Simulation of Effects of Ischemia in 3D Human Ventricle

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Abstract

In this paper, we present an integrated model of 3D human ventricle to simulate the effects of ischemia on wave propagation. To deal with the no-flux boundary conditions, a phase-field method is employed. The major advantage of the method is that it can automatically handle the boundary conditions. Through the increasing of concentration of extracellular K^+ and ischemic size, the propagation of spiral wave under different ischemia symptoms is simulated. The experimental results show that with the increasing of ischemia severity and ischemic size, spiral waves are more and more instable, but when the tip of spiral wave stays inside the ischemic region, the spiral wave maintains stabilization.

1. Introduction

Cardiac failure is the most common heart disease, which is closely associated with abnormal wave propagation caused by reentrant sources of excitation. The mechanisms underlying the initiation and subsequent excitation of reentrant sources in the human heart are still not well revealed. Thus it would be of great importance to study the modeling of cardiac electrical activity using biophysically detailed cellular models with realistic 3D anatomical geometry and to study the behavior of reentrant waves and their relation to arrhythmias [1].

Monodomain model provides a simplest description of action potential propagation, which assumes cardiac tissue as an excitable medium of transmembrane potential [2]. One such model is the TNNP model. TNNP model uses new ionic current formulations based on recent experimental data on human ventricular cell, which consists of 17 variables for all major ionic currents [3]. It keeps a better balance between electrophysiological property and computational efficiency. Using the TNNP model, we present an integrated model of 3D human ventricle to simulate the effects of ischemia on wave propagation. The geometrical structure of human ventricular tissue is provided by Visible Human Project (http://www.nlm.nih.gov/research/visible/visible_human.html).

Due to the complex geometries of ventricular tissue, precise treatment of boundary conditions would be complicated. Many researchers have used Neumann no-flux boundary conditions for the monodomain model [4, 5]. In this paper, to deal with the no-flux boundary conditions, a phase-field method is employed [6]. The major advantage of the method is that it can automatically handle the boundary conditions by introducing an auxiliary field to smooth the interface between the interior and the exterior of ventricular tissue, which decreases the complexity of computation on the premise of maintaining the accuracy [7, 8].

In this paper, we simulate the wave propagation of human ventricular tissue with ischemia symptom through the increasing of concentration of extracellular K^+ and ischemic size [9]. We further simulate the propagation of spiral wave under different ischemia symptoms and explain the underlying mechanism that caused arrhythmia under myocardial ischemia. Finally, we simulate the scroll wave in the 3D anatomically detailed model of human ventricle. The results show that with the increasing of ischemia severity and ischemic size, spiral waves are more and more instable, but when the tip of spiral wave stays inside the ischemic region, the spiral wave maintains stabilization.

2. Methods

2.1. Model of cardiac tissue

To represent the excitable dynamics of cardiac tissue, we use the TNNP model of human ventricular tissue, given by the following equation for the transmembrane voltage V:

$$\begin{cases} \dfrac{\partial V}{\partial t} = -\dfrac{I_{ion}+I_{stim}}{C_m} + \nabla\cdot(D\nabla V) \\ I_{ion} = I_{Na}+I_{K1}+I_{to}+I_{Kr}+I_{Ks}+I_{CaL}+I_{NaCa}+I_{NaK}+I_{pCa}+I_{pK}+I_{bCa}+I_{bNa} \end{cases} \quad (1)$$

where ∇ is the gradient operator, C_m denotes the cellular capacitance, I_{ion} is the sum of all transmembrane ionic currents, I_{stim} is the externally applied stimulus current, D is the diffusion tensor, which can be found from the fibre

direction and orientation of the ventricle sheet plane. All the parameter values are the same as Ref. [3].

2.2. Numerical approach

To avoid no-flux boundary conditions, a phase-field algorithm is employed. We introduce an auxiliary field ϕ, which has a value of 1 for points inside the ventricle, and 0 outside the ventricle. We solve the following equation to determine the values of ϕ:

$$\frac{\partial \phi}{\partial t} = \xi^2 \nabla^2 \phi - \frac{\partial G(\phi)}{\partial \phi} \quad (2)$$

where ζ is a parameter which controls the width of the interface. When ζ is small enough, the no-flux boundary condition is recovered. G(ϕ) is any double-well function with minima at ϕ=0 and ϕ=1. Here, we have:

$$G(\phi) = -\frac{(2\phi-1)^2}{4} + \frac{(2\phi-1)^4}{8} \quad (3)$$

Therefore, Eq. (1) is modified to:

$$\phi \frac{\partial V}{\partial t} = -\phi \frac{I_{ion} + I_{stim}}{C_m} + \nabla \cdot (D\phi \nabla V) \quad (4)$$

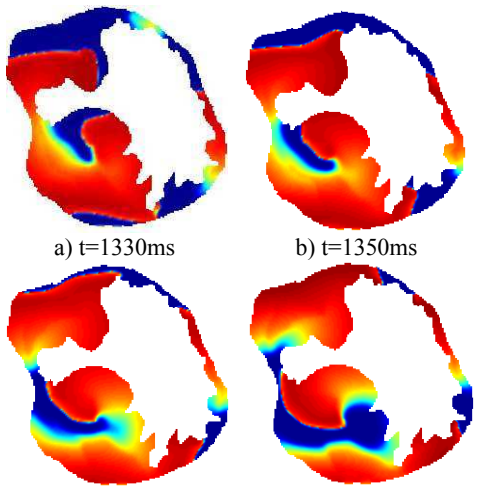
In this paper, Eq. (4) is integrated using the forward Euler method with a space step of x=0.5mm and a time step of t=0.02ms. ζ=0.5mm.

