health disparities research. He brings with him additional outside mentors, including Alvaro Alonso, MD, PhD as a core mentor for his F32 fellowship, and Emelia J. Benjamin, MD, ScM as part of his fellowship with the AF Genetics Consortium, both who are well-recognized cardiovascular epidemiologists. The faculty mentor, Ravi Ranjan, MD, PhD is an electrophysiologist and clinical researcher with extensive extramural funding and experience in the clinical management of AF. In particular, Dr. Ranjan leads efforts to provide care to rural and underserved populations, including having rural clinics in Vernal and Blanding, UT. This team is supported by postdoctoral and clinical fellows with expertise in research study design and cardiovascular disease management, as well as division-wide cardiovascular biostatisticians.

This team composition ensures a synergistic approach, combining epidemiological expertise, clinical experience in rural settings, advanced statistical capabilities, and cutting-edge signal processing. The collaboration between epidemiology and clinical practice will enable us to translate findings into actionable insights for improving AF care in underserved areas. The integration of biostatistics and electrophysiology expertise will allow for robust analysis of complex, multidimensional data, enhancing our understanding of AF progression in relation to SDoH.

## Timeline and Deliverables

Our project timeline spans the upcoming year, with key activities and deliverables aligned with our 10-month funding period. In the first 3-6 months, we will focus on developing mobile technology and integrating it with ECG/telemetry data. Participant enrollment will commence in late fall, allowing us to begin collecting follow-up data from months 6-10. During this latter period, we will conduct preliminary analyses to assess feasibility. Key deliverables, both inside and outside of the immediate funding period, include:

* A technological product demonstrating the workflow for integrating AF rhythm burden and symptoms. -Preliminary data analysis and feasibility assessment by the end of the 10-month period.
* A poster presentation at a national meeting on epidemiology/social determinants, showcasing our initial findings and methodology.
* Continued data collection over the subsequent two years.
* Manuscript publication within 1-2 years of project initiation.
* Submission of an R21 or K23 grant application to further explore health disparities in AF management.

Long-term, we aim to incorporate our findings into the EPIC system, enhancing clinical decision-making for AF patients in underserved areas. We also intend to expand our findings into other symptom-driven disease conditions, such as congestive heart failure. This timeline and set of deliverables allow us to establish the foundation of our integrated monitoring system, begin data collection, and set the stage for future in-depth analyses and broader implementation.

## Research Environment

The University of Utah provides a supportive environment for cardiovascular and health equity research. Key resources include:

* Health Sciences Center (HSC): Offers a comprehensive biobank, large datasets, and collaborative opportunities with the School of Medicine, College of Nursing, and Department of Biomedical Informatics.
* Center for High Performance Computing (CHPC): Provides resources for large-scale data analysis and computational modeling.
* Community Engagement: Extensive network of outreach clinics in urban and rural areas, ensuring diverse participant recruitment and strong community ties.
* Support and Training Mentorship and Professional Development: Experienced faculty mentors, regular seminars, workshops, and journal clubs. = Grant Writing and Research Support: Office of Sponsored Projects (OSP) assistance for grant writing, budget preparation, and regulatory compliance.

The University of Utah’s dynamic research environment, with its advanced facilities, collaborative opportunities, and strong institutional support, is well-suited to support the proposed study on the impact of social determinants on atrial fibrillation symptom burden and management.

## Data Sharing Plan

The data generated from this study will be de-identified and available upon reasonable request from other investigators at the University of Utah.

# EXTRAMURAL FUNDING PLAN

The proposed research aligns well with the NIH’s strategic goals to address health disparities and leverage technology to improve health outcomes. Based on the scope and innovative nature of our project, we plan to pursue the following extramural funding opportunities:

*NIH R21 Exploratory/Developmental Research Grant*

We intend to submit an R21 application to the National Heart, Lung, and Blood Institute (NHLBI) for the June 16, 2025 application deadline. The R21 mechanism is ideal for our novel, high-risk/high-reward approach to understanding the impact of social determinants of health (SDoH) on atrial fibrillation (AF) progression in underserved areas.

Our application will emphasize:

* The innovative use of remote monitoring in rural AF populations
* The potential for developing novel AF progression phenotypes
* The critical need for understanding geographical and SDoH impacts on AF management

*NIH K23 Mentored Patient-Oriented Research Career Development Award*

Concurrently, the principal investigator will apply for a K23 award from the NHLBI, with an expected application date of June 12, 2025. This career development award will support the PI’s growth as an independent clinical researcher focused on AF disparities and patient-centered outcomes.

