Simulating ECG Changes during Acute Myocardial Ischemia

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Abstract

In this paper the changes in ECG waveforms during the first 20 minutes of an ischemic event are studied in a simulation model. A new method, based on the shortest path algorithm, is introduced for simulating the effects of the reduced propagation velocity within an ischemic zone on the timing of the depolarization sequence throughout the entire myocardium and the resulting ECG changes.

1. Introduction

Acute myocardial ischemia (AMI) can cause permanent damage to myocardial myocytes within less than half an hour. The changes in the ECG occurring in this period are rarely recorded in humans. This study uses a computer model to simulate the changes in ECG at different stages following an ischemic event.

In this study the equivalent double layer surface source model of cardiac electric activity and a volume conductor model based on Magnetic Resonance Imaging were used. The simulated ECG wave forms during sinus rhythm have previously been validated, and have been implemented in the software package ECGSIM (www.ecgsim.org) [1]. This simulation tool permits the study of the effect of acute ischemia resulting from changes in the magnitude of the transmembrane potential (1) in regions of arbitrary location and extent. Provisions for handling the effect of changes in the propagation velocity within the ischemic region (2) and the effect of the accompanying shortening of the action potential duration (3) were not implemented. In the current study methods have been developed for also simulating the effects (2) and (3). The influences of all three factors on ECG morphology were studied.

Two sets of parameter values were identified for simulating successive phases of acute myocardial ischemia: the earliest phase directly following the event (after one minute), and the phase occurring after approximately 5-10 minutes. The results found were in agreement with data available from literature. The methods developed will be implemented in ECGSIM, which will permit the interactive study of all three effects.

2. Methods

Forward model

Any description of the genesis of electrocardiographic potentials requires the specification of the current sources generated by the biochemical reactions at the cell membrane: the source model. In addition a specification is required of the properties (extent and conductivity values) of the medium in which the potential field is set up: the volume conductor model. In this study the relevant geometry of heart and the volume conductor were derived from MRI images of a healthy 22-year old human male. The geometries of the atria and ventricles were reconstructed at the onset of the P wave.

Source model

The model of the cardiac current generator used was the equivalent double layer surface source model (EDL), located at the closed surface S_h bounding the myocardium, comprising epicardium and endocardium. The double layer may be viewed as a sheet of current dipoles directed along the local surface normal of S_h. This source model has a direct link with electrophysiology and has previously been shown to be very effective in the simulation of the potentials during depolarization and repolarization of the atria [2,3] and ventricles[1,4].

The time course of the local strength of the double layer is that of a stylized version of the transmembrane potential (TMP) of healthy myocytes. It is specified by the magnitude of the upstroke of the TMP (a_n) at any node n of the surface S_h, its timing of depolarization (δ_n) (Figure 1), and its activation recovery interval (α_n) (ARI), a specific measure of the action potential duration. The ARI is defined as the time difference between the depolarization moment δ_n and the inflection point during repolarization (Figure 2). Accordingly, the source strength at node n at time instant t can be denoted as $S(t,\delta_n,\alpha_n,a_n)$. Based on this source model, the potential on any lead ℓ on the surface of the thorax is calculated as:

$$\phi_\ell(t) = \sum_{n=1}^{N} A(\ell,n)\ \ S(t,\delta_n,\alpha_n,a_n), \quad \text{Eqn.(1)}$$

where $\boldsymbol{A}(\ell,n)$ is the transfer matrix expressing the involved volume conductor effects [3] .

From normal to ischemic activation sequences

The basis of the method used for simulating the changes in activation sequence during ischemia is the shortest path algorithm [5]. This algorithm is widely used for, *e.g.*, finding the *shortest* route between any two locations. It has previously been introduced for generating cardiac activation sequences propagating at uniform velocity [6]. In its current application, locally different propagation velocities are considered, as are used by any route finder for computing the *fastest* route between any two locations. The algorithm used is referred to as the fastest route algorithm (FRA).

