Non-invasive Location of Re-Entrant Propagation Patterns during Atrial Fibrillation

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Abstract

Functional rotors have been defined as a mechanism responsible for the maintenance of atrial fibrillation (AF). These re-entrant patterns can be identified in the atrial wall by detecting phase singularities (PS) in the epicardial phase maps. In this study, we evaluate the potential role of body surface phase maps to non-invasively locate atrial sites that may harbor rotors. This technology could be of great interest for diagnosis and treatment of AF.

In the present study, we make use of mathematical models of atrial activity to evaluate the representation of PS on the torso and inside the passive volume between heart and torso. A filament was defined as a line connecting in time and space the SPs detected on the different layers. Filaments from permanent rotors reach the torso and remain stable over time. Filaments arising at the fibrotic area cancel out with each other at increasing distances from the atria until a single filament reaches the surface with a wider meandering than that of a stable rotor.

These results show that the electrical propagation pattern in the atria during AF is reflected in the electrocardiogram. Our simulations demonstrated that rotors that remained stable on the epicardium can be detected noninvasively.

1. Introduction

Atrial fibrillation (AF) is one of the arrhythmias that more health spending generates in occidental countries, due to the high volume of hospital admissions. The main pitfall in the treatment of this cardiac disease is the lack of knowledge about their mechanisms of initiation and maintenance and so the pharmacological therapies do not have the expected success.

Since the ablation of certain sites of the atria has demonstrated to be a procedure which can terminate AF episodes, several ablation methods have been developed to improve the success ratios and decreasing the impact on the patient [1]. It has been shown that ablation of atrial sites responsible of AF onset and/or perpetuation is successful in terminating the arrhythmia and therefore its location in the atrial wall is of great interest [2]. Recently, novel recording techniques have demonstrated that functional re-entries, or mother rotors, can be a mechanism responsible of the maintenance of AF processes [3]. These functional re-entries are a self-sustained propagation pattern which can generate fibrillatory processes. Mother rotors can be identified in the atrial wall by studying the phase map of electrograms (EGM), since the location of re-entrances corresponds to phase singularities [4]. In addition, there is evidence that phase maps from surface recordings during episodes of AF can also show phase singularities.

In this study, mathematical models of the atrial electrical activity have been used in order to study the relation between phase singularities that appear on the atrial wall due to the presence of mother rotors and phase singularities that can also appear in body surface phase maps recorded at the torso. Whether there is any connection will be determined and if this relationship can be used to study and plan ablation procedures.

2. Methods

2.1 Mathematical models of atrial activity

Propagation patterns were obtained in a sphere with radium 2.5 cm with 160.000 nodes. The action potential of each node was mathematically constructed using the formulation proposed by Courtemanche [5]. Neighboring cells were coupled by a coupling conductance g, which was adjusted to obtain a realistic conduction velocity. The evolution of the transmembrane voltage of each cell (i.e. \( V_i \)) for the i-th cell) \( V_i \) was controlled by the following first-order, time-dependent ordinary differential equation:

\[
\frac{dV_i}{dt} = \frac{1}{C_i} (I_i - g(V_i - V_{SDR}))
\]
\[
\frac{dV_i}{dt} = -\frac{1}{C_m} \left( I_{\text{total},i} + \sum_j g_{i,j} \{V_i - V_j\} \right)
\]

where \( I_{\text{total},i} \) summarizes the contribution of all transmembrane currents, \( C_m \) is the transmembrane capacitance, and \( g_{i,j} \) is the conductance between neighbor cells \( i \) and \( j \). The differential equations system of the Courtemanche cell model was solved using the Runge-Kutta integration method with an adaptive temporal step, over a numerical calculation structure based on graphic processors and implemented with CUDA code [6].

Two propagation patterns were simulated. The first simulation consisted on a uniform sphere with two stable functional rotors placed on the atrial surface (Fig. 2.A), in the second simulation the sphere was divided into two hemispheres (Fig. 3.A): one hemisphere harbored a stable functional rotor whereas the other hemisphere was implemented as a fibrotic tissue, where the 57% of their nodes were disconnected (the \( g_{i,j} \) conduction of that nodes was equal to zero).

The Aitoff cartographic representation of a sphere has been used during the article to represent the complete sphere in a single map (Fig 1.C).

Figure 1. (A) Scheme of the spherical atrial model (inside) and the concentric layers. (B) Color map used in phase representations. (C) Cartographic mapping of the sphere.

2.2. Forward problem

The electrical potential was obtained in 20 concentric spheres of 2562 nodes with increasing radii from 2.5 cm to 12.5 cm (Fig. 1.A). The external sphere was defined as the torso surface and the internal layers were included to observe how the potential between the atrial wall and the torso evolves. In order to obtain the electric potential, the forward problem of the electrocardiography was solved by using the Boundary Element Method (BEM).

According to the BEM formulation [7], potentials on the surface of the torso can be computed from potentials on the heart surface by using (2).

\[
\Phi_T = A\Phi_H = (D_{TT} - G_{TH} G_{HH}^{-1} D_{HT})^{-1} \cdot (G_{TH} G_{HH}^{-1} D_{HH} - D_{TH}) \Phi_H
\]

where \( \Phi_H \) is the potential on the surface of the heart, \( \Phi_T \) is the potential on the surface of the torso, \( D_{XY} \) is the potential transfer matrix from surface X to surface Y and \( G_{XY} \) is the potential gradient transfer matrix from surface X to surface Y.