All simulations are coded in C++. The 2D and 3D simulations are run on a 3, 000-MHz processor of IBM xSeries 206m machine. In 3D, we implement a volume rendering pipeline with ray casting scheme and Visualization ToolKit (VTK) for the visualization of the left ventricle and wave patterns.

3. Results

3.1. 2D left ventricular sheet

In this section, we simulate the spiral wave propagation of the human left ventricular tissue. We initiate a spiral wave with an S1-S2 protocol in the normal area whose core is outside the ischemic area, and the S2 stimulus is applied in the refractory tail of the S1 wave. Their strength is two times threshold for both. Figure 1 shows the propagation of spiral wave under normal conditions.



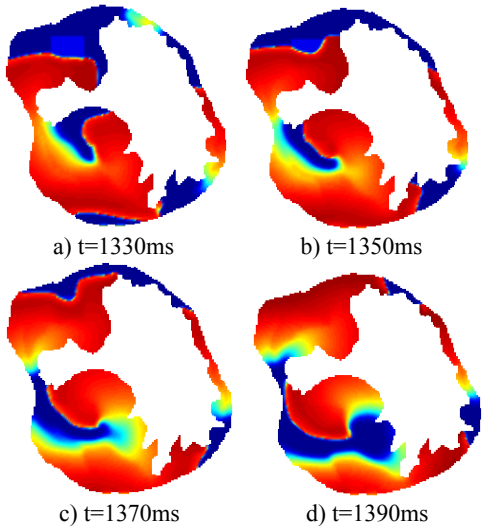
a) t=1330ms b) t=1350ms

c) t=1370ms d) t=1390ms

Fig.1. The propagation of spiral wave under normal conditions

3.1.1. Wave patterns of different ischemia symptoms

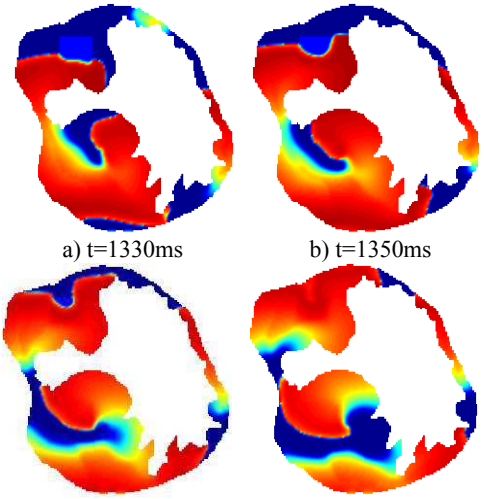
We simulate the spiral wave propagation of human ventricular tissue with ischemia symptom through the increasing of concentration of extracellular K^+. A simulated ischemic area is set up in the 2D ventricular sheet by increasing the $[K^+]_o$ inside the ischemic area. The light blue square area in the upper-left corner of the sheet represents the ischemic area. Grid size of the ischemic area is 20×20. Three situations of different ischemia symptoms are listed below: mild ischemia, moderate ischemia and severe ischemia. The $[K^+]_o$ is 7.5mM in the mild ischemic area, 9.0mM in the moderate ischemic area and 11.0mM in the severe ischemic area, corresponding to resting potential -79mV, -75mV and -69mV, respectively.



a) t=1330ms b) t=1350ms

c) t=1370ms d) t=1390ms

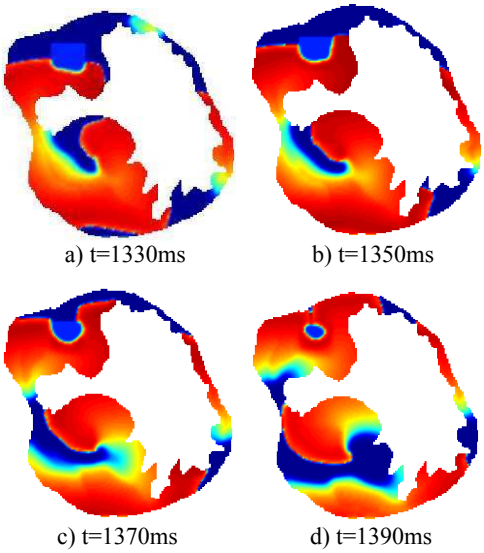
Fig.2. The propagation of spiral wave under regional mild ischemia



