Theoretical Research on the Influence of Defibrillator Paddle Position on the Human Ventricular Myocardium

IM Graf, G Seemann, O Dössel

University Karlsruhe (TH), Germany

Abstract

Considering the high importance of the electrical defibrillation therapy and also the fact that the phenomena behind it have not been totally explained, research in this area is vitally needed. This article shows the reaction of a human ventricular myocardium to electrical stimuli applied through electrodes positioned in different places near to the myocardium. The reaction was obtained using a mathematical computer simulation. The study was done with a model representing a three-dimensional ellipsoidal section of human ventricular myocardial tissue immersed in bath. A realistic fiber orientation and curvature was implemented along with electrophysiological heterogeneity. For obtaining information strictly related to the influence of paddles positioning, the cardiac muscle to which the electrical stimulus is applied is initially resting. A feature of interest was the observation of the regions from which the wave fronts started to propagate. Regions, which contained cell uncoupling were also implemented. The temporal evolution of the transmembrane voltage was registered for around 500 ms. It was observed that the existence of a region with cell uncoupling induces a different reaction of the myocardium to an electrical shock. Even though it could be of immediate help in cardiac defibrillation, it may reinduce fibrillation.

1. Introduction

Since defibrillation therapy was discovered, many scientists have researched the phenomena associated with it. Despite the invested efforts, there are still unsolved enigmas. This challenges people to proceed in investigating the complex cardiac system and its reactions to various stimuli. The human myocytes (30–100 μm long and 8–20 μm wide) are forming a complex structure. An interstitial fluid surrounds the cells, which are densely packed. The points coupling the cells, i.e. the nexus, connect the intracellular domain of neighboring myocytes via gap junction channels. It was observed that nexa occur predominantly at the ends of cells and in a lesser extent along the sides of cells [1]. Various circumstances can induce their destructions. From these the most studied were: chronic pacing [2], ischemia [3] and heart failure [4]. The acute electrical shocks, which are associated to defibrillation are known to produce both electroporation and cell uncoupling. Recently the existence of damaged nexa produced by high electric shocks was correlated to the perturbation of virtual electrodes polarization (VEP) [5]. A clear agreement between disappearance of VEP pattern and increase in pacing thresholds was experimentally demonstrated [5].

The distribution of the electrical current in the myocardium depends on many factors: distribution of conductivity in the myocytes, the curvature of the fibers [6] and heterogeneity of electrophysiologic properties [7].

2. Materials and methods

The used mathematical model describes in detail the electrocardiac system. The electrophysiological features correspond to the human left ventricle myocardium. The implemented sum of ionic currents, which give the transmembrane current I_{mem} and ionic concentrations were related to the transmembrane voltage V_m according to Priebe-Beuckelmann model [8]. The membrane, which has a specific capacity, C_m contains channels and gates through which ions are passively and actively transported. The flow of ions, which varies permanently in time, is influenced by electrochemical gradients and protein kinetics. It is represented in the model by a set of membrane currents. As an effect V_m is temporally modified. The mathematical relation, which defines this, is:

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

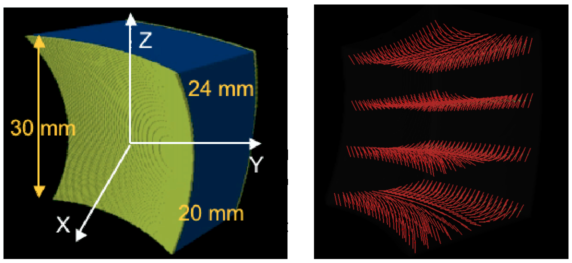
The electrical activity in cardiac tissue is calculated with the use of the bidomain model [9]. The formulas were deduced from Poisson equations, describing the potential in the intracellular and extracellular space. Each of the domains are described by specific conductivity tensors denoted by σ_i in the intracellular space and σ_e in the extracellular space.

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

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

$$V_m = \Phi_i-\Phi_e. \quad (4)$$

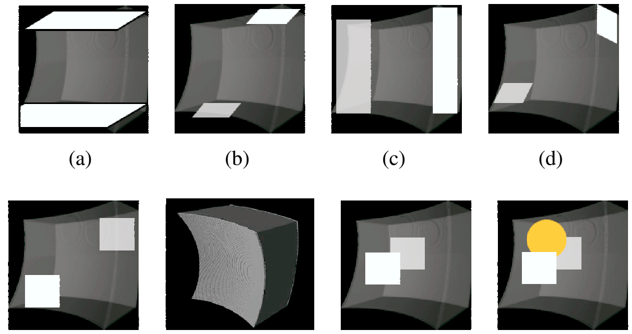
For generating and solving the systems of equations in V_m and Φ_e Finite Difference Method and Gauss-Seidel technique were used.



