Investigation of the Influence of Electric Fields on Human Ventricular Myocardium Including Realistic Fiber Orientation: A Simulation Study

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Abstract

The aim of this work is to enlarge the knowledge about the electrophysiological phenomena that describes the defibrillation procedure. We simulated this using a three-dimensional computer model in which the human cardiac tissue is incorporated in blood bath medium. Two initial situations were imposed: the tissue being in a resting state and the tissue being half resting, half depolarized, before the electrical shock was applied. For obtaining a more detailed look over these situations we varied the fiber orientation and the magnitude of the electrical impulse. The effects of intracellular electrical discontinuities represented an important target in our study. The temporal evolution of the transmembrane voltage was always followed until the tissue went back into the resting phase.

1. Introduction

Cardiac fibrillation is the disorganized electrical behavior of the heart and in consequence coordinated contraction is lost. Electrical defibrillation, as an application of strong electric shocks to the heart, is the most effective therapy for this otherwise lethal disturbance of cardiac rhythm. During defibrillation first and foremost the shock current must access the bulk of myocardial mass. The exogenous current traverses the myocardium along convoluted intracellular and extracellular domains. This redistribution results in changes of transmembrane voltage: regions of membrane hyper- and depolarization of extent larger than a single cell are induced in the myocardium by the defibrillation shock. Tissue inhomogenities also contribute to local membrane depolarization in the myocardium, which is superimposed over the large-scale depolarization associated with the fiber orientation of the myocardium. The article presents the investigation of the influence of external electric fields on a human ventricular myocardium, using a computer model of cardiac tissue.

Mathematical computer models, rooted in the underlying biophysics, can yield information that cannot practically be obtained in any other way. The study of variation of transmembrane voltage in the cardiac tissue provides important information that can be used in enlarging the understanding of the cardiac defibrillation process. The used cardiac computer model consists of two parts: a description of the membrane ion kinetics (offering a cardiac microscopic view) and a representation of the electrical properties of the tissue (offering a cardiac macroscopic view).

Myocardium consists of densely packed cells (30–100 μm long and 8–20 μm wide) arranged into fibrous bundles. The cells are embedded in an interstitial fluid, which is separated from the intracellular fluid by the cell membrane (a lipid bilayer). The point where two membranes join, the nexus (represented in the physical model by gap junction), connects the intracellular compartments of the neighboring cells via connexon protein channels. Nexa occur predominantly at the ends of cells and in a lesser extent along the length of cells [1].

Cardiac structure presents extra- and intracellular anisotropic electrical properties in which the average conductivity is greater along fibers than on transversal direction. This feature is important in determining the path preferred by the electrical current.

The orientation of myocytes in the ventricular wall is dependent on the depth [2, 3]. The orientation can be approximated by the helix angle of a fiber path through the myocardium parallel to the local epicardium. In human left ventricle an angle of -75° was measured epicardial and 70° endocardial, with 0° in midmyocardium.

2. Ionic cell model

The electrophysiological behavior of cells is modeled with a human left-ventricle myocardial model proposed by Priebe-Beuckelmann [4]. The presentation of the electrophysiological behavior of a cell is done with a set of nonlinear coupled differential equations, which describes in sum the changes of the transmembrane voltage and represent intra- and extracellular ionic concentrations, mainly of calcium, sodium and potassium. The concentrations are changed by passive and active transport mechanisms of the cell membrane channels. The transport of ions is time dependent and influenced by gradients of the concentrations and the electrical potential and is represented in the model by a set of membrane currents.

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The temporal changes of the transmembrane voltage is defined by:

$$\frac{\partial V_m}{\partial t} = -\frac{1}{C_m}(I_{mem} - I_{stim}) \quad (1)$$

with the membrane capacity C_m, the sum of the transmembrane currents I_{mem} and the stimulus current I_{stim}.

3. Excitation propagation

For the simulation of electrical activity in cardiac tissue the bidomain model is used [5]. The equations arise from electrostatic formulations describing the potentials in the intracellular and extracellular tissue. These domains are coupled through a non-linear model describing the current flow through the cell membrane.

