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Research paper

Spontaneous termination of reentrant activity under myocardial acute ischemia: Role of cellular conductivity and its relation to ischemic heterogeneities

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ABSTRACT

The relation between reentrant activity and occurrence of cardiac arrhythmias still is a topic of intensive investigation. Reentries are strictly related to and enhanced by the complex structure of cardiac tissue, characterized by multi-sized electrophysiological and spatial heterogeneities. However, the structure and the function of the tissue can sometimes also promote phenomena of spontaneous termination of waves. The role played by the tissue in this scenario is not well understood and yet under investigation. In this study, we implemented a bidomain formulation of the phase I of the Luo and Rudy action potential model in 2D under ischemic conditions. We investigate how the size of ischemic heterogeneities and tissue conduction properties may affect the system dynamics and drive it towards maintenance of reentrant activity or quiescence.

The main findings show that: (a) for the stability of the waves, changes of conductivity in the intracellular space are more critical than alterations in the extracellular space; (b) the maintenance or the self-termination of pinned spirals is strongly dependent not only on the size of the heterogeneities but also on the degree of intracellular anisotropy.

These findings confirm and extend results obtained from previous investigations. In addition, since experimental values of conductivity tensors reported in the literature are not consistent, an overview of possible scenarios arising from a broader range of assumed anisotropy values is provided in relation to different sizes of ischemic heterogeneities. In this perspective, simulations are shown to compare the impact of different degrees of tissue anisotropy on wave dynamics.

1. Introduction

There is strong evidence in literature suggesting that reentrant activity is one of the main causes of the occurrence of cardiac arrhythmias [1–3], among which some (like ventricular tachycardia (VT) and ventricular fibrillation (VF)) can be seriously life threatening if not properly treated and can lead to sudden cardiac death [4,5]. Reentries are highly promoted

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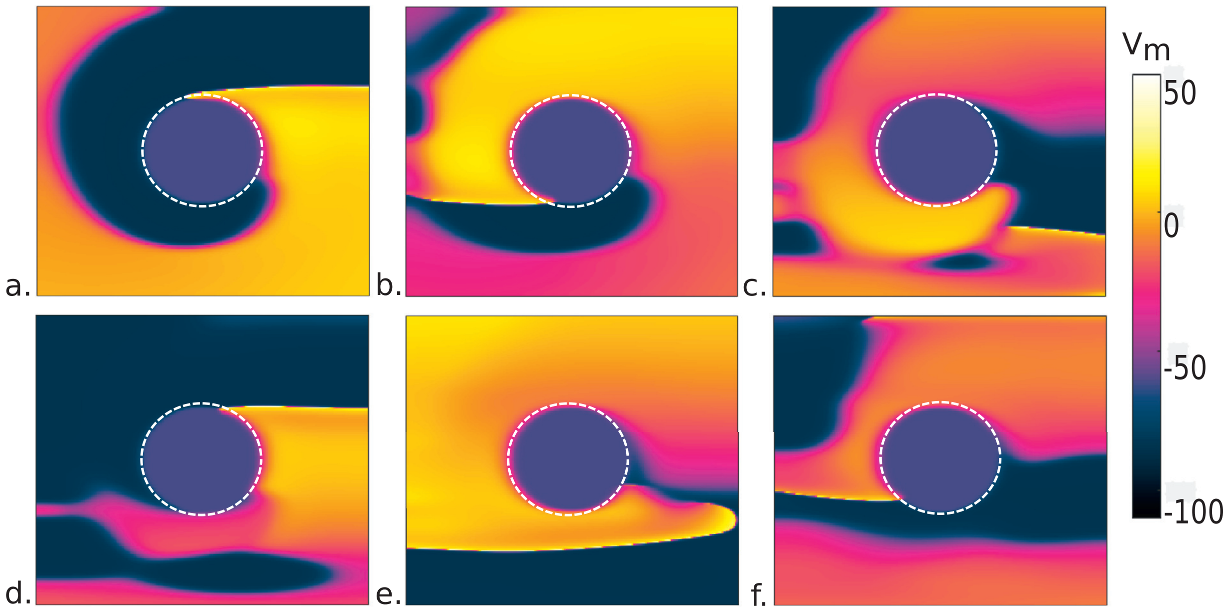

