Modeling Structural Abnormalities in Equivalent Dipole Layer Based ECG Simulations

Manon Kloosterman[1], Machteld J Boonstra[1], Folkert W Asselbergs[1], Peter Loh[1], Thom F Oostendorp[2], Peter M van Dam[1]

[1]University Medical Centre Utrecht, Department of Cardiology, Utrecht, The Netherlands
[2]Donders institute for Brain, Cognition and Behaviour, Radboud University Medical Centre, Nijmegen, The Netherlands

Abstract

The relation between abnormal ventricular activation and corresponding ECGs still requires additional understanding. The presence of disease breaks the equivalence in equivalent dipole layer-based ECG simulations. In this study, endocardial and epicardial patches were introduced to simulate abnormal wave propagation in different types of substrates. The effect of these different types of substrates on the QRS complex was assessed using a boundary element method forward heart/torso and a 64-lead body surface potential map (BSPM). Activation was simulated using the fastest route algorithm with six endocardial foci and QRS complexes corresponding to abnormal patch activation were compared to the QRS complexes of normal ventricular activation using correlation coefficient (CC). Abnormal patch activation affected both QRS morphology and duration. These QRS changes were observed in different leads, depending on substrate location. With insights obtained in such simulations, risk-stratification and understanding of disease progression may be further enhanced.

1. Introduction

The electrocardiogram (ECG) is widely used as a diagnostic tool to provide insight in the electrical activity of the heart. In progressive cardiomyopathy, the shape and magnitude of the measured body surface potentials (BSP) change over time.[1] The relation between abnormal ventricular activity on corresponding ECG abnormalities still requires additional understanding which can be obtained through invasive electro anatomic mapping and ECG simulation studies. Using the latter, slight changes in underlying ventricular activation can be simulated, achieving more detailed insight and understanding of electrical substrates.

Two types of models are required to simulate the ECG; a cardiac source model, representing electrical currents generated by ventricular cells, and a volume conductor model representing the effect of these generated currents on the ECG.[2] The equivalent dipole layer (EDL) is such a cardiac source model. The EDL is positioned at the endocardial and epicardial surface bounding the myocardium. The local source strength at each element of this surface model is defined by the local transmembrane potential. Changing local depolarization and repolarization times result in changes in the simulated ECG.[3]

In EDL based modelling, the presence of diseased myocardium breaks the equivalence of the dipole layer. To restore the equivalence, in order to adequately simulate abnormal substrate activation, an additional boundary between healthy and diseased myocardium was incorporated, referred to as patches. In this simulation study, we explore the use of such patches representing different types of substrates to simulate abnormal wave propagation and to study their effect on the ECG.

2. Methods

2.1. Simulation of normal activation

We used a CT-based anatomical model (57y male) with a 64-lead ECG set-up. The anatomical model contained the triangulated surface meshes of the ventricular myocardium, blood pools, thorax and lungs with the following assigned conductivities: 0.2 S/m, 0.6 S/m, 0.4 S/m and 0.2 S/m respectively. The discrete transfer matrix was computed using the boundary element method from each triangle of the discretized ventricular surface towards each observation point at or within the torso.[3]

The EDL was used as a cardiac source model.[3] First, the described patient specific (57y male) anatomical model was used to simulate normal activation. Activation sequences were simulated using the fastest route algorithm with six endocardial foci.[4] The source strength at each

node is proportional to the local transmembrane potential with its shape defined by δ and ρ, the local depolarization and repolarization time respectively (**Figure 1A**).[3]

2.2. Simulation of diseased myocardium

To simulate abnormal substrate activation, additional boundaries (patches) were incorporated between healthy and diseased myocardium. At four different locations, endocardial and epicardial patches were embedded within the ventricular model (**Figure 1B**).

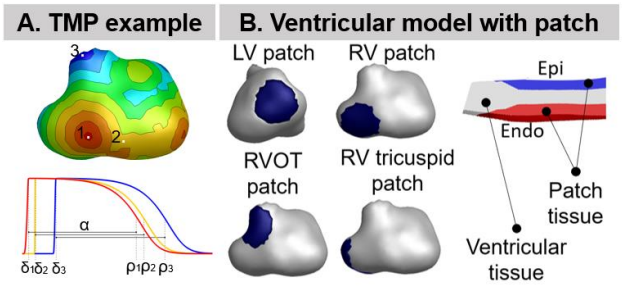

Figure 1. A. Simulated activation sequences from red (early) to bleu (late) with corresponding local transmembrane potentials. With α indicating transmembrane potential duration, δ activation timing and ρ repolarization timing. **B.** CT- based ventricular model with patches (bleu region). Patches were embedded within the ventricular model (red endocardial, blue epicardial).

