Impact of CRT Device Settings on Interventricular Dyssynchrony: An Analysis Using Non-Invasive Activation Map Reconstruction

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Abstract

Cardiac Resynchronization Therapy (CRT) is an effective treatment for heart failure patients with Left Bundle Branch Block (LBBB). However, selection of the optimal interventricular delay (VV) of CRT device remains challenging due to patient-specific variability. This study aimed to improve CRT efficacy by means of a non-invasive method to reconstruct cardiac activation maps and choose optimal VV delay. Retrospective data from five LBBB pattern patients who underwent CRT were analyzed. A previously developed algorithm generated patient-specific activation maps using 12-lead electrocardiogram (ECG) and computed tomography data. To model torso potential distributions, a forward ECG problem was solved and machine learning compared the simulated and real 12 lead signals. ECG recordings at different VV delays were tested using Spearman's correlation coefficient. The overall mean correlation was 0.73 ± 0.09, demonstrating quite high quality in the mapping technique. The variability in dyssynchrony indices across patients highlights the need for personalized selection of VV delay in the CRT device. These results suggest that the integration of imaging and computational modeling may improve CRT outcome by tailoring therapy to individual characteristics.

1. Introduction

Cardiac resynchronization therapy (CRT) has been shown to be effective in restoring regional synchronous activation, thereby improving heart contractility and mechanoenergetic efficiency [1]. However, a significant non-response rate persists due to factors such as suboptimal patient selection and lead placement [2]. Current guidelines emphasize the use of QRS duration and left bundle branch block (LBBB) pattern for pre-CRT patient selection, while the post-CRT stimulated QRS value serves as a significant predictor of long-term response [3].

Previous studies have highlighted the importance of tailoring CRT device settings and lead position based on left and right ventricular (LV and RV) activation characteristics [4,5]. Using a non-invasive multichannel mapping system, it has been shown that the assessment of RV and LV activation during biventricular pacing correlates more closely with the final response to CRT than do measures of electrical activation derived from the surface ECG [6].

Our current study is based on three-dimensional (3D) cardiac mapping to evaluate dyssynchrony parameters in modes with various interventricular (VV) delays programmed using a CRT device. The main objective is to identify differences in characteristics of electrical dyssynchrony.

2. Methods

2.1. Clinical data

This study utilized retrospective clinical data from five cases. All patients had a primary implanted CRT device. Data collected included cardiac computed tomography (CT) images and 12-lead electrocardiogram (ECG) recordings obtained both before CRT implantation and one year after operation.

Preoperative ECG recordings comprised the patients' intrinsic rhythms with LBBB pattern. Postoperative ECGs captured pacing modes with various VV delays ranging from -50 to 50 ms. These delays reflect the time difference between the onset of cardiac pacing from the active RV and LV poles. A positive value of VV delay means that the active pole of the RV lead starts pacing first. Negative value of VV delay means that the active pole of the LV lead starts pacing first. A zero value of VV delay means that the active poles of both electrodes start pacing simultaneously.

In each case, our cardiologist created a 3D geometric model of the heart, torso, and lungs tailored to the patient. For this purpose, semi-automated segmentation methods applied to cardiac CT images were used, providing an accurate representation of individual anatomical structures.

The position of active poles of CRT device leads was also marked by the cardiologist.

2.2. Non-invasive mapping system

In this study, we used a non-invasive cardiac activation map reconstruction algorithm originally developed in our previous work [7]. The algorithm integrates the solution of the forward ECG problem with machine learning techniques to generate accurate and patient-specific cardiac activation maps. The forward ECG problem was approached by simulating the potential distribution on the torso surface using the eikonal equation in conjunction with the lead-field method. This step involved varying the conductivity and activation source parameters to generate a wide range of potential activation maps and ECG signals.

To obtain an activation map corresponding to patient ECGs, we utilized a machine learning algorithm. The process began by transforming the ECG signals into a latent space representation using a convolutional variational autoencoder. This step allowed us to extract essential features from the ECG data in a compressed, lower-dimensional form. Next, the algorithm searched for the activation maps that produced simulated ECGs most closely matching the patient's observed ECGs within this latent space. The corresponding activation maps were averaged to produce the final patient-specific cardiac activation map.

