Towards the Validation of a Digital Twin Pipeline on Patients with Bundle Branch Block

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Abstract

Digital twin technologies offer promising tools for personalized diagnosis and therapy planning in cardiac electrophysiology. However, few studies have validated these methods in clinical settings. In this work, we evaluate a digital twin pipeline applied to two patients with left bundle branch block (LBBB) by comparing simulation results to surface electrocardiograms (ECGs) acquired during clinical electrophysiology studies. Using patient-specific cardiac geometries derived from magnetic resonance imaging (MRI) and 12-lead ECGs recorded during sinus rhythm and controlled pacing at the apex and right ventricular outflow tract (RVOT), we calibrated and tested personalized electrophysiological models. In both cases, the models accurately reproduced the ECG morphology corresponding to each stimulation site, correctly identifying the origin of activation. During sinus rhythm, the inferred activation pattern in one patient revealed the absence of Purkinje conduction in the left ventricle (LV), consistent with LBBB physiology. In the second case, optimization convergence was suboptimal, indicating the need for more robust parameter estimation methods. These findings demonstrate the feasibility of ECG-driven digital twin personalization and provide a step towards clinical validation and refinement of the pipeline.

1. Introduction

Digital twins have emerged as powerful tools for simulating patient-specific cardiac electrophysiology, enabling non-invasive assessment of electrical activation patterns and supporting clinical decision-making [1, 2]. Their potential is particularly significant in the context of conduction disorders, such as LBBB, where the electrical activation of the ventricles is markedly altered, often leading to mechanical asynchrony and increased risk of heart failure. Accurate digital reconstructions of such pathological activation patterns, informed by readily available clinical data such as 12-lead ECGs and cardiac MRI, could enhance diagnosis, therapy planning, and patient stratification.

However, despite the growing interest in digital twin technologies for cardiac applications, few studies have focused on their validation in clinical settings [3]. This study addresses this gap by generating digital twins for two patients diagnosed with LBBB and comparing the simulation results against surface ECGs acquired during clinical electrophysiology studies. Patient-specific heart geometries were reconstructed from cardiac MRI, and electrophysiological models were personalized using 12-lead ECG recordings obtained during both sinus rhythm and controlled pacing at the apex and RVOT.

The resulting digital twins accurately reproduced the ECG morphologies corresponding to each stimulation site, correctly identifying the origin of activation. During sinus rhythm, the inferred activation sequence in one patient revealed the absence of Purkinje conduction in the LV, consistent with the expected LBBB pattern. In contrast, the second case showed limitations in the optimization process, underscoring the need for more robust calibration methods. These results demonstrate the potential of ECG-driven digital twin personalization for capturing key features of pathological conduction and support further development and clinical validation of the pipeline.

2. Materials and Methods

2.1. Patients' Report

The first patient, a 61-year-old Caucasian male with a history of smoking, presented symptoms of fatigue, orthopnea, dyspnea NYHA III, and paroxysmal nocturnal dyspnea. ECG findings revealed a heart rate of 98 bpm, first-degree atrioventricular block, LBBB, left atrial

enlargement, and left ventricular hypertrophy. Doppler echocardiogram and MRI confirmed dilated cardiomyopathy with severe biventricular dysfunction, significantly enlarged left and right ventricles, and substantial left atrial enlargement. Delayed enhancement sequences identified fibrosis patterns typical of non-ischemic heart disease.

The second patient is a 79-year-old Caucasian female with a history of smoking, alcohol use, and hypertension, diagnosed with dilated cardiomyopathy and LBBB. The patient experiences brief episodes of chest discomfort at rest along with pre-syncope and nocturnal cough. Cardiac MRI findings revealed significant left ventricular dilatation with severe dysfunction and notable interventricular septal dyssynchrony, accompanied by mild right ventricular impairment. Late enhancement sequences detected subepicardial fibrosis predominantly in the antero-inferoseptal regions. The ECG confirmed sinus rhythm with left axis deviation (55 bpm) and LBBB, while the electrophysiological study did not provoke any sustained tachyarrhythmia.

