Study of Self Maintaining Spatial Spiral Waves in Ventricular Tissue

Sándor M Szilágyi[1], László Szilágyi[2]

[1]Petru Maior University, Tîrgu Mureş, Romania
[2]Sapientia University of Transylvania, Tîrgu Mureş, Romania

Abstract

Aims: This study focuses on the most important cardiac malfunction cases responsible for sudden cardiac death and on detailed visualization of all formation phases of the deadly, self maintaining spiral waves (SW) that may occur in the ventricular tissue and develop ventricular fibrillation (VF).

Methods: We developed a spatio-temporal computerized model of the whole heart that handles half millimeter sized compartments using 1μs time step. We employed the effect of muscle fiber direction, laminar sheets, depolarization period and other parameters. In presence of ischemia, normal parameter values were no longer maintained. In our simulation the depolarization wave (DW) conduction speed of the injured–but still functioning–tissue was decreased by up to 20 times, while the chance of spontaneous ectopic-firing (SEF) was increased by up to 1000 times.

Results: Under normal conditions the development probability of the SW was under 2% using 1-hour simulated period and had a 90% correlation with ventricular stimulation speed, and 75% with minimal depolarization period of the ventricular tissue.

Conclusion: Large size and low conducting speed of the injured ventricular tissue and the high probability of SEF are the main generating factors of SW.

1. Introduction

In developed countries ventricular fibrillation (VF) represents the leading reason of cardiac death. Despite decades of intensive research, the mechanisms responsible for VF are only partially discovered [1].

The main reason of slow progress represents the partially understood heart excitation and contraction functioning. The dysfunction of electrical impulse propagation may develop cardiac arrhythmias that perturb pumping activity [2]. Despite significant progress in the visualization of the heart's electrical dynamics, many details of arrhythmias are still unknown. To properly understand the behavior of the cardiac conduction system and pumping function under pathological conditions, several long duration measurements have to be taken.

In the last decades several studies have suggested that in the presence of a functional obstacle in cardiac muscle, a depolarizing wave may form a reentry circuit. These reentry waves are believed to develop cardiac fibrillation [3]. In addition, ionic heterogeneity of the cardiac tissue cells may have crucial role in the development of spiral waves and in their transition to an irregular shape forming VF.

The fast development of advanced mathematical modeling and intelligent computational methods makes possible to perform real-time computerized simulations as a useful tool to study cardiac dynamics. Computerized simulation of cardiac dynamics has the following advantages:

- is not perturbed by data acquisition errors;
- the values of all variables are known during the whole simulation;
- many pathological cases may be simulated without disturbing consequences;
- the simulation may be stopped every time for further improvements;
- several pathological cases may be simulated in the same time on a massive parallel architecture.

Despite all above mentioned advantages, performing a high-resolution spatial computerized simulation remains difficult. The main performance limiting factor consists in the internal error, introduced by the erroneous starting values of the model's parameters. Another annoying factor is represented by the high computational power needed to perform the simulation using proper spatial and temporal resolution. By performing calculation using low spatial or temporal resolution, we may introduce unmanageable error levels, depriving simulation to yield useful results.

Visual representation of the spatial simulation results is much harder than in case of planar simulations, because the 3D structures are usually projected onto a 2D image. Frequently, to improve visualization, spatial results are represented by a set of 2D slices [4].

It is essential to correctly distinguish the onset of

arrhythmias that may cause fibrillation on various heart structures, from those ones that do not favor these events [5]. Cardiac robustness depends on details such as the heart's size [6], geometry [7], mechanical [8] and electrical state [9], anisotropic fiber structure [10], and inhomogeneity [11].

The main goal of this paper is to present the possible onset of spiral waves and its transform to irregular waveform. The rest of the paper is organized as follows: Section 2 gives a detailed description of the cardiac excitation and contraction for normal and pathological cases. Section 3 presents and discusses several aspects of the spiral waves and the results of simulations. In Section 4, the conclusions are formulated.

2. Methods

The electric and mechanic modeling of ventricular tissue must take into consideration several aspects of the modeled organ. The first important step of modeling consists in the description of the cell's properties. As we want to simulate spiraled waves and various pathological phenomena, we consider that the structure of the modeled organ is far from being homogeneous.

The simulation cannot be performed in real time on nowadays computers, if we have to model each cardiac cell separately. The ventricular tissue of a healthy adult person contains more than one billion cells, while in the presence of hypertrophies the cell count may rise by up to three times. If each cell is modeled separately, applying a short temporal resolution (order of microseconds), the necessary computation power to determine the surface potential of each cell for each time slice exceeds about one hundred times the capabilities of top supercomputers.

