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Analysis of Epicardial Mapping Electrogram of Sustained Atrial Fibrillation Based on Shannon Entropy

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***Abstract*[1]—The mechanisms of sustained atrial fibrillation (AF) are not well understood. And predicting the development of AF is a problem of great clinical interest. This paper proposed an AF analysis method by evaluating, based on Shannon entropy, the complexity of atrial activation in various AF stages. The first step was to preprocess and characterize electrograms. Then, Shannon entropy analysis and statistical analysis were applied to find the significance of interval entropy in sustained AF. Study results proved that interval entropy presented a degressive tendency in the process of sustained AF and some sites with high activation frequency but low entropy was possibly related to ectopic driver of AF.**

Keywords: atrial fibrillation, epicaridal mapping, entropy

I. INTRODUCTION

Atrial fibrillation (AF) is the most common atrial arrhythmia. Approximately 2.3 million people suffer AF in North America. In China the standardized rate of prevalence of AF is 0.61% and increases with age [1]. Studies of past have described several mechanisms of AF including ectopic focus, multiple reentrant wavelets and single reentrant circuit [2]. And the technique of epicardial mapping has been playing a vital role in these studies. Therefore, our lab have achieved an epicardial mapping system [3] and carried out 6 animal experiments with this system.

In information theory, Shannon entropy is a measure of the uncertainty associated with a random variable. Many authors have developed various methods based on Shannon entropy from surface electrocardiogram (ECG) to explore mechanisms of arrhythmias [4-5]. Since the atrial electrogram (AEG) of AF is characterized by variable activation intervals, in this paper, Shannon entropy was applied to evaluate the extent of interval variability of AEGs. Moreover, the significance of interval entropy in sustained AF has been discussed.

We analyzed epicardial mapping electrograms from animal experiments. The first step was to preprocess AEGs with a LMS adaptive filter, followed by characterizing activation times of them. Activation interval was got directly from the difference of two neighbor activation times. Then, the technique of Shannon Entropy was introduced to characterize the spatial distribution of interval variability during sustained AF. Finally, statistical analysis was used to compare the entropy distribution in various stages of sustained AF and on various mapping regions.

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II. METHOD

A. Fibrillation and Mapping

Sustained AF was induced by burst pacing (> 300bpm) on left atrium appendage (LAA) or right atrium appendage (RAA) of canine heart. 128 uniploar electrodes were placed on the atrial epicardial surface and their distribution was shown in the Figure 1. In animal experiments, atrial electrograms were recorded simultaneously for more than 5 minutes, along with ECG lead II.

B. Processing

A technology of least mean square (LMS) adaptive filter was introduced to cancel noises and ventricular artifacts in some records (mainly due to problems with electrode contact or environment of operative rooms). In this stage, we employed ECG lead II as the input of an adaptive filter, while contaminated AEG as the desired signal. Consequently, the error signal of the filter would be the optimum estimate of desired AEG [6].

C. Characterization

Activation time was defined as the time corresponding to the apex of activation waveform. Being similar to QRS complex of ECG, the activation morphology of AEG is characterized by sharp slope and large amplitude. Here, we used a method proposed by JiaPu Pan[7] to characterize activation times of AEG.

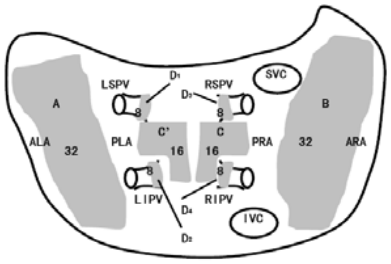

Fig. 1. Diagrammatic representation of epicardial surface of atrium, including orifices of pulmonary veins (PV: left superior PV - SPV, right superior PV – RSPV, left inferior PV – LIPV, right inferior PV - RIPV), superior vena cava (SVC), interior vena cava (IVC), anterior right atrium (ARA), anterior left atrium (ALA). Areas shaded in gray represent positions of mapping regions. Numbers represent in areas shaded the number of uniploar electrodes on respective region.

D. Entropy analysis

Activation intervals of AEGs were subjected to entropy analysis to evaluate interval variability of AF. The original definition of entropy proposed by Shannon required the probability distribution of discrete variable with the form of following equation.

$$H_n(X) = -k\sum_{i=1}^{n} p(x_i)\log_2 p(x_i) \quad (1)$$

where X is a discrete random variable with possible values $\{x_1, \ldots x_i, \ldots x_n\}$ and p denotes the probability mass function of X.