Depending on the electrical connection between ventricular and patch tissue (**Figure 2**), nodes directly in contact with the ventricular model were assigned the same activation timing as the ventricular nodes. The patch activation sequence was then computed using the fastest route algorithm together with a set propagation velocity.

Different types of patch activation were simulated (*e.g.* homogeneous and inhomogeneous delay) to assess the effect on simulated BSP. Homogeneous patch activation was simulated by reducing patch propagation velocity from 0.85 m/s (normal) to 0.25 m/s (severe delay). Inhomogeneous patch activation was simulated adding Gaussian noise (0-90 ms).

The patch was activated continuous or discontinuous (**Figure 2**). The part of the patch in direct contact with the myocardium was either fully connected with the ventricular model (continuous activation) or only the outer ring of the patch was connected to the ventricular model (discontinuous type 1), or only the latest 25% of the outer ring were connected to the ventricular model (discontinuous type 2).

Normal ventricular activation was compared to all cases of abnormal patch activation by assessing QRS duration and QRS morphology. Most affected leads were determined as the lead with the lowest Pearson's correlation coefficient (CC).

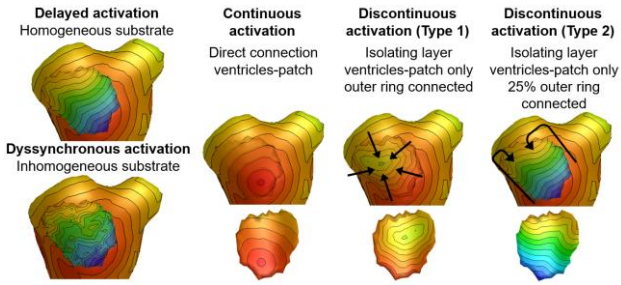

Figure 2. Different types of activation sequences (delayed, dyssynchronous, continuous and discontinuous) of the patches. Activation sequences are displayed as local activation timing maps from red (early) to blue (late)

2.3. Clinical case

Brugada Syndrome is characterized by fibrofatty tissue in the right ventricular outflow tract (RVOT). During Ajmaline provocation, the typical Brugada ECG pattern may become apparent. We created a patch at the epicardial surface in the RVOT and Ajmaline provocation was simulated by decreasing overall myocardial propagation velocity. In the patch, activation wave disruption was amplified and current-to-load mismatch was simulated by decreasing local transmembrane potential amplitude.

3. Results

In total, 153 abnormal patch activation sequences were simulated. When using the same propagation velocity for the patch and the ventricles, simulated BSP were the same as the original model. The presence of diseased patch activation affected both QRS morphology and duration (**Figure 3**). The presence of an epicardial versus endocardial patch resulted in an opposing electrical vector observed in BSP.

An inhomogeneous substrate compared to a homogeneous substrate resulted in more evident changes in both QRS morphology and duration (**Figure 3**). Discontinuous patch activation due to an 'isolating' layer between patch and normal ventricular myocardium (**Figure 4**), resulted in a patch activation initiated at the edge of the patch. The direction of activation through the patch differed depending on the connection between the ventricular myocardium and the patch.

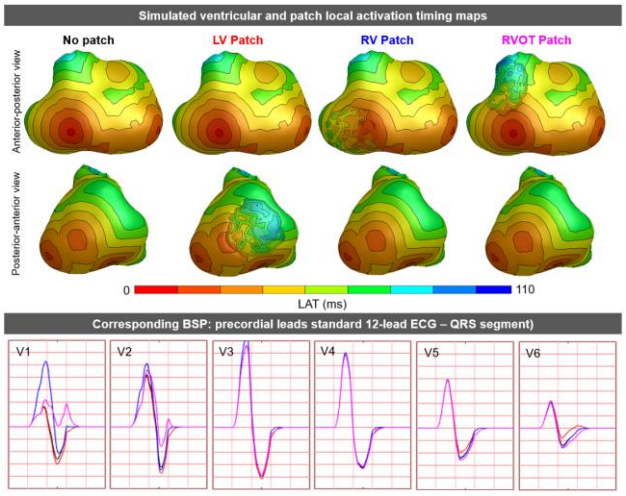

Figure 3. Effect of abnormal patch activation on the computed 12-lead ECG. In all cases, conduction velocity of the myocardium was set at 0.85 m/s and of the patch at 0.45 m/s. An inhomogeneous substrate was simulated in all cases using a patch with ranging activation times (0-30 ms).