a) t=1330ms b) t=1350ms

c) t=1370ms d) t=1390ms

Fig.3. The propagation of spiral wave under regional moderate ischemia



a) t=1330ms b) t=1350ms

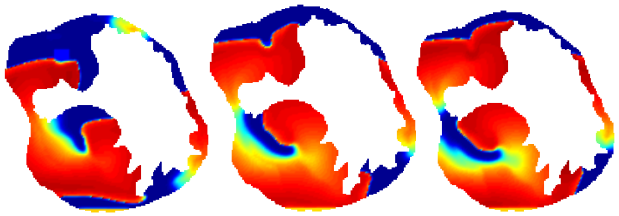
c) t=1370ms d) t=1390ms

Fig.4. The propagation of spiral wave under regional severe ischemia

Figures 2 ~ 4 show that the wave conduction in the ischemic area is obviously slower than the other area. The wave is broken in the ischemic area. Then the wavefront skirts round the ischemic area and converges to advance. Finally the wave can propagate through the ischemic area. Regional mild ischemia has little effect on wave propagation. But if $[K^+]_o$ is too high, there will be complete conduction block in the ischemic area, the spiral wave is instable and hardly passes through the ischemic area. The above results indicate that ischemic severity can affect the wave propagation. In our simulation experiments, the severer ischemic symptom there is, the more instable the spiral wave will be, and ventricular tachycardia is easier to be induced to ventricular fibrillation by the dynamic changes.

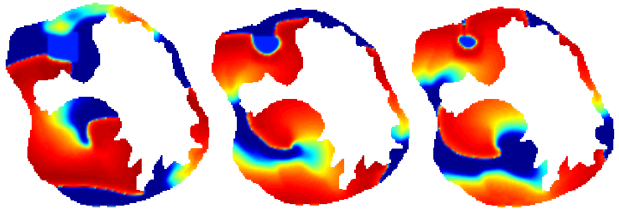
3.1.2. Wave patterns of different ischemic size

The size of ischemic area is very important to the spiral wave propagation even under the same ischemic severity. In this paper, for the sake of simplicity, we only set up different ischemic area under the severe ischemia in the 2D left ventricular sheet. Grid size of the ischemic area is 10×10, 20×20, 30×30, respectively.



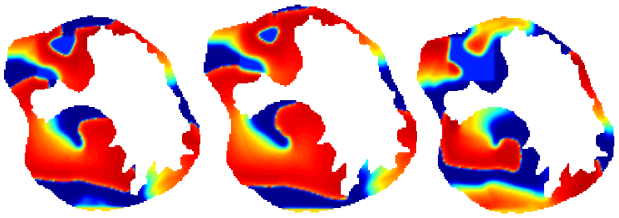
a) t=1330ms b) t=1350ms c) t=1370ms

Fig.5. The propagation of spiral wave in a 10×10 size regional ischemic tissue under severe ischemia



a)t=1320ms b)t=1370ms c)t=1390ms

Fig.6. The propagation of spiral wave in a 20×20 size regional ischemic tissue under severe ischemia



a)t=1330ms b)t=1350ms c)t=1390ms

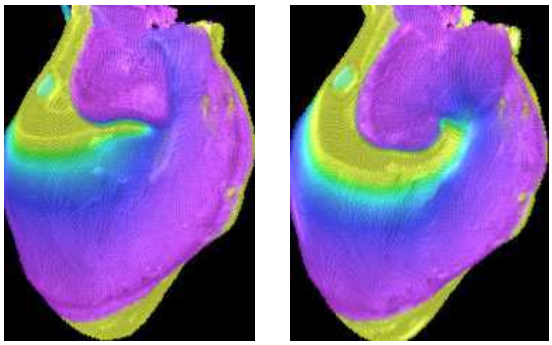
Fig.7. The propagation of spiral wave in a 30×30 size regional ischemic tissue under severe ischemia

Figures 5 ~ 7 show that if the ischemic area is smaller, it will take less time for the spiral wave to pass through the area, and the wave propagation is not affected to a large extent. With the increasing of ischemic size, the ischemic area blocks the wave propagation obviously. At a certain moment, the spiral wave behaves as a chaos state. When the tip of spiral wave stays inside the ischemic region, the spiral wave maintains stabilization. The above results indicate that the size of ischemic area can also affect the wave propagation.

3.2. Whole left ventricle

Scroll wave can be initiated by applying an S1-stimulus at the posterior side of the left ventricle, then an

S2 stimulus to the refractory tail of the S1 wave at the left lateral side of the ventricle. Figure 8 shows the propagation of spiral wave located in the free wall of the left ventricle in the TNNP model.



a) t=1350ms b) t=1370ms

Fig.8. Spiral wave activity in the left ventricle

4. Conclusions

In this paper, we present an integrated model of 3D human ventricle to simulate the effects of ischemia on wave propagation. The experimental results show that with the increasing of ischemia severity and ischemic size, spiral waves are more and more instable, but when the tip of spiral wave stays inside the ischemic region, the spiral wave maintains stabilization.

Acknowledgements

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