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Electropathological Substrate Detection of Persistent Atrial Fibrillation – A Novel Method to Analyze Unipolar Electrograms of Noncontact Mapping

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Abstract— **Radiofrequency catheter ablation as a curative method for atrial fibrillation (AF) has become increasingly popular. Patients with paroxysmal AF have been treated by catheter ablation with great success, but so far this treatment has been less effective for patients with persistent AF. Usually there are multiple triggers or substrates during persistent AF and their exact locations are unclear. On the other hand, the non-contact mapping system (Ensite 3000, St Jude Medical) producing thousands of virtual endocardial electrograms, has gradually become accepted as a powerful tool to use on patients before and after ablation. Effective mathematical tools to detect the substrates of AF from unipolar electrograms produced by the non-contact mapping are few, though many methods are available for performing this task with bipolar electrograms. In this work, we introduce for the first time a simple and efficient approach to automatically and systematically determine the substrate of persistent AF in order to guide catheter ablation via the non-contact mapping.**

I. INTRODUCTION

Radiofrequency catheter ablation has emerged as a promising effective treatment for patients with atrial fibrillation (AF) and this procedure is still evolving [10]. The most commonly employed techniques for AF ablation today are pulmonary vein (PV) isolation and substrate based ablation. The latter approach includes linear ablation, complex fractionated atrial electrograms (CFAE) or dominate frequency analysis via Fast Fourier Transform (FFT) guided ablation. Paroxysmal AF, initiated by rapid electrical firing predominantly in the PVs, has been treated by catheter ablation with more than an 80% success rate. However, persistent AF, which normally occurs with multiple triggers/substrate and is less dependent on the PVs, has only $\sim$50% success rate even with the "optimally" combined ablation approach [11]. Therefore, it is very important to comprehensively study the substrate of persistent AF in order to improve the success rate of AF ablation.

Identification of critical regions of persistent AF with conventional contact mapping technologies based on point-by-point sequential acquisition suffers from several problems including being time consuming, lacking flexibility, as well as the difficulty of assessing temporal electrical variation. The non-contact mapping system (Ensite 3000, St Jude Medical) ([5], [9]) allows automatic generation of isopotential maps of a left atrium (LA) from a single beat by the simultaneous reconstruction of up to 3,600 virtual endocardial electrograms, which are crucial for studying the electropathology of AF. The non-contact mapping has been widely validated in many previous studies ([7], [8]).

The purpose of this study is to develop a robust method to systematically determine the substrate of persistent AF in order to guide catheter ablation via non-contact mapping.

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II. METHODS

A. Unipolar electrograms

A LA endocardial geometry was reconstructed and non-contact mapping was performed prior to ablation in a patient with persistent AF (age: 47 y, AF duration 4 m, LA diameter: 39 mm). Electrical activity from the LA was recorded for 4.2 sec. Atrial electrograms were reconstructed at 2048 locations. All these electrograms were sampled at 1200 Hz and a voltage sensitivity of 10 μm. LA geometry information and all electrical recording data were processed using custom-written Matlab (Mathworks) applications. In this work, six sites were selected from the LA (Figure 1A) for analysis: site I is in the antero-superior septum (ASS), II is from the mitral valve (MV), III the left superior pulmonary vein (LSPV) sleeve, IV the veno-atrial junction of the right inferior pulmonary vein (RIPV), V the roof and VI the floor.

B. QRS subtraction

To study atrial electrograms properly, ventricular activities (with comparatively larger magnitude) have to firstly be removed. There exist a range of methods to subtract ventricular signals using the standard 12-lead surface ECG data ([1], [2], [3]) recorded simultaneously. These methods take advantage of the consistent concurrency between ventricular activities and waveform oscillations in surface ECG data. In our work, a template matching and interpolation technique was used to subtract QRS ([3], [4]) from original unipolar signals. The six selected unipolar electrograms are displayed respectively in the Figure 1B after removal of ventricular activities.

