

# Selecting Cardiac Resynchronization Therapy Strategy for Left Bundle Branch Block at Different Levels: In Silico Comparative Study

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## Abstract

*This pilot in silico study compares the effects of novel cardiac resynchronization therapy (CRT) strategies, including His bundle pacing (HBP), left bundle branch pacing (LBBP), and combined optimized therapies (HOT-CRT and LOT-CRT), in treating proximal and distal left bundle branch block (LBBB). Using a detailed computational heart model based on the clinical data from a patient (ECG and cardiac computed tomography (CT)), we reproduced specific anatomical and electrical characteristics to simulate different LBBB types and several CRT strategies. Over 100 computational experiments were performed to assess the impact of each CRT technique on cardiac electrical activity, focusing on ventricular activation times and electrical uncoupling. Our results indicate a variable efficacy of CRT modalities depending on the location of the conduction block. Specifically, HBP and HOT-CRT were most effective for proximal LBBB, whereas LBBP and LOT-CRT showed significant benefits in distal LBBB. Conversely, BiV-CRT showed consistent efficacy in both proximal and distal LBBB. This in silico method provides a promising avenue for refining therapeutic interventions in a patient-specific manner, potentially improving both diagnostic accuracy and outcomes in CRT and CSP.*

## 1. Introduction

Cardiac conduction system pacing (CSP) has recently been proposed in the 2021 European Society of Cardiology [1] and 2023 American Heart Association [2] clinical guidelines as a potential alternative to biventricular pacing (BiV-CRT) for cardiac resynchronization therapy (CRT). One of the key selection criteria for CRT is left bundle branch block (LBBB) [3, 4], which identification presents significant challenges due to the heterogeneity of conduction block levels. In particular, in cases of distal LBBB, His bundle pacing (HBP) fails to narrow the QRS complex despite the successful lead placement [5]. This limitation

may be overcome by left bundle branch pacing (LBBP), in which the lead is positioned more distally.

To the date, five CRT strategies have been proposed: BiV-CRT, HBP, LBBP, and HIS/LBB optimized CRT (HOT-CRT/LOT-CRT) which combines the latter with ventricular pacing. These strategies may offer superior outcomes for patients with specific patterns of LBBB [6–9]. However, the variability in the level of conduction block and anatomic differences between patients' hearts make comprehensive comparative clinical trials challenging for all CRT strategies.

A promising approach involves the use of patient-specific computer models of the heart, integrating cardiac imaging data with personalized models and machine learning techniques. Such models have demonstrated enhanced accuracy in predicting CRT outcomes [10–13]. Despite this progress, previous models simulated LBBB without specifying the location of the conduction block and focused exclusively on BiV-CRT.

**Aim.** This study aims to evaluate effects of pacing on the ventricular activation during five CRT strategies in the cases of proximal and distal LBBBs.

## 2. Materials and methods

### 2.1. Patient-specific ventricular model

To develop a patient-specific ventricular model, we utilized clinical data from a patient who underwent BiV-CRT implantation for chronic heart failure with a reduced left ventricular ejection fraction. Comprehensive clinical evaluations were performed post-implantation, including a 12-lead ECG and contrast-enhanced CT. A biophysically detailed computational heart model was subsequently constructed using clinical data. The model development pipeline included the following steps, as described in our previous work [13]: 1) Finite element models of the torso, lungs, and ventricles were constructed based on semi-automatic segmentation of CT data. 2) A rule-based ap-

proach was used to simulate myocardial fiber architecture [14]. 3) To simulate activation patterns, a Purkinje network for both RV and LV was generated using the model proposed by Costabal et al. [15]. 4) The Eikonal model [16] was used to calculate electrical activation times at each node of the ventricular grid. 5) The Lead-Field approach [17], given activation times and an action potential model [18], was used to calculate 12-lead ECG signals. 6) To improve the physiological accuracy of the model, we incorporated a fast endocardial layer. The fast endocardial layer was modeled in the following manner: the subendocardial surfaces of the left and right ventricles were extracted, and an undirected weighted graph was constructed on all nodes and edges of the obtained surface meshes.