The patients' data were collected at the cardiology outpatient clinic at the University Hospital of the Federal University of Juiz de Fora, where patients underwent cardiac MRI examinations and electrophysiology studies.

2.2. Cardiac Digital Twin Pipeline

Cardiac Mesh Generation. Patient-specific biventricular geometries were reconstructed from short-axis 2D cardiac MRI scans using the software SEGMENT [4]. The resulting 3D cardiac model was converted into a finite element mesh using GMSH [5], and further processed through an automated mesh handling and labeling pipeline described in [6].

Electrophysiological Model. The electrical activation was simulated using an Eikonal model, widely adopted in cardiac electrophysiology due to its ability to efficiently approximate the ventricular activation sequence [1]. In this model, ventricular activation is reduced to the moment the wave arrives at each point in the myocardium, which is interpreted as a weighted graph, where the edge weights represent the travel time between nodes. This turns the problem into a shortest-path search, solved with Dijkstra's algorithm. This model was driven by root nodes—early activation sites on the endocardial surface—and allowed estimation of activation times that best fit the patient's ECG data.

Purkinje Network Generation. For sinus rhythm simulations, the pipeline also incorporated a Purkinje network model, using a ruled-based algorithm, following the guidelines presented in the work from Camps et al [1]. Candidate early activation sites were sampled from anatomically plausible regions of the endocardium, with preferential distribution in septal and free wall regions, and connected to the His–Purkinje system using the aforementioned algorithm.

Personalization via Inverse Modeling. Personalization of the activation sequence was achieved using Sequential Monte Carlo Approximate Bayesian Computation (SMC-ABC) [7]. This probabilistic inference method iteratively adjusted the parameters defining the earliest activation sites by comparing the 12-lead clinical ECG with the simulated ECG, which was reconstructed using a pseudo-ECG formulation, with electrode positions following the American Heart Association standard for limb and precordial leads. At each iteration, the discrepancy between simulated and clinical ECGs guided the resampling of parameters, progressively improving the fit.

Simulation Parameters and Experiments. For all inference simulations, the candidate parameter population was set to 100, ensuring sufficient coverage of the parameter space while maintaining computational efficiency. Each iteration employed a maximum of 100 Markov Chain Monte Carlo (MCMC) steps to explore the local landscape before updating the population. During sinus rhythm, the number of root nodes was allowed to vary between 3 and 9 to reflect physiological variability. For the stimulation protocols—where clinical data specified the pacing site—the number of root nodes was fixed at 1, with no Purkinje network included. In these cases, the first patient received pacing at the apex, while the second was paced at the RVOT. All other simulation parameters followed the default values defined in the open-source pipeline.

ECG Comparison. The ECG's were normalized and compared using the Pearson's correlation coefficient (PCC), the root mean squared error (RMSE) and standard deviation (STD) throughout the leads.

3. Results

For the first patient, Figure 1 shows the distribution of activated root nodes obtained through the digital twin pipeline, mapped onto a 17×2 endocardial segment chart for both sinus rhythm and the apex-stimulated case. In Figure 1A, under sinus rhythm, the model inferred complete inactivation of the LV and a dispersed distribution of root nodes within the right ventricle. This is consistent with the expected pattern of LBBB. In Figure 1B, when the patient was paced at the apex, the inference correctly localized the activation origin to the apical region, with a highly concentrated root node distribution. These results demonstrate that the digital twin accurately captured both physiological and stimulated activation patterns for this patient, validating the model's ability to reflect distinct conduction scenarios based solely on surface ECG data. In addition, the simulated ECG traces closely matched the corresponding clinical recordings, as shown in Figures 2 and 3. Despite some variability across the population of inferred parameter sets, the results demonstrated good overall stability.