The effect of the decrease in the propagation velocity within ischemic areas is implemented by means of the FRA. It requires a heart model in which the propagation velocity between any pair of the set of nodes representing the heart surface is known. The normal velocity $v_{i,j}$ along each connection over the surface or within the myocardium was derived from the distance through the myocardium, $d_{i,j}$, between nodes i and j and the delay, $t_{i,j}$, between the reference activation times at these nodes [6]. These reference values were estimated from the timing of depolarization found by means of a dedicated inverse procedure [6],

$$v_{i,j} = \frac{d_{i,j}}{|t_{i,j}|} \qquad \text{Eqn. (2)}$$

The effectiveness of these velocity estimates and the FRA were tested by computing the full activation sequence as initiated at the six locations nodes f_1.. f_6, (k=1…6) of early breakthrough indicated in Figure 1, as well as their timing, t_k. The timing of depolarization at the remaining nodes (n=1500-6) was computed as follows. First, six depolarization sequences ($\boldsymbol{t}_{dep}(k)$) were computed, each originating from one of the given foci: starting at t=t_k.

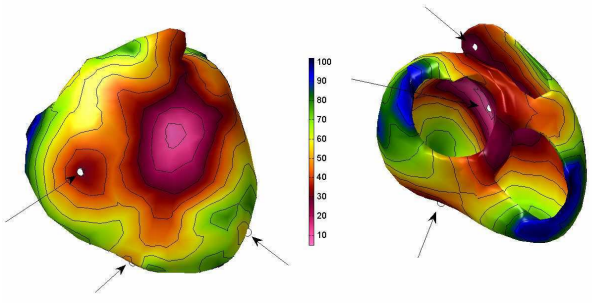

Figure 1. Isochrones of the reference timing of ventricular depolarization during sinus rhythm. Six sites of breakthrough are marked (arrows pointing at the white dots, the foci f_1..f_6). Left: anterior view; right: posterior-basal view. Isochrones are drawn at 10 ms intervals.

The timing of depolarization at any node i for sequence $\boldsymbol{t}_{dep}(k)$ is assigned the value $t_i(k)$= t_k + $t_{i,k}$, with $t_{i,k}$ computed as $t_{i,k}$=$d_{j,k}$/$v_{j,k}$ using the velocities estimated from the reference timing. Finally, the depolarization time at node i in the presence of all (active) foci was taken to be

$$t_i = \min_k\left(t_i(k)\right), \qquad \text{Eqn. (3)}$$

i.e., first come first served. The resulting timing matched the full reference timing at all nodes exactly.

During acute myocardial ischemia the propagation velocity within the infarcted area is reduced [7]. The effect on the total activation sequence was simulated by using the FRA and the estimated velocities, while reducing the values inside the ischemic zone. Along all connections to nodes within the ischemic zone the velocities were reduced by a factor. If a focus was found to be located within an ischemic area, the corresponding node was no longer treated as a focus.

Ischemic action potential duration and amplitude

The repolarization process following depolarization is relatively slow and may continue up to the next activation. During ischemia myocardial cells repolarize faster, i.e. the ARI shortens (α_n in Figure 2).

In the normal state the resting potential is about -90 mV (a_0 in Figure 2). During ischemia the resting potential rises over time up to maximally -60 mV. At a resting potential level greater than -60 mV the cells generally remain depolarized.

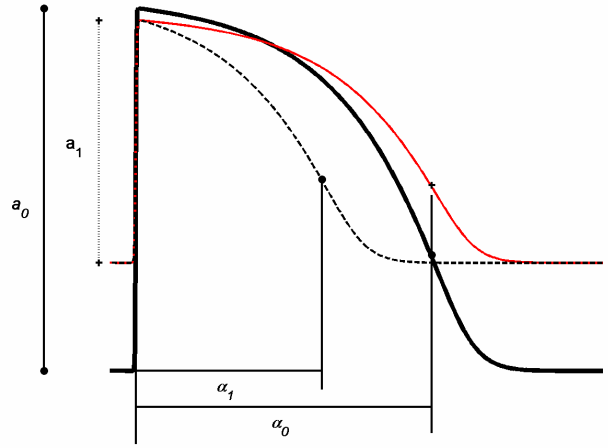

Figure 2. Stylized transmembrane potentials (TMP) at a ventricular node acting as sources for simulating the electrical signals. The TMP at each node n is specified by the timing of depolarization (δ_n) its activation recovery interval (α_n) and its amplitude (a_n). Three cases are shown: 1) normal case (thick solid black line, α_0, a_o), 2) reduced amplitude (thin solid line, α_0, a_1), and reduced amplitude and duration (dashed line, α_1, a_1).

