Quantitative localization of premature ventricular contractions using myocardial activation ECGI from the standard 12-lead electrocardiogram

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Abstract

Background: The precise localization of the site of origin of a premature ventricular contractions (PVC) prior to ablation would facilitate the planning and execution of the electrophysiological procedure. Current electrocardiographic imaging (ECGI) techniques require body surface maps, a costly and complex procedure, that requires as many as 256 leads to localize the PVC origin. We developed and tested a novel myocardial activation based ECGI technique utilizing the readily available 12-lead ECG to localize the PVC origin.

Methods: The major components of the 12-lead ECGI method are: the source model, proximity effect and spatial orientation, volume conductor, and patient specific model of the heart, lungs, and thorax as derived from magnetic resonance imaging (MRI). For the PVC origin localization, the fastest route algorithm is used on patient specific models created by newly developed morphing software. PVC localization by the 12-lead ECGI was correlated to the site of successful ablation.

Results: Seven patients that underwent electrophysiological mapping and ablation of PVCs were studied. All patients (7/7) had accurate prediction of the PVC origin. However in two patients, no specific MRI was used for localization that resulted in an incorrect switch between the RV free wall and septum of the RVOT. With patient-specific models, these latter two cases would likely be localized correctly.

Conclusions: This feasibility study of a novel myocardial activation-based ECGI using only the standard 12-lead ECG shows promise to localize the origin of PVC. This ECGI method yields activation estimates of isochrones on both ventricles from which the PVC origin location is derived. This method has the capability to localize the PVC from any part of the ventricular endocardium, intra-myocardium or epicardium.

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Introduction

Catheter ablation has been shown to be an effective therapy for treatment of symptomatic premature ventricular contractions (PVC). Prior to the ablation procedure, an anatomic estimate of the PVC origin is commonly derived from only qualitative descriptions of the standard 12 lead ECG waveforms. Recently, electrocardiographic imaging (ECGI) has been successfully applied in clinical research to determine complex ventricular activation. Because ablation sites can be estimated from activation maps, ECGI has the potential to provide valuable information for catheter ablation. However, current ECGI methods are based on body surface maps (BSMs) derived from multiple leads (64–256). In addition, the patches of the electro anatomical mapping system might prevent the correct placement of the BSM electrodes. Furthermore, an ECGI method that can localize the PVC origin specific to the endocardium, intra-myocardium, or epicardium would be of significant clinical benefit.

In a recent study by Wang et al., BSM based ECGI method was shown to be accurate for predicting the site of origin of PVC and ventricular tachycardia (VT). This study demonstrated the power of ECGI methods to plan the ablation of arrhythmias. However, this method mainly localizes the PVC and VT to the epicardium. Although, the local morphology of the QRS may estimate the transmural depth of the PVC.
current study, we investigated the feasibility of our newly developed cardiac isochrone positioning system (CIPS) based ECGI method using the standard 12-lead ECG to localize PVC origins to the endocardium or epicardium of the right and left ventricle and septum.

Methods

Components of myocardial activation based ECGI

The ECGI method used is based on models representing the electric currents generated by the heart called the source model and on the electric volume conductor properties of the body tissues surrounding the heart that effect the potential field observed on the body surface (ECGs). To better understand the mathematical models used in this study, we have organized the activation based ECGI method into the following major components:

1) Cardiac current source model that is linked to electrophysiological findings
2) Proximity and spatial orientation of the 9 ECG electrodes,
3) Electrical volume conductor,
4) Patient’s specific geometry from Magnetic Resonance Imaging (MRI),

The first component, the cardiac current source model, is the equivalent double layer (EDL) model. The EDL represents the currents generated during the depolarization spread through the myocardium, which is equivalent to the result of all the coupled myocardial cells as recorded at endo- and epicardial surfaces. Consequently the EDL is referred to the endocardial and epicardial surface of the myocardium (Fig. 1a, c). In the mathematical model, the local source strength at node $n$ of the triangulated ventricular surface follows the local transmembrane potential (TMP), analytically defined by the depolarization time $\delta_n$ and repolarization time $\rho_n$ at that node $n$ (Eq. 1, Fig. 1c).

