On the Use of the Bidomain Model for Computing the Position and Size of Ischemic Regions; a Validation Study

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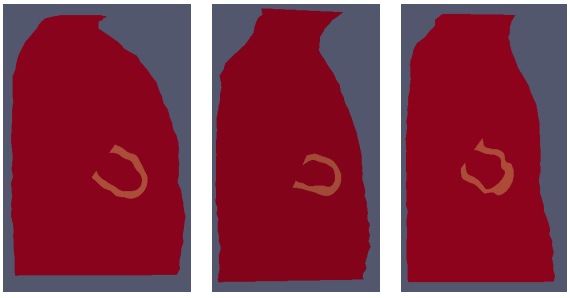
Abstract

In this paper we discuss a framework involving exercise ECG testing and mathematical models for identifying ischemic regions in the heart. More precisely, the ischemic regions are identified by minimizing the difference between recorded and simulated multi-channel ECG signals. Furthermore, we investigate how geometrical changes of the heart, lungs and torso affect the size and position of the ischemic regions that are calculated. To validate our findings, the computed ischemic regions are visualized in terms of images and compared with images taken with perfusion scintigraphy.

1. Introduction

Ischemia is a *temporary* shortage of oxygenated blood at the cellular level. For individuals with plaque narrowing of the coronary arteries, such shortage may arise when vigorous exercise triggers an increased need of blood to the heart muscle. The transient mismatch in supply and demand of oxygen that occurs causes no permanent damage to the myocardial tissue, but it can be extensive enough to temporary affect the electrical activity of the suffering cells. The *Exercise ECG* aims at temporary altering the electrical activity by performing physical exercise while recording ECG.

Exercise ECG is an inexpensive, immediate, repeatable and non-invasive test that has been extensively validated. However, it is reported that the sensitivity and spesificity of exercise ECG are approximately 70 percent each. Consequently, there are a substantial number of false negative and false positive tests, see [1]. Since individuals with an ischemia will be put at risk for developing myocardial infarction, the challenge of improving the diagnostic accuracy of ECG has drawn a lot of attention among researchers. One branch of this research has been to combine mathematics and computer simulations with ECG measurement to increase the diagnostic value of ECG [2, 3]. However, by introducing such a methodology, realistic 3D grids of each patient are needed. A description for generating patient specific 3D grids can be found in [4]. An example of three patient specific geometries is shown in Figure 1. For visualization purposes, only 2D slices of these geometries are shown. Please note the differences in the heart and body shape, as well as in the position and rotation of the heart.



(a) Geometry 1 (b) Geometry 2 (c) Geometry 3

Figure 1. 2D slices (sagittal view) of the different 3D geometries that are used in this study. Each slice is positioned approximately 5 cm to the left from the vertical midline of the body.

Based on these geometrical variations, an interesting question would be *how sensitive are the computer simulations with respect to different geometries?*. In the following we will investigate how geometrical changes of the heart, lungs and body shape affect the size and position of the ischemic regions that are computed.

2. Mathematical framework

Let H denote the domain occupied by the heart and consider the stationary model (a simplification of the bidomain model [5, 6])

$$\nabla \cdot ((M_i + M_e)\nabla u) = -\nabla \cdot (M_i \nabla v) \quad \text{in } H, \tag{1}$$

where M_i and M_e are the intra- and extra-cellular conductivities tensors, whereas v and u represent the transmembrane and extracellular potentials, respectively. In general, both v and u are unknown functions, but according to lab measurements, the transmembrane potential v can be approximated by certian constant values during the PR[1] and ST[2] segments of the the heart cycle. Furthermore, during these two time segments, the values for v depend upon whether a supply/demand imbalance does occur, i.e. whether ischemic tissue is present or not [7]. Typical values for v during relaxation and at maximum workload are given in Table 1 and in Table 2, respectively. Below, we let D denote the ischemic region in the heart.

Table 1. Approximate values for v before exercise.

