Simulation of Arrhythmia using Adaptive Spatio-temporal Resolution

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Abstract

Aims: This study is aimed to present the simulation of several types of cardiac arrhythmias using adaptively selected spatio-temporal resolution, involving the accuracy analysis of the experiment.

Methods: We developed a spatio-temporal adaptive whole-heart simulation algorithm that handles automatically and regionally the proper resolution. The limits of upper and lower resolutions (0.2-5 mm; 1-500 μs) are a priori established, while the granularity at a given moment depends on the type, place and state of each modeled compartment. We employed the effect of muscle fiber direction, laminar sheet effect, average and minimal depolarization period, and cell inhomogeneity.

Results: The estimation errors were maximal during fast depolarization phase of the activation potential. Under normal circumstances, tachycardia and bradycardia, a 2/5/10/20 times lower spatial resolution induced an about 3%/7%/12%/20% estimation error of the depolarizing front line's shape. In the presence of AF/VF, under similar simulation conditions, the estimation error raised to 7%/15%/22%/34%.

Conclusion: The simulation of cardiac arrhythmia demands high spatio-temporal resolution during fast depolarization phase and in presence of AF/VF due to the irregular spread of depolarization.

1. Introduction

The leading mortality factor in the developed countries represents the ventricular fibrillation (VF) induced by cardiac arrhythmia. Due to the complex anatomical structure of the heart and the only partially understood cardiac physiology, currently the mechanisms responsible for arrhythmia and VF are only superficially discovered [1]. The partially known heart excitation and contraction phenomena, and the dysfunction of electrical impulse propagation may develop cardiac arrhythmias, thereby perturbed pumping activity occurs [2].

The main obstacle in exploring most details of the onset of the cardiac arrhythmia is represented by the poor measure of the inner parameters [3]. Several studies have emphasized that in the roots of arrhythmia are situated in the inhomogeneous depolarization of the cardiac tissue [4].

In the last decades, numerous mathematical models and intelligent computational methods were developed in order to perform real-time computerized simulations of the whole heart, creating a useful tool to study cardiac dynamics [2, 5]. These simulations possess several advantages: they are not perturbed by data acquisition errors, the simulated values of all internal variables may be visualized and studied in real time, the size and nature of the healthy and injured cardiac tissue may be studied before the real intervention, and the simulation may be stopped at any moment for further improvements [6].

In spite of the intensive research and significant progress, a proper recognition of the dangerous situations that can develop arrhythmias and therefore VF still remains an unresolved problem [7]. To enhance our physiological event estimation capabilities, it is imperial to involve in our simulation several heart-related parameters such as: size, geometry, mechanical and electrical state, anisotropic fiber structure, and inhomogeneity.

In the following, we present a multi-structural, adaptive whole heart model that can uncover the root of arrhythmia development. This model handles the effect of highly inhomogeneous and injured cardiac tissue, accentuated fibrosis, obstructed depolarization and diverse re-entry circuit development, which predisposes the organism to the development of dangerous arrhythmias and VF.

The rest of the paper is organized as follows: Section 2 gives a detailed description of the multi-structural, adaptive heart model. Section 3 presents and discusses several aspects of the altered depolarization, formulation of arrhythmias, and presents the results of simulations. In Section 4, the conclusions are formulated.

2. Methods

We performed the adaptive whole organ modeling using an enhanced cellular automata system (CAS). The developed multi-subsystem-based model is based on the work described in [6], where a patient specific electro-mechanic heart model was presented.

Although the main simulation steps are similar in our new simulation as in the old one [6], several important aspects were changed. First of all, a partially new set of cellular models were used to serve simplification or efficiency reasons.

The cellular activity of the sino-atrial node was performed using the equations of Noble and Noble [8], while the atrial cells simulation is based on the work of Nygren et al [9]. Inada et al published an atrio-ventricular node model that involves atrio-nodal, nodal, and nodal-his cells [10]. This complex model was included in our simulation in order to handle the whole depolarization retentive sub-system of the heart. The electric activity of the ventricular cells was modeled by the Luo-Rudy II model [11-12], while the Purkinje cells were modeled using the equations of McAllister et al [13]. In all models we applied a 1μF/cm^2 membrane capacity, and a 37°C temperature.

In several pathological cases the inner structure of the cardiac tissue suffers serious deterioration. For example aging, diverse injuries and infarcts usually trigger from a mild up to an accelerated fibrosis that predisposes the cardiac tissue to develop many highly inhomogeneous islands, thereby creating the root of later developed arrhythmias.

In order to properly simulate such nasty pathological cases, the introduction of a new depolarization concept was necessary. The old-fashioned compartment-based excitation model had to be extended, forming a multi-subsystem-based (MSSB) simulation environment. In this newly created model several sub-systems complement each other in order to precisely describe the depolarization of an inhomogeneous tissue.

The first sub-system is made up of the conventional compartments, which handle the effect of cell type, cell state, size, shape of the activation potential function. To cope with some extended cardiac properties, such as laminar sheets, inhomogeneous conduction and structure, a wider area of compartments had to be involved, determining the connection network among them.