However, considering the probability mass function of activation interval of AEG was unknown, we actually used another equation to estimate the entropy of activity intervals. This Equation [8] could calculate entropy merely resting on observed values in the form:

$$H(m,n) = \frac{1}{n}\sum_{i=1}^{n} \ln \frac{y_{i+m} - y_{i-m}}{2m/n} \quad (2)$$

where y_1, y_2 ... y_n ($y_1 \leqq y_2 \ldots \leqq y_n$) are the order statistics of observed values and m is a positive integer smaller than $n/2$.

E. Statistical analysis

To compare the entropy distribution in different stages of sustained AF and on various mapping regions, we divided AEG records into segments per two seconds. In each segment, entropy of activation interval of every uniploar signal was independently calculated, and then areas with highest or lowest entropy in mapping regions would be obvious. Finally, we computed the average entropy of eight mapping regions respectively and then as a whole.

III. Results

Sustained AF was induced in 6 live dog hearts with the method mentioned above. The following results were firstly got from a Sustained AF record of experiment 3, which had the longest duration, 25.7 minutes, among all atrial electrograms records. And then we found similar results in records of other experiments.

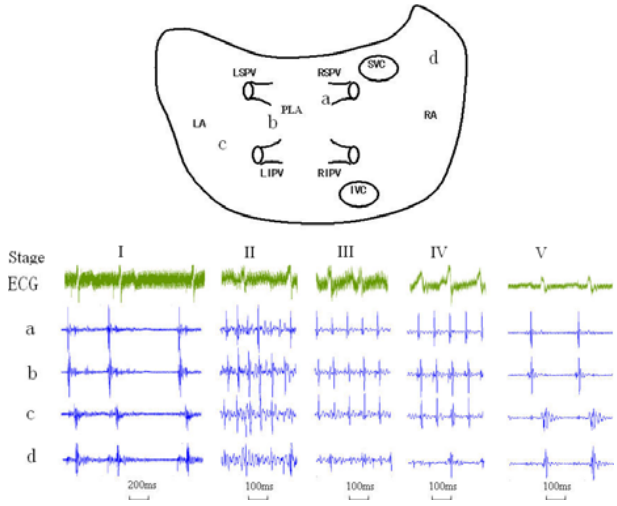

Fig. 2. Representative signals of various sustained AF. Bottom panel shows selected uniploar AEGs from sites a to d (shown in top panel) along with ECG Lead II. There are five group AEGs and ECG, respectively representing five stages of sustained AF. Note that the time scale of group I is different from others. Abbreviations as in Fig. 1.

A. Stages of Sustained AF

The record from experiment 3 contained a complete process from the initiate of AF to the termination of it. Resting on the activation frequency and morphology of AEG and ECG II lead, this record was classified into five stages in time sequence, and Figure 2 showed representative signals of various stages:

- Stage I, before the initiate of sustained AF. The dog heart was under the influence of premature beat, which was derivate from right superior pulmonary vein (RSPV) and finally triggered AF. Both atrial and ventricular rate are 90 bpm.
- Stage II, the initiate of sustained AF. Average atrial rate sharply rose to 720 bpm from 90 bpm. Meanwhile, the ventricular rate reached 210 bpm. And the morphology of most AEGs were abnormal and with fractionation. This stage last mere 2 seconds.

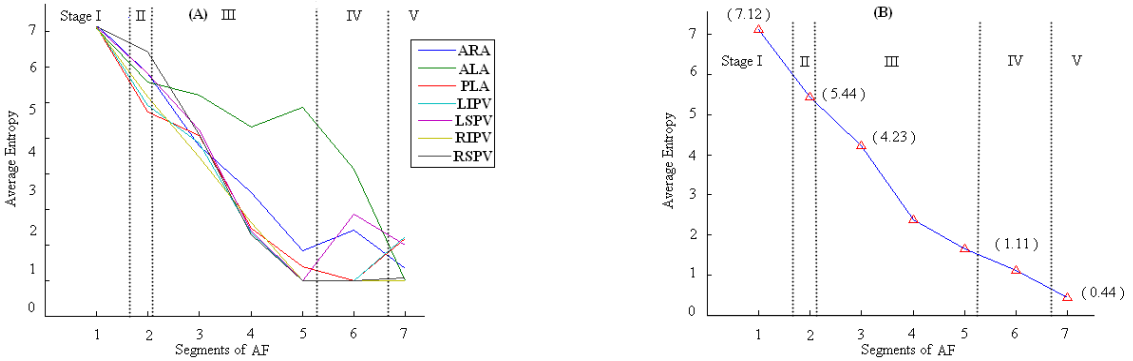

Fig. 3. Average Entropy in various sustained AF. A, average entropy of mapping regions respectively. B, average entropy of all uniploar AEGs. Vertical dashed lines present the boundaries of AF stages. Abbreviations as in Fig. 1.