* The PI’s commitment to a career in patient-oriented research on AF disparities
* The strong mentorship team available at our institution
* The potential for this research to lead to larger, multi-center studies on AF management in underserved populations

Both of these funding mechanisms will allow us to expand upon the preliminary data generated from this pilot grant. The R21 will provide resources to scale up our remote monitoring approach and conduct more comprehensive analyses of SDoH impacts on AF progression. The K23 will support the PI’s protected research time and additional training in advanced statistical methods and health disparities research. By pursuing both mechanisms, we aim to establish a strong foundation for a long-term research program addressing AF disparities, with the ultimate goal of improving outcomes for underserved AF patients.

# REFERENCES

1. Lip GYH, Fauchier L, Freedman SB, et al. Atrial fibrillation. Nature Reviews Disease Primers 2016;2:16016. Available at: [http://www.nature.com/articles/nrdp201616.](http://www.nature.com/articles/nrdp201616)

2. Darbar D, Roden DM. Symptomatic burden as an endpoint to evaluate interventions in patients with atrial fibrillation. Heart Rhythm 2005;2:544–549. Available at: [https://linkinghub.elsevier.com/retrieve/pii/S1547527105002006.](https://linkinghub.elsevier.com/retrieve/pii/S1547527105002006) Accessed March 27, 2024.

3. Magnani JW, Norby FL, Agarwal SK, et al. [Racial Differences in Atrial Fibrillation-Related Cardiovascular Disease and Mortality: The Atherosclerosis Risk in Communities (ARIC) Study](https://doi.org/10.1001/jamacardio.2016.1025). JAMA Cardiol 2016;1:433–441.

4. Sarraju A, Maron DJ, Rodriguez F. [Under-Reporting and Under-Representation of Racial/Ethnic Minorities in Major Atrial Fibrillation Clinical Trials](https://doi.org/10.1016/j.jacep.2020.03.001). JACC: Clinical Electrophysiology 2020;6:739–741.

5. Spertus J, Dorian P, Bubien R, et al. [Development and validation of the Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT) Questionnaire in patients with atrial fibrillation](https://doi.org/10.1161/CIRCEP.110.958033). Circ Arrhythm Electrophysiol 2011;4:15–25.

6. Essien UR, Kornej J, Johnson AE, Schulson LB, Benjamin EJ, Magnani JW. Social determinants of atrial fibrillation. Nat Rev Cardiol 2021;18:763–773. Available at: [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8516747/.](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8516747/) Accessed February 16, 2024.

7. Benjamin EJ, Thomas KL, Go AS, et al. Transforming Atrial Fibrillation Research to Integrate Social Determinants of Health: A National Heart, Lung, and Blood Institute Workshop Report. JAMA Cardiology 2023;8:182–191. Available at: [https://doi.org/10.1001/jamacardio.2022.4091.](https://doi.org/10.1001/jamacardio.2022.4091) Accessed November 20, 2023.

8. Holmes DN, Piccini JP, Allen LA, et al. Defining Clinically Important Difference in the Atrial Fibrillation Effect on Quality-of-Life Score. Circulation: Cardiovascular Quality and Outcomes 2019;12:e005358. Available at: [https://www.ahajournals.org/doi/10.1161/CIRCOUTCOMES.118.005358.](https://www.ahajournals.org/doi/10.1161/CIRCOUTCOMES.118.005358) Accessed April 8, 2024.

9. Shah AS, Ongtengco A, Qiao V, et al. Association Between Family History and Early‐Onset Atrial Flutter Across Racial and Ethnic Groups. Journal of the American Heart Association 2024;13:e032320. Available at: [https://www.ahajournals.org/doi/full/10.1161/JAHA.123.032320.](https://www.ahajournals.org/doi/full/10.1161/JAHA.123.032320) Accessed May 27, 2024.

# BIOGRAPHICAL SKETCHES

## 

NIH-formatted biosketches on the following pages for…

## Principal Investigator - Anish S. Shah, MD, MS

## Faculty Mentor - Ravi Ranjan, MD

OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 01/31/2026)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

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|  |
| --- |
| NAME: Shah, Anish |
| eRA COMMONS USER NAME (credential, e.g., agency login): anishshah |
| POSITION TITLE: Postdoctoral Fellow |

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

|  |  |  |  |
| --- | --- | --- | --- |
| INSTITUTION AND LOCATION | DEGREE (if applicable) | END DATE MM/YYYY | FIELD OF STUDY |
| Brookhaven Community College, Farmers Branch, TX | OTH | 05/2007 | Emergency Medical Technician |
| Emory University College of Arts and Sciences, Atlanta, GA | BS | 05/2011 | Linguistics; Neuroscience & Behavioral Biology |
| Texas A&M University College of Medicine, College Station, TX | MD | 06/2016 | Medicine |
| Emory University, Atlanta, GA | MS | 05/2020 | Clinical Research |
| Emory University School of Medicine, Atlanta, GA | Resident | 06/2019 | Internal Medicine |
| University of Illinois, Chicago, IL | Fellow | 06/2024 | Cardiology Fellowship |
| University of Utah, Salt Lake City, UT | Fellow | 06/2026 | Electrophysiology Fellowship |

### A. Personal Statement

My long term goal is to become an independently funded clinical-investigator in neurocardiology with a focus on computational techniques to understand the role of the autonomic nervous system in sudden cardiac death and arrhythmia, including from the perspective of neuropsychological pathology. I aim to leverage my clinical knowledge, background in computer programming and data science, and my current research studying autonomic dysfunction by noninvasive measures, to better understand the neurocardiac axis.