2.3. Biventricular pacing modes

The algorithm returns not only the cardiac activation map, but also the specific conductivity parameters optimized to match the observed ECG signals. These conductivity parameters are important as they reflect the individual patient's tissue properties, which were used in subsequent simulations to evaluate different pacing strategies.

Using these personalized conductivity parameters, we proceeded to solve the forward ECG problem for the biventricular pacing mode, wherein the positions of the stimulating electrodes corresponded to those of the implanted CRT device. The VV delay, a critical parameter influencing the synchronization of the ventricles, was set according to the configurations determined by the clinician and corresponded to recorded ECGs.

To evaluate the optimal criteria for setting the VV delay in CRT device, two distinct dyssynchrony indices were considered:

1. Interventricular dyssynchrony index ($LVRV_{dyss}$). This index quantifies the difference in activation times between the RV and LV. For computational simplicity, the index was calculated as the sum of the absolute differences between the onsets and offsets of activation times for both ventricles divided by the total activation time. It reflects the percentage of time when ventricles are activated asynchronously.

2. Intraventricular dyssynchrony index (LV_{Dyss}). This index is defined as the sum of the absolute difference in activation times between the septal and lateral walls divided by the total LV activation time.

2.4. Validation and analysis

To validate the quality of the reconstructed cardiac activation maps, we compared the simulated ECGs generated by our model with the real ECGs recorded during CRT pacing with various VV delays. The primary metric used for validation was the Spearman correlation coefficient, which measures the rank-order correlation between the simulated and recorded signals. A higher correlation coefficient indicates a closer match between the simulated and real ECGs, thus validating the quality of the activation maps generated by our algorithm. The mean Spearman correlation coefficient across the five patients was calculated to provide an overall measure of the model performance.

3. Results

3.1. Validation of biventricular pacing activation maps

The comparison between simulated and real ECGs was performed by measuring the Spearman correlation coefficients across all patients during CRT pacing with various VV delays. The overall mean Spearman correlation coefficient was 0.73 ± 0.09, indicating a sufficient degree of similarity between the model-generated and real ECG data.

The mean correlation coefficients varied between patients and programmed VV delays, with an interquartile range from 0.66 to 0.79. This diversity is illustrated in Figure 1, which shows a bar plot of mean Spearman correlation coefficients between VV delays for each patient. The observed differences suggest that individual patient characteristics such as cardiac anatomy, myocardial properties, or lead placement may influence the quality of non-invasive mapping.

The analysis revealed that the Spearman correlation coefficients were affected by changes in the VV delay settings. For example, as shown in Figure 2, negative VV delays (the active pole of the LV lead initiated pacing first) demonstrated lower mean correlations compared to the others.

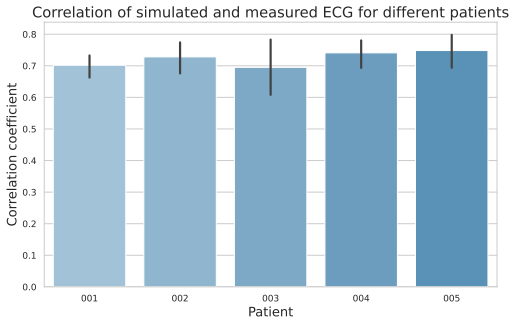

Figure 1. Spearman correlation of simulated vs. measured ECGs across patients.

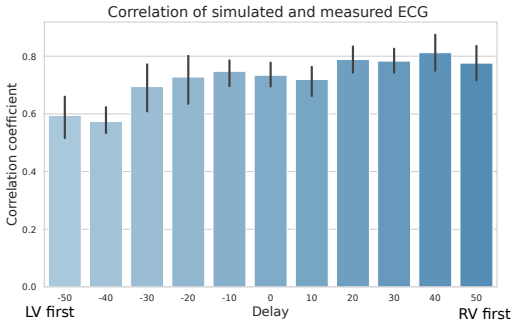

Figure 2. Spearman correlation of simulated vs. measured ECGs across different VV delays.