- Stage III, the maintaince of sustained AF. Average atrial rate slowed down to 600 bpm and morphology of most AEGs reverted to be normal. But in some regions, like the top of ARA and the center of ALA, abnormal atrial activations were still obvious. This stage last more than 20 minutes.
- Stage IV, the termination of sustained AF. The ECG went back to regularity. This stage last about 2 minutes.
- Stage V, after the termination of sustained AF. The dog reverted to sinus rhythm, and both atrial and ventricular rate were 180 bpm.

B. Variation tendency of Entropy

As mentioned above, we studied the distribution of activation interval entropy of atrial electrograms in various AF stages. Seven representative segments had been selected in time sequence. Figure 3A showed average entropy of various mapping regions in these segments, while Figure 3B showed average entropy of all uniploar signals.

Scrutinizing Figure 3, one could find an apparent variation tendency of Entropy in the complete process of sustained AF. Upon the whole, the average entropy continuously descended from 7.12 (before the initiate of AF) to 0.44 (after the termination of AF). On the other hand, on each mapping regions, the variation of average entropy also basically presented a degressive change over time.

Another finding from Figure 3 was that the average entropy of anterior left atrium (ALA) was kept on the highest level among all mapping regions in the whole stage III (i.e., the maintaince of AF). This finding would be explained in next section.

C. ALA habored ectopic driver

Figure 4A showed a representative distribution of entropy and activation frequency on the ALA in AF stage III. Site a with minimum activation frequency (300 bpm) showed synchronous activations with ECG lead II. Site b showed variable abnormal signals, including fractionation and held both the highest entropy (6.52) and the maximal activation frequency (690 bpm). Site c with lowest entropy (2.50) showed continuous and regular activations.

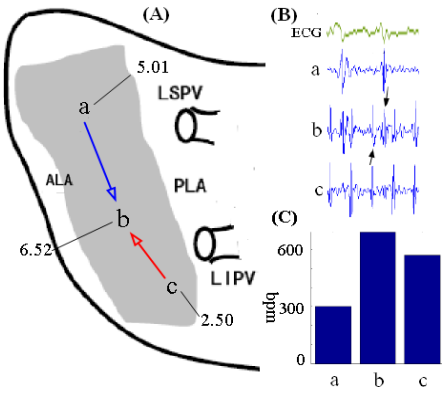

Fig. 4. Representative distribution of entropy and activation frequency on the ALA in AF stage III. A, diagrammatic representation of left atrium. Numbers attached to sites a to c are the values of interval entropy. And arrow heads present possible directionality of activation propagation. B, AEGs from sites a to c along with ECG Lead II. C, activation frequency.

By analyzing the activation sequence of sites above and ECG Lead II, we found that the highest entropy on site b was resulted from that this site had participated in activations propagated both from site a and from site c. Also apparent is site a and its neighborhood were dominated by sinus due to the synchronization between it and ECG. On the other hand, considering high activation frequency and regular interval, it's believable that site c was an ectopic driver or, to say at least, dominated by an ectopic driver. This driver transmitted high frequency activations upwards on the ALA and met activations from sinus in the central area, thus finally lead to the continuously high entropy on ALA in the AF stage III.

IV. DISCUSSION

In this study of sustained AF, one of our major findings is the degressive tendency of activation interval entropy of AEG in the process of AF. Therefore, entropy could be effective in the area of evaluating sustained AF extent and predicting its development. For example, if the entropy were sharply descending to certain level, it would be possible that the AF would terminate by itself, without any invasive interfere. On the other hand, the distribution of entropy on atrium contributes to localize the area of wave fractionation and ectopic driver. As mentioned before, a site with high activation frequency but low interval entropy is possibly related to an ectopic driver.

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