As an undergraduate, I acquired skills in computer programming and data management during my linguistics thesis focused on word-processing and phonetics. During a summer research scholarship as a medical student, I enriched my programming and statistical skills conducting an investigation under the guidance of Scott Blackman, MD, PhD at John Hopkins University. We focused on detecting individuals at risk for cystic fibrosis related diabetes using GWAS analysis. As a medical resident, I continued to expand my research skills under the mentorship of Amit J. Shah, MD, MSCR, and began my work on heart rate variability (HRV) as a measure of autonomic function. My TL1 award allowed me to complete a Master of Science in Clinical Research, through which I am gaining additional skills in quantitative epidemiology, biostastistics, and grant writing. During my F32 award and cardiovascular fellowship, I developed additional signal processing computational genetics techniques, under the mentorship of Dawood Darbar, MD, to better understand the mechanisms behind arrhythmias - focusing particularly on that of atrial fibrillation. With a multidisciplinary team of electrophysiologists, geneticists, and epidemiologists, I have a network that can support my development into an independent investigator and clinical cardiac electrophysiologist.

Most recently, I have focused on understanding the triggers behind atrial fibrillation events, including the psychosocial factors that may contribute to the onset of episodes, and the weight and importance of symptom burden. This work has been supported by Ravi Ranjan, MD PhD, who serves as a clinical electrophysiologist and federally funded researcher, as well as Emelia J. Benjamin, MD, ScM, a cardiovascular epidemiologist. My goal for a future K23 award is to include how symptoms are manifested and affected in different clinical phenotypes of atrial fibrillation. Building towards that, I would like to develop a cohort that identifies different psychosocial factors that affect AF, which will be aided by the University of Utah Health Equity Pilot Award.

1. Shah A, Vaccarino V, Moazzami K, Almuwaqqat Z, Garcia M, Ward L, Elon L, Ko Y, Sun Y, Pearce B, Raggi P, Bremner J, Lampert R, Quyyumi A, Shah A. Autonomic Reactivity to Mental Stress is Associated with Cardiovascular Mortality. 2024.
2. Vaccarino V, Almuwaqqat Z, Kim JH, Hammadah M, Shah AJ, Ko YA, Elon L, Sullivan S, Shah A, Alkhoder A, Lima BB, Pearce B, Ward L, Kutner M, Hu Y, Lewis TT, Garcia EV, Nye J, Sheps DS, Raggi P, Bremner JD, Quyyumi AA. Association of Mental Stress-Induced Myocardial Ischemia With Cardiovascular Events in Patients With Coronary Heart Disease. JAMA. 2021 Nov 9;326(18):1818-1828. PubMed Central PMCID: PMC8579237.
3. Shah,Anish S.,. Stress Reactivity: Disturbances of the Neurocardiac Axis. Emory University; 2021. Available from: https://etd.library.emory.edu/concern/etds/tx31qj818
4. Shah AS, Lampert R, Goldberg J, Bremner JD, Li L, Thames MD, Vaccarino V, Shah AJ. Alterations in heart rate variability are associated with abnormal myocardial perfusion. Int J Cardiol. 2020 Apr 15;305:99-105. PubMed Central PMCID: PMC8019069.

### B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

|  |  |
| --- | --- |
| 2024 - 2026 | Electrophysiology Fellow, University of Utah, Salt Lake City, UT |
| 2020 - 2024 | Cardiology Fellow, University of Illinois Chicago, Chicago, IL |
| 2019 - 2021 | Postdoctoral Fellow, Emory University, Rollins School of Public Health, Department of Epidemiology, Atlanta, GA |
| 2016 - 2019 | Internal Medicine Resident, Emory University, School of Medicine, Atlanta, GA |
| 2013 - 2013 | Research Assistant, Johns Hopkins University School of Medicine, Department of Pediatric Endocrinology, Baltimore, MD |
| 2011 - 2012 | Tutor, Northlake College, Department of Physics, Irving, TX |
| 2010 - 2010 | Cellular Biology Teaching Assistant, Emory University, Department of Biology, Atlanta, GA |
| 2008 - 2009 | Research Fellow, College of Arts and Sciences, Emory University, Atlanta, GA |
| 2005 - 2007 | Learning Disability Tutor, Brainworks, Inc, Carrollton, TX |