Minor discrepancies were observed in the precordial leads, but the key waveform features and activation patterns were consistently reproduced, further supporting the reliability of the personalized digital twin.

In this sense, a PCC analysis was performed on the sinus rhythm and apex-stimulated ECGs results comparing them to the corresponding clinical data, which revealed good correspondence throughout both cases, with average PCC's from the leads readings of 0.95 and 0.77, respectively. In addition, root mean squared errors (RMSE) and standard deviations (STD) were calculated throughout the leads, comparing the normalized ECG's, which resulted in average RMSE's and STD's of 0.16 ± 0.12 and 0.23 ± 0.14 respectively.

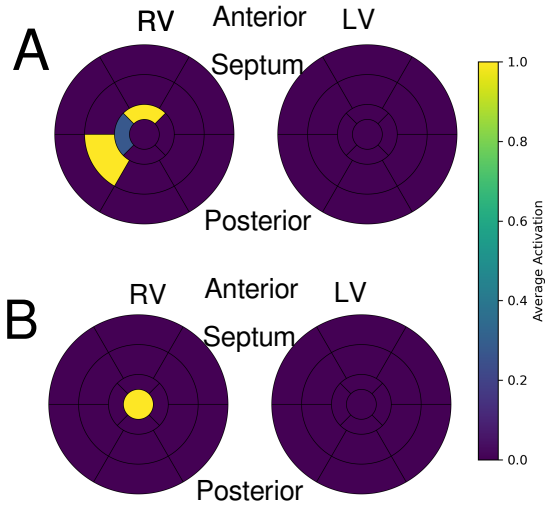

Figure 1. Root node activation over a 17x2 endocardial segment chart for sinus rhythm (A) and apex-stimulation (B) for the first patient.

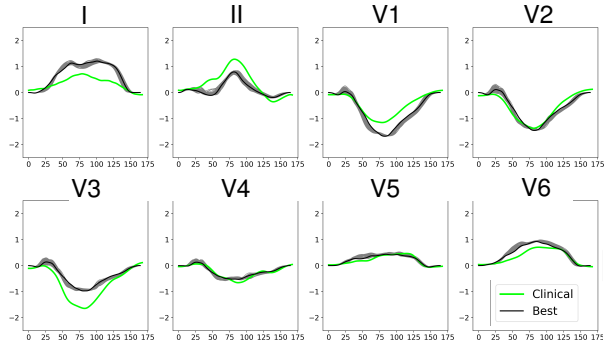

Figure 2. Comparison between the first patient's ECG inference match and the clinical one for the sinus rhythm scenario (PCC = 0.95, RMSE = 0.16 ± 0.12).

For the second patient, the stimulation at the RVOT was accurately localized by the model, as illustrated in Figure 5B, and further supported by the close match between the simulated and clinical ECGs, depicted in Figure 6, reporting PCC of 0.79 and RMSE + STD combination of 0.28 ± 0.10. The inference for sinus rhythm also presented a high correlation score (PCC = 0.92), with low errors (0.22 ± 0.07). However, when analyzing the root node activation pattern in Figure 5A, a few root nodes were identified in the LV, which required a thorough analysis of the local activation times (LATs). This investigation revealed that some activation in the LV was later than in the RV, which agrees with the left bundle branch block diagnosis (Figure 4).

4. Conclusion

This study demonstrates the feasibility and accuracy of using a digital twin pipeline to infer patient-specific ventricular activation sequences directly from clinical 12-lead ECGs and cardiac MRI from two patients with LBBB. For the first patient, the method successfully reproduced both sinus rhythm (PCC = 0.92) and apex-paced activation (PCC = 0.77) patterns, accurately localizing stimulation sites and identifying characteristic conduction abnormalities. In the second patient, we could correctly infer the activation in the RVOT (PCC = 0.79). For the sinus rhythm case (PCC = 0.92), the results showed that some nodes in the left ventricle were activated. Although some nodes were activated later than the right ventricle nodes, which is consistent with the left bundle branch block condition, this observation highlights opportunities for improving the method.