3. Results

We simulated the ischemic situation resulting from an occlusion in the left anterior descending artery (LAD). By occluding the LAD the anterior ventricular wall and the septum become ischemic (Figure 3a,b). Two successive ischemic phases were defined to simulate ischemia; an early and late phase. Initially the occlusion only causes ischemia in the epicardial layer of the muscle tissue (early ischemia), whereas after several minutes the endocardium also becomes ischemic (late ischemia).

When modeling the early phase, the propagation velocity was reduced by 10%, the TMP amplitude was reduced by 5%, and the ARI was shortened by 25 ms. In the late phase both propagation velocity and amplitude of the TMP were reduced by 25%, and the ARI was shortened by 75 ms.

The effect of the reduction in propagation velocity is shown in Figure 3. In the early phase only the ischemic epicardial area is affected. During the late ischemic phase the septal focus was deactivated and the ischemic area encompassed the whole myocardial wall, i.e. including the endocardial wall (Figure 3b). As can be seen, the reduced velocity in the ischemic region not only resulted in changes in the timing inside the ischemic area, but also in the remainder of the heart (Figure 3c). The septum was activated up to 50 ms later than the reference timing.

The 12 lead ECGs corresponding to the early and late situations are shown in Figure 4. For early phase ischemia small changes in the QRS complex are visible on the leads close to the ischemic area (V2-V3). The changes in ST-T wave morphology are most pronounced on leads V2, V3 and V4. The removal of the septal focus in the case of late ischemia shows a slightly prolonged QRS complex, with clear changes in all leads. The changes in the T wave are relatively small compared to the changes made, i.e., the 25% decrease in TMP magnitude and an ARI shortening of 75 ms.

The maps of changes in the ST level, a clinical measure for ischemia, are shown in Figure 5. The ST amplitude at 80 ms after the end of the QRS-complex was evaluated in both situations and compared to the ST value of the reference ECG. The delta ST maps at the early and late stages show patterns with a positive shift below V2 and V3 and a negative shift above V1. Note that the shifts during the early stage are greater than in the later one.

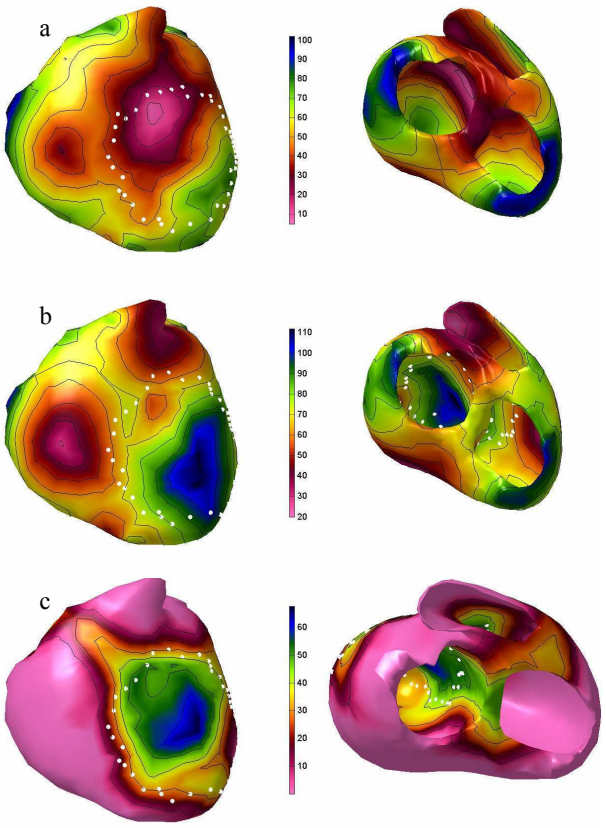

Figure 3. Simulated ischemic activation sequences and the difference in timing compared to the reference activation timing (Figure 1). Panel a: Activation sequence with reduced propagation velocity of 10% in the ischemic region. Panel b: As in panel a; velocity reduced by 25%. Panel c; the difference between the timing in panel b and the reference timing shown in Figure 1. All panels, left: anterior view; right: posterior-basal view (In panel c the right view has been rotated such that the septum is visible). Isochrones are drawn at 10 ms intervals. The white dots indicate the border of the ischemic area.