Honors

|  |  |
| --- | --- |
| 2021 - 2024 | F32 Postdoctoral Fellow, NIH, NHLBI |
| 2019 | Georgia Clinical and Translational Science Alliance TL1 Postdoctoral Research Training Award (TL1TR002382, PI: Blumberg; and UL1TR002378, PIs: Garcia, Ofili, Phillips, Taylor), NIH/NCATS |
| 2018 | AHA Scientific Sessions Top Donors Meetin, American Heart Association – special invitation to discuss research with AHA leadership and top philanthropists |
| 2017 | Doctor's Dilemma (Medical Jeopardy) Emory Resident Team, Georgia ACP |
| 2015 | Research Symposium - 1st Place Oral Presentation, Texas A&M University College of Medicine |
| 2013 | Medical Student Research Program in Diabetes, National Institute of Diabetes and Digestive and Kidney Diseases |
| 2009 | Delores B. Aldridge Excellence in Service to a Diverse Community Award, Emory University |
| 2009 | Speaker to His Holiness the XIV Dalai Lama, Emory-Tibet Partnership – selected to represent Emory students in a meeting with the Dalai Lama in MacLeod Gange, India |
| 2008 | Scholarly Inquiry and Research at Emory - Research Fellow, Emory University |
| 2007 | EMT National Competition - 1st Place, Health Occupation Students of America |

### C. Contribution to Science

1. **Evaluation of interaction between stress and cardiovascular disease:**

The neurocardiac response to stress is manifest by the autonomic nervous system, and maladaptive responses can lead to autonomic dysfunction and cardiovascular disease. Heart rate variability (HRV), a marker of sinoatrial node function and a measure of sympathovagal balance, can be extracted from electrocardiography through signal processing techniques. Using HRV as a surrogate for the dynamic state of the autonomic nervous system, I was able to evaluate how multiple cardiovascular systems are affected by psychosocial stress. This has led to multiple first-author and co-authored manuscripts, as below. I have generally found that stress, both acutely and chronically, can lead to decreases in vagal activity and decreases in sympathetic activity, and associate with both future psychosocial distress, as well as maladaptive coronary physiology. The maladaptive response to stress particularly is of interest as I have shown it strongly associates with future cardiovascular mortality, despite known traditional cardiovascular risk factors and disease. My work has been supported by a TL1 award and an F32 award previously with my mentorship team.

* 1. Shah AS, Alonso A, Whitsel EA, Soliman EZ, Vaccarino V, Shah AJ. Association of Psychosocial Factors With Short-Term Resting Heart Rate Variability: The Atherosclerosis Risk in Communities Study. J Am Heart Assoc. 2021 Feb;10(5):e017172. PubMed Central PMCID: PMC8174247.
  2. Shah,Anish S.,. Stress Reactivity: Disturbances of the Neurocardiac Axis. Emory University; 2021. Available from: https://etd.library.emory.edu/concern/etds/tx31qj818
  3. Shah AS, Lampert R, Goldberg J, Bremner JD, Li L, Thames MD, Vaccarino V, Shah AJ. Alterations in heart rate variability are associated with abnormal myocardial perfusion. Int J Cardiol. 2020 Apr 15;305:99-105. PubMed Central PMCID: PMC8019069.
  4. Shah A, Alonso A, Whitsel E, Soliman E, Vaccarino V, Shah A. Association of Psychosocial Factors With Heart Rate Variability: The Atherosclerosis Risk in Communities Study. ; ahajournals.org (Atypon); c2020. Available from: https://www.ahajournals.org/doi/10.1161/circ.141.suppl\_1.P542 DOI: 10.1161/circ.141.suppl\_1.P542

1. **Atrial fibrillation phenotyping**:

I received specific training by electrophysiologists, epidemiologists, and geneticists who study mechanisms behind atrial fibrillation, including mentorship by members of the Atrial Fibrillation Genetics Consortium. My work has evaluated how electrocardiography-based changes in atrial fibrillation may represent genetic mechanisms behind atrial fibrillation. I have also assessed how machine learning can help distinguish between different genetic variants and their contributions to atrial fibrillation, particularly in underrepresented populations. This work has primarily led to try to better understand atrial fibrillation phenotypes, and how symptom burden may be affected by environmental factors. I will expand this work by understanding symptoms in AF in future research, and as part of my future K23 award.