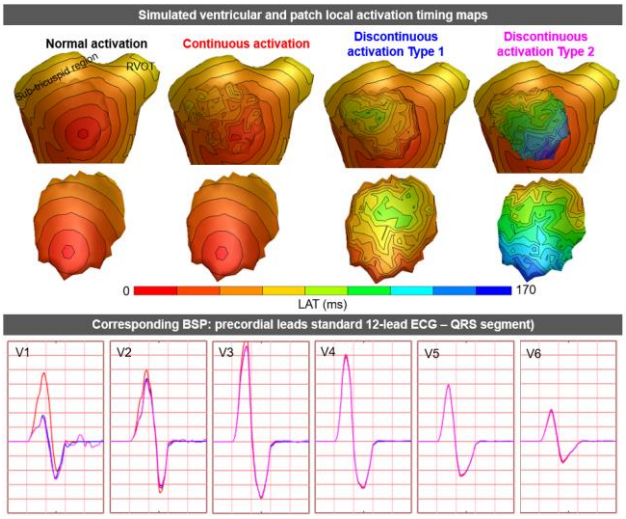

Figure 4. Effect of abnormal patch activation on the computed 12-lead ECG. In all cases, conduction velocity of the myocardium was set at 0.85 m/s and of the patch at 0.45 m/s. An inhomogeneous substrate was simulated in all cases using a patch with ranging activation times (0-30 ms) with different connection types between patch and ventricles.

Depending on substrate location, the agreement between QRS complexes was different amongst leads (**Figure 5**). Overall QRS-CC was 0.99 [0.9 ;1.00], but higher for a homogeneous versus inhomogeneous substrate (1.00 [0.99;1.00] vs. 0.97 [0.92;0.99], p<0.001).

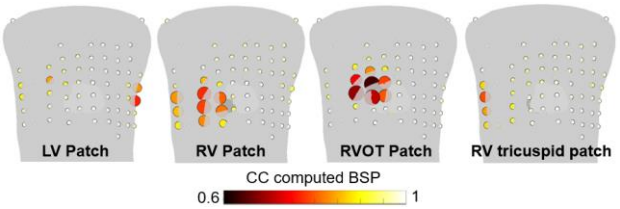

Figure *5*: Effect of patch location on computed BSP. Mean ± standard deviation of correlation coefficient per BSP lead between normal and diseased BSP is displayed. Each dot represents an electrode with the color representing average CC and the size magnitude in standard deviation.

When simulating Ajmaline provocation in Brugada Syndrome (**Figure 6**), patch activation was further disrupted, resulting in the typical Brugada QRS changes, *e.g.* increased R'-wave amplitude, QRS duration prolongation and J-point/ST-segment elevation (**Figure 6B**). Especially leads V1 and V2 of the standard 12-lead ECG were mostly affected. When assessing the Brugada leads (**Figure 6C**), even bigger QRS changes were observed.

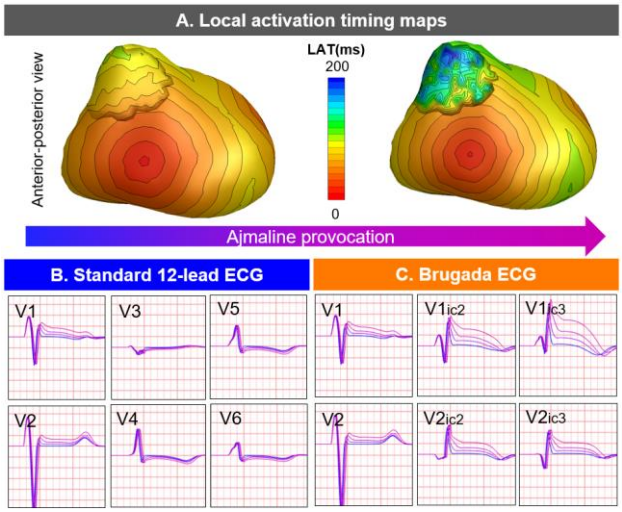

Figure *6* Ajmaline provocation in Brugada Syndrome. Progressively increasing QRS duration, changing QRS morphology and ST-segment elevation can be observed by simulated ajmaline administration in lead V1, lead V2 and the Brugada leads V1ic2, V1ic3, V2ic2 and V2ic3.