The second component involves the proximity of the ECG electrodes with respect to the spatial orientation to the heart (see $B(\ell, n)$ in Eq. 1). The potential generated by an activation front depends on the solid angle subtended by that front at an electrode location (see Fig. 1d). This solid angle is comparable to the ‘3D view cone’, as described for the heart by Wilson et al. in 1933 and as described for triangulated heart computer model by van Oosterom et al. The proximity of the wave front determines largely the solid angle; distant wave fronts have smaller solid angles compared to wave fronts in close proximity to the electrode (see Fig. 1d). Electrodes on the lateral side of the chest have different solid angles (‘views’) on a particular wave front compared to electrodes near the sternum that are at near right angle views.

The third component is the electrical volume conductor effect dominated by tissues having electric conductivity values that differ prominently from those of the surrounding tissues.
tissues (Fig. 1b, see $B(\ell, n)$ in Eq. 1). The volume conductor model is composed of the blood in the ventricular chambers and the air in the lungs (Fig. 2). The major effect is the zero electric conductivity of the air surrounding the thorax.

The mathematical method used to solve this volume conductor problem in a numerical way is referred to as the Boundary Element Method (BEM). With the BEM a transfer matrix $B$ can be computed taking into account the full complexity of the discretized volume conductor model (Eq. 1). The conductivity values used in this study were for the thorax and ventricular muscle tissue 0.2 Siemens/meter (S/m), for the lungs 5 times less than this conductivity (0.04 S/m) and for blood 3 times better (0.6 S/m). The potentials ($\varphi$) at thorax node of the 12 lead electrodes are equal to

$$\varphi(t; \ell) = \sum_n B(\ell, n)S(t; \delta_n, \rho_n),$$

in which $S(t; \delta_n, \rho_n)$ is the local time dependent EDL source strength, and $B(\ell, n)$ the BEM derived transfer function relating the contribution of $S$ at node $n$ to the potentials $\varphi$ at thorax node $\ell$.

The fourth component relates to patient-specific geometries of the heart, lungs and thorax derived from MRI (see Fig. 2). Previous studies have shown the importance of patient-specific models. These models were created with new morphing software. This software was created, because no commercial software is available to generate models that can directly be used in our ECGI method. With this software the boundaries of all relevant tissues were identified manually. For the ventricles these boundaries are the left and right endocardium, epicardium, aorta and pulmonary artery. To capture the spatial orientation from the 12 lead electrodes, the epicardium and endocardium, lungs, and thorax of reference models are automatically morphed to match the manual drawn contour points — patient specific geometries. The use of reference models enables the use of clinical recorded cardiac MRIs, with relative large distances between the subsequent MRI cross-sections of the heart.

The ECG technique

The standard 12-lead ECGs sampled at 1000 Hz were recorded during the ablation procedure. From these ECGs, a representative PVC of the clinical ECG waveforms was selected for each patient. Fiducial points, i.e. onset and end QRS, were determined manually. Subsequently the ECG was baseline corrected between two successive QRS onsets. No additional filtering was applied to any of the ECG signals. To simplify the calculations, the ECGI procedure is executed on nine signals $V_R, V_L, V_F, V_1-\overline{V}_6$ referenced to the Wilson central terminal.

Patient-specific MRI-based models

In all patients, the newly developed morphing software was used to reconstruct MRI based anatomical models of heart, lungs, and thorax. In five patients, models were

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Fig. 2. Patient-specific model and anatomic variation. The two in the top row are the models taken from the ECGsim website: normal young male and the 40 year normal male. The other two are the patient specific cased reconstructed for this study. In all versions, the orientation of the heart and lung distribution within the thorax differs significantly per patient. The dark red shows the right ventricular blood cavity, the light right represents the left blood cavity. Note the great variation of heart sizes and positions. Color illustration online.
Algorithm, as used in every map navigation system. This activation isochrones is computed using the fastest route procedure. The result of this fine tuning procedure matched ECG waveforms with a correlation of more than 98%. Patients. For the other 5 patients realistic models were used. The location of the PVC origin matched well with the ablation site for these two patients, these models were obtained from the individual and gender only, due to the limited size of our database. In two patients, these models were obtained from the individual recorded MRI. Two of the models in the database are also available on the ECGsim website (www.ecgsim.org). On all individual thorax models, the ECG electrodes were positioned to the standard 12-lead locations.

