Simulation of MCG Signal in 2D Cardiac Tissue Sheet with Ischemic Condition

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Abstract

Magnetocardiogram (MCG) is a noninvasive and noncontact technology for measuring weak magnetic signals generated by cardiac electrical activities, which are possible to become a routine tool for clinical diagnosis of cardiac disease. The relationship between excitation propagation in 2D cardiac tissue sheet and MCG signal has not been well investigated yet. In this paper, the simulations were performed on a 2-D 1.0cm × 1.0cm cardiac tissue sheet with and without ischemia condition. Ten Tusscher's human ventricular cell model was used as the basic unit, and with some modifications in order to get lower computation expense. The electrical properties caused by ischemia were realized by raising external potassium concentrations from 4.5 mM to 10 mM and adding ATP-sensitive K^+ (K_{ATP}) current. The mono-domain equation was used to simulate the excitation propagation, and the MCG/Electrocardiography (ECG) signals were calculated using the boundary element method. The simulation results showed that the MCG signal is more sensitive to identify myocardial ischemia than the ECG signal, and thus suggest that the MCG would be a useful tool for cardiovascular disease research.

1. Introduction

Electrophysiological properties of single ischemia cardiomyocyte have long been recognized. Many studies found that hyperkalemia, acidosis and hypoxia together could successfully reproduce ischemia behaviours [4]. Besides, Weiss's group described ischemia in tissue level by central ischemic zone (CIZ) and border zone (BZ) [1]. They also carried out a simulation on a 3-D ventricle model and calculated ECG signals in a human torso. In cardiovascular research, MCG is used for imaging the current distribution on heart surface, through which we can get information about area and location of infarctions and other dysfunctions [2]. In this work, we developed two virtual cardiac tissue sheets with or without ischemia condition, and then implemented excitation propagation simulation in these two sheets. We computed ECG and MCG signals of each sheet and made a thorough comparison. The results show that MCG is more sensitive to identify myocardial ischemia and it may become another useful tool for cardiovascular disease research.

2. Methods

2.1. Cellular electrophysiology model

Ten Tusscher electrophysiological model acted as the basis of our single cell level simulation [3]. This model is based on experimental data on ionic currents: the fast sodium, L-type calcium, transient outward, rapid and slow delayed rectifier, and inward rectifier currents. A simple but computation-efficient calcium dynamics is included in this model, which makes this model more precise. Equations of calcium dynamics is shown below:

$$I_{leak} = V_{leak}(Ca_{sr} - Ca_i) \tag{1}$$

$$I_{up} = \frac{V_{\max up}}{1 + K_{up}^2 / Ca_i^2} \tag{2}$$

$$I_{rel} = (a_{rel}\frac{Ca_{sr}^2}{b_{rel}^2 + Ca_{sr}^2} + c_{rel})dg \tag{3}$$

$$Ca_{ibufc} = \frac{Ca_i \times Buf_c}{Ca_i + K_{bufc}} \tag{4}$$

$$\frac{dCa_{itotal}}{dt} = -\frac{I_{CaL} + I_{bCa} + I_{pCa} - 2I_{NaCa}}{2V_cF} + I_{leak} - I_{up} + I_{rel} \tag{5}$$

$$Ca_{srbufsr} = \frac{Ca_{sr} \times Buf_{sr}}{Ca_{sr} + K_{bufsr}} \tag{6}$$

Ten Tusscher and his co-workers used this model to simulate 1-D and 2-D propagation and successfully produced spiral waves and ECG, which mean the model is sufficient for macro research.

2.2. Ischemic condition

Ischemia effects include increasing the extracellular potassium concentrations, decreasing PH, and activating ATP sensitive potassium current. We raised $[K^+]_o$ from 4.5mM to 12mM to simulate hyperkalemia [4]. In order to simulate acidosis, we decreased conductance of I_{Na} by 25%, reduced conductance of I_{CaL} by 50% and decreased $[K^+]_i$ to 125nM as Yoram Rudy et al. suggested in their paper [4]. Also, we adopted formulation of I_{Katp} as follow to take into the effects of hypoxia [4]:

$$I_{K(ATP)} = \overline{g}_{K(ATP)} \cdot (V_m - E_k) \tag{7}$$

$$\overline{g}_{K(ATP)} = G_{K(ATP)} \cdot P_{ATP} \cdot ([K]_o / [K]_{o,normal})^n \tag{8}$$

$$G_{K(ATP)} = 195 \cdot 10^{-6} / Nichols_{area} (nS / cm^2) \tag{9}$$

$$P_{ATP} = \frac{1}{1 + (\frac{[ATP]_i}{k_{0.5}})^H} \tag{10}$$

E_k : potassium reversal potential,

$Nichols_{area} = 5 \cdot 10^{-3} \text{cm}^2$ [10],

$[ATP]_I$=3.0mM for integrated ischemia model,

n=0.24, H=2, $k_{0.5}$=0.250 μM .

2.3. 2-D sheet and stimuli protocols

Propagation simulation was carried on a 2-D 1.0cm ×1.0cm cardiac tissue sheet. There are totally 60×60 Endo-cells on this sheet, which means the distance between two cells is about 0.017cm. Time step was set to 0.02 ms and conductivity coefficient 0.001 for normal tissue. Stimuli was put on cells whose ordinal numbers were between 29 and 32 on both X and Y direction.

2.4. The mono-domain equation

Excitation propagation was governed by computation system below [11]:

$$\frac{\partial V}{\partial t}(\underline{x},t) = \frac{1}{C_m}[-I_{ion}(\underline{x},t) - I_{app}(\underline{x},t) + \frac{1}{\beta}(\frac{\kappa}{\kappa+1}) \nabla \cdot (M_i(\underline{x}) \nabla V(\underline{x},t))] \tag{11}$$

$$V(\underline{x}, t=0) = V(\underline{x}) \tag{12}$$

$$\underline{n} \cdot V(\underline{x},t) = 0 \quad \text{(no-flux BC)} \tag{13}$$

V: transmembrane potential,
C_m: membrane capacitance per unit area,
I_{ion}: sum of ionic currents per unit area,
κ: anisotropic ratio,
β : surface-to-volume ratio,
Mi: conductivity tensor.

2.5. MCG simulation

Shou and his co-workers simplified MCG computation by BEM method [5]. All equations are shown below:

$$\phi_\infty(r) = -\frac{1}{4\pi\sigma_S} \int_{V_H} J_P(r') \cdot \nabla \frac{1}{R} dV_H' \tag{14}$$

$$B_\infty(r) = \frac{\mu_0}{4\pi} \int_{V_H} J_P(r') \times R / |R|^3 \, dV_H' \tag{15}$$

$\phi_\infty(r)$ is the potential field in an infinite homogeneous media. $B_\infty(r)$ is the magnetic field in an infinite homogeneous media. They are generated by the primary current density J_P in cardiac region V_H.

3. Results

We simulated normal and ischemia ventricular single endocardial cell membrane potential during 1000ms accordingly, and the results are shown below.

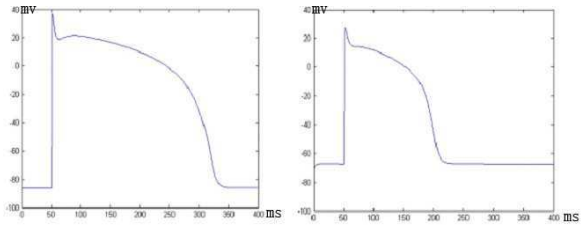

Figure 1. Endocardial cell membrane potentials of different states. The left picture corresponds to normal state, while the right one corresponds to ischemia state.

From this figure, we conclude that our ventricular endocardial cell model is able to reproduce the following electrical changes in ischemia condition: reduction of upstroke velocity, shortening of APD and elevation of resting membrane potential.

In figure 2, we investigate excitation propagation in two sheets. And choose five time points to illustrate the results. Excitation propagates slower on ischemia sheet because the reduction in membrane excitability and the prolongation of recovery of excitability [4].