* 1. Hill M, Chalazan B, Tofovic D, Chen Y, Shah A, Barney M, Diaz A, Konda S, Darbar D. Prevalence of disease-associated cardiomyopathy gene variants in ethnic minorities with atrial fibrillation. ; jacc.org (Atypon); c2023. Available from: https://www.jacc.org/doi/10.1016/S0735-1097%2823%2900465-5 DOI: 10.1016/S0735-1097(23)00465-5
  2. Shah AS, Ongtengco A, Qiao V, Chen Y, Diaz A, Hill M, Bhan A, Tofovic DS, Darbar D. Association Between Family History and Early-Onset Atrial Flutter Across Racial and Ethnic Groups. J Am Heart Assoc. 2024 May 21;13(10):e032320. PubMed Central PMCID: PMC11179838.

1. **Computational approaches in epidemiology and biostatistics**:

With a strong mathematical and biostatistical background, strengthened by my Master of Science training, and my previous experience as a computer programmer, I have worked to develop several open source software toolkits, published primarily in the R language on a peer-reviewed system called the Comprehensive R Archival Network (CRAN). These software publications on CRAN focus on the interpretation of cardiovascular data, including echocardiography and coronary catheterization records as well as signal processing approaches to manipulate electrocardiography and intracardiac recordings of electrophysiology studies. My work has also touched on causal-based modeling and biostatistical techniques, including developing harmonic regression approaches for rhythmic data. My software has been shared online, and has been utilized by hundreds of other researchers across the world.

* 1. Shah,Anish S,. card: Cardiovascular Applications in Research Data. R package v0.1.0; 2020.
  2. Shah,Anish S.,. rmdl: Language to Manage Many Models. 2024 May 02.
  3. Shah,Anish S.,. EGM: Evaluating Cardiac Electrophysiology Signals. 2024 May 23.

OMB No. 0925-0001/0002 (Rev. 10/2021 Approved Through 09/30/2024)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.  
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Ranjan, Ravi

eRA COMMONS USER NAME: RRANJAN

POSITION TITLE: Professor of Medicine

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

| INSTITUTION AND LOCATION | DEGREE  (if applicable) | Completion Date  MM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| Indian Institute of Technology, Kanpur, India | B. Tech | 05/1992 | Electrical Engineering |
| Johns Hopkins University, Baltimore, MD | MSE | 05/1995 | Biomedical Engineering |
| Johns Hopkins University, Baltimore, MD | PhD | 05/1998 | Biomedical Engineering |
| Harvard Medical School, Boston, MA | MD | 06/2002 | Medicine |
| Massachusetts General Hospital, Boston, MA | Internship | 06/2003 | Internal Medicine |
| Massachusetts General Hospital, Boston, MA | Residency | 06/2005 | Internal Medicine |
| Johns Hopkins Hospital, Baltimore, MD | Fellowship | 06/2008 | Cardiovascular Medicine |
| Johns Hopkins Hospital, Baltimore, MD | Fellowship | 06/2010 | Clinical Electrophysiology |

# A. Personal Statement

I have extensive training and background in the field of cardiac electrophysiology. My work in this field ranges from studying ion channels at the subcellular level to doing whole organ level experiments and computational modeling. On the computational side, I have made models of individual sodium channels concentrating on the pore region to propagation of electrical activity on the surface of the heart. On the experimental side my experience ranges from doing single channel patch clamp experiments to isolated whole heart experiments and large animal chronic studies. My training and experience in the field of clinical electrophysiology has given me a detailed understanding of numerous arrhythmias and more importantly has generated numerous intriguing questions ranging from disease mechanisms to using technology to improve outcomes of electrophysiological procedures. My research has continuously been extramurally funded from the beginning.

My current research interests include arrhythmia mechanisms and ablation lesion formation. We are using large animal models of atrial fibrillation including a tachy-pacing canine and transgenic goat model to develop a better understanding of atrial fibrillation. We are doing serial high density mapping to see if there are any stable drivers that help in sustaining atrial fibrillation and if they are present how to identify them in a clinically useful manner. As post ablation lesion characterization we are developing ways to better create long term lesions while minimizing reversible edema formation. We have been going computational modelling of atrial and ventricular arrhythmias with the goal of identifying critical regions that sustain these arrhythmias that can be targeted with ablation.

In this project we are going to explore the use of radiation as a means of non-invasively ablating ventricular tissue for ventricular tachycardia. We are going to systematically study the structural and functional effects of radiation on cardiac tissue in a pre-clinical model using a combination of functional and imaging studies to establish the timeline of changes. We will make computational models to identify critical regions to target making use of the extensive expertise in MRI and computational modeling. We will test this in a pre-clinical model of ventricular tachycardia as well as patients who have VT. We have assembled an outstanding team covering Cardiac Electrophysiology, Radiation Oncology, Medical Physicists, MRI physicists, Biomedical Engineering and Biostatistics for this project with most of whom I have been collaborating for many years.

Ongoing and recently completed projects that I would like to highlight include:

1I01CX002758 (Ranjan, PI) 04/01/24-03/31/28

VA (CSRD) MERIT Award

Computational modeling guided ablation for atrial flutters

The goal of this project is to develop computer models of individual patients’ fibrosis and scar substrate and use that information to predict the most effective ablation therapy to terminate atrial fibrillation.