These findings highlight the potential of digital twins for non-invasive, patient-specific assessment of conduction abnormalities. Further validation in larger cohorts will be essential to advance their clinical translation towards scalable, data-driven personalized diagnostics and therapy planning.

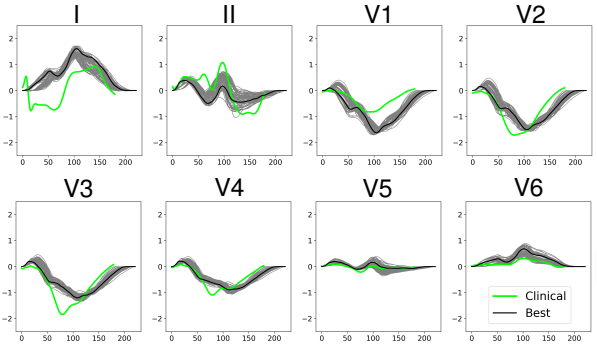

Figure 3. Comparison between the first patient's ECG inference match and the clinical one for the stimulated case (PCC = 0.77, RMSE = 0.23 ± 0.14).

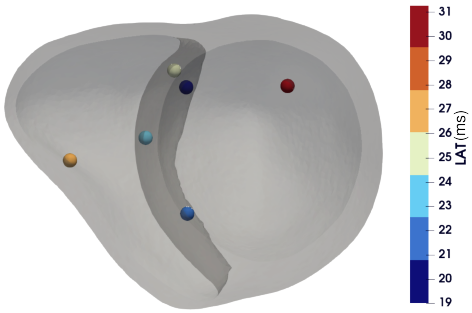

Figure 4. LATs of the active root nodes selected in the sinus rhythm stimulation for the second patient.

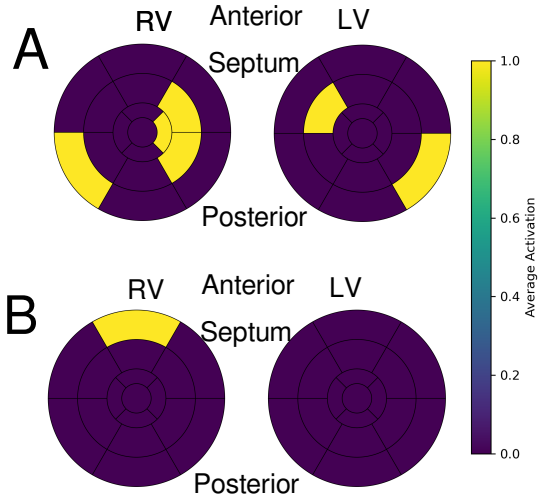

Figure 5. Root node activation over a 17x2 endocardial segment chart for normal sinus rhythm (A) and RVOT case (B) for the second patient.

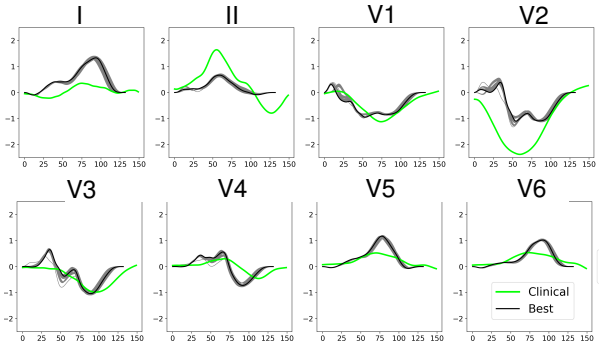

Figure 6. Comparison between the second patient's ECG inference match and the clinical one for the RVOT stimulated case (PCC = 0.79, RMSE = 0.28 ± 0.10).

Acknowledgments

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