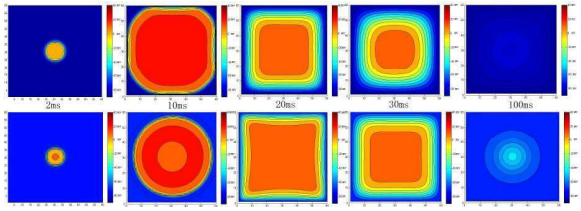

Figure 2. Excitation sequence at 2ms,10ms,20ms,30ms and 100ms. At each time point, two sub-pictures are recorded. The top sequence corresponds to normal sheet, and the bottom one corresponds to ischemia sheet.

ECG and MCG during excitation propagation at point (0.003m, 0.003m, 0.001m) are calculated and results are normalized. In following figures, one unit in x axis equals to 0.02ms.

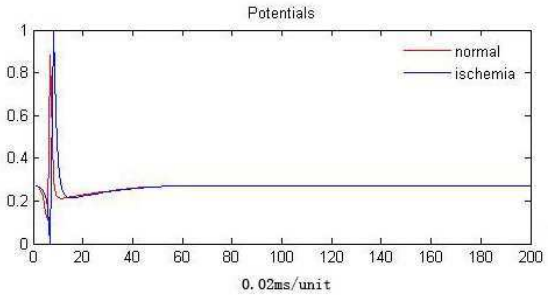

Figure 3. ECG during propagation.

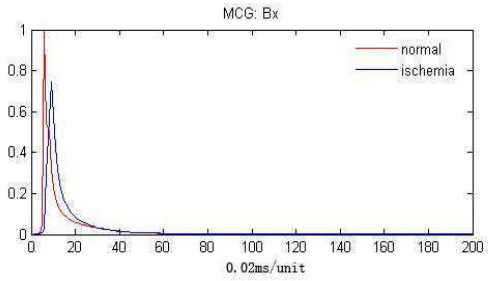

Figure 4. MCG signal in x direction.

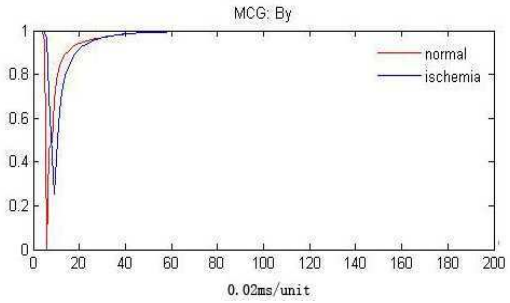

Figure 5. MCG signal in y direction.

Table 1. Compare of amplitude between different signals.

		Normal	Ischemia	Absolute difference
ECG	Max value	0.8806	1	0.1194
	Min value	0.1143	0	0.1143
MCGx	Max value	1	0.7449	0.2551
MCGy	Min value	0	0.2551	0.2551

A complete comparison of amplitude is carried and results are listed in table 1.

In x direction, MCG's absolute difference of max value is 2.1365 times as greater as ECG. In y direction, MCG's absolute difference of min value is 2.2318 times as greater as ECG.

Besides these, the peak value appears 2ms later in ischemia sheet's ECG than in normal sheet's ECG. But this delay time is 6ms for MCG in both x and y directions.

From these two aspects, we conclude that MCG is more sensitive to differentiate ischemia myocardial sheet from normal one.

4. Discussion and conclusions

By calculating MCG, we get three figures. In x and y directions, absolute difference between peak value(x direction) or valley value(y direction) of two sheets is greater then in ECG. Also, time delay of peak or valley value appearance in MCG is longer than in ECG. So we can say MCG is more sensitive to identify ischemia tissue in 2-D dimension then ECG to a certain degree.

Although our work has proved that MCG is more sensitive then ECG, it still has some limitations of our suggestion. Firstly, we only calculated MCG in one point above the tissue. We need to calculate MCG map at different vertical height above the tissue. This may help us to find optimized height value for this problem. Secondly, in this paper, we did not simulate spiral wave, and we may change stimulation protocol to induce spiral wave and to see whether MCG would change heavily or not. Thirdly, in future work, we may use a normal tissue with a certain ischemia part in it. This kind of tissue is more common in real world and calculating MCG of it may be more meaningful.

There're many literatures discussing clinical use of MCG [6-9]. But still lots of theoretical problems need to be solved. We hope our work would contribute to it.

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