To perform real-time simulation using a strong PC, but not a supercomputer, we had to use homogenous cellular compartments, where the size of compartments and the temporal resolution of the simulation may be modified adaptively. It is considered that the highest spatial and temporal resolution is needed in the depolarization wave's frontline, due to the fast voltage rise caused by fast sodium current [5].

In the presence of pathologic phenomena the depolarization frontline may divide or break, so the applied spatial and temporal resolution must be increased. In this situation each compartment may have altered state, so the investigated phenomena may be properly simulated.

The adaptively modified compartments can be used for all cardiac cell types. The state of each compartment is modeled separately, so the differences for normal and pathologic cases can be visualized permanently. This model allows describing the electrical and mechanical behavior of each compartment. The connections among compartments are a priori determined, so we can properly model the propagation of the depolarization wave and the mechanical contraction of the compartments.

Several higher level parameters are included in cardiac tissue modeling. The connection among compartments varies with both space and time. For example, ventricular muscle conducts the depolarization wave much more slowly than atria, but in presence of cardiac muscle injury in the atria, the conduction speed may decrease drastically or even may drop to zero.

Several time- and state-dependent tissue-related parameters were involved in our model. These parameters greatly influence the anatomy-related tissue parameters, such as fiber direction, anisotropy, average depolarization period, laminar sheets and spontaneous cell inhomogeneity. The used component models enable us to determine the electrical excitation and mechanical contraction of the cardiac muscle, thus supporting the volumetric analysis for atria and ventricles.

In this study, the tissue level excitation mechanism is based on Fast's work [12], while the activation potential is based on Luo-Rudy II (LR) model [13-14]. In this stage, each tissue element works as a secondary generator element. These elements can generate a depolarization wave if the adjacent elements are repolarized; otherwise, the wave propagation is swooned [15].

The LR model has ionic equation formulated as in the Beeler-Reuter model [16], and is the first dynamic mammalian ventricular cell model that describes the mathematical relation of the ionic currents and determines the shape of the activation potential [13-14]. This model accounts for dynamic changes of ionic concentrations, so it can properly handle several pathological cases. An important aspect of this model is its simplicity. Although it contains few dozen parameters instead of several hundreds used in newer ventricular models [17], all pathological causes of spiral wave formation can be simulated.

In our simulation we applied half millimeter sized compartments and 1μs time step. This minimal spatio-temporal step can be increased if the compartment is not in the fast depolarizing phase. In the presence of spiral waves or irregular contraction the minimal spatio-temporal step was only slightly increased, while in normal situations the increment was considerably larger.

For the case of healthy cardiac functioning we employed the effect of muscle fiber direction (the ratio between longitudinal and transversal conductivity varies from 2 to 10), normal and minimal depolarization period (considered 80-250 ms), laminar sheet effect (in-sheet transversal conduction 2-5 times faster than trans-sheet conduction), and cell inhomogeneity (using conduction speed differences for base-apex gradient (5%-20%), transmural epicardial–endocardial gradient (5%-35%), left-right ventricular gradient (5%-15%)).

In the presence of ischemia, normal parameter values were no longer maintained. The disturbed or inhibited cell

pumping functionality cannot maintain normal ionic concentration levels, so in our simulation the depolarization wave (DW) conduction speed of the injured–but still functioning–tissue was decreased by up to 20 times, while the chance of spontaneous ectopic-firing (SEF) was increased by up to 1000 times.