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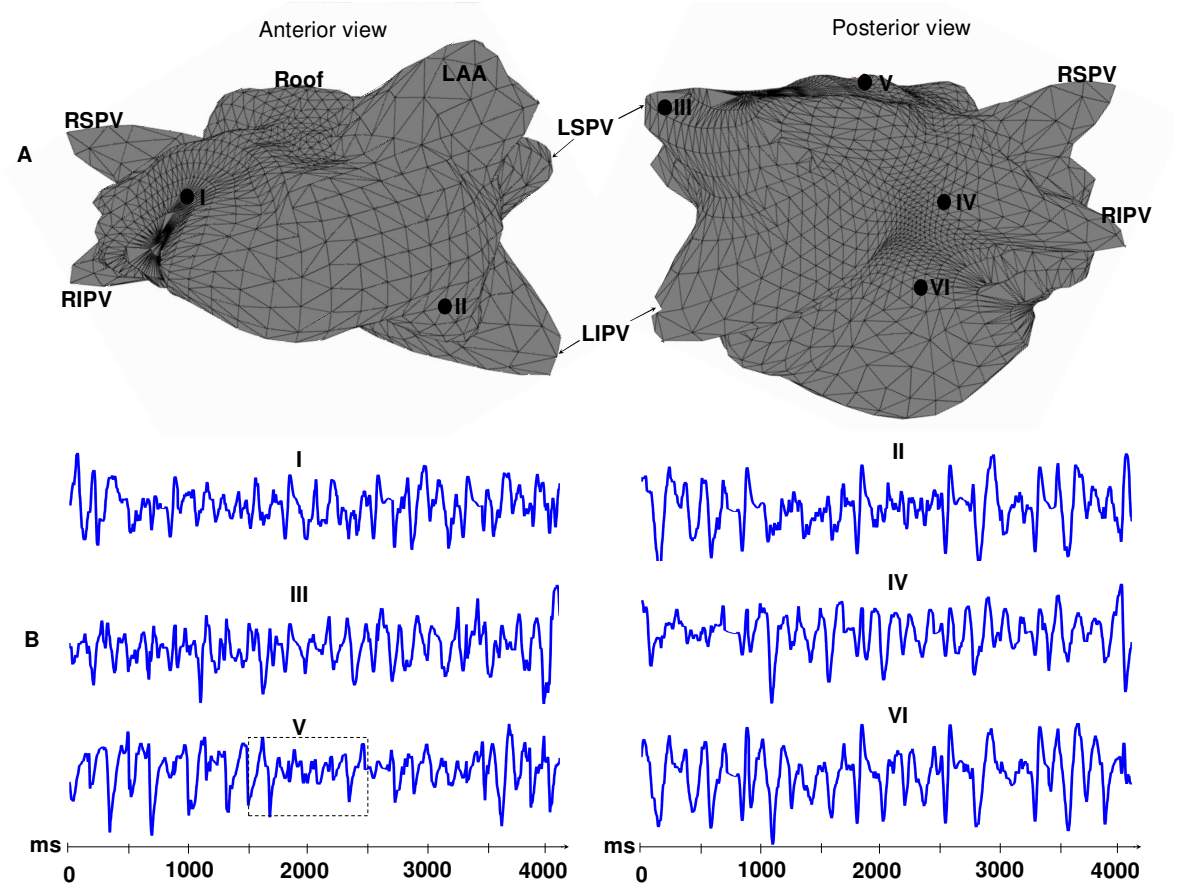

Figure 1: Six selected sites: at I in the ASS, II the MV, III the LSPV sleeve, IV the veno-atrial junction of the RIPV, V the atrial roof and VI the floor, are shown in **(A)**, and their unipolar electrograms are displayed respectively in the **(B)**.