(a) (b)

Figure 1. Model of the ventricular wall used for the simulations. a) The three tissue types, edocardium, myocardium and epicardium are represented with different colors. b) The red lines represent the fiber twist of the model.

The study was done with a model representing a three-dimensional ellipsoidal section of human ventricular tissue, bordered by endocardium and epicardium, which was immersed in bath (see fig.1). Realistic fiber orientation was implemented. The model is composed of 2.1 million active voxels, each of them having a side length equal to 0.2 mm. The virtual preparation is 16 mm thick and 30 mm high. The radius corresponding to the top section of the model is 26 mm. The curvature of the bottom section is specific to a 16 mm radius. As a selected condition, the myocardium was in the resting phase before it was activated by the electrical shock. A pair of rectangular electrodes were placed in the immediate vicinity of the myocardium. Their orientation and surface was varied from case to case. The chosen configurations for the electrodes were the following ones: 1) cathode 1310.4 mm^2 at the apical border, anode 1310.4 mm^2 at the top (fig. 2a); 2) cathode 80 mm^2 top right epicardium, anode 80 mm^2 bottom left endocardium (fig. 2b); 3) cathode 840 mm^2 at y=minimum, anode 840 mm^2 at y=maximum (fig. 2c); 4) cathode 80 mm^2 at y=minimum top, anode 80 mm^2 at y=maximum bottom (fig. 2d); 5) cathode 1080 mm^2 at x=minimum, anode 1080 mm^2 at x=maximum (fig. 2e); 6) cathode 1080 mm^2 at x=maximum, anode 1080 mm^2 intersects the axis of symmetry of the model (x=0) (fig. 2f); 7) cathode 4 mm^2 at x=maximum, anode 4 mm^2 intersects the axis of symmetry of the model (x=0) (fig. 2g). The duration of applied electrical shock of 10 ms with an amplitude of the electrical impulse was 200 mV. A special case was included in the study: the reaction of the myocardium to the same type of electric shock when a region of the cardiac tissue presents cells uncoupling. Considering the seventh configuration described, we identified the most affected region by the electrical shock by studying both the distribution of the extracellular potential and the transmembrane voltage. The cathode was immersed in bath 4 mm away from the endocardium. Because of this distance and the fact that the curvature of the virtual preparation was varying along Z axis, the most affected region by the electrical stimulation was not focused under the surface of the cathode. It was 6 mm displaced in the direction of the top (fig. 2h). Its core had a volume of 2 mm^3. In that part of the virtual preparation cell uncoupling of different degrees were implemented. The calculation time step is 10 μs. The simulations were performed on a 2 GHz Power Mac G5. The average time needed for each computation was 150 hours.



(a) (b) (c) (d)

(e) (f) (g) (h)

Figure 2. Models of the chosen configurations of electrodes for the study.

3. Results

With the imposed conditions it was revealed that VEP plays an important role. The surface of the tissue immediately depolarized after the start of the electrical shock was larger than the one neighboring the cathode. The VEP covered the entire area near to endocardium and epicardium. The transversal propagation of the front waves can be observed in fig. 3, which presents the variation of the extracellular potential and fig. 4, which shows the temporal evolution of V_m. The myocardium was sectioned

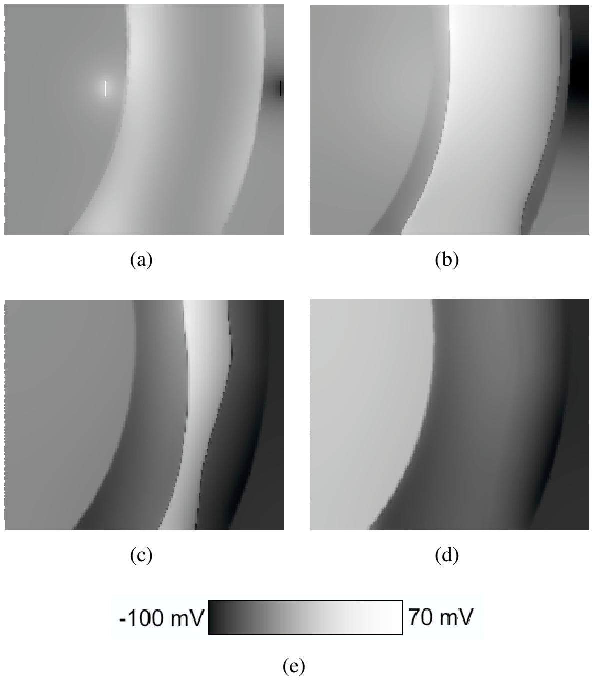


Figure 3. The evolution of extracellular potential in an heterogeneous left ventricle myocardium with realistic fiber orientation after (+200 mV, -200 mV) electrical signal is applied through the sixth electrodes configuration: a) 1 ms, b) 10 ms, c) 40 ms, d) 60 ms, e) color code for Ve.

