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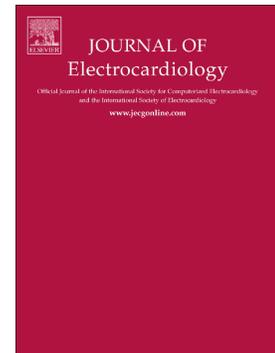
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Combining Endocardial Mapping and Electrocardiographic Imaging (ECGI) for Improving PVC Localization: A Feasibility Study

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Abstract

Introduction: Accurate reconstruction of cardiac activation wavefronts is crucial for clinical diagnosis, management, and treatment of cardiac arrhythmias. Furthermore, reconstruction of activation profiles within the intramural myocardium has long been impossible because electrical mapping was only performed on the endocardial surface. Recent advancements in electrocardiographic imaging (ECGI) have made endocardial and epicardial activation mapping possible. We propose a novel approach to use both endocardial and epicardial mapping in a combined approach to reconstruct intramural activation times.

Objective: To implement and validate a combined epicardial/endocardial intramural activation time reconstruction technique.

Methods: We used 11 simulations of ventricular activation paced from sites throughout myocardial wall and extracted endocardial and epicardial activation maps at approximate clinical resolution. From these maps, we interpolated the activation times through the myocardium using thin-plate-spline radial basis functions. We evaluated activation time reconstruction accuracy using root-mean-squared error (RMSE) of activation times and the percent of nodes within 1 ms of the ground truth.

Results: Reconstructed intramural activation times showed an RMSE and percentage of nodes within 1 ms of the ground truth simulations of 3 ms and 70%, respectively. In the worst case, the RMSE and percentage of nodes were 4 ms and 60%, respectively.

Conclusion: We showed that a simple, yet effective combination of clinical endocardial and epicardial activation maps can accurately reconstruct intramural wavefronts. Furthermore, we showed that this approach provided robust reconstructions across multiple intramural stimulation sites.

1 Introduction

Accurate electrical wavefront reconstructions are important in clinical cardiac electrophysiology. Many different tools, both invasive and non-invasive, provide clinicians with the overall direction, orientation, and earliest sites of activation.² These parameters provide clues to interpret the clinical pathology and

then to design and implement treatment strategies. However, these activation wavefront reconstructions are only surface reconstructions on either the epicardium or endocardium. Mapping techniques typical only include one surface, which means they capture only a surface projection of intramural information, *i.e.*, how the wavefront propagates through the three-dimensional myocardium. Without intramural information, it is difficult to correctly identify, visualize, and treat complex cardiac arrhythmia formation dependent.

Recent advancements in invasive and non-invasive epicardial mapping have opened the door for intramural reconstruction of wavefronts throughout the myocardial volume. Electrocardiographic imaging (ECGI) has been shown to non-invasively compute activation times on the epicardial surface^{2,6} and even both epicardium and endocardium simultaneously.^{14,15} An obvious step would be to combine both the non-invasive ECGI epicardial measurements and invasive endocardial measurements to create volumetric reconstructions of the intramural cardiac activation.

This study aims to develop and show feasibility of a novel approach to reconstruct intramural activation times by combining endocardial and epicardial activation maps. We assessed such a reconstruction approach using simulated activation time measurements paced from 11 different sites distributed over the left ventricle at various intramural depths. Additionally, we replicated real-world ECGI geometric error by translating the epicardial activation time maps in orthogonal directions to determine the robustness of the combined approach. We showed wavefront reconstructions that were adequate to guide ablation therapies and thus illustrate feasibility of this novel approach.

2 Methods

2.1 Image-based model and simulations of intramyocardial activation sequences

The Cardiac Arrhythmia Research Package (CARPentry) software suite provides all the tools needed to simulate ventricular activation from premature ventricular contraction (PVC),¹ which we conducted from 11 separate pacing sites at regularly spaced depths (1.7 mm apart) along a radial line spanning the entire left ventricular freewall (see Figure 1 upper row, leftmost column). The required geometric model (650 μ m resolution mesh, 63,000 nodes, and 3.2 million elements) included cardiac anatomy acquired with MRI from animal experiments as described previously.^{7,16} Activation times were computed throughout the myocardium using an eikonal formulation of the spread of excitation so as to match total activation times from the experimental recordings from similar pacing-site locations.⁷ The result was a set of 11 different intramyocardial activation sequences from the entire ventricles of a single subject.