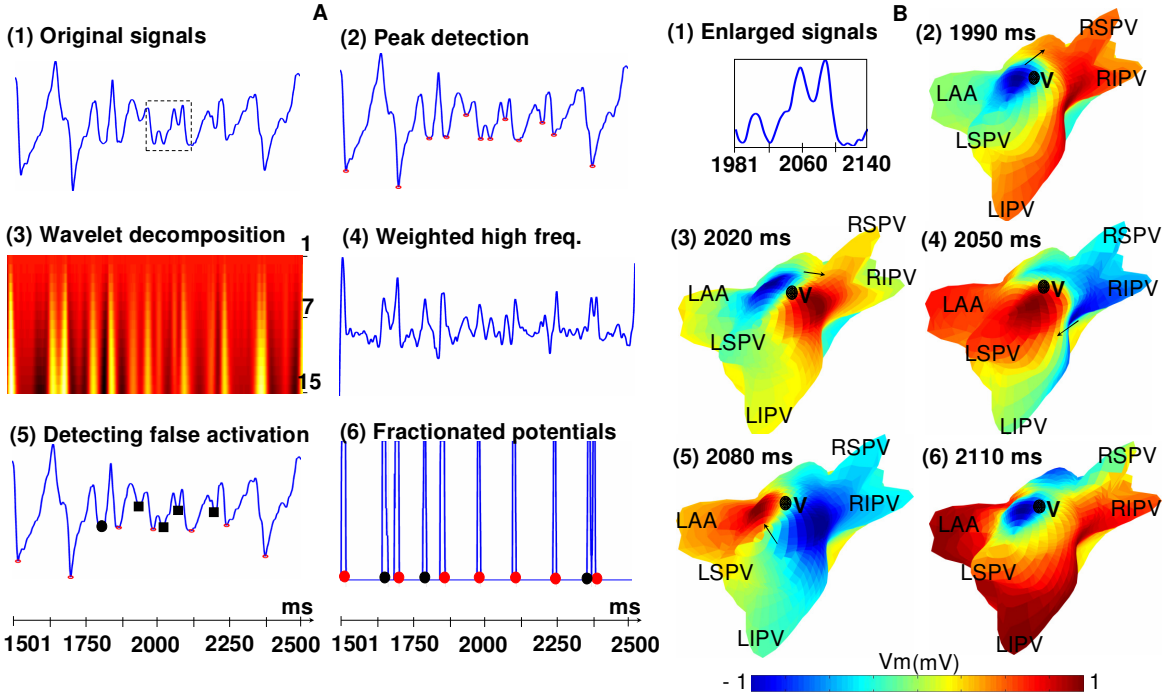

Figure 2: (A) Peak detection and wavelet filtering were applied to the atrial electrograms of the atrial roof from 1501 to 2500 ms at site V (Figure 1B). electrograms were displayed (1);peak detection was applied (2); wavelet decomposition into 1-15 scales (3); Weighted short-duration high frequency (4); black squares, false electrical activation, detected by wavelet method and black dots eliminated for short activation duration (<70 ms) in (5);detecting fractionated potentials (6). **(B)** Electrical propagations on the LA from 1990 to 2120 ms (postero-lateral view). See text for details.

C. Electrogram unification

The electrical waveform magnitude varies dramatically among the six locations, even after the QRS subtraction. The largest absolute magnitude at the site VI (the floor) is as low as 0.5 mV, while at the site V (the roof) it can reach as high as 2.5 mV. Thus, it is necessary to convert all signals to unit electrograms before employing frequency analysis.

D. Negative peak detection

The important part of our proposed method for analyzing the activation frequency is to design a robust method for detection of major signal valleys. First, all local minima, where the derivative changes from the negative sign to positive, were detected. Then a threshold value, indicating the depth of the valleys relative to surrounding data, was chosen. For a larger threshold value, the algorithm is more selective at finding peaks. For our data set, 0.2 proved to be the most effective. In Fig. 2, the peak detection was applied to the atrial electrograms of the site V on the atrial roof from 1501 to 2500 ms as shown in Fig. 1B. Negative peaks with red bars underneath were selected based on the chosen waveform magnitude threshold (Fig. 2A2).

E. Wavelet filtering

Wavelet decomposition using the first derivative of a Gaussian waveform was employed to filter out false electrical activation. The wave length of the electrograms consists of the short-duration high frequency (scales 1-7) and long-duration low frequency (9-15) (Fig. 2A3). The amplitude of each scale was color coded with positive correlations ranging from red to black and negative ones from red to yellow. Local electrical activities were constructed by calculating the exponentially weighted sum of the first seven high frequency scales (Fig. 2A4), and distal disturbances were also created similarly using the seven low frequency scales. False electrical activations (black squares in Fig. 2A5) were filtered out by an algorithm using the relative amplitudes of the local electrical activities and distal disturbances[15]. Positive peaks above a certain threshold value in local electrical activities (Fig. 2A4) were used to analyze fractionated potentials. In Fig. 2A6, red circles display primary activation times, and black ones show fractionated potentials.

F. Rejecting short fractionated electrograms

Cardiac cells can only be electrically excited again after a recovery period. The shortest temporal interval of two successive electrical conduction is 70 ms [21]. Shorter wave fractionation (<70 ms) could imply cell partial recover due to local or distal activities. In Fig. 2A5, black circles display the rejected short fractionated potentials.

G. Automatic processing of all data on the LA

Magnitude and spatial intervals of unipolar oscillations vary not only temporally, but also spatially. However, after normalizing the electrogram magnitude on all 2048 sites on the LA, a global threshold value suitable for all locations could be found. Frequency values were obtained across the LA using the procedure B-F discussed above.