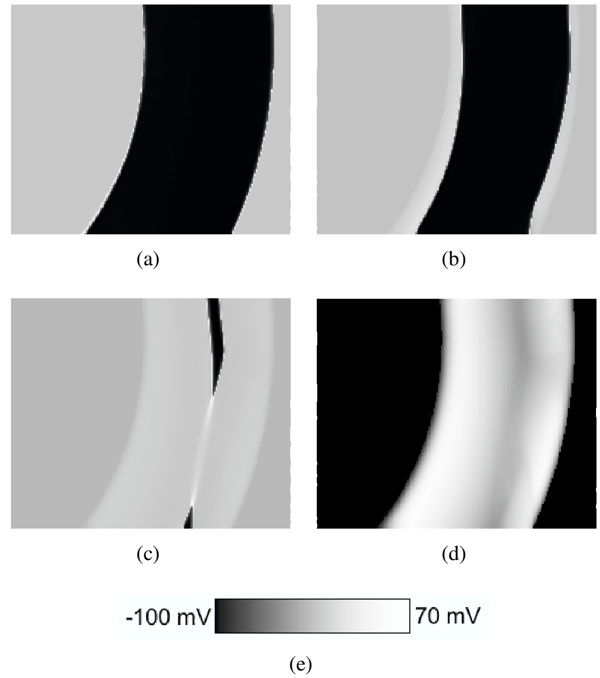


Figure 4. Temporal evolution of transmembrane voltage in an heterogeneous left ventricle myocardium with realistic fiber orientation after (+200 mV, -200 mV) electrical signal is applied through the sixth electrodes configuration: a) 1 ms, b) 10 ms, c) 50 ms, d) 60 ms, e) color code for Vm.

and the generated two-dimensional images are shown for better visualization. The figures are visualizing the model from two perspectives: 1) a plane which intersects the middle of the electrodes, Y axis being maintained constant, 2) a slice through the middle of the model, in which Z axis is maintained constant. Fig. 3 and 4 consider the first perspective. Both of them present the temporal reaction of the tissue after (+200 mV, -200 mV) electrical signal is applied through the seventh electrodes configuration. Only in the configuration 3 (see fig. 5) and configuration 4 a longitudinal propagation of the front wave appeared together with the transversal one. Under these circumstances the time needed by the tissue to be completely depolarized was 57 ms. In rest of the cases the time varied between 63 ms (configuration 1) and 65 ms.

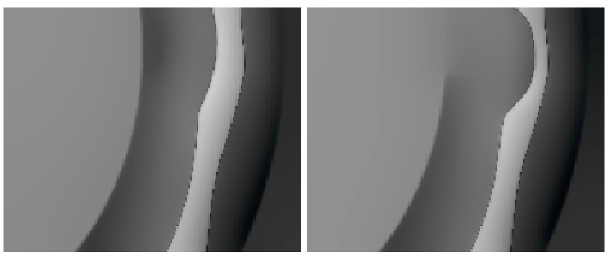
The inclusion of cells uncoupling also modified the length of the temporal intervals specific to the phases through which the tissue passed after the application of the electrical shock. Considering the seventh configuration we identified the most affected region by the electrical shock. The 2 mm^3 core of this region was selected and first was implemented in it 25% cell uncoupling. Following the reaction of the tissue to the electrical shock and comparing it to the normal tissue case we concluded that the differences are negligible. The enlargement of the percentage of the cell uncoupling to 75% modified the shape of the wavefront near to that region (see fig. 6 a) and it decreased the time needed by the tissue to be completely depolarized with 4 ms. Further on the volume of the myocardium, which contains cell uncoupling was extended to 64 mm^3. The core of the region had 75%, while in the surrounding space just 50% cell uncoupling was implemented. The shape of the wave front was strongly affected as can be seen in fig. 6 b. The tissue was totally depolarized 7 ms faster than in the previous case. In average 410 ms passed until the tissue regained the resting state.