2.2 Extraction of surface activation times and reconstruction of intramyocardial sequence

Our approach was to reconstruct volumetric activation times from surface maps sampled from either the endocardium or combined endocardium and epicardium. Endocardial maps were extracted from the simulation results described above to approximate catheter-based endocardial mapping density and coverage,⁵ *i.e.*, in a grid pattern with 1 mm spacing covering a 25x25 mm regions on the endocardium. The parameters to extract epicardial maps approximated non-invasive ECGI measured activation times *i.e.*, a 35x35 mm grid with 1 mm spatial resolution. Interpolation into the intramyocardial volume was by means of thin-plate spline radial basis functions.⁷

2.3 Perturbations of epicardial mapping locations

For each of the 11 pacing sites, we translated the locations of epicardial activation maps to simulate common geometric registration errors from ECGI. The translated locations of activation values moved by 7 mm over the epicardium in four orthogonal directions, parameters selected based on reported performance of epicardial ECGI activation time calculations.¹¹

2.4 Comparisons between reconstructed and ground-truth activation times

We analyzed the accuracy of the wavefront reconstruction by computing errors in activation times reconstructed throughout the myocardial wall. Along with the root-mean-squared error (RMSE) differences for each pacing site, we determined the proportion of nodes with interpolated activation times within 1 ms of the ground-truth value.

3 Results

Fig. 1 contains an example reconstruction of interpolated intramural activation times from both endocardial alone and epicardial/endocardial combined activation times, compared to ground-truth values from the original simulations. As shown, there is good agreement of the reconstructed activation times and wavefront patterns when using the combined endocardial/epicardial approach (RMSE = 3.0 ms). By contrast, reconstruction based only on endocardial values was poor (RMSE = 18.3 ms).

Statistical results supported these observations, with reconstructions based on endocardial activation maps alone producing RMSE values ranging from 26 to 10 ms, depending on the depth of the activation site. Results improved considerably using the combined endocardial/epicardial approach, where RMSE values were approximately 3 ms across all pacing sites Fig. 2 summarizes these results for all pacing sites with the black circles and yellow six-pointed stars. Fig. 3 show the proportion of nodes with an absolute error under 1 ms using endocardial mapping alone (black circles), which ranged from 18 to 28%, with the largest percentage occurring at the most epicardial pacing site. Result improved considerably when we included both endocardial and epicardial activation maps, with between 60 and 72% of nodes showing errors below 1 ms.

3.1 Epicardial perturbations

Results changed, at times substantially depending on the metric, in the face of geometric errors created by systematically translating the epicardial maps and re-interpolating from both endocardium and epicardium. Following perturbations, the RMSE increased only from 3 ms to, at worst, 6 ms (Fig. 2). The proportions of nodes with under 1-ms error showed a more prominent effect; in the worst case, values decreased from 60% to 30% in one translational scenario(Fig. 3). There were also differences between the effects of each type of shift that also depended on the pacing site.

4 Discussion

This study implemented and assessed the feasibility of a novel intramural activation time reconstructions using clinically acquirable endocardial and epicardial activation maps. Our simulation-based analysis showed a high intramural reconstruction accuracy, with over 60% of nodes having an activation times within 1 ms of the ground-truth values for the combined endocardial-epicardial approach across all tested

