

Simulation of ECG under Ischemic Condition in Human Ventricular Tissue

Weigang Lu^{1,2}, Kuanquan Wang¹, Henggui Zhang^{1,2}, Wangmeng Zuo¹

¹School of Computer Science and Technology, Harbin Institute of Technology, Harbin, China

²School of Physics and Astronomy, University of Manchester, Manchester, U.K

Abstract

In this study, we developed a 2D model of human left ventricular tissue based on the anatomical structure of human heart. Using the model, we explored the functional effects of ischemia-induced electrical properties of cardiac cells on ventricular electrical wave conduction. The ischemic model takes into account of three main pathophysiological consequences of ischemia that include hyperkalaemia, acidosis, and anoxia. The effects of ischemic level and size on the characteristics of ECG were quantified. It was shown that under ischemic conditions, the action potential durations of ventricular cells were abbreviated. And in most cases, the larger the size of ischemic region or the more severe the ischemic level, the more dramatic the changes in the amplitude of ST-T wave were observed.

1. Introduction

Myocardial ischemia, which is caused by reduced coronary blood flow to the heart, is the foremost precursor of cardiac arrhythmias that cause morbidity and mortality. The cardiac electrophysiological abnormality is quite dangerous. However, the functional effects of ischemia-induced electrical properties of cardiac cells on ventricular electrical wave conduction have not been fully understood yet. Electrocardiogram (ECG) is one of the most powerful tools for clinical investigations, which provides information for diagnosis and treatment of the cardiac abnormality. Therefore, it is of great importance to establish a mechanistic relationship between ischemia-induced electrophysiological change of cardiac cells and ECG waveform.

In clinical diagnosis, ECG ST segment depression is recognized as a sign of sub-endocardial ischemia while its elevation as a sign of transmural ischemia [1]. With the increasing or decreasing of ischemic level and size, ECG waveform will be bound to change. But the casual link between the two is still unclear.

To address the above question, in this study, we developed a 2D human left ventricular model that incorporates both the electrical heterogeneity and anatomical structure of human heart. The ischemic model

takes into account of three main pathophysiological consequences of ischemia: hyperkalaemia, acidosis, and anoxia. Using the model, we quantified the effects of ischemic level and size on the waveform of ECG, particularly on ST-T wave depression or elevation.

2. Method

In the 2D model of human cardiac tissue, to represent the ventricular electrophysiological properties, we used the TNNP2006 model [2], which is described as follows:

$$\frac{\partial V_m}{\partial t} = -\frac{I_{ion} + I_{stim}}{C_m} + \nabla \cdot (D \nabla V) \quad (1)$$

where V_m is transmembrane potential, C_m is the membrane capacitance, I_{ion} is the sum of ionic currents, I_{stim} is the externally applied stimulus current, and D is the diffusion tensor.

Under ischemia condition, we took into account of three main pathophysiological consequences: hyperkalaemia, acidosis, and anoxia. The hyperkalaemia condition was modeled by increasing the concentration value of extracellular K^+ ($[K^+]_o$), the acidosis condition was modeled by decreasing the maximum conductances of the inward Na^+ and L-type Ca^{2+} channels. For anoxia condition, as intracellular ATP concentration ($[ATP]_i$) is reduced during ischemia, ATP sensitive K^+ channels are activated. Thus we incorporate $I_{K(ATP)}$ into I_{ion} , which is formulated as in Reference [3].

According to Ref. [3,4,5,6,7,8], under acute ischemia, in the ischemic region we define the condition of mild ischemia as $[K^+]_o=7.5$ mM, $[ATP]_i=6$ mM, $[ADP]_i=50$ uM, the maximum conductances of the inward Na^+ and L-type Ca^{2+} channels are decreased by 10%, and the condition of severe ischemia as $[K^+]_o=11$ mM, $[ATP]_i=4.6$ mM, $[ADP]_i=99$ uM, the maximum conductances of the inward Na^+ and L-type Ca^{2+} channels are decreased by 20%. Under normal condition, $[K^+]_o=5.4$ mM, $[ATP]_i=6.8$ mM, $[ADP]_i=15$ uM.

The ECG (pseudo-ECG) formulation is described as follows [9]:

$$ECG = \int \frac{D \nabla V_m \cdot \vec{r}}{r^3} dV \quad (2)$$

where V is the area of 2D tissue (or the volume of the whole ventricle), \vec{r} is the vector from the recording electrode to a point in the tissue, and r is the distance from the recording electrode to the point. For the 2D ventricular tissue, we placed the recording electrode 2cm from the left end of the tissue.

3. Result

3.1. Cellular simulation

Under acute ischemia, the resting membrane potential is elevated, and the action potential duration (APD) is shortened. Figure 1 shows the action potentials of endocardial cell in control, mild ischemia, and severe ischemia conditions with BCL=1000 ms. With the increase in the ischemic level, the resting membrane potential is elevated and the APD is decreased gradually. With the model, the APD is abbreviated about 11.5%~19.2% in the endocardial cell, 17.7%~29.8% in the endocardial cell and 9.4%~16.0% in the epicardial cell between mild ischemia and severe ischemia.

