Personalization of ventricular cardiac conduction system models to reproduce patient electrocardiogram

Fernando Barber\(^1\), Peter Langfield\(^2\), Miguel Lozano\(^1\), Ignacio Garcia-Fernandez\(^1\), Josselin Duchateau\(^2\), Meleze Hocini\(^2\), Michel Haissaguerre\(^2\), Edward Vigmond\(^2\), Rafael Sebastian\(^1\)

\(^1\) CoMMLab, University of Valencia, Valencia, Spain
\(^2\) IHU Lyric, Bordeaux, France

Abstract

Cardiac electrical activation is a fundamental mechanism that controls cardiac function. It is key for a computational model to be able to reproduce the patient ECG and the underlying sequence of activation of the ventricles. In this study, we propose to personalize the activation sequence by estimating a compatible cardiac conduction system (CCS) for a given patient from his electroanatomical map. We perform the study on five subjects in sinus rhythm from which we estimated the CCS and performed forward simulations to obtain the virtual ECG. Errors at the endocardium were in average 5.72ms, and correlation between clinical and simulated ECG ranged between 0.75 and 0.90. We concluded that the methodology is feasible to personalize the sequence of activation with the advantage of providing an underlying structure for the CCS.

1. Introduction

A fundamental mechanism underlying cardiac function is the electrical sequence of activation, which results from the fast activation of the cardiac conduction system (CCS) in the ventricles. Therefore, computational heart models require a custom setup in order to personalize the sequence of activation to each patient and reproduce the patient-specific 12-lead ECG [1]. There are available several sources of clinical data that can be obtained to carry out this task. The standard 12-lead electrocardiogram (ECG) is the most routinely non-invasive modality used to record the electrical activity of the heart, but it does not provide direct quantitative information about the activation sequence in the heart.

In the past, to obtain information concerning the time course and instantaneous distribution of the excitatory process of the normal human heart, exvivo studies were made on isolated human hearts using intramural terminals [2, 3]. Results from such studies have been widely used to impose a normal activation sequence in non-personalized computational models. More recently, non-invasive electrocardiographic imaging, also called ECGI, was presented as an invivo alternative that overcomes at least some of the limitations of the standard ECG. ECGI combines information from many surface electrodes with knowledge of the geometry of the heart and torso of the patient to depict the electric activity of the heart. It can be used to reconstruct potentials, electrograms, and activation and repolarization patterns on either the epicardium or, less commonly, the endocardium [4–6]. However, ECGI requires a large number of electrodes placed on the patient’s torso both at the time of geometry acquisition using cardiac imaging, and during the clinical intervention, thus requiring dedicated technical support and additional costs. Therefore, despite the advantages, its adoption in the clinical workflow is still limited. An alternative that has been proposed is the combination of patient-specific computational modeling and the 12-lead ECG in an optimization process that tries to match simulated and recorded ECG [7]. In general, those techniques optimize a set of parameters such as the conduction velocity, and the location of early activated sites in the endocardium, to obtain the full 3D activation sequence [8]. The last alternative to simulate the patient-specific 12-lead ECG is to include the underlying CCS. In human hearts, the ventricular CCS extends over the right (RV) and left ventricular (LV) endocardium as well as within the trabeculae carnae, allowing a faster and more synchronized activation of the myocardium, and an efficient contraction [9]. Clinically, the PKN structure is very relevant since it is responsible for the initiation and maintenance of certain life-threatening arrhythmias [10]. Therefore, it is important not only to reproduce the patient’s sequence of activation and ECG but doing it including the underlying CCS. In that line, there have been developed generic models [11] that do not reproduce patients’ ECG, and personalized ones that reproduce either the electroanatomical maps [12–14] and the ECG [15].

In this study, we apply a methodology to estimate the CCS of a patient from an EAM, and following we solve...
the forward problem to obtain the virtual 12-lead ECG. We analyze the data requirements to obtain accurate results in a set of 5 exemplary cases.

2. Material and Methods

2.1. Patient data

We have included in this study 10 EAMs datasets (5 from LV and 5 from RV), that is, 5 biventricular patient data. They were acquired at Bordeaux University Hospital using CARTO 3 system (Biosense Webster, Inc., Diamond Bar, CA, USA), and different catheters namely, NaviStar ThermoCool ablation catheter and PentAray. For each EAM a set of discrete electrical signals is acquired from which the local activation time (LATs) can be calculated. The LATs provided by the system are not completely reliable and therefore, we re-annotated them as follows. The LAT was set as the time between the R-peak in the V5 ECG lead and the deflection on the distal bipolar signal (M1-M2) closest to the point of maximum negative slope on the distal unipolar signal (M1). Note that all the endocardial samples that were not in contact with the reconstructed endocardial EAM surface were discarded. As a result of this re-annotation the LAT maps were smoother and more spatio-temporally coherent. Fig. 1 (first row) shows the differences for one of the EAMs before and after processing it. Note that for visualization purposes after the re-annotation of the samples, a linear interpolation was performed to obtain the LAT on every point of the 3D mesh. In addition, the LAT maps have been projected from the endocardial mesh to a unitary 2D disk using a quasi-conformal projection (QCM).