Segment	Potential
PR	$v(x,t_1) \approx -96mV, \quad x \in H$
ST	$v(x,t_2) \approx 0mV, \quad x \in H$

Table 2. Approximate values for v at maxmium workload.

Segment	Potential
PR	$v(x,t_3) \approx \begin{cases} -96mV, & x \in H \setminus D \\ -60mV, & x \in D \end{cases}$
ST	$v(x,t_4) \approx \begin{cases} 0mV, & x \in H \setminus D \\ -20mV, & x \in D \end{cases}$

Since myocardial ischemia results whenever there is a transient imbalance between coronary blood flow and myocardial work, we are interested in an approximation for the shift h in the transmembrane potential, i.e. the transmebrane potentials at maximum workload *relative* to the potentials during relaxation

$$h(x) = \underbrace{\overbrace{v(x,t_4)}^{\text{ST}} - \overbrace{v(x,t_3)}^{\text{PR}}}_{\text{maximum workload}} - \Big[\underbrace{\overbrace{v(x,t_2)}^{\text{ST}} - \overbrace{v(x,t_1)}^{\text{PR}}}_{\text{relaxation}}\Big] \tag{2}$$

The associated shift r in the extracellular potential u is defined as

$$r(x) = \underbrace{\overbrace{u(x,t_4)}^{\text{ST}} - \overbrace{u(x,t_3)}^{\text{PR}}}_{\text{maximum workload}} - \Big[\underbrace{\overbrace{u(x,t_2)}^{\text{ST}} - \overbrace{u(x,t_1)}^{\text{PR}}}_{\text{relaxation}}\Big]. \tag{3}$$

Since (1) must hold for all t, and thereby for $t = \{t_1, t_2, t_3, t_4\}$ for all $x \in H$, it follows from (1), (2) and (3) that

$$\nabla \cdot ((M_i + M_e)\nabla r) = -\nabla \cdot (M_i \nabla h) \quad \text{in } H. \tag{4}$$

Further, by using (2) and the values in Table 1 and Table 2, an approximation for h is given as

$$h(x) \approx \begin{cases} 0mV, & x \in H \setminus D \\ -56mV, & x \in D. \end{cases} \tag{5}$$

During an exercise ECG test, the electrical potentials are recorded on the surface of the body. Therefore, an equation representing r also outside the heart must be included in our model. Outside the heart there are no sources, and thus r is governed by a standard homogeneous potential equation:

$$\nabla \cdot ((M_o \nabla r) = 0 \quad \text{in } T, \tag{6}$$

where M_o represents the conductivity in T, and T is defined as the domain surrounding the heart H. Details concerning suitable interface and boundary conditions for model (4) and (6) can be found in [2].

2.1. Inverse solution

The approximate recovery of h from ECG data d is accomplished by dividing the left ventricle into 60 subunits and assigning a basis function to each of these units:

$$N_1(x),\ N_2(x), \ldots,\ N_{60}(x),$$

where

$$N_j(x) \approx \begin{cases} 0\text{mV}, & x \text{ outside subunit } j, \\ -56\text{mV}, & x \text{ inside subunit } j, \end{cases} \tag{7}$$

for $j = 1, 2, \ldots, 60$. In this paper we have only studied subendocardial ischemic regions. Therefore, the support of N_j was restricted from endocardium and 3/5 of the endocardium-epicardium distance into the heart wall.

