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OPTIMA: Personalized Treatment of Persistent Atrial Fibrillation in a Simulation-driven Clinical Trial

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The most common cardiac rhythm disorder is atrial fibrillation (AF), which is characterized by irregular rhythms in the upper chambers of the heart. In the current standard-of-care, clinicians use catheter ablation to terminate the arrhythmia by creating scar tissue that electrically isolates the pulmonary veins (PVI). However, patients with persistent AF (PsAF) who develop atrial fibrosis exhibit arrhythmias which are often resistant to this procedure. We address this challenge with Optimal Target Identification via Modeling of Arrhythmogenesis (OPTIMA), which has served as the subject of a prospective clinical trial (N=10) as well as an ongoing FDA-approved phase II randomized clinical trial.

In the OPTIMA method, we build patient-specific three-dimensional bi-atrial models from late gadolinium-enhanced magnetic resonance imaging. These models serve as the basis for simulations that characterize wave propagation initiated by pacing sites throughout the atria and specifically identify the circulating electrical signals called rotors, or re-entrant drivers, which sustain AF. We use virtual ablation to target these sites and eliminate both clinically manifested rotors along with latent rotors which emerge following ablation. These targets are delivered to the clinic before the procedure.

OPTIMA is built on a complex, semi-automated computational pipeline which integrates detailed modeling, image interpretation, and mapping tools to build personalized biophysical simulations of cardiac electrophysiology. Deep learning methods assist with anatomical segmentation while a host of supporting software tools manage and interpret the big and deep data required for each prediction. OPTIMA is powered by state-of-the-art high-performance computing platforms which make it possible to optimize the ablation strategy for each patient.

Here we review the computational methods required to support this trial and present

findings gleaned from the existing cohort. The rich data produced at each stage of the pipeline yields insights into mechanistic features of PsAF models, namely the spatial distribution of fibrosis, and the prevalence and multiplicity of the unique rotors required to sustain AF. While the OPTIMA clinical trial measures success in a controlled fashion, the underlying modeling process yields a trove of granular patient-specific data, and the lessons we extract from these data can guide ongoing efforts to optimize the application of computational cardiology tools in clinical settings.