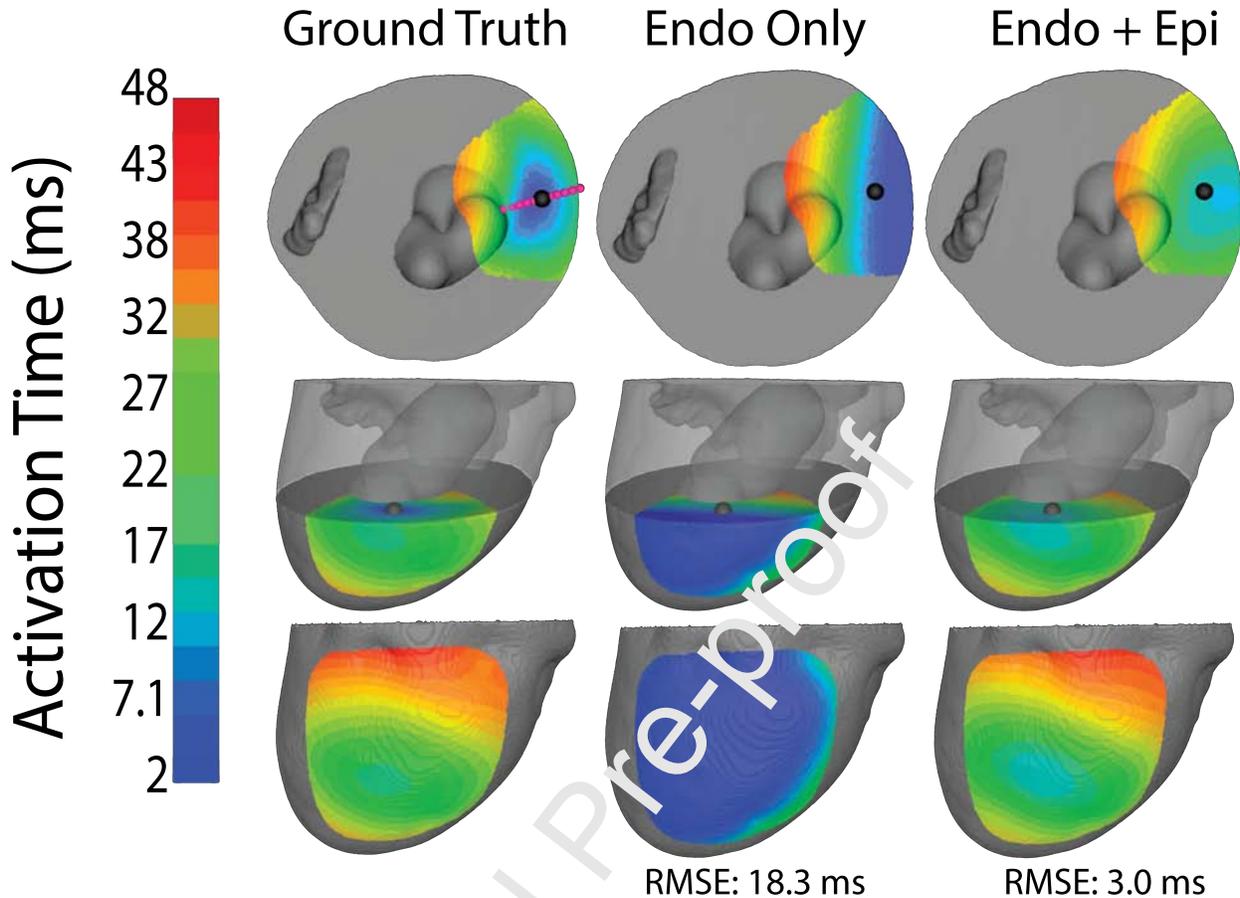


Figure 1: Example intramural activation time reconstructions (all units in ms). Row 1: axial cross section of heart. Row 2: long-axis cross section in the anterior-posterior view. Row 3: complete epicardial activation time reconstructions. Left column, ground truth simulated activation times for a mid-myocardial pacing site. Middle column, reconstructed activation times from endocardial only values. Right column, reconstruction from combined epicardial/endocardial values. Black spheres correspond to a mid-myocardial pacing site and the red spheres correspond to the locations of other 10. RMSE values for the two reconstructions are displayed below the respective columns.

pacing sites. The average RMSE values never rose above 4 ms for any condition we tested, at least when the locations of the epicardial mapping sites were known accurately (within 1 mm). When we applied geometric registration error noise to the epicardial activation maps, there was a drop in wavefront reconstruction accuracy, however, all reported metrics showed acceptable reconstructions with RMSE staying below 8 ms and percentage of nodes within 1 ms staying above 30%.