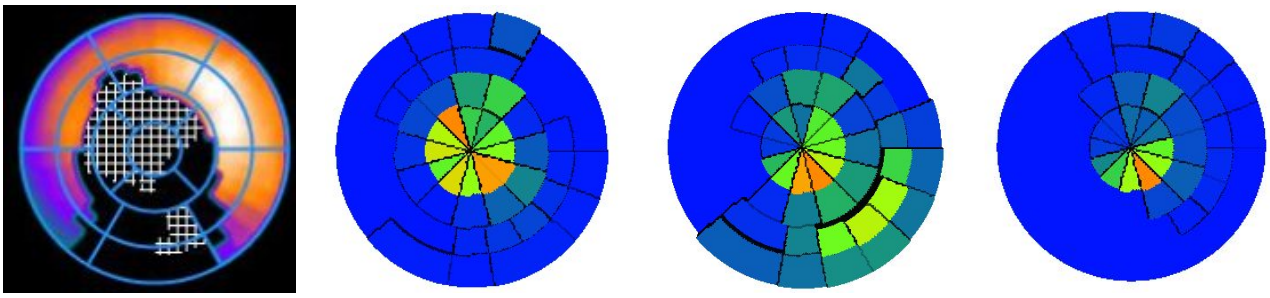
The shift in the transmembrane potential was discretized by putting

$$h(x) = \sum_{j=1}^{60} p_j N_j(x). \tag{8}$$

Our scheme for identifying ischemic zones is based on the output least squares approach. More specifically, assuming

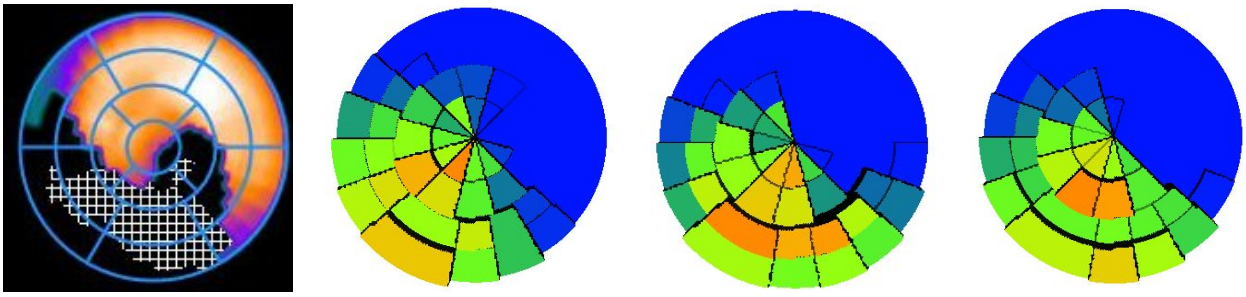
[1] The PR segment is assumed to occur 1-25 ms before onset of the QRS complex.

[2] The ST segment is measured 60-80 ms after the end of the QRS complex.



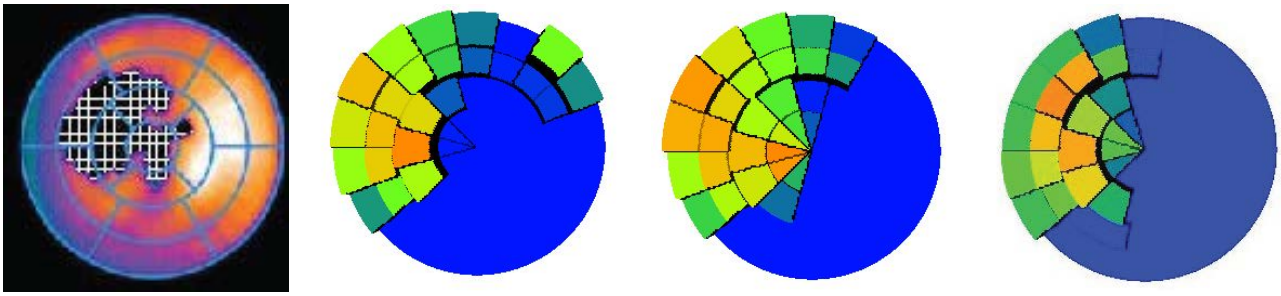
(a) Scintigraphy patient 1 (b) Result with geometry 1 (c) Result with geometry 2 (d) Result with geometry 3

Figure 2. The inverse problem was solved using ECG from patient 1 along with geometries from either patient 1, 2 or 3. The size and position of the computed ischemic region are visualized in terms of a bullseye plot, see (b), (c) and (d). These bullseye plots should be compared with each other and against the scintigraphy (hashed region).



