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A preliminary study on atrial epicardial mapping signals based on Graph Theory

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ABSTRACT

In order to get a better understanding of atrial fibrillation, we introduced a method based on Graph Theory to interpret the relations of different parts of the atria. Atrial electrograms under sinus rhythm and atrial fibrillation were collected from eight living mongrel dogs with cholinergic AF model. These epicardial signals were acquired from 95 unipolar electrodes attached to the surface of the atria and four pulmonary veins. Then, we analyzed the electrode correlations using Graph Theory. The topology, the connectivity and the parameters of graphs during different rhythms were studied. Our results showed that the connectivity of graphs varied from sinus rhythm to atrial fibrillation and there were parameter gradients in various parts of the atria. The results provide spatial insight into the interaction between different parts of the atria and the method may have its potential for studying atrial fibrillation.

1. Introduction

Atrial fibrillation (AF) is the most common type of arrhythmia which increases the cardiovascular morbidity and mortality worldwide [1]. Currently, the main treatment for AF is curative ablation of pulmonary veins (PVs) [2,3]. This treatment is more effective for paroxysmal AF while the relapse rate of persistent AF is relatively higher [4]. Recently, dominant frequency (DF) analysis expands the target sites of ablation from PVs to left and right atrium. It suggests that myocardial cells with higher activation frequencies may be the drivers maintaining AF [5,6]. Yet, Berenfeld et al. observed multiple DF sites in a given individual, and although ablation at each site resulted in the slowing of the AF process, termination was observed at other sites in addition to the maximal DF site [7]. Therefore, the definition of the optimal ablative pathways remains to be explored in a further study.

It seems that the above methods focus on the focal sites separately while neglect the correlation and interaction between different sites of the atria. However, it is shown that ectopic electrical activities can shift from one site to another by the interconnection between different parts of the atria [8]. As an effective tool to study the relations of different entities, Graph Theory has been introduced to study cardiac arrhythmia. Cycle network [9], visibility graph [10] and recurrence networks [11,12] have been applied to research cardiac arrhythmia such as congestive heart failure (CHF) [13], ventricular fibrillation (VF) [14] and AF [15], etc. Limited by the number of mapping channels, these methods apply single-channel data to study temporal interactions through tools and concepts borrowed from the complex network study.

In this study, a different perspective is applied to the analysis of the spatial association of multi-channel data by examining the atria as a whole. We combine Graph Theory with epicardial mapping to study atrial electrograms (AEG) acquired from various parts of the atria. Each electrode was mapped to a graph vertex. Whether an edge was exhibited between two vertices was determined by the cross-correlation coefficient of the AEG acquired from the corresponding mapping electrodes. By studying the topology, the connectivity and the parameters of these graphs, we can get an insight into the correlations of AEG from different electrodes.

Our study is based on the rationale that if two atria sites are repeatedly affected by the same driver (this driver may be the sinoatrial node (SAN) under normal rhythm or an ectopic reentrant wavelet during AF), AEG from these two sites should have a more similar morphology so as to have a larger cross-correlation coefficient. On the other hand, for those atria sites affected by different drivers, the activation rate and the morphology of the AEG would be not relevant enough to exhibit an edge. Four basic parameters of graph structure were analyzed in our study. Average degree and

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graph density were used to evaluate the average similarity of AEG from various parts of the atria, which reflects the regularity and synchronization of the atria activation process. Average clustering coefficient was to characterize the clustering of myocardial cells during the atria activation process. Q value evaluates the strength of dividing the atria into separate ectopic modules. Specially, during AF, vertices categorized into the same module in the graph reflect those atria sites affected by the same driver, which may help identify the ectopic sites maintaining AF so as to provide guidance for ablation targets in AF treatment.

2. Methods

In order to study AF by examining the atria as a whole with Graph Theory, we devised animal experiments to collect real-world data using eight living canine subjects. These data during sinus rhythm and AF were pre-processed and analyzed with the following methods.

2.1. Fibrillation and mapping

Eight living mongrel dogs (weight 13.4 ± 2.9 kg) were studied. After thoracotomy and suspension of the pericardium, the canine heart was exposed. A total of 95 unipolar electrodes were placed on six flexible patches, denoted as A, B, D1, D2, D3 and D4. Each electrode was 1.5 mm in diameter. The unipolar electrodes were carefully arranged in these flexible patches to match the size of the canine atrium in a surgical setting. Four flexible patches (D1–D4) were rolled and placed around the root of PVs. The distribution of the patches was shown in Fig. 1. The electrical activity of the aortic root was acquired as an electrical reference ground. In addition, a separate electrode was sewn onto the apex of the heart (located in the left ventricle) to provide a ventricular reference signal. All of these electrodes were connected to the epicardial mapping system (model: FDEMS-2) our lab has developed [16]. Each hardware channel had isolated amplifier and filter with adjustable gain (25–2000) and a fixed bandwidth (3.5–600 Hz). Unipolar AEGs and the ventricular reference signal were simultaneously recorded and digitized at a 2 kHz sampling rate and 16 bit precision. AF was induced by rapid pacing (>1000 bpm) of the left atrial appendage (LAA) or the right atrial appendage (RAA) of the canine heart with an intravenous injection of acetylcholine. Thus, our model was essentially a model of cholinergic AF.