3. Results and discussion

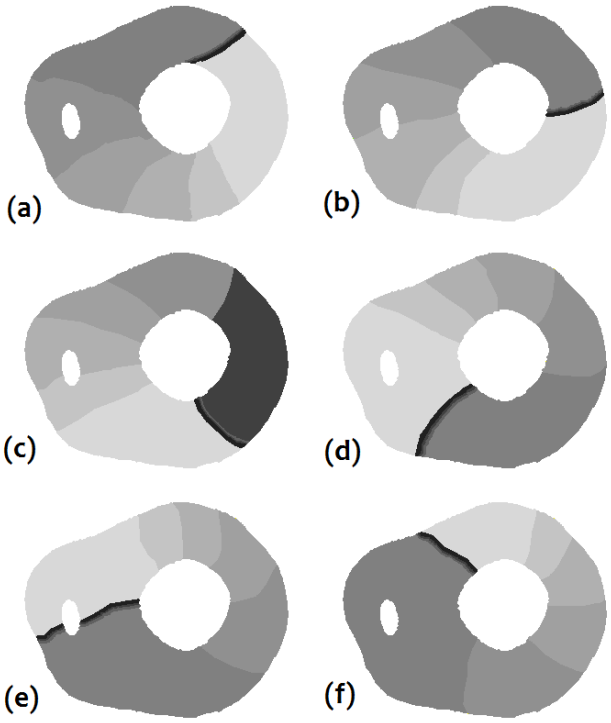

Figure 1. Simulation of reentrant arrhythmia in human ventricular tissue (VT). The simulated slice is situated approximately 30mm from apex. The reentrant period is 270ms, so the consecutive images are at 45ms distance from each other. The dark grey represents the recently excited cells, the lightest part of the slices consist of excitable ventricular cells.

Figure 1 shows that in the ventricular tissue a reentrant arrhythmia may occur, developing VF. The chance to develop such dangerous arrhythmia depends on several factors, such as homogeneity of ventricular tissue, excitation frequency, presence of accessory pathways and depolarization period of the ventricular tissue.

Table 1 presents the chance to develop SW in a given simulation period in presence of various pathological cases. It can be observed that SW did not appear in a complete healthy cardiac tissue even when we simulated 24 hour duration. In the presence of diverse pathological cases the SW was developed. The combined cardiac deficiencies produced the highest SW incidence. Among the single pathological cases the high level VT inhomogeneity represents the highest danger.

Table 1. The obtained probability of developing SW in the presence of diverse pathological cases.

Simulated period	1m	1 h	6 h	24 h
Healthy cardiac tissue	0 %	0 %	0 %	0 %
Reduced inhomogeneity in VT	0 %	3 %	7 %	12 %
Severe VT inhomogeneity	0 %	6 %	12 %	25 %
High level VT inhomogeneity	0 %	8 %	15 %	31 %
Presence of accessory pathway	0 %	6 %	11 %	19 %
High excitation frequency	0 %	3 %	7 %	12 %
Low depolarization period	0 %	1 %	3 %	6 %
All deficiencies are present	1 %	14 %	29 %	47 %

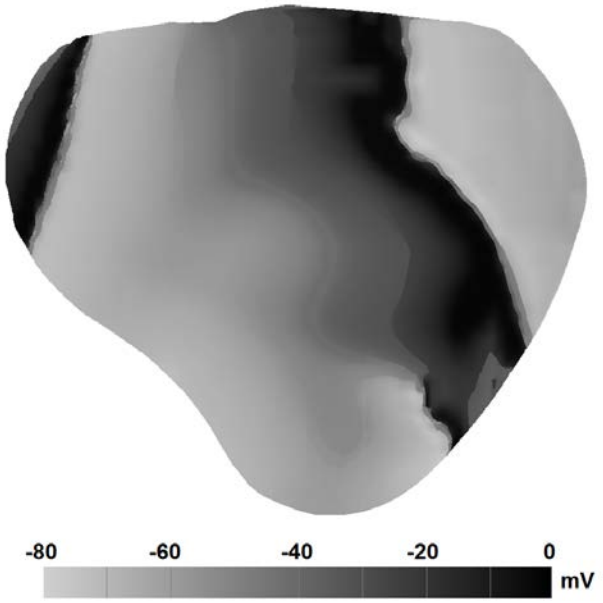

Figure 2. The surface potential expressed in mV of the ventricular tissue in the presence of SW. Dark shades represent the high, while light ones the low surface potentials.

Under normal conditions (but in presence of low level VT inhomogeneity) the development probability of the SW was under 2% using 1-hour simulated period and had a 90% correlation with ventricular stimulation speed, and 75% with minimal depolarization period of the ventricular tissue.

In the presence of ischemia the low-conducting ventricular tissue deflected the DW and generated perturbations on the wave front; the strength of deflections are directly proportional with the size of low-conduction area. If DW was maintained for at least half a repolarization period, the SW appeared in few seconds.

SEF promotes SW with 95% specificity.

The low depolarization period represents a possible danger by increasing the time window, when a pathological excitation may occur.

A patient suffering from hypertrophy has an increased VT size that represents a longer depolarization period. Low DW conduction speed of the VT also increases the depolarization period. Both above mentioned factors produce longer depolarization, so reentry waves may form more easily.