The system of equations is coupled by the relation describing the variation of transmembrane current density, I_{stim}, through the cell membrane as a function of the transmembrane voltage V_m, which is defined as the difference between intra- and extracellular space. The conductivities of the two domains are denoted by σ_i and σ_e. They can be modified by the fiber orientation.

$$\nabla\left((\sigma_i + \sigma_e)\nabla V_e\right) + \nabla\left(\sigma_i \nabla V_m\right) = 0 \quad (2)$$

$$\nabla\left(\sigma_i \nabla V_m\right) + \nabla\left(\sigma_i \nabla V_e\right) \quad = \quad -I_{stim}. \quad (3)$$

Finite difference method generates systems of equations in V_m and V_e (extracellular potential), which are solved with the Gauss-Seidel preconditioning technique.

4. Simulation parameters

The applied underlying three-dimensional structure of the model consists of a virtual wedge preparation of the myocardium described by 50 x 50 x 100 cubic voxels. It includes blood bath medium 5 voxels wide, at both sides. The orientation of fibers was varied from isotropic properties to realistic fiber twist. A pair of planar electrodes, 50 x 50 x 1 cubic voxels in size, are placed in the immediate vicinity of the bath at the ends of the z axis. The electrical sources are not placed directly on the myocardium for obtaining more precise spatial distribution of membrane polarization in the cardiac tissue during the initial phase of electrical stimulation [6]. The duration of applied electrical shock was 1 ms and the side length of the voxels was always fixed at 0.2 mm. The calculation time step is 10 μs.

In the first part of the study, the value of electrical shock supplied by the electrodes was varied between 1 V and 5 V at the left end (z = 0) and -1 V and -5 V at the right end (z = 99).

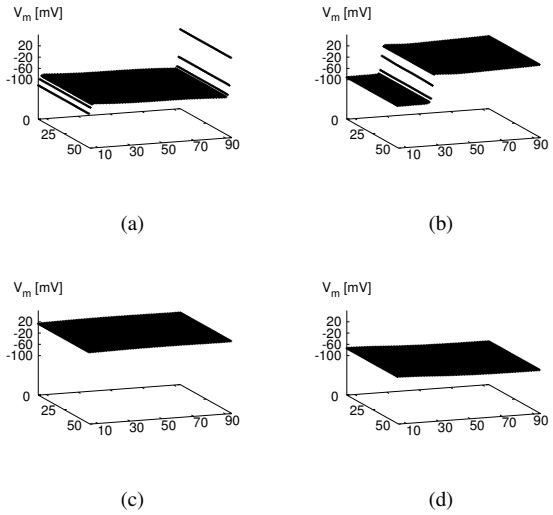

Figure 1. Temporal evolution of transmembrane voltage, as a function of distance, measured in voxels, in a tissue with 70° fiber orientation after (+1V, -1V) electrical signal is applied: a) 1 ms, b) 50 ms, c) 100 ms, d) 410 ms.

5. Results

All simulations include the following phases: hyper- and depolarization near to blood bath medium, spreading of the depolarization front from the place where the cardiac tissue was firstly depolarized (right end) until the entire tissue is characterized by the same value of the transmembrane voltage, followed by repolarization, a phenomena which is ended with the resting state.

During the first phase the exponential decay of the transmembrane voltage with the distance along the fiber can be observed [7].

The major recorded differences between the chosen models consist of the time needed by the cardiac tissue to pass from one phase to the other and also the repolarization patterns. The model with realistic fiber orientation depicted a special behavior during repolarization: the part of the tissue which was firstly depolarized was repolarizing faster than the rest, so the tissue does not maintain in an isopotential state like the model with 70° fiber orientation, shown in fig. 1.

