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A novel closed-loop method for real-time suppression of repolarization alternans *in vivo*: Implications for arrhythmia susceptibility

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Introduction: Repolarization alternans (RA) has been implicated in the pathogenesis of ventricular tachyarrhythmias (VTEs) and sudden cardiac death.

Methods: We developed a real-time closed-loop system to display and analyze multi-channel body surface and intracardiac ECG signals. Spectral analysis of RA was used to adjust electrical pacing stimuli delivered during the absolute refractory period (ARP) aimed to reduce RA. The signed derivative of the normalized T-wave integral at points with significant alternans was used to determine the phase of RA. Balloon occlusion of the left circumflex coronary artery was used to induce spontaneously occurring RA in 6 swine.

Results: 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 the body surface, CS and LV leads as 0.04 ± 0.02 [0.93 ± 0.73], 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 mV level RA following acute myocardial infarction. Overall, pacing during the ARP resulted in a significant decrease in alternans voltage (71.1% reduction, $p<0.0001$) and Kscore (79.3% reduction, $p<0.0001$) in a triangular LV-CS lead system (n=6).

Conclusion: We have demonstrated that electrical stimulation during the APR can be used to suppress RA, *in vivo*. Our findings may have important implications in developing methods to prevent the onset of VTEs.

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