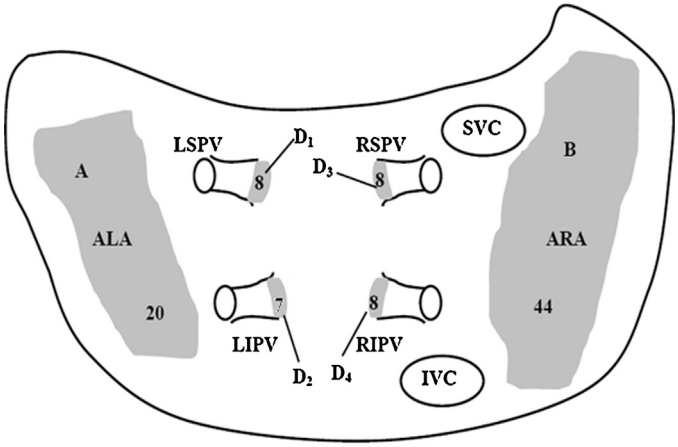

Fig. 1. An atrial epicardial mapping schematic diagram. A: anterior left atrium (ALA), B: anterior right atrium (ARA), D1: left superior PV (LSPV), D2: left inferior PV (LIPV), D3: right superior PV (RSPV), D4: right inferior PV (RIPV), superior vena cava (SVC), interior vena cava (IVC). The areas shaded in gray represent the mapping regions. The numbers in the shaded areas represent the numbers of unipolar electrodes in the regions. The horizontal and vertical spacing between the electrodes on different patches are as follows: A and B: 3.5 mm, 3.5 mm; D1–D4: 3 mm, 2 mm. The specific spacing between electrodes in each patch is determined by the area and the number of electrodes of the patch.

2.2. Pre-processing

The hardware of our mapping system conducted the signal conditioning work, which included amplifying and filtering. Software pre-processing mainly solved the problem of the ventricular artifacts. A least mean square (LMS) adaptive filter was introduced [17,18]. The contaminated AEG signals were filtered through an adaptive LMS filter taking a reference signal from the apex of the heart (located in the left ventricle). The model of the adaptive filter is noise-canceller [17]. Consequently, the error signal of the filter provided an optimum estimate of the desired AEG signals.

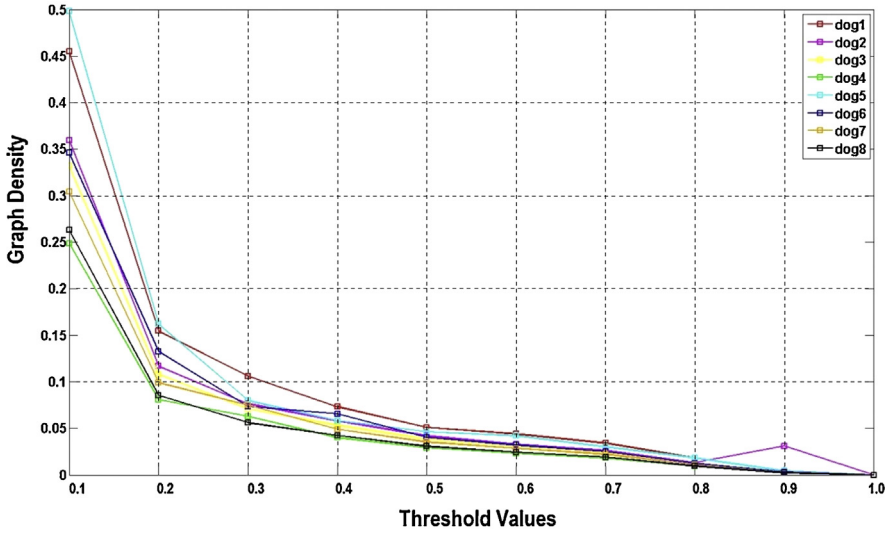

Fig. 2. Average graph density curves of overall atria graphs under AF via different threshold values. Curves of different dogs were represented in different colors. When the threshold value changed from 0.1 to 1.0, the graph densities become smaller and smaller. The trends of the curves were similar. In the range of 0.5–0.8, the graph densities were in the same magnitude level.