The second sub-system consists of the network of the fast conducting Purkinje fibers. The introduction of this new Purkinje fibers system (PFS) significantly reduces the spread propagation errors. PFS is important during a normal depolarization, but in pathological cases it possesses an even greater role.

The third or further sub-systems are introduced in several pathological cases, such as in presence of Wolff-Parkinson-White syndrome, where the set of accessory pathways forms a sub-system. The simulation of re-entry circuits also demands the inclusion of sub-systems. Since reentry circuits predispose the heart to develop arrhythmias, these partially understood phenomena can be investigated more precisely using the above mentioned MSSB modeling.

All sub-systems work parallel and independently contribute to the spread of the depolarization wave. Considering that in most cases the second and all further sub-systems play an imperial role in electric conduction but their direct effect on the surface ECG in most cases can be neglected (the tissue quantity involved in an accessory pathway is less than the tissue in the ventricles by several orders of magnitude), they usually do not possess own weight (during simulation), and their position is determined by the a priori specified connections to the elements (compartments) of the first sub-system.

As the tissue from the compartments (first sub-system) possesses the total or almost total mass, thereby determines the shape of the generated surface ECG, therefore it is imperial to correctly determine the excitation moment and direction of the compartments.

In our model we implied that among the sub-systems, the first one conducts slowest the depolarization, and if in one compartment there are involved at least two elements from more than one secondary sub-system, the excitation automatically propagates among them with the conduction speed of the compartment.

The depolarization moment of a compartment is determined using several rules. First of all, we determine the main parameters of the neighbor compartments set: $S_{NC}(x_i, y_i, z_i, cs_i, m_i, dt_i)$, where beside the spatial coordinates, the conduction speed *cs*, the mass *m* and the depolarization time *dt* is involved. Starting from the elements of S_{NC}, we deduce the minimal depolarization time using formula:

$$dt(S_{NC}) = \min_i \left\{ d(C, C_i) \frac{m_C cs_C + m_{C_i} cs_{C_i}}{m_C + m_{C_i}} + dT_{C_i} \right\},$$

where $d(A,B)$ represents the Euclidean distance between *A* and *B*. A similar operation has to be performed for all other sub-systems ($j = 1...k$), where the formula will become:

$$dt(S_{NS_j}) = \min_i \left\{ d(C, S_{j,i}) \cdot cs_C + dT_{S_{j,i}} \right\}.$$

The determined depolarization time of the compartment will be: $dt_C = \min\{dt(S_{NC}), dt(S_{NS_j})\}$.

There are several pathological cases, where a small region of cardiac tissue has altered properties. Usually during an injury these developed tissue-islands reduce the conduction speed (by up to 100 fold) or totally inhibit the propagation of the depolarization wave (DW). These injuries may predispose the heart to develop various

arrhythmias, so their proper modeling needs to use a high local spatial resolution.

In order to reduce the necessary computational power, we used an adaptive resolution selection method. Typically an increased spatio-temporal resolution is necessary at the fast depolarization phase of a normal compartment, or when the front-line of the DW divides or breaks. In our simulation we applied a regionally variable spatio-temporal resolution [14-15]. The limits of upper and lower resolutions (0.2-5 mm; 1-500 μs) are a priori established, while the granularity at a given moment depends on the type, place and state of each modeled compartment.

In normal circumstances the effect of muscle fiber direction (the ratio between longitudinal and transversal conductivity) varies from 2 to 15, while the normal and minimal depolarization period is considered in the 70-280 ms interval. The laminar sheet effect may modify significantly the DW's shape (the in-sheet transversal conduction is 2-6 times faster than trans-sheet conduction). The effect of ventricular tissue inhomogeneity was also included. The conduction speed difference for base-apex gradient is 5%-25%, the transmural epicardial–endocardial gradient is 5%-45% and the left-right ventricular gradient is 5%-20%.

3. Results and discussion

In Fig. 1 the formation of a reentry wave is presented. The minimal re-excitation period is 240ms. The time elapsed between consecutive images from (a) to (h) is 30ms, while from (h) to (l) is 90 ms. The simulation covered a 12x10 cm region. In the central region of the images, the contour of a slow conducting injured tissue is marked. After the initial depolarization (a), when the tissue is only partially repolarized, a self ectopic excitation occurs in the borderline of the injured region. The surrounding partially excitable media directs the DW to the lower side of the images. In the images (b) - (f) the upper side of the DW continuously swooned by the not-yet excitable media, while the lower side of the DW can propagate with no barriers. In the image (f) the lower side of the injured tissue becomes excitable, so the DW penetrates into the injured region, and propagates in it with a reduced speed. In the images (f) – (j) the formulation of the main re-entrant circuit is presented (this anatomical reentry can be developed not only in case of an unexcitable scar, produced by an infarct, but also in slow conducting, sufficiently large injured regions). In case of a sufficently large injury, the period of the formed re-entrant circuit can exceed the repolarization period of the ventricular cells, so the formed circular activity is self maintaided. This phenomenon may develop ventricular fibrillation (VF), but even if VF is not formed, the inhibited cardiac pumping functionality induces sudden cardiac death.