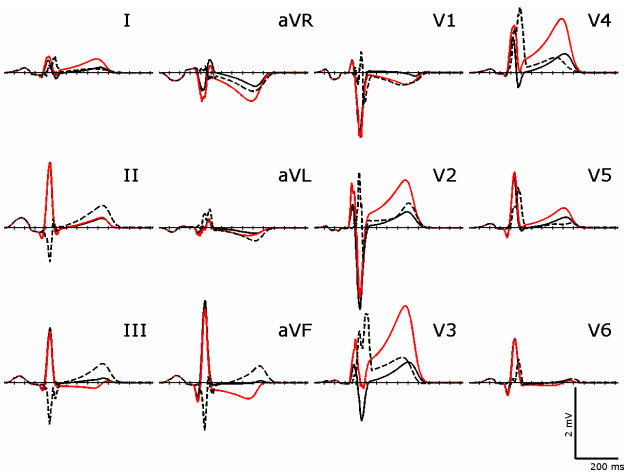

Figure 4. Simulation of 12 lead ECG during ischemia due to occlusion of the left anterior descending artery within 1-2 minutes after occlusion (early phase, gray line) and after several minutes (late phase, dashed line). The black solid line shows the reference ECG (see also Figure 1).

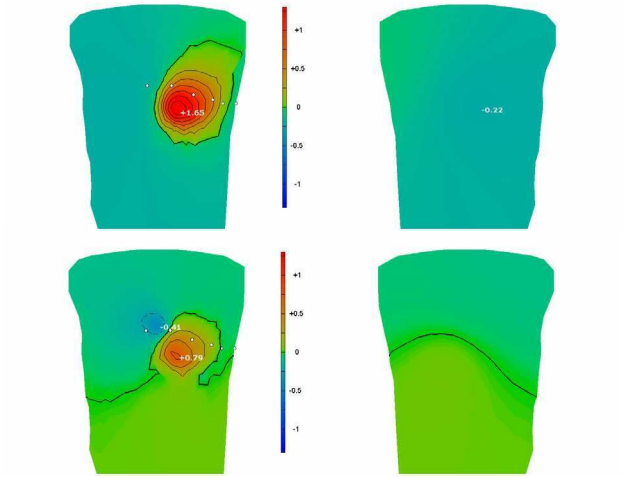

Figure 5. Delta ST maps during LAD based ischemia during the early phase (top panels) and late phase (bottom panels). Range for the early phase: [+1.65.. -0.22] mV. Range for the late phase: [+0.79 .. -0.41] mV. The front of the torso is shown on the left, the back on the right. All values in mV. Isopotential lines are drawn at 0.25 mV intervals.

4. Discussion and conclusions

Based on a reference timing of depolarization at the nodes on the ventricular geometry and the geometry itself, the velocities within and over the surface of the ventricles were estimated. From these velocities the FRA was found to accurately recapture the reference, i.e. the normal activation sequence. The simulation of an ischemic activation sequence was obtained by a local reduction of the propagation velocity.

In the early ischemic phase the propagation velocity is reduced by only 10%. Despite this small reduction in velocity and accordingly small change in activation sequence (Figure 3a) the effect on the QRS complex is visible (Figure 4). The late ischemic phase shows clearly that the timing outside the ischemic area is also affected (Figure 3c), as is found in clinical studies. The ECG during this phase is more fractionated since one of the foci within the ischemic area has been deactivated.

The patterns of the simulated delta ST maps during the early phase show a close match with data recoded during a PTCA procedure [8]. However, the magnitude of the delta ST values was larger. This might be due to the fact that the geometry data used in our study were those of a slim subject, in whom the distance between body surface and heart is generally smaller, thereby causing larger ST segment shifts. The ST changes corresponding to other areas of ischemia and during other phases, not presented here, qualitatively matched results described in the literature [9-11].

The model introduced here can be useful in identifying ischemic areas in patients displaying delayed activation in specific regions. In its interactive use, this can be done by testing the effect of a reduced local propagation velocity in a suspect region and comparing the resulting ECG with that of the individual patient.

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