Pre-Procedure Application of Machine Learning and Mechanistic Simulations Predicts Likelihood of Paroxysmal Atrial Fibrillation Recurrence Following Pulmonary Vein Isolation

Julie Shade[1,2] BS, Rheeda L. Ali[1] PhD, Dante Basile[1,2], Dan Popescu[1,3] BS, Tauseef Akhtar[4] MD, Joseph E. Marine[4] MD, David D. Spragg[4] MD, Hugh Calkins[4] MD, Natalia A. Trayanova[1,2,5] PhD

[1]Alliance for Cardiovascular Diagnostic and Treatment Innovation, Johns Hopkins University, Baltimore, MD USA.
[2]Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD, USA.
[3]Department of Applied Math and Statistics, Johns Hopkins University, Baltimore, MD, USA.
[4]Division of Cardiology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA.
[5]Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA.

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Highlights

- A combination of machine learning (ML) and mechanistic simulations of atrial fibrillation (AF) induction (SimAF) predicts AF recurrence following pulmonary vein isolation (PVI) with an average **validation sensitivity of 82%, specificity of 89%, and area under the curve (AUC) of 0.82.**
- Inclusion of features extracted from SimAF leads to **highly generalizable (excellent validation and testing results) AF recurrence risk prediction with minimal training data.**

Background

- Untreated AF leads to **stroke and heart failure.**[1]
- PVI leaves only **78% of patients free from AF** 12 months later.[2]
- **AF recurrence results in morbidity**, often requires repeat ablation with additional fibrotic substrate modification.[3]
- It is unknown how to determine, *before the PVI procedure*, which patients are likely to experience AF recurrence and might benefit from a more extensive initial ablation strategy targeting pro-arrhythmic regions of fibrosis.[4]
- **Goal:** to develop a methodology that combines personalized multi-scale modeling and machine learning to predict the risk of AF recurrence after PVI using only pre-procedural clinical images.

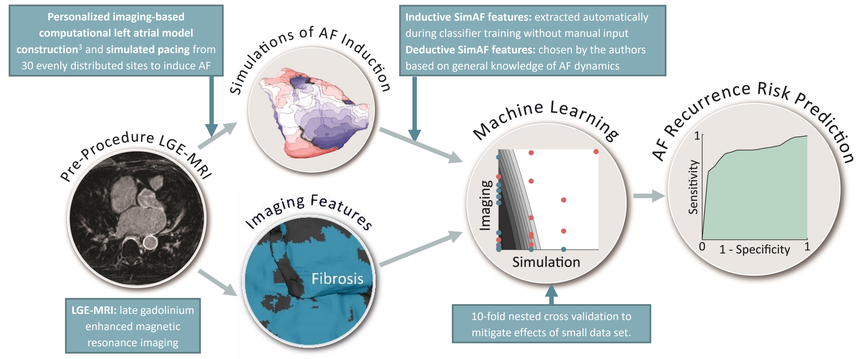
Overview

Characteristics of PxAF cohort

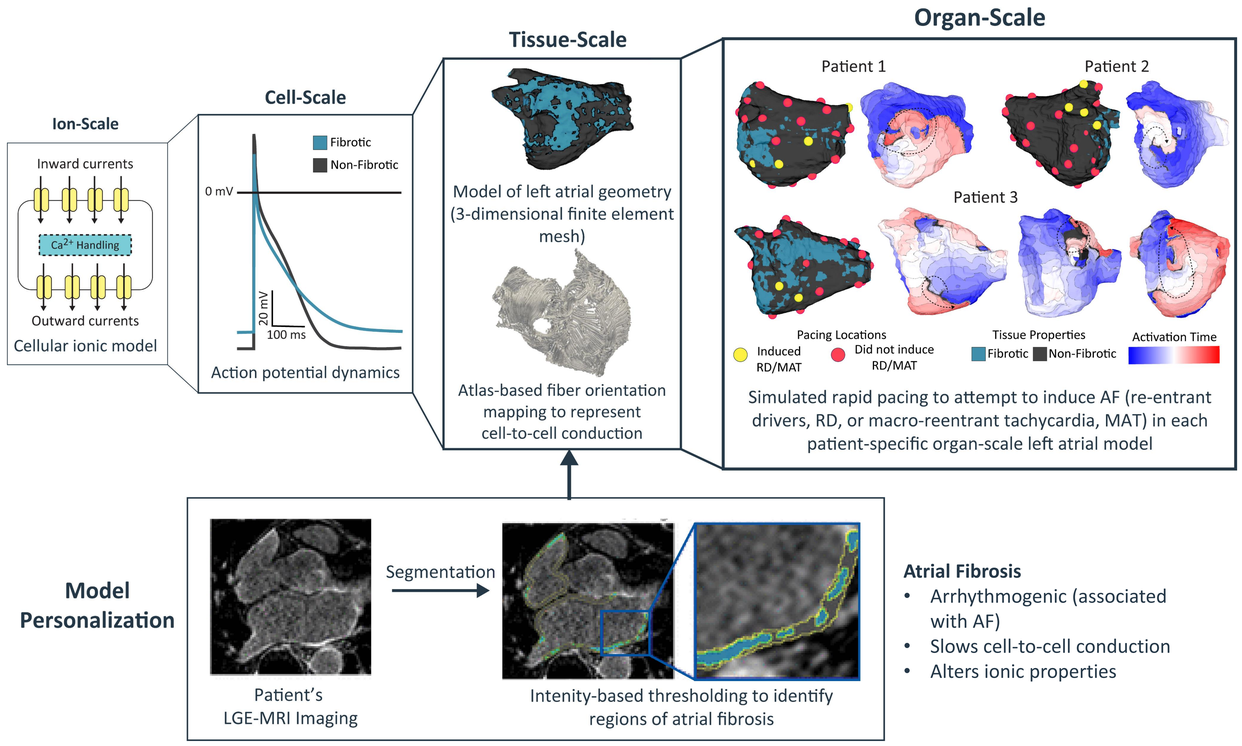
Clinical Characteristics	Freedom from AF (n=20)	AF Recurrence (n=12)	p
Age (years)	63 ± 8	63 ± 9	0.87
Male sex	9	4	0.71
Body mass index (kg/m^2)	27 ± 6	27 ± 5	0.99
Hypertension	10 (50%)	7 (58%)	0.73
Impaired Glucose or Diabetes	5 (25%)	1 (8%)	0.63
Congestive heart failure	4 (20%)	2 (17%)	1
Ablation Procedure Details			
Cryo Ablation	3 (15%)	1 (8%)	1
Flutter Line	5 (20%)	3 (25%)	1

