

Methodology Considerations in Phase Analysis and Clinical Application of
Electrocardiographic Imaging in Patients with Long QT Syndrome

by

Ramya Vijayakumar

Doctor of Philosophy in Biomedical Engineering

Washington University in St. Louis, 2016

Professor Yoram Rudy, Chair

Cardiac arrhythmias affect people worldwide leading to morbidity and mortality. A thorough understanding of the mechanisms and the underlying substrate is essential for accurate diagnosis and successful treatment of arrhythmias. Electrocardiographic Imaging (ECGI) is a noninvasive imaging modality for studying the cardiac electrical activity in the intact human heart under physiological conditions. With its panoramic mapping feature and its ability to generate high resolution maps of cardiac activation and repolarization on a beat-by-beat basis, ECGI has emerged as an important tool for characterizing abnormal electrophysiologic substrate and providing mechanistic insights into complex arrhythmia patterns.

A novel phase mapping algorithm was implemented to analyze ECGI-reconstructed epicardial electrograms in the presence of spatio-temporal cycle length (CL) variations, as occur during atrial fibrillation (AF). Phase maps were consistent with time-domain activation maps for various ventricular and atrial activation sequences. Phase mapping highlighted rotational wave fronts (rotors) and determined their center of rotation (singularity point) using a precise mathematical definition. This property can facilitate understanding of wavefront dynamics

during complex arrhythmias, such as AF and ventricular fibrillation (VF). However, phase mapping has the propensity to introduce false rotors during complex activation patterns, such as wavefront propagation about a line of block. Therefore, mapping and analysis of complex arrhythmias should be based on a combined approach using both time-domain activation maps and phase maps that account for CL variations.

Clinically, ECGI was used to characterize the electrophysiological properties of the substrate in congenital Long QT Syndrome. Maps of epicardial activation, recovery time (RT) and activation-recovery intervals (ARI; surrogate for local action potential duration (APD)) were reconstructed and compared with those of healthy volunteers. Activation was normal in all patients. However, RT and ARI were prolonged relative to control, indicating delayed repolarization and abnormally long APD. ARI prolongation was spatially heterogeneous, with repolarization gradients much steeper than control. This defines a substrate for reentrant arrhythmias, not detectable by surface ECG. Steeper dispersion of repolarization in symptomatic patients suggests a possible role for ECGI in risk stratification.

The present work contributed to the continued development of ECGI signal analysis. It also demonstrated the feasibility and clinical importance of ECGI as a noninvasive tool for diagnosis and arrhythmic risk stratification in human.