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*A Simulation Study of the Effects of His Bundle Pacing in Left  
Bundle Branch Block*

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**Abstract:** His bundle pacing (HBP) has emerged as a feasible alternative to right (RVP) and biventricular pacing (BVP) for Cardiac Resynchronization Therapy (CRT). This study sought to assess, in ex-vivo experimental models, the optimal setup for HBP in terms of electrode placement and pacing protocol to achieve superior electrical synchrony in the case of complete His-Purkinje block and left bundle branch block (LBBB). We developed a 3D model of His bundle and bundle branches, embedded in a patient-specific biventricular heart model reconstructed from CT images. A monodomain reaction-diffusion model was adopted to describe the propagation of cardiac action potential, and a custom procedure was developed to compute pseudo-ECGs. Experimental measurements of tip electrode potential waveforms have been performed on ex-vivo swine myocardium to determine the appropriate boundary condition for delivering the electrical stimulus in the numerical model. An extended parametric analysis, investigating the effect of the electrode orientation and helix length, pacing protocol, and atrioventricular delay, allowed us to determine the optimal setup for HBP therapy. Both selective (S-HBP) and non-selective (NS-HBP) His bundle pacing were tested, as the variable anatomical location of the His bundle can result in the activation of the surrounding myocardium. Our study indicates a perpendicular placement of the electrode as the most advantageous for restoring the physiological function of the His-Purkinje system. We found that higher-energy protocols can compensate for the effects of an angled placement though concurring to potential tip fibrosis. Promisingly, we also revealed that an increased electrode helix length can provide optimal resynchronization even with low-energy pacing protocols. Our results provide informative guidance for implant procedure and therapy optimization, which will hopefully have clinical implications further improving the procedural success rates and patients' quality of life, due to reduced incidence of lead revision and onset of complications.

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