2.2. CCS Estimation

To estimate a patient CCS compatible with the endocardial activation sequence we follow the next pipeline. First, we re-annotated the LATs from the EAMs to have a consistent activation map (see Figure 1, first row). Second, we estimate conduction velocity on the tissue ($CV_T$), the location of the early activated sites (Purkinje myocardial junctions, PMJs), and their corresponding activation times by solving the backward Eikonal problem from the acquired EAM samples (see Figure 1, second row, small spheres on the endocardial surface). For a detailed description of the method see [13]. Although we can use the estimated PMJs to simulate the electrical activation, we choose to estimate also the branching structure of the CCS. Therefore, from the estimated PMJs, we create iteratively an structure that is compatible with their activation times, considering that at t=0ms the bundle branch (first section of the CCS in the ventricles) is activated. For details on the algorithm see [15]. In summary, given a conduction velocity in the CCS ($CV_{PK}$), branches are created as geodesic lines on the endocardial surface to connect the PMJs to the existing branching structure (initially only a fix branch that extends from the atrio-ventricular node to the apex is created). See Figure 1, second row, branching structure on endocardial surface. Each branch is connected in such a way that the corresponding PMJ will activate at the estimated time, permitting a maximum activation error of 5 ms. The branches are created first for PMJs that activate earlier and show the smallest error when connected. After processing all unconnected PMJs several times, those with errors larger than 5 ms are removed.

2.3. Simulation of ECG

Since we do not have the MRI sequence for each of the patients, we used a fix heart-torso geometry obtained from [16]. We fit the estimated CCS models on the LV and RV of the reference model, and connected the PMJs to the tissue. To simulate the electrical propagation, we made use of the Stewart ionic cell model [17] for the CCS tissue.
Figure 2. Results for four patients. For each patient P1 (a) to P4 (d), the 2D disk plots for the re-annotated EAM are shown together with that obtained from simulation with estimated CCS. The corresponding ECG for leads V1 and V5 is shown. Solid red lines correspond to the acquired on the patients, and solid black line for the simulated, respectively.

3. Results

The estimation of the CCS gave rise to simplified CCS that could reproduce the sequence of activation on the endocardium of the ventricles. Figure 2 shows the results for cases (a) P1 to (d) P4. For each of the cases, the 2D disks show the LV LAT maps of the EAM data (top) and the simulated LV model (below) using the estimated CCS. As can be observed, the early (blue) and late (red) activated regions match properly between clinical and simulated maps. Although data were re-annotated, there were certain spatio-temporal inconsistencies, that were observed as large gradients in reduced areas. Those effect cannot be reproduced by the 3D models that show a smoother propagation in tissue and a constant electrical wave propagation.

Table 1 shows the number of estimated PMJs for each LV model, which ranges between 18 and 34, and will produce the early activated areas. The errors between the simulated and the clinical data (measured at the location of acquired points) are summarized in the column labeled as $\epsilon_t$. Average error was 5.72 ms. Since errors are measured at points were clinical samples are acquired, when a sample is not explained by any of the PMJs, the error at that point is high.

With respect to the simulated 12-lead ECG, the correlation between simulated and clinical signals was very high, ranging from 0.75 to 0.90 (see Table 1). The polarity and morphology of the signals matched in all cases for the 12 leads, as can be observed in Figure 2 for V1 and V5. The amplitude was the only parameter that was not properly reproduced, probably due to differences in the torso anatomy of each patient, which were not taken into account.

Table 1. Results from simulations with estimated CCS.

<table>
<thead>
<tr>
<th>Study</th>
<th>$CV_T$</th>
<th>$CV_{PK}$</th>
<th># PMJs</th>
<th>$\epsilon_t$ (ms)</th>
<th>$\rho_{ECG}$ (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>0.8</td>
<td>1.7</td>
<td>20</td>
<td>6.9</td>
<td>0.88</td>
</tr>
<tr>
<td>P2</td>
<td>0.9</td>
<td>1.7</td>
<td>18</td>
<td>4.4</td>
<td>0.75</td>
</tr>
<tr>
<td>P3</td>
<td>0.6</td>
<td>1.9</td>
<td>32</td>
<td>6.1</td>
<td>0.81</td>
</tr>
<tr>
<td>P4</td>
<td>0.7</td>
<td>2.1</td>
<td>34</td>
<td>4.5</td>
<td>0.9</td>
</tr>
<tr>
<td>P5</td>
<td>0.5</td>
<td>1.9</td>
<td>33</td>
<td>6.7</td>
<td>0.89</td>
</tr>
</tbody>
</table>
4. Conclusions

We have presented a procedure to personalize the activation of a computational model, based on the estimation of the patient CCS from his EAM. Results in 5 cases showed good agreement between simulated and acquired clinical 12-lead ECG. Including the CCS structure in the model, instead of a set of early activation sites, would permit to simulate complex arrhythmia reentries that are sustained by the CCS.

Acknowledgments

This study has been supported by Programa Propi d’Investigació del Vicerectorat d’Investigació de la UV, convocatória d’Accions Especials, expedient UV-INV-AE-1546534; the Leeduq Foundation and GENCI computing resources, allocation A0080310517; and from the French Government as part of the “Investments of the Future” program managed by the National Research Agency (ANR), Grant reference ANR-10-IAHU-04.

References


Address for correspondence:
Dr. Rafael Sebastian
Av. de la Universidad s/n, 46100, Burjassot, Valencia, Spain
rafael.sebastian@uv.es