4. Conclusions

The study shows that the formation of VEP near to endocardium and epicardium is invariant to the position in which the bath electrodes were placed. Supplementary regions from which depolarization spread were observed when one of the electrodes was placed at the apical border of the myocardium while the other one was fixed at its top. The additive effect implied the shorting of the time needed until the myocardium was overall depolarized. According to this aspect such electrodes configuration can

(a) (b)

Figure 5. Temporal evolution of transmembrane voltage in an heterogeneous left ventricle myocardium with realistic fiber orientation after (+0.2V, -0.2V) electrical signal is applied through the third electrodes configuration: a) 10 ms, b) 40 ms. Same color code as in fig. 4.



(a) (b)

Figure 6. Reaction of an heterogeneous left ventricle myocardium with realistic fiber orientation, which includes a) 75% cell uncoupling in the core of the affected region by a strong electrical shock, b) 75% cell uncoupling in the core of the region and 50% in a small surrounding volume, 40 ms after the electrical stimului were applied through the sixth electrodes configuration. Same color code as in fig. 3.

increase the defibrillation efficiency. From this point of view our research is a major step for optimizing internal defibrillators.

Our article also presents a theoretical research, which was focused on damaged tissue associated to high electrical shocks. It was shown that the myocardium, containing a quantity of destroyed nexa that surpassed a certain limit, had a different reaction to the electrical stimuli. The variation of the myocardium response to the electrical stimulation depends on the volume of the tissue, which contains cell uncoupling and also on the concentration of damaged nexa. The results pointed that the shape of the depolarization wave is critically modified. This implies a small reduction of the time necessary for the myocardium to be completely depolarized. The temporal intervals between cardiac phases are not drastically reduced because the electrical conduction in the damaged area is lowered. With this study we enlarged the theoretical knowledge of a serious clinical problem.

Acknowledgments

This work was supported by the Research Training Group 786 'Mixed Fields and Nonlinear Interactions' of the German Research Foundation (DFG).

References

[1] Hoyt RH, Cohen ML, Saffitz JE. Distribution and three-dimensional structure of intercellular junctions in canine myocardium. Circ Res 1989;64:563–574.

[2] Patel P, Plotnikov A, Kanagaratnam P, Shvilkin A, Sheehan C, Xiong W, Danilo PJ, Rosen MR, Peter NS. Altering ventricular activation remodels gap junction distribution in canine heart. J Cardiovac Electropysiol 2001;12:570–577.

[3] Beardslee MA, Lerner DL, Tadros PN, Laing JG, Beyer EC, Yamanda KA, Kleber AG, Schuessler RB, Saffitz JE. Dephosphorylation and intracellular redistribution of ventricular connexin43 during electrical uncoupling induced by ischemia. Circ Res 2000;87:656–662.

[4] Kostin S, Rieger M, Dammer S, Hein S, Richter M, Klovekorn WP, Bauer EP, Schaper J. Gap junction remodeling and altered connexin43 expression in the failing human heart. Mol Cell Biochem 2003;242:135–144.

[5] Sambelashvili TA, Nikolski PV, Efimov IR. Virtual electrode theory explains pacing threshold increase caused by cardiac tissue damage. J Physiol 2004;286:H2183–H2194.

[6] Streeter DD. Gross morphology and fiber geometry of the heart. In Bethesda B (ed.), Handbook of Physiology: The Cardiovascular System, volume I. American Physiology Society, 1979; 61–112.

[7] Seemann G, Sachse FB, Weiß DL, Dössel O. Quantitative reconstruction of cardiac electromechanics in human myocardium: Regional heterogeneity. J Cardiovasc Electrophysiol Oct. 2003;14(S10):S219–S228.

[8] Priebe L, Beuckelmann DJ. Simulation study of cellular electric properties in heart failure. Circ Res 1998;82:1206–1223.

[9] Henriquez CS, Muzikant AL, Smoak CK. Anisotropy, fiber curvature and bath loading effects on activation in thin and thick cardiac tissue preparations: Simulations in a three-dimensional bidomain model. J Cardiovasc Electrophysiol May 1996;7(5):424–444.

Address for correspondence:

Iulia Mihaela Graf
Institute of Biomedical Engineering / University Karlsruhe (TH)
Kaiserstr. 12 / 76128 Karlsruhe / Germany
tel./fax: ++49-721-608-8035/2789
Iulia.Graf@ibt.uni-karlsruhe.de