The first novel component of this study was to use both epicardial and endocardial activation maps to reconstruct activation times within the myocardial wall. Routine clinical wavefront reconstructions have been limited to one cardiac surface (more often endocardial), with any projection into the wall fraught with errors like those we documented in Fig. 1. It is simply impractical to measure both endocardial and epicardial activation times simultaneously in patients.¹² However, as electrocardiographic imaging (ECGI) has become more robust and clinically available, it has become practical to reconstruct epicardial activation non-invasively² and even to reconstruct both endocardial and epicardial activation simultaneously.^{14,15}

The preliminary results from our approach suggest that incorporating maps from both surfaces would

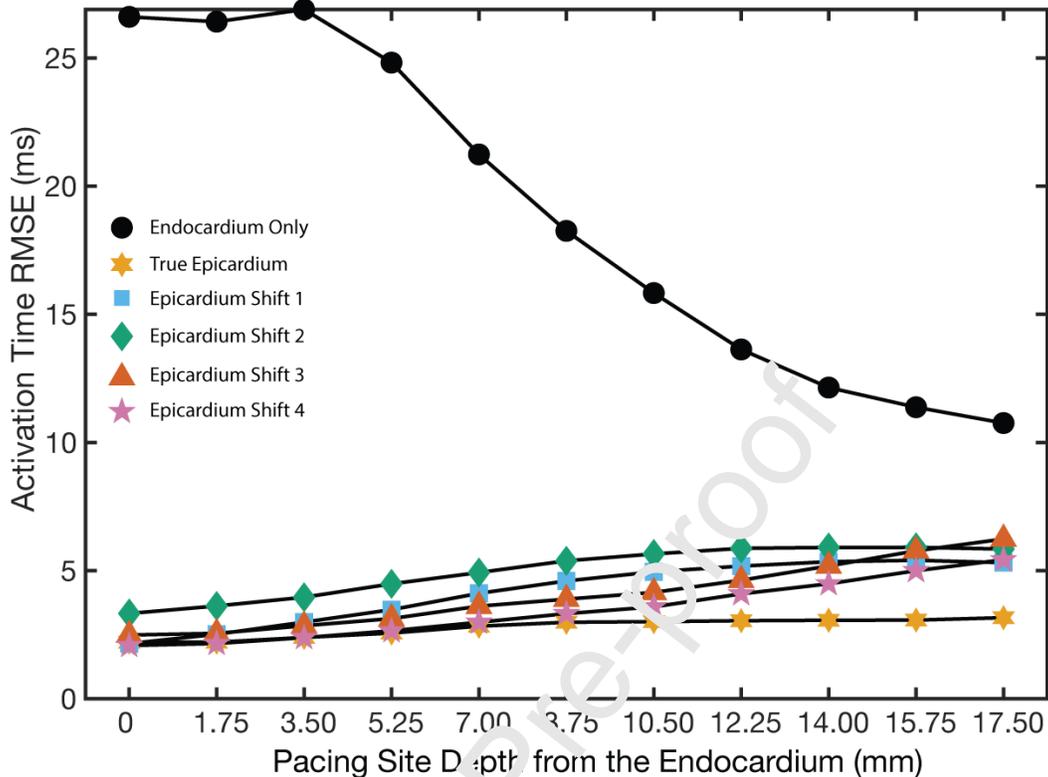


Figure 2: Average activation time RMSE (in ms) stratified by pacing site. Each line indicates a different reconstruction scenario including reconstruction based only on endocardial maps, and from epicardial + endocardial maps with ground-truth epicardial map placement and four translations of the epicardial activation times. Pacing sites are arranged according to depth from the endocardium in mm.

provide adequate results for clinical utility. We used a fairly simple reconstruction approach based on radial basis functions to interpolate activation times throughout the myocardial volume. Across a line of pacing sites that spanned the LV freewall, the reconstruction accuracy remained high. Furthermore, visual inspection showed that the combined endocardial/epicardial technique produced acceptable propagation wave patterns, orientations, and directions compared to ground truth activation profiles.

We simulated a small range of activation sequences by varying the pacing site across the LV freewall to determine if activation might affect wavefront reconstructions. The combined approach was most accurate for endocardial pacing and dropped only slightly as pacing approached the epicardium—for RMSE from 3 to 4 ms or for the proportion of values with error below 1 ms, from 70 to 60%. This robustness to activation sequence is a crucial finding because it is often challenging to determine the origins the PVCs using non-invasive 12-lead ECG alone.