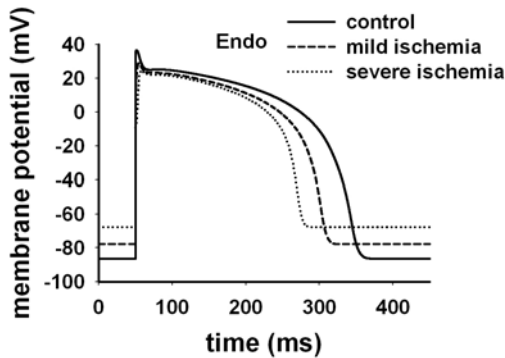


Figure 1. Action potentials of endocardial cell in control, mild ischemia, and severe ischemia

3.2. Ischemia-induced changes in the ECG

The anatomical structure of human heart is based on the Visible Human Project. From the female dataset, we extracted a slice of the left ventricle on a regular Cartesian grid with a spacing of 0.33 mm. We further segmented it into the endocardial layer, the midmyocardial layer and the epicardial layer with a proportion of cells of 25%, 35%, and 40% respectively.

In the 2D human left ventricular slice, endocardial ischemia and transmural ischemia are modeled as shown in Figures 2a and 2b. By increasing the ischemic level and size, we quantified the effects of ischemia-induced electrical properties of cardiac cells on pseudo-ECG waveform.

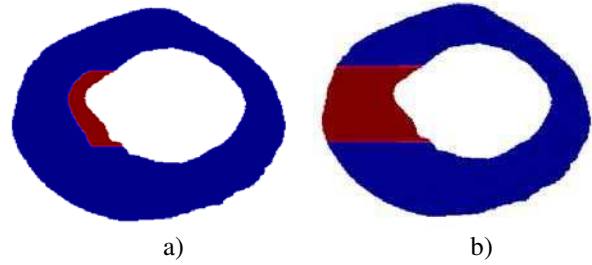


Figure 2. Definition of a) sub-endocardial and b) transmural ischemic region in the 2D human left ventricular slice. Red region is ischemic, and blue region is healthy, separated by a border zone

3.2.1. ECG under sub-endocardial ischemia

Figures 3a and 3b show the pseudo-ECGs under different levels and sizes of sub-endocardial ischemia respectively. Since the APDs of sub-endocardial ischemic cells are shortened, the repolarisations of ischemic cells are advanced. And during repolarisation, the ischemic cells make more contribution to the positive gradients of membrane potential, thus ST segment is depressed, and T wave is advanced.

Under the same size of sub-endocardial ischemia (here we choose the ischemic size as 80x50 pixels), as shown in Figure 3a. Compared with mild ischemia, APDs of ischemic cells are further reduced under severe ischemia, and during repolarisation the ischemic cells make more contribution to the positive gradients of membrane potential, therefore the ST segment depression is larger, T wave is advanced and the inverted magnitude becomes greater.

Under the same level of sub-endocardial ischemia (we take the mild ischemia as an example), we define the small size ischemia as 80x40 pixels, the large size ischemia as 80x50 pixels, as shown in Figure 3b. Compared with small size ischemia, as a result of more number of ischemic cells under large size ischemia, the cells make more contribution to the positive gradients of membrane potential. Therefore the ST segment depression is larger, T wave is further advanced and the inverted magnitude becomes greater.

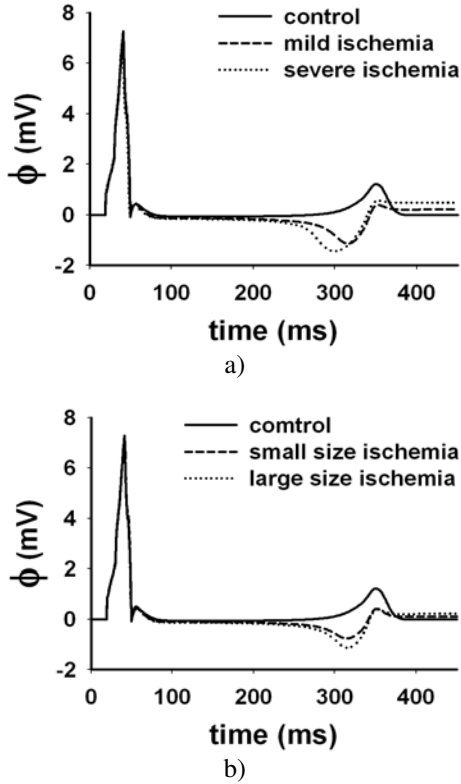


Figure 3. Pseudo-ECGs under different a) levels of sub-endocardial ischemia and b) sizes of sub-endocardial ischemic region

3.2.2. ECG under transmural ischemia

Figures 4a and 4b show the pseudo-ECGs under different levels and sizes of transmural ischemia respectively. Since the APDs of transmural ischemic cells are shortened, the repolarisations of ischemic cells are advanced. And during repolarisation, the ischemic cells make more contribution to the negative gradients of membrane potential, thus ST segment is elevated, and T wave is advanced.

