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Modeling Sources of Atrial Fibrillation on a Triangulated Sphere

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A model of atrial fibrillation as a cellular automaton on a triangulated sphere, a weighted undirected graph, is presented. We show the results of simulation for study of mechanisms of formation and stability of propagation of rotary excitation waves with heterogeneity of excitation propagation velocity and refractoriness of the myocardium. The simulation shows the possible existence of a stable rotor in a minimum area of pathological zone of 14 mm^2 (diameter 4.3 mm) with the parameters of myocardium in pathological zone: velocity 0.1 m/s, refractoriness 100 ms; the main myocardium: velocity 1 m/s, refractoriness 200 ms.

Introduction

Heart tissue is an active environment in which autowaves can propagate. Autowave phenomena of different nature are usually described by parabolic differential equations in partial derivatives with nonlinear free member. This approach can be seen in the modeling of complex fractionated electrograms [1]. Complex fractionated signals are recorded in some areas of the atrial myocardium in patients with atrial fibrillation (AF) during cardiac electrophysiological studies [2].

To describe the process of excitation wave propagation in heart tissues, Norbert Wiener in 1946 proposed a model in which a cardiomyocyte (an element of the model) was described by a set of discrete states that succeeded each other at discrete intervals according to certain rules. This field was developed in the works of other researchers [3, 4], who used cellular automata (CA) to simulate the excitation propagation in the myocardium.

It is now estimated that the pathological regions of the myocardium provoke the formation of rotors and ensure their stability [5]. The most promising method for the treatment of atrial fibrillation is considered to be selective catheter ablation, which targets regions of rotary activity of the myocardium.

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Materials and Methods

The goal: to develop a mathematical AF model for investigation of the mechanisms of formation and stability of propagation of rotary excitation waves with heterogeneity of excitation propagation velocity and refractoriness of myocardium.

To achieve this goal, there is no need to simulate the exact shape of the electrogram signal. Electrophysiological processes in the myocardium in this case are of no interest. The area of interest is the relative characteristics of the functioning of the atrial myocardium, such as velocity of the excitation wave front, duration of the refractory state, and dimensions of pathological and normal myocardial tissue. The AF model was developed based on CA on a triangulated surface of a sphere. Using a sphere simplifies the algorithm as it eliminates the problem of solution closure by boundaries and allows observing the process on a curved surface in three-dimensional space [6]. Additionally, the simulation object is a closed surface that is best represented in the form of a sphere. An icosahedron was selected as an approximation of a sphere, which performs best of all regular polyhedra for triangulation of the sphere by recursive partitioning with minimal distortion of the resulting triangles.

The simulation area limited by the triangulated sphere includes 40,962 nodes a_i and can be visualized as a two-dimensional structure by the algorithm, making visualization of the excitation fronts clearer. The CA of the AF model is a simple undirected flat-weighted graph $G = (A, E, W)$, where $A = \{a_i | i = 0, 1, \ldots I\}$ – set of nodes; $E = \{e_j\}$ – set of edges; $W = \{w_j\}$ – set of weights of edges of graph G.

The set $W = \{w_j\}$ contains a weighting function of the edge, which represents the value of n and determines the number of sampling steps needed to transmit the excitation between nodes. The value of n is determined by the given initial conditions of the propagation velocity of the excitation front v_j in the relevant areas of the model and the distance between nodes S_j:

$$n = S_j/(dt \cdot v_j),$$

where dt – a fixed step by sampling time.

CA nodes can be in one of the states that are cyclically varying:

$$a_i(t) = \{0, 1, ..., k - 1, k\}.$$

The developed algorithm has the following CA states: rest state, activity state, refractory state. For each node, the initial conditions set any of these conditions, as well as additional "off" state. The "off" state is used to simulate the valve structures and completely nonexcitable areas (scars), a node with such state is not subjected to transition rules, and it is constantly at rest. The active state of a CA node is retained until all adjacent nodes are activated. The transition from the active state to the refractivity is performed when all adjacent nodes are in active or refractory state. The transition conditions are determined by the state of the adjacent nodes taking into account the weight of the edge between them. The number of sampling steps that determine the duration of the refractory period in node R (the period corresponding to the excitation of the myocardium) is $m = R/dt$, i.e. each node of the set $V = \{v_i\}$ is a set value of m specifying the refractory period. Switching of CA state is performed synchronously by the general rule of transition:

$$a_i(t + 1) = \varphi(a_i(t)|a_i(t) \in P),$$

where P – set of adjacent nodes that make up the neighborhood of the CA.

The simulating program was developed, and for 3D-visualization of the results of modeling the activation of the atrial myocardium, the working program of electromagnetic navigation system Biotok was used (http://biotok.ru/RU/products#arhythmology-navigation); a screenshot of the working window of the program is shown in Fig. 1.