PVC localization

After having created a model using all the components that translate the activation isochrones into ECG waveforms, the next step is to rematch every ms of the modeled ECG with the actual measured ECG. The process has been described in detail in van Dam et al. In short: Initially a rough estimate of the activation isochrones is computed using the fastest route algorithm, as used in every map navigation system. This fastest route algorithm computes activation isochrones originating from every discrete node on the triangulated ventricular surface (Fig. 1c). For each set of activation isochrones originating from a node, the 12 lead ECG was computed (Eq. 1). The first estimate of the activation isochrones is the one with the highest correlation between the actual ECG measured and model ECG computed. The correlations found for these initial estimates ranged between 80% and 90% due to modeling errors in each of the components and algorithms. This rough tuning mismatch in ECG waveforms was reduced by fine tuning the activation isochrones using a Levenberg–Marquardt based optimization procedure. The result of this fine tuning procedure matched ECG waveforms with a correlation of more than 98%. 

Results

Seven patients undergoing electrophysiological mapping and ablation of symptomatic PVCs were retrospectively studied (Table 1). The electro-anatomical maps (NAVX, CARTO) were the gold standard for the 12-lead localization ECGI algorithm. With this algorithm the PVC origins were localized correctly in patients 1 to 5 (Table 2) and localized correctly in patients 6 and 7 to the RVOT. However in patient 6, the PVC was incorrectly located to the RV septum and not to the close epicardial RV free wall, and in patient 7 it was incorrectly located to the RV free wall and not to the close RV septum (Table 2). In contrast, using specific MRI derived models, the PVC origins were localized correctly in both patients 1 (Fig. 3) and 2 (Table 2).

Discussion

The results of this feasibility study show the ability of the myocardial activation based ECGI technique to locate PVC origins using only the 12 lead ECG. When using an MRI derived model, all the patients studied had the origin of the PVCs correctly localized. However, in patients 6 and 7, a part of the localization was incorrect, patient 6 was in the RV septum and not the close RV free wall and patient 7 was in the RV free wall and not in the close RV septum. Since the localization errors of these 2 patients were close and reversed, they would probably be corrected by using patient specific MRIs. 

Current clinical practice uses the 12-lead ECG for localization and pre-procedural planning of PVC ablation procedure. In this approach qualitative descriptions of specific ECG lead waveforms are used to localize the PVC origin. The limited accuracy of this qualitative 12-lead ECG analysis restricts the capabilities to support the planning of the ablation procedure. These limitations also apply to the BSM based ECGI methods capable of only localizing PVCs to the epicardium.

To our knowledge, no other ECGI method is available to localize quantitatively the PVC origin from the 12-lead ECG. In this feasibility study, the accurate correlations obtained are likely attributed to structure of our ECGI method that permits the use of rough and fine tuning of the activation isochrones from the ECG. This tuning capability was the result of using the simple fastest route algorithm to generate the activation.

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age</th>
<th>EF %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>39</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>31</td>
<td>48</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>36</td>
<td>38</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>46</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>15</td>
<td>56</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>51</td>
<td>65</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>50</td>
<td>65</td>
</tr>
</tbody>
</table>

None of the patients had a history of myocardial infarction. During the ablation procedure no scar was found except in patient 3 in whom a large area of scar was found along inferobasal and mid inferior segments of the left endocardial ventricle.

Table 2

Comparison between the localization of ablation site from the electroanatomical maps and the origin of the PVCs based on myocardial activation based ECGI.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Location ablation site</th>
<th>Activation based ECGI localization</th>
<th>Patient model</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LV Superior Septum</td>
<td>LV Superior Septum</td>
<td>Specific</td>
</tr>
<tr>
<td>2</td>
<td>RVOT Septal</td>
<td>RVOT Septal</td>
<td>Specific</td>
</tr>
<tr>
<td>3</td>
<td>Mid Left Endocardial Lateral Wall</td>
<td>Mid Left Endocardial Lateral Wall</td>
<td>Database</td>
</tr>
<tr>
<td>4</td>
<td>RVOT Endocardial Anterior</td>
<td>RVOT Endocardial Anterior</td>
<td>Database</td>
</tr>
<tr>
<td>5</td>
<td>RVOT Mid Septal</td>
<td>RVOT Mid Septal</td>
<td>Database</td>
</tr>
<tr>
<td>6</td>
<td>RVOT Anterosuperior Septal</td>
<td>RVOT Anterosuperior Free Wall (Epicardial)</td>
<td>Database</td>
</tr>
<tr>
<td>7</td>
<td>RVOT Anterosuperior Free Wall</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The first 2 patients had MRI data from which a patient specific model was constructed. The PVC origin coincided well with the ablation site for these two patients. For the other 5 patients realistic models were used. The location of the PVC origin matched well with the ablation site for the patients 3–5. For patients 6 and 7 the PVC origin was located correctly in the RVOT region.
Isochrones. This computer program can be further tuned by incorporating fiber direction or the slow activation as the result of fibrosis.  