Under the same size of transmural ischemia (here we choose the ischemic size as 80×90 pixels), as shown in Figure 4a. Compared with mild ischemia, APDs of ischemic cells are further reduced under severe ischemia, and during repolarisation the ischemic cells make more contribution to the negative gradients of membrane potential, therefore the ST segment elevation is larger, T wave is advanced and the upright magnitude becomes greater.

Under the same level of transmural ischemia (we take the mild ischemia as an example), we define the small size ischemia as 80×90 pixels, the large size ischemia as 120×90 pixels, as shown in Figure 4b. Compared with small size ischemia, as a result of more number of ischemic cells under large size ischemia, the cells make

more contribution to the negative gradients of membrane potential. Therefore the ST segment elevation is larger and the upright magnitude of T wave becomes greater.

Due to the same level of ischemia, the repolarisation time of the same type of ischemic cells is equivalent, thus the time that T wave forms is same.

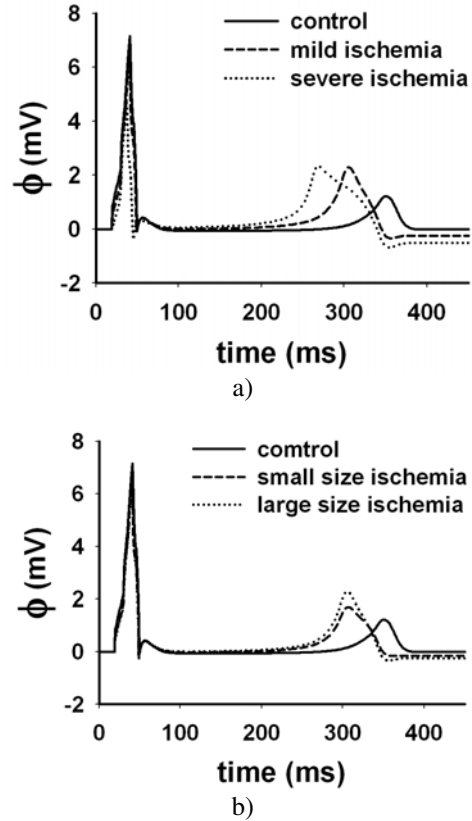


Figure 4. Pseudo-ECGs under different a) levels of transmural ischemia and b) sizes of transmural ischemic region

Note that, it is not absolute for above situation that ST-T wave changes with the increasing of ischemic size. Let us take the sub-endocardial severe ischemia as an example. Figures 5a and 5b show the changes of ST segment and T wave in the 2D human ventricular tissue under sub-endocardial ischemia for varying ischemic size. ST segment and T wave are measured as the difference between the base line and the minimum of ST segment or T wave. We fix the width of ischemic region to 80 pixels, the length of ischemic region increases linearly from 0 to 90 pixels (at 90, sub-endocardial ischemia has evolved into transmural ischemia). The scale 1 of horizontal axis describes the ischemic size as 80×10 pixels, 2 as 80×20 pixels, and so on.

With the growing of ischemic region extending to epicardial layer, in the beginning the degree of ST-T

wave depression increases monotonically. And when ischemic region is close to the ventricular wall, ST-T wave stops depressing and transforms to elevate. Under transmural ischemia, ST segment elevates and T wave displays the upright formation.

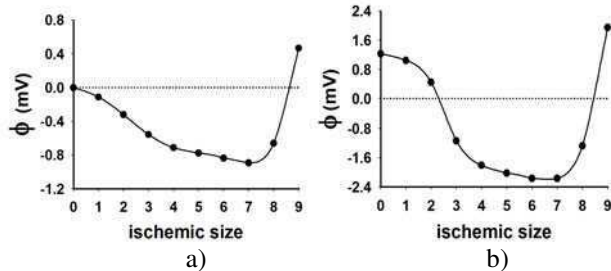


Figure 5. a) ST segment, b) T wave changes with the increasing of ischemic size under sub-endocardial ischemia

4. Conclusions

In conclusion, we have developed an integrated human ventricular ischemic model by taking into account three main pathophysiological consequences of ischemia: hyperkalaemia, acidosis, and anoxia. Using the model, we quantified the waveform of ECG under ischemia. The simulation results show that under ischemia, action potential durations are reduced. And in most cases, the larger the size of ischemic region or the more severe the ischemic level, the more dramatic the changes in the amplitude of ST-T wave are observed. Our model can be successfully implemented to simulate the electrical activity of human ventricular tissue affected by myocardial ischemia.

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Address for correspondence

Kuanquan Wang
Mailbox 332, Harbin Institute of Technology
Harbin 150001, China
E-mail: wangkq@hit.edu.cn