Input parameters for the simulation program: diameter of the sphere – 100 mm; number of nodes – up to 100,000; number of pathological zones – up to 10; position and size of the zones are defined by mouse pointer; parameters of the main and changed myocardium are given by velocity of the excitation front and duration of the refractory state.

Results

Simulation modeling was performed on a 50-mm diameter sphere. The main area has parameters of

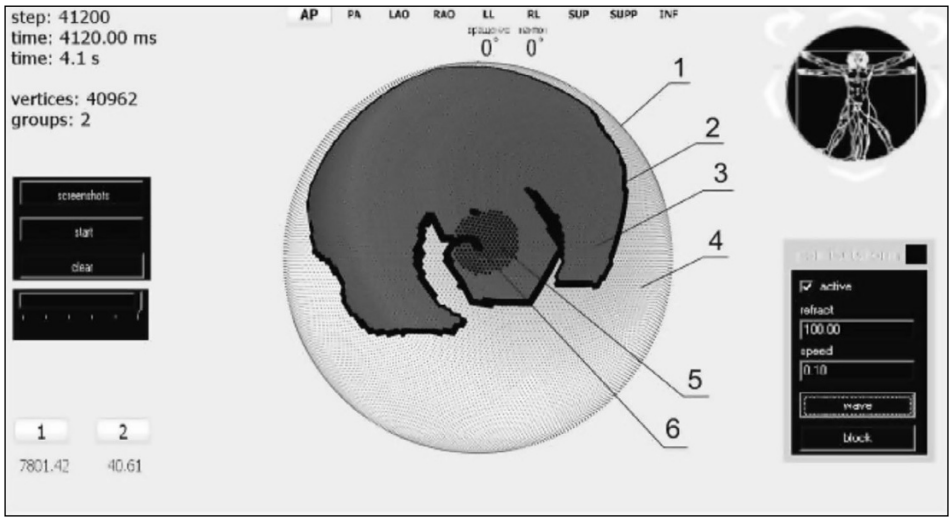

Fig. 1. Program window during modeling process: 1) triangulated sphere; 2) excitation wave front; 3) active state of myocardium; 4) rest state; 5) area of pathology; 6) front rotor.

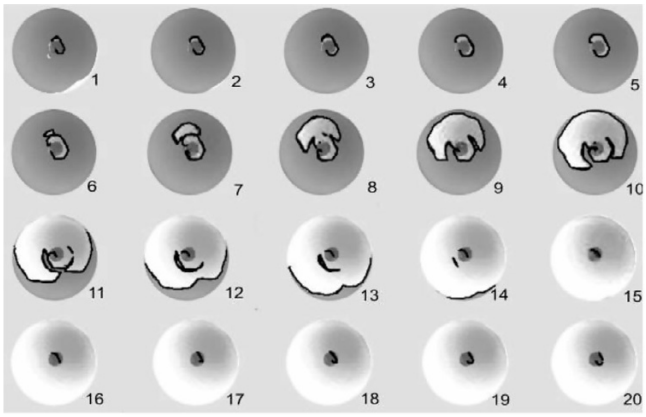

Fig. 2. Simulation of excitation front with a steady rotor in a pathological region.

"healthy" myocardium: velocity – 1 m/s; refractoriness – 0.2 s [7]. With these parameters, there are no conditions for the existence of more than one excitation wave up to frequencies of 300 beats/min. For pathological (or partially adaptive) changes of the conduction speed up to 0.1-0.5 m/s and for refractoriness up to 0.1 s, conditions arise for simultaneous existence of several excitation waves of the atrial myocardium. The sources of excitation of such waves in the real myocardium can be muscle tissue of the pulmonary veins, local areas of pathological changes that have their own automatism, and spiral autowave (rotors) formed at the discontinuities of excitation wave fronts due to myocardium heterogeneity caused by the dispersion of the propagation velocity of excitation waves and refractoriness.

Figure 2 shows an example of the simulation of an excitation front consisting of a sequence of images of the program. In the center, an area with pathological parameters is defined: velocity – 0.1 m/s; refractoriness – 0.1 s. A rotor formed in the center of the zone. When the myocardium surrounding the area comes out of refractory state (frame 1), the excitation from the rotor comes out of the boundaries of the zone (frames 2-10), and, as the velocity parameters of the front outside the zone are much higher, the excitation front covers the area (frames 11 and 12) and quickly propagates, activating the rest of the "healthy" myocardium and translating it into the refractory state. The rotor remains in the same zone, in which there are conditions to maintain it. The refractory state, in which the surrounding myocardial tissue is at this stage, limits its zone of influence and does not allow moving out of the pathological zone (frames 13-20). Further, the tissue surrounding the pathological area is released from the refractory state and the rotor forms another excitation front in the "healthy" myocardium. The stable rotor in the simulation was obtained with a minimum area of 14 mm^2 (diameter – 4.3 mm) with myocardium parameters: velocity – 0.1 m/s; refractoriness – 0.1 s. The depth of the excitation front is 10 mm, and assuming that such wave excitation covers nonexcitable annular structure, its diameter is approximately 3.2 mm. The modeled rotor rotates inside an excitable structure, so it requires slightly more space. The CA element has finite dimensions.