R01 HL162353 (Ranjan, MPI) 03/01/22 – 2/28/26

National Institutes of Health, NHLBI

Improved imaging of fibrosis in atrial fibrillation.

The goal of this project is to improve and validate atrial tissue substrate imaging for fibrosis.

R01 (Ranjan, PI) 09/01/2018-08/31/2023

National Institutes of Health, NHLBI

Myocardial substrate driven mechanistic insights into atrial fibrillation.

The goal of this project is to develop a mechanistic understanding of atrial fibrillation in a canine model.

Citations:

1. Lange M, Kwan E, Dosdall DJ, MacLeod RS, Bunch TJ, **Ranjan R.** Case report: Personalized computational model guided ablation for left atrial flutter. Front Cardiovasc Med. 2022;9:893752. eCollection 2022. PubMed PMID: 36187013; PubMed Central PMCID: PMC9521648.
2. Kamali R, Kump J, Ghafoori E, Lange M, Hu N, Bunch TJ, Dosdall DJ, Macleod RS, **Ranjan R.** Area available for atrial fibrillation to propagate is an important determinant of recurrence after ablation. JACC Clin Electrophysiol. 2021 Feb 19. Epub ahead of print. PMID: 33640348.
3. Swenson DJ, Taepke RT, Blauer JJE, Kwan E, Ghafoori E, Plank G, Vigmond E, MacLeod RS, DeGroot P, **Ranjan R.** Direct comparison of a novel antitachycardia pacing algorithm against present methods using virtual patient modeling. Heart Rhythm. 2020 Sep;17(9):1602-1608. PMID: 32438017.
4. Ghafoori E, Kholmovski EG, Thomas S, Silvernagel J, Angel N, Hu N, Dosdall DJ, MacLeod R, **Ranjan R.** Characterization of gadolinium contrast enhancement of radiofrequency ablation lesions in predicting edema and chronic lesion size. *Circ Arrhythm Electrophysiol.* 2017 Nov;10(11). PMID: 29079664; PMCID: PMC5693314.

# B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

01/2024 - Chief, Arrhythmia Service, University of Utah Hospital

07/2022 - SSPT NHLBI Study section member (terms ends in 2026)

01/2022 Plenary Speaker for Personalized AF Meeting: European Union Horizon 2020 Research

And Innovation Program.

01/2022 - Associate Editor: Journal of Interventional Cardiac Electrophysiology

03/2021 Reviewer for NIH: Small Business: Cardiac and Surgical Devices Study Section

07/2021- Professor of Medicine (Tenured), University of Utah

07/2021- Adjunct Professor of Biomedical Engineering, University of Utah

11/2020 Reviewer for NIH: Small Business: Cardiac and Surgical Devices Study Section

07/2020 -12/23 Director, Electrophysiology Labs, University of Utah Hospital

07/2020 - Editorial Board: JACC EP

03/2020 Reviewer for NIH: Special Emphasis Panel ZRG1-SBIB-A-90

01/2020 Reviewer for NIH: Special Emphasis Panel ZRG1-PSE-D-55

12/2019 - Editorial Board: Heart Rhythm O2

10/2019 Reviewer for NIH: Emerging Imaging Technologies and Applications Study Section

06/2019 Reviewer for NIH: Imaging Guided Interventions and Surgery Study Section

03/2019 Reviewer for NIH: Secondary Analyses of Existing Datasets in Heart, Lung, and Blood Diseases and Sleep Disorders

02/2019 Reviewer for NIH: NHLBI Clinical Trial Pilot Studies (R34), (2) Single-Site Investigator-Initiated Clinical Trials (R61/R33), and (3) Clinical Coordinating Center for Multi-Site Investigator-Initiated Clinical Trials (Collaborative UG3/UH3) and Data Coordinating Center for Multi-Site Investigator-Initiated Clinical Trials (Collaborative U24).

11/2018 Review for NIH: SBIR Phase IIB Awards

07/2017 Grant Reviewer for NIH: Bold New Bioengineering Methods and Approaches for Heart, Lung, Blood and Sleep Disorders and Diseases (R21)

02/2017 Ad Hoc Reviewer, Electrical Signaling, Ion Transport, and Arrhythmias Study Section [ESTA] study section, National Institutes of Health

02/2017- Investigator, Norah Eccles Harrison Cardiovascular Research and Training Institute (CVRTI), University of Utah

01/2017 - Editorial Board: Journal of Interventional Cardiac Electrophysiology

01/2017 Reviewer for NHLBI special session on SBIR contract proposals.