The development of VF and diverse arrhythmias often depends from subtle details, so the proper modeling of these events is imperial.

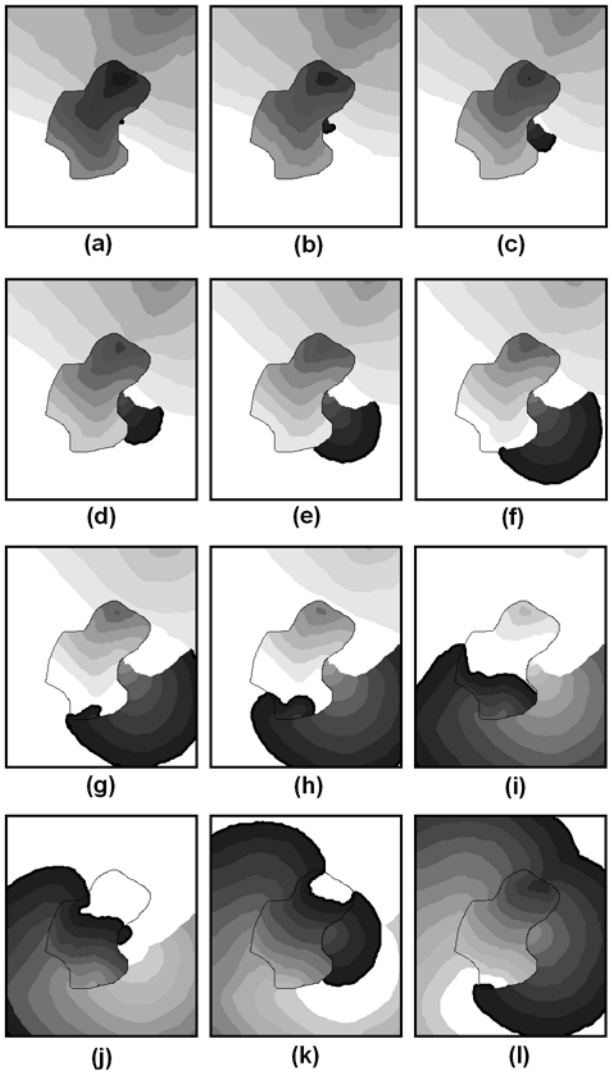

Figure 1. 2D simulation of reentrant arrhythmia development in injured human ventricular tissue.

In Fig. 2 and 3 the spreading speed of depolarization is presented. It can be seen that the DW speed decrement is slightly less in case of spatial resolution reduction than in case of temporal resolution reduction. The fast changing depolarization waveform's speed is more sensible to resolution, so the AF and VF demand fine granularity. In the slow changing cases (normal case, tachycardia and bradycardia), the model's sensibility to resolution is almost constant. From these results can be concluded that a low resolution carries with him the inadequate estimation of the depolarization and repolarization phenomena, obstructing the proper simulation of the reentry circuits.

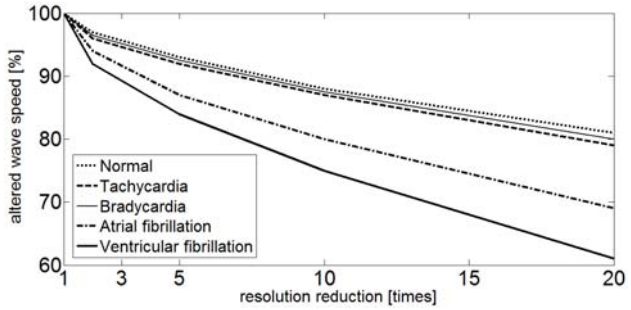

Figure 2. The depolarization wave's speed plotted against spatial resolution reduction in presence of various phenomena.

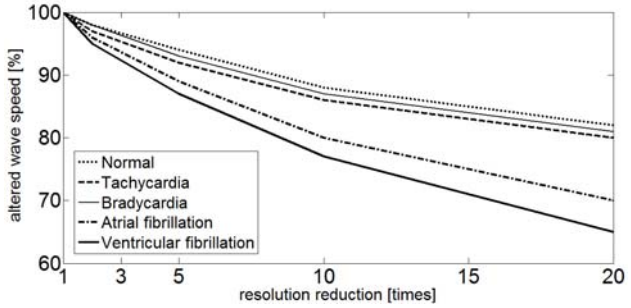

Figure 3. The depolarization wave speed plotted against temporal resolution reduction in presence of various phenomena.

4. Conclusion

The promoted computerized simulation of cardiac dynamics, using various spatial and temporal resolutions, provides a better appreciation of cardiac excitation and reentry wave development. This analysis may throw light upon the limits and necessary granulation of modeling during several cardiac rhythm malfunctions such as tachycardia, bradycardia, atrial and ventricular fibrillation, and uncovers the formation of arrhythmia.

The simulation of cardiac arrhythmia demands high spatio-temporal resolution during fast depolarization phase and in presence of AF/VF due to the irregular spread of depolarization. An adequate simulation platform may be used to recognize the most dangerous situations, thus contributing to the efficiency of computerized health care.

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