2.3. Phase maps

Phase maps of each concentric layer were obtained from the EGM phase signal of each node by using (3):

\[
\text{Phase signal} = \angle(HT(E G))
\]

where \( \angle() \) is the phase operator and \( HT(\cdot) \) is the Hilbert Transform. The phase signal ranges from 0 to 2\( \pi \) and represents the relative delay of each signal in one period (Fig. 1.B).

2.4. Phase singularity definition and detection

A phase singularity (PS) was defined as the point in a phase map which is surrounded by phases from 0 to 2\( \pi \). The phase value was obtained in 3 circles around each evaluated point, with radii of 0.08·R, 0.15·R and 0.2·R, where R was the radius of the layer (1 cm, 1.8 cm and 2.5 cm at torso). A point was defined as a PS when the phase of at least two of these three circles was gradually monotonically increasing or decreasing.

2.5. Filaments definition and detection

A filament was defined as the connection between layers and across time of the PSs. Specifically, two PSs in different layers were connected to construct a filament when the distance between these PSs was less than 0.4·R. Additionally, the distance between PSs at consecutive time instants should be less than 0.4·R to be connected, where R is the radius of the sphere at which PSs are found.

Finally, only filaments present during enough time to make a complete rotation in their most internal layer or in the torso were consider as functional rotors. All other filaments were discarded.

3. Results

Figure 2.A shows the propagation pattern and phase maps of the EGMs for the uniform model. The potential map exhibits the position of the two stable functional...
rotors and the phase map of the internal layer (R=2.6 cm) shows two PSs at that location. The location of both PSs is similar in intermediate and external layers (R=5 and R=12.5 cm), although the phase map does not evidence the shape of functional reentries. Fig. 2.B shows the temporal behavior of filaments. Two filaments arise from the rotors in the atria and terminate in the torso, remaining stable in time. In Figure 2.C the temporal evolution of PSs found in the atrial wall (that defines the rotor meandering) and at the torso can be observed. In this case, the trajectory of the PSs on the torso and on the atrial wall was found to be similar.

Fig. 3.A shows the propagation patterns and phase maps of the EGMs for the non-uniform model. This simulation contains a single stable rotor and the phase map of the internal layer (R=2.6 cm) shows a PS at the location of the rotor. The position of the PSs that arises from the main rotor is similar in the intermediate and external layers (R=5 and R=12.5 cm). In Fig. 3.B it can be observed that the filament arising from the main rotor reaches the torso straightly, whereas the filaments from the fibrotic tissue cancel out with each other. Sixteen PSs were found in the fibrotic area (see Fig. 3D) but the number of PSs of the fibrotic hemisphere decreases in intermediate layers with increasing distances from the epicardium and a single PS reaches the torso. The rotor PS at torso can be distinguished from the fibrotic PSs by their meandering area (Fig. 3C) since the area where the rotor’s PS meanders is smaller than the area of the fibrotic PS (0.18% of the sphere surface vs. 0.8%).

4. Discussion

Mathematical models of atrial electrical activity have been used in this study in order to establish the relation between the atrial propagation patterns and the surface body potential during AF. Previous works have demonstrated that PSs in the EGM’s phase signal indicates the position of functional re-entries [4]. This work presents the possibility that these PSs provoked by stable rotors could be also observed on body surface potentials. Relation between the PSs of atrial and torso activity have been summarized into filaments, and the behaviour of filaments with different propagation patterns have been analysed. Our results showed that stable re-entrant propagation patterns exhibit filaments that remain stable on the torso. In case of unstable propagation patterns, in our case fibrotic propagation, the number of PSs produced on the atrial wall around fibrotic patches decreases with increasing distance to the atria. Our results showed that, although PSs detected on body surface phase maps may be caused by unstable propagation patterns in the atrial wall like fibrotic tissue, PS produced by stable propagation patterns showed a higher spatial and temporal stability than PSs produced by unstable propagation patterns.

Since Haïssaguerre demonstrated that ablation of certain atrial sites can terminate the AF episodes [1], several studies have been developed in order to improve the outcome of ablation procedures. Some authors have defended that AF can be maintained by atrial regions that have highest activation rates [2], and ablation of this unique sites can terminate the AF episodes. Jalife et. al demonstrated that a possible mechanism responsible of the maintenance of the arrhythmia and higher activation rates is the functional re-entry (or mother rotor) [3].
Additionally, several studies have shown that atrial electrical activity is reflected on the body surface potential during AF [8]. Therefore, it seems reasonable to speculate that the analysis of the surface electrical signal may contain information regarding the mechanism of maintenance of the arrhythmia and the location of the maintaining region. This study opens the door to the use of this type of signal analysis in the treatment of AF in order to plan ablation procedures non-invasively.

In the present study we used geometrically simple mathematical models in order to ensure that anatomical inhomogeneity were not affecting filaments behaviour. However, in order to evaluate the potential role of this technology in the clinic, realistic models and clinical recordings should be used.

5. Conclusion

Electrical propagation patterns in the atria during AF are reflected in the electrocardiogram. Phase maps that allow locating functional reentries in the epicardium could also be used to identify functional rotors from noninvasive recordings.

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References


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