To account for the patient’s intrinsic LBBB rhythm, we implemented a calibration procedure for the His-Purkinje system:

1. **Right Bundle Branch (RBB) calibration:** We generated 10 different configurations of the RBB, varying the branching patterns and terminal Purkinje-myocardial junctions (PMJs). For each configuration, we calculated the activation map and 12-lead ECG. The RBB configuration that produced the least discrepancy with the patient’s clinical ECG signal was selected for the patient-specific model.
2. **Left Bundle Branch (LBB) modeling:** Since the native LBBB rhythm did not manifest LBB activation, we generated 10 different configurations of the LBB. These configurations varied in their branching patterns and PMJ locations to represent potential anatomical variations. All 10 LBB configurations were retained for subsequent simulations to account for uncertainty in the LBB structure.
3. **Model calibration and validation:** The model was calibrated by adjusting tissue conductivities and Purkinje system properties to match the patient’s ECG morphology and QRS duration. The final model was validated by comparing simulated activation sequences and ECG waveforms with the patient’s clinical data.

## 2.2. Simulation of LBBB levels and CRT strategies

Based on the patient-specific computer model, two types of LBBB were simulated: proximal LBBB with complete conduction block in the left bundle; and distal LBBB with conduction block distal to the left bundle bifurcation. When modeling the distal block across all three branches of LBBB, the activation pattern was close to the proximal LBBB. In this regard we generated combinations of two branch blocks: anterior-posterior, anterior-septal, and posterior-septal. We found that only the distal conduction block of both anterior and posterior branches resulted in a QRS complex prolongation exceeding 120 ms. Therefore, in cases of distal LBBB, we modeled the conduction block beyond the bifurcation of the LBBB, with preserved

conduction through the septal branch (Figure 1).

Five CRT strategies were evaluated (Figure 1):

1. **BiV-CRT.** This strategy involved RV-LV pacing at the sites of the implanted electrode projections. The RV lead was located in the RV apex and the LV lead was located in the basal segments of the lateral LV wall.
2. **HBP.** Pacing was applied directly to the His bundle.
3. **LBBP.** Pacing was applied to the anterior fascicle of the left bundle branch.
4. **HOT-CRT.** A combination of BiV-CRT and HBP with 40 ms delay of the latter.
5. **LOT-CRT.** This strategy combined BiV-CRT with LBBP with 40 ms delay of the latter.

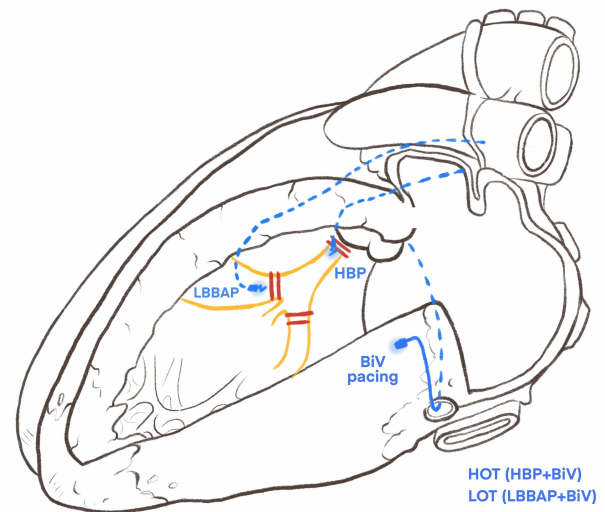


Figure 1. Schematic representation of various levels of conduction block in the left bundle branch and different strategies for cardiac resynchronization therapy.

## 2.3. Ventricular activation measurements

For each LBBB level, structural configurations of the bundle branches and CRT strategy, we evaluated QRS duration (QRSd), and four ventricular activation characteristics. The total activation time (TAT) of the heart ventricles was determined by computing the time interval between the earliest and latest activation among cardiac mesh points. The activation times of the LV (LVAT) was calculated as the differences between the time of the latest activation and the time of the earliest activation within the LV. Ventricular electrical uncoupling (VEU) was defined as the difference between the mean LV and RV activation times.

## 3. Results

Through 100 computational experiments, we systematically compared the ventricular activation patterns and ECG

