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Real-time detection and suppression of repolarization alternans as antiarrhythmic therapy

Background: This study investigates the spatio-temporal variability of intracardiac repolarization alternans (RA) and its relationship to arrhythmia susceptibility in a swine acute myocardial ischemia (MI) model.

Methods & Results: We developed a real-time multi-channel repolarization signal acquisition, display and analysis system to record electrocardiographic signals from catheters in the right ventricle, coronary sinus and left ventricle prior to and following circumflex coronary artery balloon occlusion. We found that RA is detectable within 4 minutes following the onset ischemia, and is most prominently seen during the first half of the repolarization interval. We developed a novel, clinically-applicable intracardiac lead system based on a triangular arrangement of leads spanning the right ventricular (RV) and coronary sinus (CS) catheters which provided the highest sensitivity for intracardiac RA detection when compared to any other far-field bipolar sensing configurations ($p < 0.0001$). The magnitude of RA was used to adjust pacing stimuli delivered during the absolute refractory period (ARP) aimed to reduce RA. We found that the pacing pulse polarity and the phase polarity are sufficient parameters to suppress RA. To calibrate the pacing stimuli, we estimated the required charge to induce one μV [one unit] change in the alternans voltage [and Kscore] on CS and LV leads as 0.05 ± 0.025 [0.32 ± 0.29] and 0.06 ± 0.033 [0.33 ± 0.37] μC, respectively. Using this approach, we demonstrated the ability to suppress spontaneous RA following acute MI. Overall, pacing during the ARP resulted in a significant decrease in alternans voltage and Kscore and reduced arrhythmia susceptibility ($p<0.01$).

Conclusion: RA can be reliably detected through a novel triangular RV-CS lead configuration. Electrical stimulation during the ARP can be used to suppress RA, *in vivo*. Our findings may have important implications in developing methods to prevent the onset of ventricular arrhythmias.

Recent Publications

1. Merchant FM and Armoundas A A. Role of substrate and triggers in the genesis of cardiac alternans, from the myocyte to the whole heart: Implications for therapy. Circulation. 2012;125:539-549
2. Sayadi O, Puppala D, Ishaque N, Doddamani R, Merchant F M, Barrett C, Singh J P, Heist E K, Mela T, Martinez J P, Laguna P and Armoundas A A. A novel method to capture the onset of dynamic electrocardiographic ischemic changes and its implications to arrhythmia susceptibility. J Am Heart Assoc. 2014;3
3. Sayadi O, Merchant F M, Puppala D, Mela T, Singh J P, Heist E K, Owen C and Armoundas A A. A novel method for determining the phase of t-wave alternans: Diagnostic and therapeutic implications. Circ Arrhythm Electrophysiol. 2013;6:818-826
4. Merchant F M, Sayadi O, Moazzami K, Puppala D and Armoundas A A. T-wave alternans as an arrhythmic risk stratifier: State of the art. Curr Cardiol Rep. 2013;15:398
5. Merchant F M, Sayadi O, Puppala D, Moazzami K, Heller V and Armoundas A A. A translational approach to probe the proarrhythmic potential of cardiac alternans: A reversible overture to arrhythmogenesis? Am J Physiol Heart Circ Physiol. 2014;306:H465-474.

Biography

Antonis A Armoundas completed his BS in Electrical Engineering from National Technical University of Athens, Athens, Greece, in 1991 and MS in Biomedical Engineering from Boston University, Boston, MA, in 1994. He received PhD in Nuclear Engineering, from the Massachusetts Institute of Technology (MIT), in 1999. He was an American Heart Association sponsored Post-doctoral Fellow at the Division of Molecular Cardiobiology and the Department of Biomedical Engineering at Johns Hopkins University. Now, he is a National Institute of Health supported Principal Investigator at Massachusetts General Hospital and an Assistant Professor at Harvard Medical School, while he maintains an appointment at M.I.T. He has authored more than 80 high-impact peer-reviewed journal articles and book chapters, and he also holds six patents. His research interests include "Biomedical signal processing, forward and inverse problem solutions, and cellular electrophysiology methods".

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