Fig. 1. Snapshots showing maintenance of a spiral wave pinned to the ischemic heterogeneity having a radius of 0.67 cm, highlighted by the white dashed circle. Simulations were run using a bidomain formulation of the phase I of the Luo and Rudy action potential model. The 2D domain was represented by a 3.67 × 3.67 cm^2 sheet of heterogeneous and anisotropic cardiac tissue, in which fibers were supposed to be aligned along the *x*-axis. The color bar indicates the membrane potential V_m in mV: (a) time = 70 ms; (b) time = 200 ms; (c) time = 350 ms; (d) time = 580 ms; (e) time = 700 ms; (f) time = 980 ms. (For interpretation of the references to color in this figure, the reader is referred to the web version of this article.)

by the complex myocardial structure, in which electrophysiological and spatial multi-sized heterogeneities represent a critical substrate. Heterogeneities can be intrinsic or can be exacerbated after the occurrence of specific diseases [6]: in both cases they affect the properties of the tissue causing reduced conduction velocity, prolonged refractory period, discordant repolarization alternans or repolarization gradients [7–15].

The concept of spiral waves was introduced in 1946 [16] with respect to reentries anchored to anatomical features of the tissue and then extended to refer to waves circulating around “functional” obstacles, i.e. not anatomical, called the core of the spiral. Once a reentry develops in the tissue, it can remain stable showing VT or it can break up into multiple wavelets, i.e. degenerating into VF. In the latter case two types of VF have been hypothesized and experimentally validated in animal models: the “mother rotor” and the “multiple wavelets” [17]: in the first case, pre-existing heterogeneities play an important role in causing conduction block of waves propagating from a stable rotor and are responsible for the development of multiple wavelets during fibrillation [18]; in the second case, instead, the fibrillation and the development of multiple waves is sustained by continuous waves break up due to dynamical instabilities [19].

In 1914 Garrey et al. [20] introduced the concept of the “critical mass hypothesis”, according to which formation and maintenance of cardiac arrhythmias is strongly affected by the size and form of the tissue. Beyond shock-induced termination [21], under certain conditions arrhythmias may also terminate spontaneously into quiescence: this may happen when the wavelength (and the refractory period) are increased in some regions of the tissue, causing a reduction of tissue size and, as a consequence, termination of reentrant activity. Beyond wavelength [22], other features have been shown by previous studies to play a role in the interactions between wave and obstacles: among them, dynamical instabilities (such as chaos) [7], size of anatomical and functional obstacles [23,24], excitability and curvature of the obstacles [25], thickness, shape and geometry of the tissue [20,24].

In this paper the effects exerted by both geometry and electrophysiological properties of the tissue on maintenance and self-termination of reentrant waves are discussed. In this perspective, we implemented a bidomain formulation of the phase I of the Luo and Rudy action potential model [26] under conditions of acute ischemia, starting from initial conditions in which reentrant waves are pinned to ischemic heterogeneities. The roles played by the size of the heterogeneities and by the change of conduction properties in the tissue are analyzed, showing interesting examples of how these parameters and their combination can highly influence wave dynamics pushing the system to persistence of reentrant activity or quiescence.

2. Maintenance and spontaneous termination of cardiac arrhythmias

Figs. 1(a)–(f) and Fig. 2(a)–(f) show snapshots from simulations of maintenance and spontaneous termination of reentrant activity, respectively. A spiral wave is pinned to an ischemic region with radius of 0.67 cm. In both cases the dynamics of the waves develops under conditions of acute ischemia and the size of the heterogeneity stays constant, but due to