4. Conclusion

An inhomogeneous VT represents a double danger: the SEF occurs more often and if SEF is occurred, the possible wave propagation obstacles in VT increase the chance of SW development.

The spacious size and low conducting speed of the injured ventricular tissue and the high probability of SEF are the main generating factors of SW.

Computerized simulation of SW represents a non-invasive visualization tool than helps to understand the inner cardiac depolarization-repolarization process in normal and various pathological cases. An adequate simulation platform may select the most endangered patients by a non-invasive method that can enhance the efficiency of health care.

Acknowledgements

This research was funded by the Hungarian Academy of Sciences, under the János Bolyai Scholarship program.

References

[1] Sekar RB, Kizana E, Cho HC, Molitoris JM, Hesketh GG, Eaton BP, Marbán E, Tung L. I_{K1} heterogeneity affects genesis and stability of spiral waves in cardiac myocyte monolayers. Circ Res 2009;104:355–64.

[2] Cherry EM, Fenton FH. Visualization of spiral and scroll waves in simulated and experimental cardiac tissue. New J Phys 2008; 10:125016.

[3] Sekar RB, Kizana E, Smith RR, Barth AS, Zhang Y, Marbán E, Tung L. Lentiviral vector-mediated expression of GFP or Kir2.1 alters the electrophysiology of neonatal rat ventricular myocytes without inducing cytotoxicity. Am J Physiol-Heart C 2007; 293:2757–70.

[4] Fenton F, Karma A. Vortex dynamics in three-dimensional continuous myocardium with fiber rotation: filament instability and fibrillation. Chaos 1998; 8:20–47.

[5] Cherry EM, Greenside HS, Henriquez CS. A space-time adaptive method for simulating complex cardiac dynamics. Phys Rev Lett 2000; 84 (6):1343–6.

[6] Winfree AT. Electrical turbulence in three-dimensional heart muscle. Science 1994; 266:1003–6.

[7] Panfilov AV. Three-dimensional organization of electrical turbulence in the heart. Phys Rev E 1999; 59:R6251–4.

[8] Sainte-Marie J, Chapelle D, Cimrman R, Sorine M. Modeling and estimation of the cardiac electromechanical activity. Comput Struct 2006; 84(28):1743–59.

[9] Coghlan HC, Coghlan AR, Buckberg GD, Cox JL: The electrical spiral of the heart: its role in the helical continuum. The hypothesis of the anisotropic conducting matrix. Eur J Cardio-Thorac 2006; 29(1):S178–87.

[10] Caillerie D, Mourad A, Raoult A. Toward a fiber-based constitutive law for the myocardium. In: Thiriet M, editor. Proceedings of Modeling and Simulation for Computer-Aided Medicine and Surgery. EDP Sciences, 2002:25–30.

[11] Antzelevitch C, Shimizu W, Yan GX, Sicouri S, Weissenburger J, Nesterenko VV, Burashnikov A, Di Diego J, Saffitz J, Thomas GP. The M cell: its contribution to the ECG and to normal and abnormal electrical function of the heart. J Cardiovasc Electr 1999; 10(9):1124–52.

[12] Fast VG, Rohr S, Gillis AM, Kleber AG. Activation of cardiac tissue by extracellular electrical shocks: formation of ‘secondary sources’ at intercellular clefts in monolayers of cultured myocytes. Circ Res 1998; 82(3):375–85.

[13] Luo CH, Rudy Y. A dynamic model of the cardiac ventricular action potential I. Simulations of ionic currents and concentration changes. Circ Res 1994; 74:1071–96.

[14] Luo CH, Rudy Y. A dynamic model of the cardiac ventricular action potential. II. Afterdepolarizations, triggered activity, and potentiation. Circ Res 1994; 74:1097–113.

[15] Szilágyi SM, Szilágyi L, Benyó Z. A patient specific electro-mechanical model of the heart. Comput Meth Prog Bio 2011; 101(2):183–200.

[16] Beeler GW, Reuter H. Reconstruction of the action potential of ventricular myocardial fibres. J Physiol 1977; 268:177-210.

[17] ten Tusscher KHWJ, Bernus O, Hren R, Panfilov AV. Comparison of electrophysiological models for human ventricular cells and tissues. Prog Biophys Mol Bio 2006; 90(1–3):326–45.

Address for correspondence:

Sándor Miklós Szilágyi
Str. Frantz Liszt nr. 8, 540068 Tîrgu Mureş, Romania
szsandor72@yahoo.com