07/2016-06/21 Associate Professor of Medicine (Tenured), University of Utah

11/2016- Adjunct Associate Professor of Biomedical Engineering, University of Utah

04/2015 Grant Reviewer, Cardiac Electrophysiology Clinical Peer Review Study Group,

American Heart Association

08/2011-11/16 Adjunct Assistant Professor of Biomedical Engineering, University of Utah

2010 Fellow, Heart Rhythm Society

08/2010-06/16 Assistant Professor of Medicine, University of Utah

Honors

05/2009 Young Investigator Award winner at the Annual Scientific Sessions of the Heart Rhythm Society.

10/2014 Finalist and Third Prize Winner at the Tenth Annual Northwestern Cardiovascular Young Investigators' Forum in Clinical Science

10/2015 Finalist and Third Prize Winner at the Tenth Annual Northwestern Cardiovascular Young Investigators' Forum in Basic Science

# C. Contribution to Science

**1. Ablation Lesion Creation and Visualization using Radiofrequency**: For the last few years my research has focused on using MRI in the field of cardiac electrophysiology with emphasis on identifying ablation lesions or lack thereof. I have been focusing on poor lesion formation as a potential cause of atrial fibrillation recurrence over time. Some of our recent work has shown that about half of delivered ablation lesions do not result in scar. Having the career development K23 award has allowed me to acquire many of the skills, especially MRI related to further carry out this work. The field of MRI in EP is new but has the potential to be quite big and impactful as it provides many unique abilities beyond the fact the there is no ionizing radiation.

1. Kholmovski EG, Silvernagel J, Angel N, Vijayakumar S, Thomas S, Dosdall D, MacLeod R, Marrouche NF, **Ranjan R**. Acute noncontrast T1-weighted magnetic resonance imaging predicts chronic radiofrequency ablation lesions. *J Cardiovasc*  *Electrophysiol.* 2018 Aug 14. doi: 10.1111/jce.13709. PMID: 30106244.
2. Thomas S, Silvernagel J, Angel N, Kholmovski E, Ghafoori E, Hu N, Ashton J, Dosdall DJ, MacLeod R, **Ranjan R.** Higher contact force during radiofrequency ablation leads to a much larger increase in edema as compared to chronic lesion size. *J Cardiovasc Electrophysiol.* 2018 Aug;29(8):1143-1149. PMID: 29777548; PMCID: PMC6105416.
3. Yamashita K, Kholmovski E, Ghafoori E, Kamali R, Kwan E, Lichter J, MacLeod R, Dosdall DJ, **Ranjan R**. Characterization of edema after cryo and radiofrequency ablations based on serial magnetic resonance imaging. J Cardiovasc Electrophysiol. 2019 Feb;30(2):255-262. doi: 10.1111/jce.13785. Epub 2018 Nov 21. PMID: 30375090
4. **Ranjan R,** Kato R, Zviman MM, Dickfeld TM, Roguin A, Berger RD, Tomaselli GF, Halperin HR. Gaps in ablation line as a potential cause of recovery from electrical isolation and their visualization using MRI. *Circ Arrhythm Electrophysiol*. 2011 Jun;4(3):279-286. PMID: 21493875

**2. Real Time MRI:** MRI allows visualizing detailed cardiac structure while doing EP procedures and as a result the ablation can be targeted to a very specific location preventing collateral damage. MRI can also provide real time feedback of ablation related tissue changes, which is a big deficiency under the current clinical practice. The field of real-time MRI is new and has the potential to fundamentally change how we do electrophysiology procedures. I have been working in the field of real-time for some time. We have used to identify gaps in real time and more recently have used to deliver cryo-ablation lesions.

1. Lichter J, Kholmovski EG, Coulombe N, Ghafoori E, Kamali R, MacLeod R, **Ranjan R.** Real-Time MRI guided cryoablation of the pulmonary veins with acute freeze zone and chronic lesion assessment. *Europace* 2018 Jun 5. PMID: 29878090.
2. Kholmovski EG, Coulombe N, Silvernagel J, Angel N, Parker D, MacLeod R, Marrouche N, **Ranjan R.** Real time MRI guided cryo-ablation – A feasibility study. J of Cardiovas Electrophysiol. 2016 May;27(5) 602-608. PMID: 26856381.
3. **Ranjan R**. Magnetic resonance imaging in clinical cardiac electrophysiology. *Critical reviews in biomedical engineering*. 2012; 40(5):409-426. PMID: 23339649
4. **Ranjan R**, Kholmovski EG, Blauer J, Vijayakumar S, Volland NA, Salama ME, Parker DL, MacLeod R, Marrouche NF. (2012) Identification and acute targeting of gaps in atrial ablation lesion sets using a real-time magnetic resonance imaging system. *Circ Arrhythm Electrophysiol*. 2012 Dec;5(6):1130-1135. PMID: 23071143

**3. Use of MRI in improving ablation procedure outcomes:** In the last 10 years we have been using MRI to better delineate the substrate leading to clinical arrhythmias, using MRI to understand the substrate progression, lesion maturation in pre-clinical models and humans and esophageal injury; all with the goal of improving outcomes and minimizing complications.