For experimental and clinical evidence of the results obtained in the simulation, a high-density multipolar electrode system was designed and manufactured (Fig. 3). The design of the electrode system was a multilayer rigid-flex printed circuit board with two rigid parts and a flexible polyamide part of bilateral printed conductors connecting the parts. One of the rigid parts of the board has 64 pads for electrodes with diameter of 0.76 mm and increments of 1 mm for the registration of electrical potentials of the heart. The size of the rigid part of the board with the electrodes is 34 mm long and 18 mm wide. Each electrode is in the form of a hemisphere of an alloy of silver and tin and is coated by immersion gold. Electrodes in the form of a hemisphere can achieve better contact and therefore a better quality of signal recording from the surface of the atria. The second rigid part of the board has a connector for mating with a con-

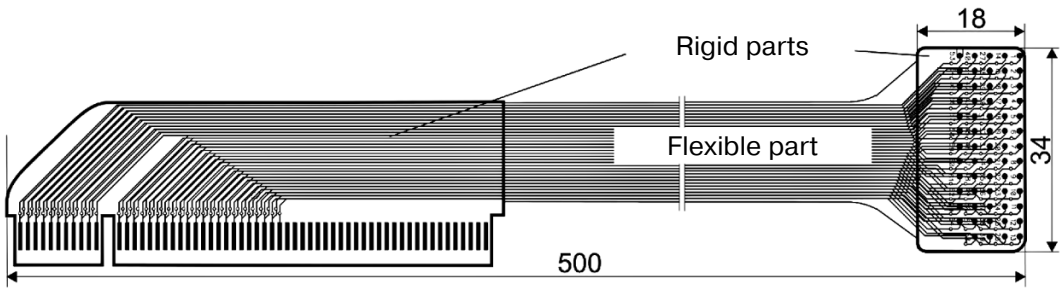

Fig. 3. Construction of high-density multipole electrode system.

necting cable of a multi-channel electrophysiology system.

Clinical studies were performed to evaluate the diagnostic value of the high-density multipole electrode system for searching and visualizing targets for electropulse and surgical effect on the myocardium in the treatment of atrial fibrillation [8]. Parallel phase analysis of signals from the multichannel electrophysiological system was used for topical diagnosis. Stable periodic rotary activity was detected in three patients, and in 12 cases, the sources of arrhythmia were unstable. Stimulation of the revealed centers of AF by high-energy electrical pulses in five patients resulted in reduction of AF, which was no longer provoked. In other cases, a repeat procedure was required.

Discussion

A rotor is stable and can exist indefinitely in the active medium simulating the myocardium, but, if destroyed, formation of a new rotor requires certain initial conditions. The presented model can be regarded as an analog of paroxysmal AF.

It is possible that regions of the myocardium that during clinical analysis are mistaken for ectopic foci [5] may not have their own automatism similar to the function of the sinus node, and, most likely, are compact areas of rotor activity.

For small size of pathological area, it would be impossible to distinguish the source of focal excitation and the rotor using conventional systems for electrophysiological studies of the heart, i.e. the compact rotor simulates ectopic focus of excitation, but its myocytes do not have their own automatism. Localization of the rotors is possible by dominant frequencies [9]; however, as shown by simulation, localization accuracy is low; in the absence of sharp edges in the characteristics of healthy and pathological myocardial regions, the dominant frequency in them will be the same.

It is proposed to a build clinical research strategy of the rotors in the direction of finding areas with slowed propagation and shortened refractory period, or, that is easier implementable, using a parallel phase analysis of electrograms of high-density multipolar endocardial electrode systems. Phase analysis can be performed by the chosen dominant frequency [8]. Visualization of the results of topical diagnosis can be made as a graded color or vector map of propagation velocity and direction of the excitation front of atrial myocardium on the surface of a realistic model synthesized using the navigation system.

Conclusion

In the course of this study, a model of atrial fibrillation as a cellular automaton on a triangulated sphere (being a weighted undirected graph) was developed. The results of the simulation were shown for the study of the mechanisms of formation and stability of propagation of rotary excitation waves with heterogeneity of excitation propagation velocity and refractoriness of myocardium of different sizes.

For the existence of a stable vortex excitation structure, the myocardium area of 14 mm^2 is sufficient with refractoriness decreasing down to 100 ms and reduced excitation propagation velocity down to 0.1 m/s; outside this area in a healthy myocardium, the rotor excitation spreads in the same way as the focal source excitation.

A high-density electrode system was developed based on flex-rigid printed circuit boards for epicardial mapping; the system is designed to perform experimental and clinical studies on the localization of AF sources.

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