Since the ventricular cardiomyocytes are not arranged in a uniformly connected continuum [8], models with structural discontinuities were also studied. First the effect of non-uniformly distributed gap-junctions was observed. In this simulation, one percent of the gap-junctions was removed from the tissue with realistic fiber orientation. The places where the connection between neighboring cells was missing presented small secondary sources which decreased the time needed for complete depolarization with

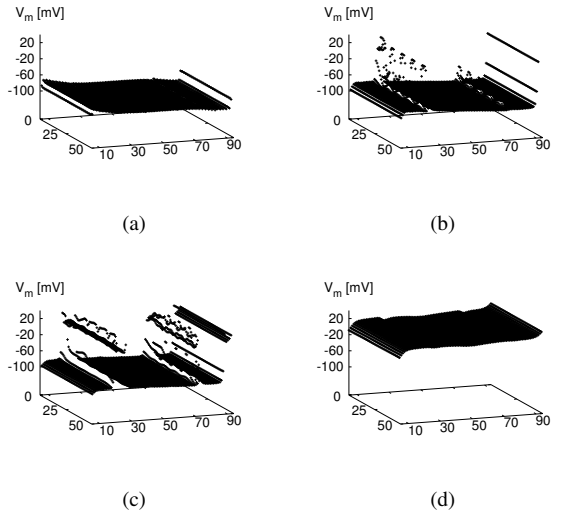

Figure 2. Transmembrane voltage, as a function of distance, measured in voxels, in a tissue with realistic fiber orientation and 2 interlaminar clefts after (+5V, -5V) electrical signal is applied, at different time steps: a) 1 ms, b) 5 ms, c) 10 ms, d) 70 ms .

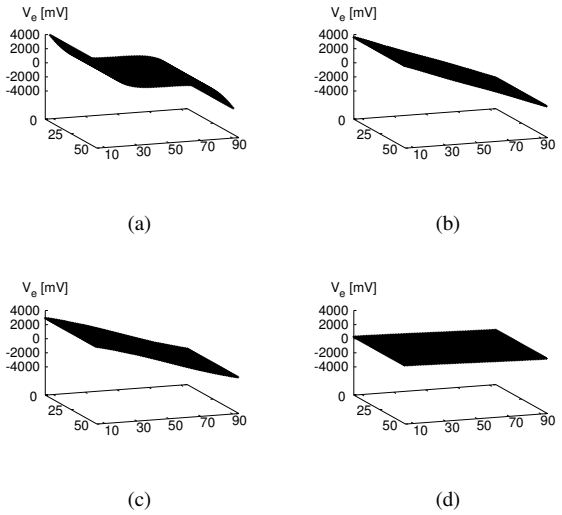

Figure 3. Extracellular potential, as a function of distance, measured in voxels, in a tissue with realistic fiber orientation and 2 interlaminar clefts after (+5V, -5V) electrical signal is applied, at different time steps: a) 1 ms, b) 5 ms, c) 10 ms, d) 70 ms .

7 ms, compared to the similar model that had uniformly distributed gap-junctions and needed 170 ms for having all cells in the plateau-phase.

A model which includes the existence of interlaminar clefts between layers of cardiomyocytes was also the subject of our studies. In this direction we considered a tissue with realistic fiber orientation that is twice intersected by isolating half filled grids. The extracellular domain remains continuous. The intracellular domain contains planes with uniformly distributed voxels of zero conductivity. We chose this geometrical pattern for having a representation which is near to the real description of the heart, that presents intersections between cardiac cleavages. The simulation showed that these planes are inducing strong secondary sources. They bring all cells in the plateau phase in 50 ms after the electrical shock is applied. After the next 70 ms the isopotential state of the tissue is established (see fig. 2).

Analyzing the time history of the extracellular potential we observed that from the moment when all cells are depolarized the value of the extracellular potential remains 0 V (see fig. 3).

The second studied situation reflects the behavior of a tissue which is initially half resting and half depolarized when an electrical shock is applied (see fig. 4).