(a) Scintigraphy patient 2 (b) Result with geometry 1 (c) Result with geometry 2 (d) Result with geometry 3

Figure 3. The inverse problem was solved using ECG from patient 2 along with geometries from either patient 1, 2 or 3. The size and position of the computed ischemic region are visualized in terms of a bullseye plot, see (b), (c) and (d). These bullseye plots should be compared with each other and against the scintigraphy (hashed region).



(a) Scintigraphy patient 3 (b) Result with geometry 1 (c) Result with geometry 2 (d) Result with geometry 3

Figure 4. The inverse problem was solved using ECG from patient 3 along with geometries from either patient 1, 2 or 3. The size and position of the computed ischemic region are visualized in terms of a bullseye plot, see (b), (c) and (d). These bullseye plots should be compared with each other and against the scintigraphy (hashed region).

that we have e electrodes, we suggest to recover such regions by minimizing the deviation between the ECG data $d = (d_1, d_2, \ldots, d_e)$ and the simulated ST shift on the body surface, i.e.

$$\min_{p_1,p_2,\ldots,p_{60}} \frac{1}{2} \left\{ \sum_{k=1}^{e} [r(y_k) - d_k]^2 + \alpha \sum_{j=1}^{60} p_j^2 \right\} \quad (9)$$

subject to

$$\nabla \cdot ((M_i + M_e)\nabla r) = -\nabla \cdot (M_i \sum_{j=1}^{60} p_j \nabla N_j) \quad \text{in } H, \ (10)$$

$$\nabla \cdot ((M_o \nabla r) = 0 \quad \text{in } T, \ (11)$$

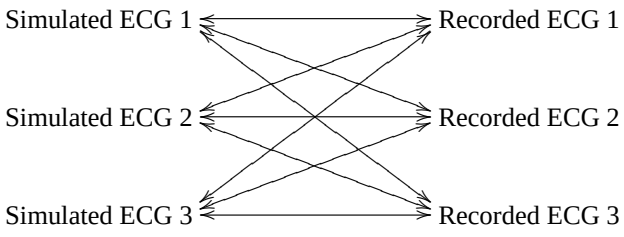
$$0 \leq p_j \leq 1 \quad \text{for } j = 1, 2, \ldots, 60. \ (12)$$

Here, $\alpha > 0$ is a regularization parameter and $y_1, y_2, \ldots, y_e$ are the positions of the electrodes.

3. Results

Three patients were included in the study, all accepted for coronary evaluation at Oslo University Hospital on the suspicion of coronary artery disease. Each patient went through an exercise ECG test with SPECT myocardial scintigrapy, and patient specific grids were generated.

Geometries from patient 1, 2 and 3 were then used to generate three sets of simulated ECG signals. Let us call these results Simulated ECG 1, Simulated ECG 2 and Simulated ECG 3, respectively. Furthermore, let us call the exercise ECG data from patient 1, patient 2 and patient 3 for Recorded ECG 1, Recorded ECG 2 and Recorded ECG 3, respectively. Now, the inverse problem was solved nine times, using each of the simulated ECGs successively along with the three recorded ECGs.



With this approach, the recorded ECGs are combined with different geometries and we can investigate how geometrical variations of the heart, lungs and body shape effect the size and position of the ischemic regions that are computed by solving (9)-(12), see figures 2-4.

4. Conclusions

In this paper we discuss a framework involving exercise ECG testing and mathematical models for identifying ischemic regions in the heart. Moreover, we investigate how geometrical changes of the heart, lungs and torso affect the size and position of the ischemic regions that are computed. To validate our findings, the computed ischemic regions were visualized in terms of images and compared with images taken with perfusion scintigraphy. An interesting observation is that the method for computing the size and position of the ischemic regions seems to be rather robust with respect to geometrical changes. Nevertheless, the method must be tested on many more patients and quantitative analyzes must be undertaken in order to assess its clinical value.

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