Other investigators have localized PVCs only to the epicardium using body surface mapping. The advantage of our ECGI method is its ability to localize quantitatively PVCs to the specific MRI based myocardial wall from the readily available digital standard 12 lead ECG to the right, left or septal ventricular wall locations and to the endocardium, epicardium, or intra-myocardium. The reason for this specific myocardial PVC localization is because this program was designed to locate ‘dipoles’ in space and time from the ECG waveforms recorded from the 9 specifically located electrodes on the body surface. In the method section, the components that produced the final isochrones on the endo- and epicardium (EDL8,9) are presented. The advantage of this approach is that the endo- and epicardial isochrones are determined in patients. Intra-myocardial locations of a PVC origin can be interpolated from activation isochrones on the endocardial and its epicardial wall. This capability of localizing PVCs is demonstrated in patients 3 and 4 with the PVC origin located on the endocardium of the mid left lateral wall and anterior RVOT, respectively. Furthermore, in patients 1, 2, and 5 the PVC origin was located correctly in the LV superior septum, septal RVOT and mid wall of the RVOT. The success of this ECGI method is based on the incorporated electro-physiological knowledge to generate the activation isochrones on the MRI derived patient specific cardiac model. These isochrones allow the quantitative localization of the PVC origin to improve the planning and execution of the ablation procedure.

Limitations

In this retrospective study, we used the ablation sites indicated on the electroanatomical maps as the gold standard for the localization of the PVC origin using the 12 lead ECG. Because the 12-lead morphology of a PVC reflects the exit site, the ablation site does not necessarily coincide with the origin of the PVC and in cases of scar, these may be more spatially and anatomically alter this origin. Further studies at localizing the exit site of scar-mediated VT are ongoing in our group. Consequently, the ablation site may not be the gold standard for localization of the origin of the PVC. Furthermore, the electroanatomical mapping technique has a limitation in the accuracy of the quantitative registration with the MRI, thereby limiting the accuracy of the calibration of the myocardial activation based ECGI method.

Another important limitation is variable and unknown location of the exact electrode placement of the 12-lead ECG for all patients. During ablation procedures most often the electrodes are not put in the standard position due to the attachment of other equipment to the patient’s chest, preventing the correct attachment of the ECG leads. Lastly, the patient models selection was based on age and gender alone and did not take weight or body surface area into account. Additional models that incorporate patient size are currently being used for prospective analysis.

Based on the present study, a large prospective study is needed and ongoing. Specifically, each case will have routine calibration by comparing the MRI or fluoroscopic images derived electrode location to the ECGI localization of the pacing electrode. Furthermore, patient-specific 3-dimensional...
location of each of the ECG electrodes should be registered to the specific MRI images of the heart, lungs and thorax. This added method would likely improve the quantitative localization of the origin of PVCs, VT, and delta waves in pre-excitation. From a practical standpoint, our technique can be integrated into electroanatomical mapping systems in order to optimize navigation during ablation procedures.

**Conclusions**

The present results of this feasibility study suggest that the CIPS based ECGI method can be used to localize accurately the origin of PVC using the standard 12-lead ECG. Patient-specific modeling is necessary to optimize this novel approach. Of importance, this ECGI method can be used before as well as during the procedure. The ability to determine the transmural location of the site of origin has important clinical value and warrants further investigation.

**Appendix A. Supplementary data**

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jelectrocard.2013.08.005.

**References**

17. van Dam PM, van Der Graaf AWM, Gotte MJW. A new 3D patient specific morphing tool enabling clinical application of non-invasive cardiac activation imaging, in ESC. Muenchen; 2012.