Assessing the Predictability of Real-Time Cardiac Digital Twins under Pathological Conditions

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Introduction: Personalized computational heart models that integrate patient-specific anatomical and clinical data within a mechanistic physiological framework – termed cardiac digital twins (CDTs) – are emerging as a key technology in precision cardiology. By construction, CDTs are expected to predict an individual patient's response to disease and therapy, thereby enhancing diagnosis, risk stratification, and treatment planning. Although methods to calibrate CDTs to a patient's current state are advancing, their ability to generalize and predict responses under unobserved pathological conditions remains untested.

Objectives: We present an ECG-calibrated CDT model incorporating a comprehensive cardiac conduction axis and evaluate ECG predictions under pathologies of the conduction axis against established diagnostic criteria.

Methods: An anatomically accurate torso–whole heart model was reconstructed from medical images of a healthy male subject and augmented with a physiologically and anatomically detailed representation of the cardiac conduction system. The model was calibrated to reproduce the subject's ECG under normal sinus rhythm. Interactive simulations were conducted to assess responses to nine pathological conditions associated with intraventricular conduction disorders and tachy-arrhythmias. Predictive performance was evaluated by comparing simulated ECGs with established diagnostic criteria.

Results and Conclusion: All simulations were executed in real time, resolving whole-heart activation and repolarization dynamics and the corresponding ECG. Across all nine pathological conditions, the model reproduced approximately 88% of expected diagnostic ECG criteria. These results demonstrate accurate CDT calibration under baseline conditions and provide initial evidence of predictive performance under previously unobserved conditions. By enabling interactive, real-time interrogation of electrophysiological responses, the framework offers mechanistic insight into the relationship between cardiac electrical sources and their manifestation in ECG phenotypes, supporting the advancement of predictive modeling in precision cardiology.