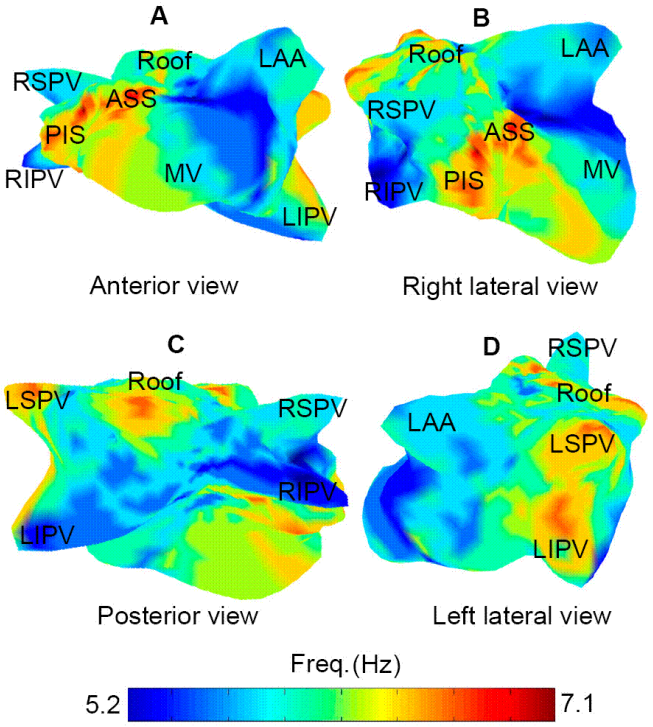

Figure 3: Frequency obtained by peak detection and wavelet filtering was superimposed on the 3D left atrium from an anterior view (A), right lateral view (B), posterior view (C), and left lateral view (D) respectively.

H. Verification

The most reliable approach is to compare electrical activation occurrence detected using frequency analysis with electrical propagations on the 3D LA anatomy simultaneously. Fig. 2B2-2B6 display electrical propagations on the LA from 1990 to 2110 ms (the left postero-lateral view). Firing of an automatic focus proximal to the site V starts in the atrial roof region at 1990 ms (Fig. 2B2). Then the electrical wave propagated around the site V (Fig. 2B3-2B6), which corresponds to smaller magnitude oscillations of the unipolar waveform in Fig. 2B1. Clearly the site V was only successfully activated at 1990 and 2110 ms, correlating with the peak detection and wavelet filtering method as displayed in Fig. 2A5, which is consistent with Fig. 2B2-2B6.

III. Results

The frequency computed by the proposed peak detection and wavelet filtering methods was superimposed on the 3D LA showing in different views in Fig. 3. The frequency in the LA of this patient with persistent AF varied from 5.2 to 7.1 Hz. Regions with activity in the upper quartile of frequencies were identified as high frequency. Multiple regions of high frequency electrical activity were seen in the patient: roof of the LA, the ASS, the PIS, two left PVs and MV. The computed frequency map is in line with 3D electrical propagation patterns.

IV. Discussion and Conclusion

The most significant advantage of a non-contact mapping system is the ability to provide a global, simultaneous view of cardiac electric activity, which is crucial for the accurate dynamic analysis of AF. As a result, we have to process virtual unipolar electrograms. FFT ([12], [13]) is commonly used for the estimation of atrial activation rates and has achieved certain success for bipolar electrograms. However, dramatically varying waveform oscillations and multiple activation deflections in the unipolar electrograms obtained by the non-contact mapping make the time averaged approach, FFT, less attractable for our problem ([14]). The CFAE ([17], [18]) is the other approach widely employed to locate substrates of AF by analyzing bipolar electrograms. The outer sites of the dominant frequency region is the area where the most fractionated activities ([19], [20]) appear. Lo et al. ([22]) have investigated the unipolar electrogram characteristics over the bipolar CFAE sites during AF, and concluded that there was no clear relationship between the unipolar morphology and the bipolar fractionated CFAE sites. The wavelet transform has emerged over recent years as a powerful tool for manipulation of complex non-stationary biomedical and biological signals ([14], [16]). The most favored advantage of wavelet decomposition over other approaches is that it can decompose over-sensing prone unipolar signals into local activities and distal disturbance simultaneously ([16]).

We have presented a novel approach which combined peak detection and wavelet filtering to automatically analyze electrical activation frequency of unipolar electrograms in detail for the first time. The initial results of this study suggest that the substrate of the patient with persistent AF are located in the atrial roof, septum, MV, and PVs. Yao and his colleagues [6] achieved a 72.1% success rate in treating persistent AF with a stepwise linear approach based on the roof line ablation, and they found the substrate of AF were mostly located in the ridge and roof areas. Currently more patient data are being included into the study to provide statistically better indications of AF substrate. Real-time frequency analysis may provide information to guide ablation in patients with persistent AF.

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