1. Yamashita K, Kwan E, Kamali R, Ghafoori E, Steinberg BA, MacLeod RS, Dosdall DJ, **Ranjan R.** Blanking period after radiofrequency ablation for atrial fibrillation guided by ablation lesion maturation based on serial MR imaging. J Cardiovasc Electrophysiol. 2020 Feb;31(2):450-456. doi: 10.1111/jce.14340. Epub 2020 Jan 21. PMID: 31916637.
2. Yamashita K, Quang C, Schroeder JD, DiBella E, Han F, MacLeod R, Dosdall DJ, **Ranjan R.** Distance between the left atrium and the vertebral body is predictive of esophageal movement in serial MR imaging. *J Interv Card Electrophysiol.* 2018 Jul;52(2):149-156. Epub 2018 Mar 12. PMID: 29532276; PMCID: PMC6033656.
3. Lichter J, Kholmovski EG, Coulombe N, Ghafoori E, Kamali R, MacLeod R, **Ranjan R**. Real-time magnetic resonance imaging-guided cryoablation of the pulmonary veins with acute freeze-zone and chronic lesion assessment. Europace. 2019 Jan 1;21(1):154-162. doi: 10.1093/europace/euy089. PMID: 29878090
4. Parmar BR, Jarrett TR, Burgon NS, Kholmovski EG, Akoum NW, Hu N, Macleod RS, Marrouche NF, **Ranjan R.** Comparison of left atrial area marked ablated in electro anatomical maps with scar in MRI. *J Cardiovasc Electrophysiol.* 2014 May;25(5):457-463. PMID: 24383404; PMCID: PMC4090328

**4. Computer Models of Cardiac Arrhythmias:** During my graduate studies, I developed and implemented models of cardiac activation ranging from single cells to tissue level. More recently, we have expanded those efforts in my group to validate more complex computer simulations. We are doing a prospective studies with me as the PI at Univ to Utah looking at using such models for guiding atrial flutter ablations. Similar model studies have been used to implant anti-tachycardia pacing in humans called the iATP and is now already implemented in the latest generation of ICDs made by Medtronic.

1. Kamali R, Kump J, Ghafoori E, Lange M, Hu N, Bunch TJ, Dosdall DJ, Macleod RS, **Ranjan R.** Area Available for Atrial Fibrillation to Propagate Is an Important Determinant of Recurrence After Ablation. JACC Clin Electrophysiol. 2021 Feb 19. Epub ahead of print. PMID: 33640348.
2. Swenson DJ, Taepke RT, Blauer JJE, Kwan E, Ghafoori E, Plank G, Vigmond E, MacLeod RS, DeGroot P, **Ranjan R.** Direct comparison of a novel antitachycardia pacing algorithm against present methods using virtual patient modeling. Heart Rhythm. 2020 Sep;17(9):1602-1608. PMID: 32438017.
3. **Ranjan R,** Tomaselli GF, Marban E. A novel mechanism of anodal stimulation predicted by bidomain modeling. *Circ Res.* 1999 Feb 5;84(2):153-156. PMID: 9933246.
4. **Ranjan R**, Ghafoori E, Blauer J, Dongdong D, Arevalo H, Prakosa A, Han F, Wall S, Freedman R, Mcgarry T, McLeod R, Trayanova N. Personalized MRI-Based Modeling Predicts Ventricular Tachycardia Vulnerability in Patients Receiving Primary Prevention ICDs. *Circulation*. 2016;134: A16247.

Complete List of Published Work:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/ravi.ranjan.1/bibliography/43869596/public/?sort=date&direction=ascending>

# BUDGET JUSTIFICATION

Our budget justification is for a total of $20,000 over a 10-month period. This budget will cover the costs of implementing a remote monitoring system for assessing patient-reported symptoms and arrhythmia burden in participants with atrial fibrillation (AF) in areas with limited access to care. We will utilize approximately 60% of the monthly budget to cover the cost of research coordinator time at the rural healthcare sites. We expect the coordinator to spend 15-20% of their weekly time on this project, including participant recruitment, training, and data collection. Approximately 30% of the budget will be allocated to the cost of developing and maintaining the mobile/web-based interface for the Atrial Fibrillation Effect on Quality-of-Life (AFEQT) questionnaire. We will collaborate with the information technology team to develop and host a web-based application for monthly completion of the AFEQT questionnaire.

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| Category | Role | Duration | Cost | Total |
| Personnel | Research Coordinator | 10 months | $1200 | $12,000 |
| Services | IT Development | 10 months | $800 | $8,000 |