No statistically significant differences in clinical characteristics between patient who did and did not experience AF recurrence.

AF recurrence risk prediction methodology



Multi-Scale Modeling of Atrial Electrophysiology

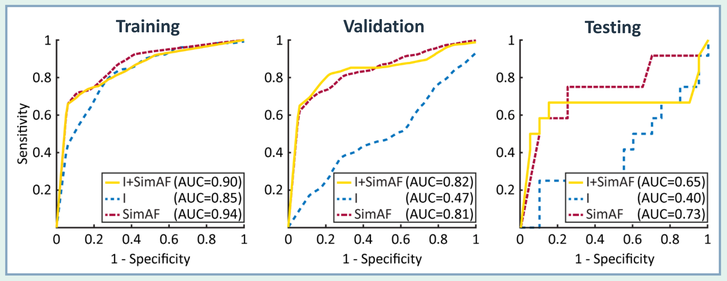


Atrial Fibrosis

- Arrhythmogenic (associated with AF)
- Slows cell-to-cell conduction
- Alters ionic properties

Results

AF Recurrence Risk Prediction with ML and Multi-Scale Modeling



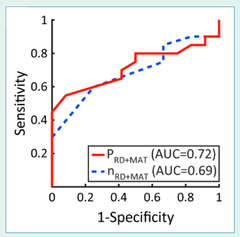
A combination of ML and multi-scale mechanistic modeling accurately predicts which patients will experience AF recurrence in a retrospective cohort of 32 patients.

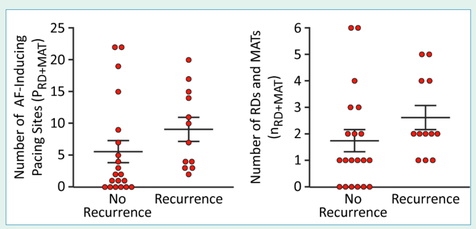
- If features extracted from SimAF are included, features extracted directly from raw clinical images (I) are not required for risk prediction.
- More training data would be needed to achieve strong generalizability if only features extracted from raw clinical images are used- **mechanistic modeling is key to achieving accurate AF recurrence risk prediction with minimal training data.**

AF Recurrence Risk Prediction with Multi-Scale Modeling Alone

Simulations alone are not sufficient for AF recurrence risk stratification, but when combined with ML, they can provide clinical explainability and mechanistic underpinning to ML classifier predictions.

- Training receiver operating characteristic (ROC) curves for prediction of AF recurrence after PVI using the number of AF-inducing pacing sites (P_{RD+MAT}, solid red line) and number of RDs and MATs (n_{RD+MAT}, dashed blue line) achieve **AUCs of 0.72 and 0.69**, respectively.





The proportion of AF-inducing pacing sites (P_{RD+MAT}) and the number of RDs and MATs (n_{RD+MAT}) are **higher** for patients who experienced AF recurrence than for patients who did not, but this is not statistically significant.

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References: *1. Calkins et al., Heart Rhythm 2017. 2. Kiz et al., Curr Cardiol Rev 2017. 3. Ali et al., Cardiovasc Res 2019. 4. Cheng et al., J Am Coll Cardiol 2019.*
Disclosures: *None*