The objective of this simulation is to identify the appropriate conditions for bringing the entire fibrillating tissue in a depolarized isopotential state. Fulfillment of this condition assures us that the tissue will be ”reseted”. When the electrical shock was 1 V in magnitude, the electrical homogeneous medium needed between 90–150 ms to get in depolarized isopotential state. In 340–390 ms they were back in the resting state. The model with nonuniform distribution of gap-junctions presented also in this case only small difference in time needed for passing from one phase to the other, compared to the tissue with realistic fiber orientation and uniformly distributed gap-junctions. The introduction of the cleavage planes in the model containing a realistic fiber orientation showed new patterns of the transmembrane voltage isopotential areas. The secondary electrical sources reduced the time needed for complete depolarization to 70 ms. After 330 ms the tissue got into the resting phase (see fig. 5). The analysis of extracellular potential can help, in this situation too, identifying the exact moment in which all cells are in the plateau phase. The value corresponding to this moment is, like in the first studied case, 0 V and it remains constant till the end of the simulation. From the studied cases with different fiber orientations (70°, 100°, 130°, 160°, 200°) the most similar from the behavior point of view to the lattice with realistic fiber orientation is the one with an angle of 100° in the first situation (in which the entire tissue was initially resting). Big similarities were observed between the tissue with 130° and the one with realistic fiber twist when the starting condition was: half depolarized, half resting medium.

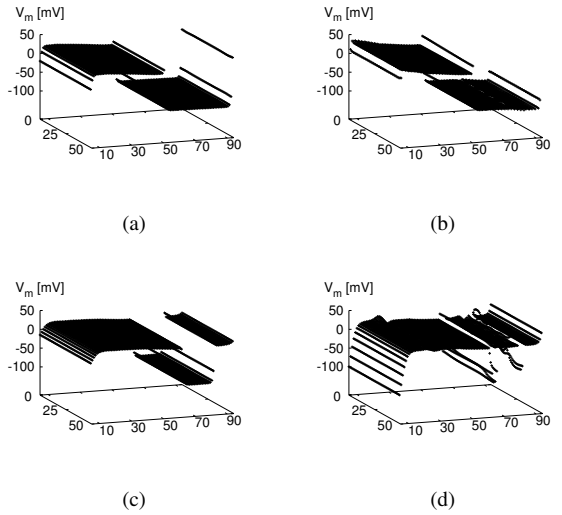

Figure 4. V_m as a function of distance in tissue with realistic fiber orientation after (+1V, -1V) electrical signal is applied, at different time steps: a), b) 1 ms, c), d) 20 ms. Tissue with continuous intracellular domain: a), c). Medium with cardiac cleavage planes: b)d).

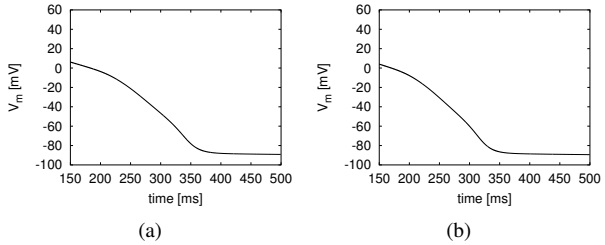

Figure 5. Temporal evolution of V_m in tissue with realistic fiber orientation, followed after the isopotential state was installed. a) Tissue with continuous intracellular domain. b) Model which includes cardiac cleavage planes.

6. Conclusions

In summary, this study reports observations that are of fundamental importance to cardiac electrophysiology, especially for electric stimulation and defibrillation. Three-dimensional simulations reflect clearly the fact that it is very important to consider the orientation of the fiber for obtaining realistic results. It also shows that the magnitude of the electrical shock influences the time needed for a medium to pass from one phase to another. In addition the transmembrane voltage patterns are modified by the fiber orientation.

The comparison between various models proves that structural discontinuities are the source of new, significant features of the results. In particular it was also observed that interlaminar cleavage planes play a very important role. Therefore a good representation of the myocardium has to take into consideration that the tissue is not continuous.

Following the time history of the extracellular potential we concluded that the data obtained in this way can be used to identify the moment when the cardiac tissue is entirely depolarized. This is the moment when the extracellular potential is zero throughout the volume. The reaction of the resting tissue to an electrical shock reflects the way healthy tissue reacts, so it is helpful for getting a general fundamental understanding of the phenomena. The response of a partly depolarized tissue to an electrical shock shows how a fibrillating myocardium behaves. Gathering the simulation data until the total repolarization of the tissue is established assures that induced defibrillation was successful. It can point out, as well, possible dangerous situations that should be avoided in practice.

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