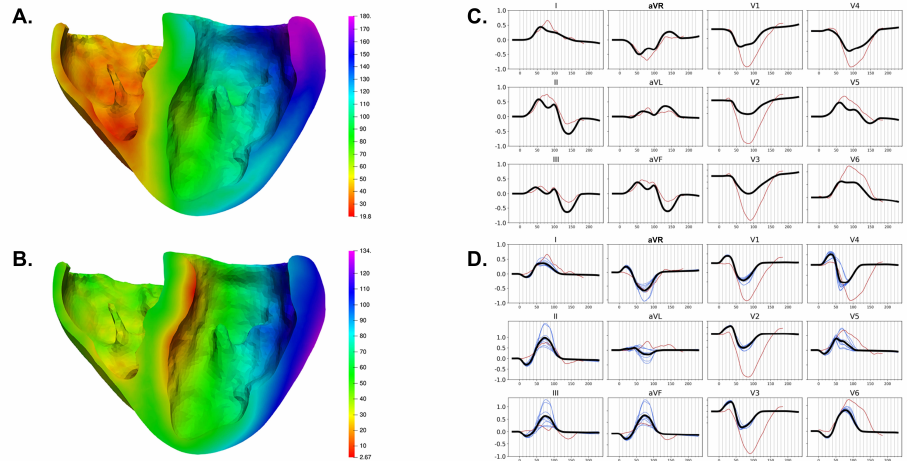


Figure 2. Activation maps (left) and 12-lead ECG (right) for proximal (A, C) and distal (B, D) LBBB models. Red colors on activation maps indicate earlier activation, purple colors indicate later activated zones. Red line on ECG signals indicate clinical ECG signals. Blue line indicate 10 model ECG signals for each conduction system configuration. Black line indicate the averaged model ECG signal

signals generated by various CRT strategies. The ECG and activation map for proximal LBBB aligned closely with clinical observations. The ECG generated for the distal LBBB showed q waves in leads I, V5, and V6. We also noted a normal transeptal activation time and a left-to-right directional flow, mirroring clinical findings associated with distal LBBB (Figure 2).

Figure 3 depicts the implications of various CRT strategies on ventricular activation. The results indicate that the efficacy of CRT modalities varies depending on the location of the conduction block.

For proximal LBBB, all strategies resulted in a reduction in the electrical dyssynchrony (VEU). However, HBP demonstrated the best reduction in ventricular activation compared to other strategies (Figure 3). BiV-CRT showed consistent efficacy in reducing electrical dyssynchrony in both proximal and distal LBBB. In distal LBBB only, HBP did not result in a significant reduction in VEU. LBBP and LOT-CRT demonstrated the most significant reduction in ventricular activation time for distal LBBB among the tested methods (Figure 2).

#### 4. Discussion and Conclusions

This pilot study demonstrates a potential of using personalised cardiac computer models to predict the efficacy of novel CRT strategies depending on the proximal or distal level of LBBB. Using a patient-specific computational heart model enriched with clinical data, the developed technology demonstrated the ability to simulate different types of LBBB and evaluate multiple CRT strategies.

The results show that the effects of CRT modalities on the ventricular activation vary with the location of the con-

duction block, illustrating the nuanced nature of cardiac therapy. HBP was identified as particularly beneficial in cases of proximal LBBB, optimizing cardiac function by directly targeting the His bundle. Conversely, LBBP and LOT-CRT demonstrated significant improvements in distal LBBB scenarios, suggesting their efficacy in more distal conduction blocks. Interestingly, traditional BiV-CRT maintained consistent results across both proximal and distal LBBB, offering a reliable, though less specialized, alternative.

These insights highlight the importance of tailoring CRT techniques based on the specific conduction block location within the heart. Such an approach not only enhances therapeutic accuracy but also aligns with the broader trend towards personalized medicine in cardiology. By refining CRT modalities to suit individual anatomical and electrical characteristics, this study paves the way for improved clinical outcomes in the treatment of LBBB, potentially setting a new standard for patient-specific cardiac therapy.

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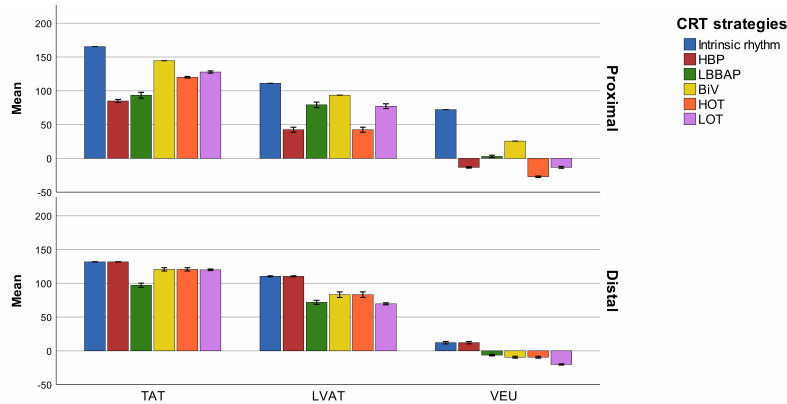


Figure 3. Ventricular activation characteristics for proximal and distal LBBB during different CRT modalities

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