3.2. Comparison of dyssynchrony indices

For each patient, dyssynchrony indices were calculated from the reconstructed cardiac activation maps generated for CRT pacing modes with different VV delays, as summarized in Figure 3. The figure presents the interventricular dyssynchrony index $LVRV_{dyss}$ and the intraventricular dyssynchrony index (LV_{Dyss}) for each VV delay value.

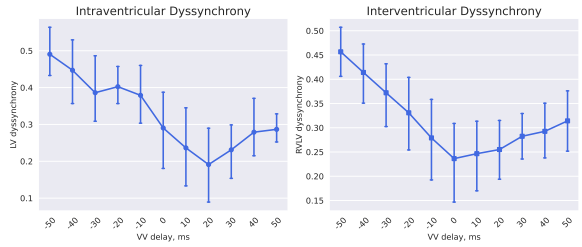

Figure 3. Interventricular and Intraventricular Dyssynchrony Indices Across VV delays. The point plots display the values of intraventricular (left plot) and interventricular (right plot) dyssynchrony indices for each VV delay setting (x-axis), with the corresponding standard error represented by error bars.

The analysis revealed distinct trends in dyssynchrony indices as the VV delay was varied. For 3 patients, a VV delay of 0 ms consistently resulted in the lowest (most favorable) $LVRV_{dyss}$, indicating improved synchronization of ventricular contractions. Conversely, delays from 0 to 20 ms were associated with a decrease in the dyssynchrony indices, indicating impaired ventricular synchrony.

Patient-specific responses to changes in VV delay were evident. For instance, Patient 4 showed a significant reduction in both $LVRV_{dyss}$ and LV_{Dyss} indices at a VV delay 20 ms, whereas Patient 1 only exhibited changes in LV_{Dyss}. This variation underscores the importance of individualizing CRT settings, as optimal VV delay vary considerably between patients.

Comparison of dyssynchrony indices before and after implantation highlighted the overall effectiveness of CRT. On average, a 20% reduction in $LVRV_{dyss}$ and a 25% decrease in LV_{Dyss} were observed after CRT. In some patients, the reduction reached 45%, indicating a significant improvement in ventricular synchronization.

4. Conclusion & Discussion

Our results demonstrate a good agreement between the simulated and measured ECGs, as well as significant variability in dyssynchrony indices across patients and different CRT pacing modes with various VV delays. These findings suggest that individual optimization of CRT settings in terms of VV delay may improve clinical outcomes.

The mean Spearman correlation coefficient of 0.73 $\pm$ 0.09 between the simulated and measured ECGs across all patients and the programmed VV delays in the CRT device confirms the quality of our non-invasive mapping approach. This result is consistent with a previous study [8] that examined non-invasive methods for reconstructing cardiac activation maps, highlighting the potential of ECG imaging in guiding CRT implantation and optimization. Our findings support the use of such techniques as a reliable alternative to invasive procedures, particularly in clinical settings where minimizing patient risk is paramount.

Also, we revealed considerable case-specific variability in the response to different VV delays. Certain patients showed optimal dyssynchrony indices in specific VV delay while others exhibited minimal changes. This variability underscores the complexity of CRT optimization and the limitations of a one-size-fits-all approach. Previous research highlighted similar challenges, indicating that anatomical differences, myocardial scar tissue, and lead placement can significantly influence CRT outcomes [9, 10]. These findings also emphasize the necessity of individualized treatment plans tailored to each patient's unique cardiac anatomy and electrical activation patterns.

The current study has several notable limitations. The sample size was small, with only five patients, which may

limit the generalizability of our findings. Additionally, while the correlation between the simulated and measured ECGs was quite high, the complexity of the heart's electrical activity means that even small inaccuracies in the model may affect the choice of the optimal VV delay in CRT device.

In conclusion, our study supports the use of non-invasive cardiac activation mapping as a valuable tool to select optimal VV delay in CRT device, with the potential to improve patient outcome through personalized therapy. The observed patient-specific variability in dyssynchrony indices underscores the need for individualized CRT programming. As the field of cardiac electrophysiology continues to evolve, such non-invasive approaches are likely to become integral to the management of heart failure patients requiring CRT.

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