4. Discussion

In this study, we introduce a novel method to study the effect of different types of abnormal cardiac electrical activity (*e.g.* substrate types) on the ECG. We observed that an inhomogeneous substrate affected QRS morphology and duration more than a homogeneous substrate. Furthermore, discontinuous patch activation resulted in a patch activation initiated at the edge of the patch with the direction of activation dependent on the connection between ventricular myocardium and the patch. With the new simulation method, we obtained local activation timing map patterns similar to the described patterns of diseased areas assessed during invasive electro anatomic mapping studies.

With the novel method, we were able to simulate the effect of abnormal ventricular activation consisting of both healthy myocardium and fibrofatty tissue. This is new compared to earlier ECG simulation studies. These studies modelled transmural scar by creating a hole in the ventricular model.[5] Thereby simulating completely electrically inactive myocardium. By using patches, we were able to restore the equivalence of the EDL and by assigning different activation characteristics different substrate types could be simulated. The use of these patches, consisting of both diseased and healthy myocardium in one patch, provides a more representative substrate in cases of old myocardial infarctions and inherited cardiomyopathies.

The possibility to study the effect of different activation characteristics (*e.g.* substrate types) on the ECG may also be used to identify the most affected leads. This may be very important in the detection of subtle disease onset in inherited cardiomyopathies like arrhythmogenic cardiomyopathy (ACM). In ACM, early disease onset is mostly observed in the basal area of the RV free wall.[6] Modelling of this substrate location resulted in QRS changes in regions outside the standard 12-lead ECG (**Figure 3).** The importance of a disease specific lead configuration is thereby indicated since subtle QRS changes may be an important sign of disease progression and an increased risk for ventricular arrhythmias.

The described patches may also be used to simulate the effect of medication in both healthy myocardium and diseased myocardium. When simulating Ajmaline provocation in the Brugada case, expected and realistic ECG and underlying cardiac activation pattern changes were observed. In particular, an increased R'-wave amplitude, QRS duration prolongation and J-point/ST-segment elevation. Although realistic activation pattern changes could be observed, expected repolarization abnormalities were absent. This is because our model is not yet able to model realistic T-wave morphologies in case of repolarization heterogeneities. Therefore, future research will focus on the transmembrane potential template to acquire realistic repolarization sequences.

Several simulation characteristics like propagation velocity and source strength were modified to simulate different substrate types. However, some of these simulation characteristics were set far below realistic physiological values. For example, patch propagation velocity (0.25 m/s compared to 0.85 cm/s) and source strength. Source strength in the patch was decreased to account for the presence of fibrofatty tissue. Although not all simulation characteristics could be set a realistic physiological value, we may conclude that our method was able to simulate realistic BSP due to the presence of different substrate types and locations.

5. Conclusion

Different types of myocardial disease with specific activation characteristics (delay, desynchrony, discontinuity) can be simulated using the described patches which directly gives insight into the effect on the ECG which can in turn be related to different cardiac diseases. In this simulation study, we observed clinically relevant characteristics to monitor substrate development. Therefore, our model may be used for teaching purposes to relate pathologies to ECG waveform changes and our model may be used for non-invasive inverse estimation of activation in the presence of inhomogeneous scar.

References

[1] Rautaharju PM, Park LP, Chaitman BR, Rautaharju F, Zhang Z-M. "The Novacode criteria for classification of ECG abnormalities and their clinically significant progression and regression" J Electrocardiol., 31, 3, 157-87, 1998

[2] van Dam PM, Oostendorp TF, van Oosterom A. "ECGSIM: Interactive Simulation of the ECG for Teaching and Research Purposes" Computing in Cardiology 37, 841-4, 2010

[3] Oostendorp T, van Oosterom A. "The potential distribution generated by surface electrodes in inhomogeneous volume conductors of arbitrary shape" IEEE Trans Biomed Eng., 38, 5, 409-17 1991

[4] van Dam PM, Oostendorp TF, van Oosterom A. "Application of the fastest route algorithm in the interactive simulation of the effect of local ischemia on the ECG" Med Biol Eng Comput., 47, 1, 11-20, 2009

[5] Oostendorp TF, Ham Wv. "Non-invasive estimation of the activation sequence of the heart: modeling of old myocardial infarctions" Biomed Tech., 46, suppl. 2, 54-6, 2001

[6] Mast TP, Taha K, Cramer MJ, Lumens J, van der Heijden JF, Bouma BJ, et al. The prognostic value of right ventricular deformation imaging in early arrhythmogenic right ventricular cardiomyopathy. JACC: Cardiovascular Imaging., 12, 3, 446-55

Address for correspondence:
Manon Kloosterman
Heidelberglaan 100, 3584 CX Utrecht, The Netherlands
Manon.kloosterman@live.com