We also assessed the robustness of the combined reconstruction approach to errors in position of the epicardial activation maps, which is one potential source of error common in ECGI. Such geometric registration errors are common in ECGI because the body geometry, heart geometry, and electrode locations can be challenging to capture noninvasively.¹⁰ Moreover, artifacts arise from patient movement, body orientation, and breathing patterns that can alter the positioning of electrodes relative to the heart and torso surface.^{3,13} To investigate the effects of the resulting errors in epicardial map location on our novel epicardial/endocardial reconstruction approach, we translated the epicardial maps by 7 mm in each

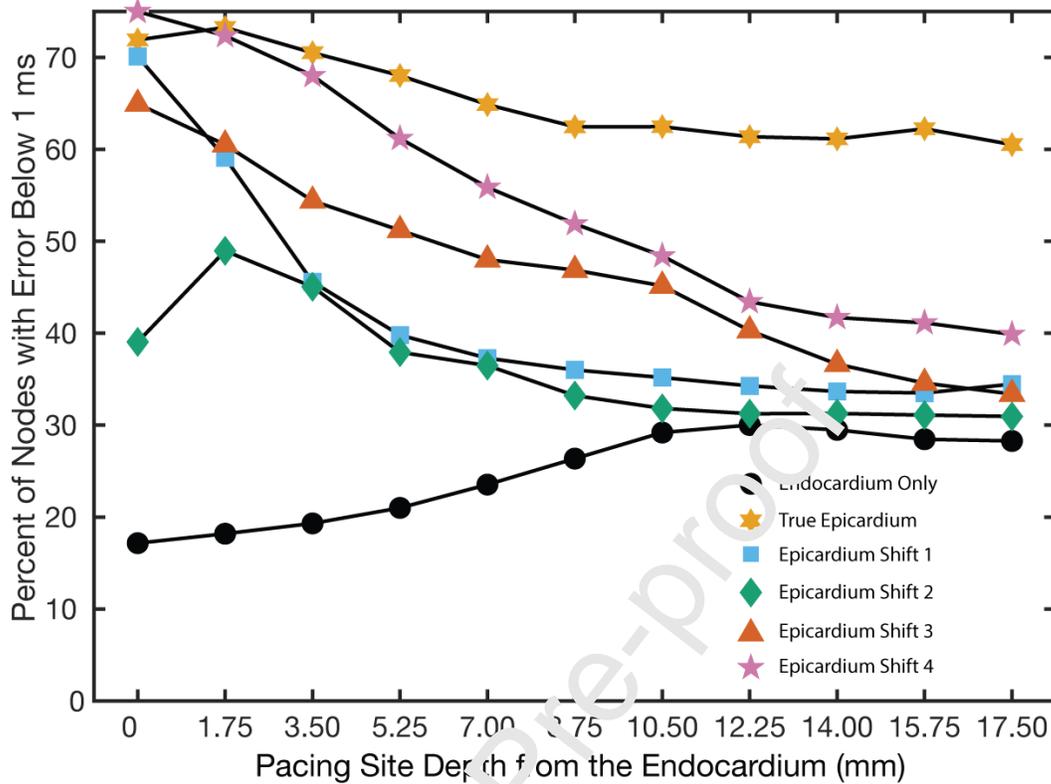


Figure 3: Proportion of nodes (in percent of total) with an absolute error under 1 ms stratified by pacing site. The data values and lines are defined as in Figure 2.

of four orthogonal directions.^{4,9,11} Results for the RMSE of activation times stayed persistently low (within 3 ms) while the proportion of nodes with error under 1 ms dropped more substantially, from 70% to 30% for some pacing sites. However, visual inspection showed that despite these statistical changes, the general patterns of the activation waves were preserved. Overall, these results suggest that the combined approach, even with added clinical variability, could still provide clinically useful descriptions of activation, specifically the locations of midmyocardial sites of origin of PVCs.

Possible limitations of this study are rooted in its nature as a test of basic feasibility to reconstruction activation in the myocardial volume from measurements on the cardiac chamber surfaces. The reconstruction approach was quite simple in concept and implementation, with origins in our experimental applications, which included intramyocardial measurements;^{8,16} there is every expectation that more sophisticated approaches might improve the results. This preliminary study is also based on a single, albeit realistic, cardiac geometric model derived from an experimental study and the pacing sites spanned only one set of transmural locations, both simplifications that ongoing studies will overcome. The results under these conditions are extremely promising and motivate extensive further study. The key point is that all aspects of the approach are technically feasible in clinical applications and can be validated more extensively than at this early stage in animal and human studies.

Acknowledgments

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We would like to move forward with the manuscript as is. Thank you so much!

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