Noninvasive Multi-Modality Studies of Cardiac Electrophysiology, Mechanics, and Anatomical Substrate in Arrhythmogenic Cardiomyopathy, Heart Failure, and Healthy Adults

Heart disease is a leading cause of death and disability and is a major contributor to healthcare costs. Many forms of heart disease are caused by abnormalities in the electrical function of heart muscle cells or the cardiac conduction system. Electrocardiographic Imaging (ECGI) is a noninvasive modality for imaging cardiac electrophysiology. By combining recordings of the voltage distribution on the torso surface with anatomical images of the heart-torso geometry, ECGI reconstructs voltages on the epicardium. This thesis applies ECGI to novel studies of human heart function and disease and explores new combinations of ECGI with additional imaging modalities.

ECGI was applied in combination with late gadolinium enhancement (LGE) scar imaging MRI in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC). The hallmark feature of ARVC is the progressive replacement of healthy myocardium with fibrous and fatty tissue. ARVC carries a high risk of sudden cardiac death. By combining ECGI and LGE in ARVC patients we found that there are signs of conduction abnormalities before structural abnormalities can be detected in ARVC patients. Electrical and structural abnormalities in ARVC patients co-localized. We also found that PVCs, potential triggers for arrhythmia, originated in regions of structural and electrical abnormalities.

ECGI was applied in combination with speckle tracking echocardiography (STE) to longitudinally image heart failure patients undergoing cardiac resynchronization therapy (CRT). STE is an echocardiographic technique for measuring strain (contraction) in the heart. CRT is a highly effective treatment for heart

failure, however, around 30% of patients do not respond to the treatment. ECGI was more effective for predicting response to CRT than the current standard ECG criteria or STE indices. The timing of peak contraction in STE did not accurately reflect the electrical activation sequence. CRT caused improvements in contraction that persisted even when pacing was disabled. CRT prolonged repolarization at the site of the LV pacing lead, which may increase the risk of arrhythmia in CRT patients.

The above studies contribute novel observations of human disease physiology and demonstrate the clinical feasibility and effectiveness of ECGI for noninvasive assessment of ARVC and CRT.