Novel Multiscale Frequency Approach to Identify the Pivot Point of the Rotor[1]

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1 Background

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and is a prognostic marker for stroke, heart failure, and even death [1]. There is now a general consensus that rotors, i.e., stable electrical sources of cardiac excitation, can cause AF [2]. The pivot points (or cores) of the rotors are believed to be good ablation targets to terminate AF in patients. About 77.8% success rate was demonstrated by ablation of such sites with the CONFIRM trial in paroxysmal, persistent, and long-standing AF patients [3]. Current mapping methods used for guiding catheter ablation such as local activation time map, complex fractionated atrial electrograms mean index map, dominant frequency (DF), phase singularity, and wave block analysis provide information about the spatiotemporal organization of AF, however, they suffer numerous limitations to accurately identify the rotor pivot points due to various noises, misleading phase, and activation times that distort these maps.

Successful ablation therapy to terminate AF requires a highly reliable technique to determine ablation sites using raw intra-atrial electrograms of AF patients. Hence, there is a clear need for a robust spatiotemporal mapping technology that can accurately identify the rotor pivot points in a patient-specific manner, which is the motivation for this research. Recently, a novel entropy-based approach was used to identify the rotor pivot point using optical mapping data from rabbit heart [4]. This approach was also used to generate 3D Shannon entropy maps for a persistent AF patient using raw intra-atrial electrograms demonstrating the feasibility to identify rotor pivot points outside the pulmonary vein (PV) region. However, challenges still remain to robustly map and

more precisely confirm the exact location of rotor pivot points for AF ablation.

It is known that the DF of a rotor is the same throughout the entire spatial area occupied by the rotor and therefore cannot accurately identify the rotor pivot point. This method uses a Fourier transform to calculate the DF and is therefore limited to a single frequency. In contrast, we hypothesize that the chaotic nature of the rotor at the pivot point yields various frequency components. In this work, the authors propose and demonstrate a novel multiscale frequency (MSF) approach that takes into account the contribution from various frequencies to yield valuable information regarding the rotor pivot point, thus allowing for its identification. We validate the feasibility of this technique to identify the pivot point of rotors using optical mapping data from isolated rabbit hearts with induced ventricular tachycardia (VT).

2 Methods

Novel MSF Approach. Band-pass quadrature filters are robust for estimating local multiscale information, such as the energy, phase, radial frequency, and orientation/angular frequency. The Hilbert transform operation transforms a real-valued signal to analytic signal with no negative frequencies, and its utility with the quadrature filter can yield MSF information by weighting the various frequency components. In this work, eight log-Gabor/normal filters were designed and used with a relative filter bandwidth B of $2\sqrt{2}$, one octave apart as described in Ref. [5]. The center frequencies for the log-Gabor filters were chosen to span a physiological range for rabbit heart rate. In addition, the signal was filtered using notch filters to remove harmonics of the DF. A wide range local MSF estimate can be obtained by weighted summation over the eight different filter pairs using the following equation:

$$i - \text{MSF} = \rho_\text{o} \left[\sum_{i=1}^{N-1} q_i \right]^{-1} \sum_{i=1}^{N-1} 2^{i+0.5} q_{i+1}$$

where q_i is the output of the ith log-Gabor filter, and ρ_0 is the center frequency of the first log-Gabor filter [5]. This index for MSF (i-MSF) is expected to be different at the rotor pivot point compared to the periphery which can enable its identification.

Optical Mapping Data From Isolated Rabbit Hearts. Optical Optical mapping experiments were performed with IACUC approval on isolated rabbit hearts which were put in the Langendorff-perfusion system, and voltage-sensitive dye di-4-ANEPPS (5 μg/mL) was added to the perfusate. After staining, 532 nm green laser was used to illuminate the epicardial surface of the heart. Fluorescence intensity was captured with two 12-bit CCD cameras, which run at 600 frames per second with 64×64 pixel resolution. VT was induced via burst pacing, and phase movies of the rotors were obtained from optical mapping recordings. The phase movies from one rabbit heart with a known pivot point were used in this work, shown in Figure 1, for processing using MATLAB software to obtain the two-dimensional (2D) DF map. MSF estimation was performed as described above to generate the 2D i-MSF map.

3 Results

Figure 1 shows a representative example of a single rotor in isolated rabbit heart in a snapshot of a phase movie, where different colors represent different phases of action potential. It is known that the convergence of different phases corresponds to a singularity point, i.e., the pivot point (core) of the rotor, which can be easily identified (see arrow). Figure 2 shows the 2D DF map with uniform DF = 7.9 Hz throughout the rotor zone. Pivot point is indicated by the arrow but it cannot be identified from the DF map itself. Figure 3 shows the 2D i-MSF map that correctly identifies the rotor pivot point with a higher i-MSF of approximately 11 Hz compared to the periphery region as indicated by the arrow.
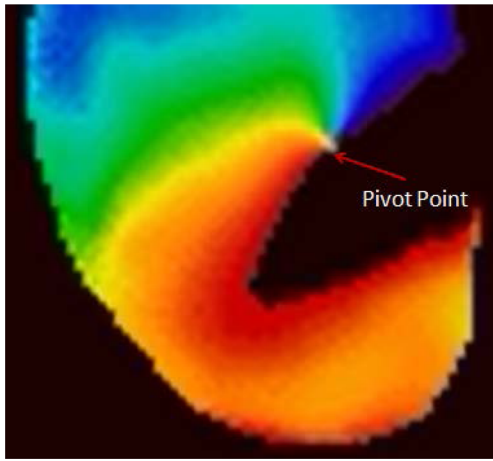
Fig. 1 Representative example of a single rotor in isolated rabbit heart from optical mapping experiments. The pivot point of the rotor is indicated by the arrow.
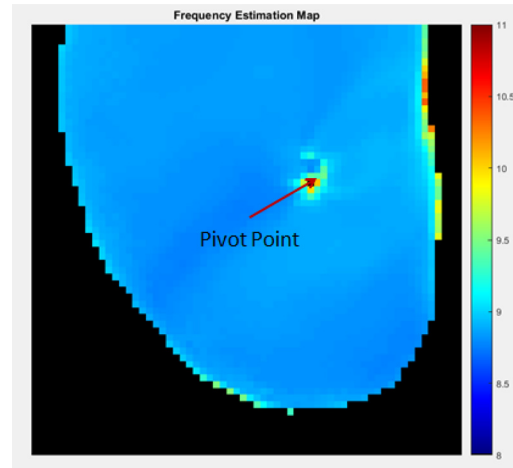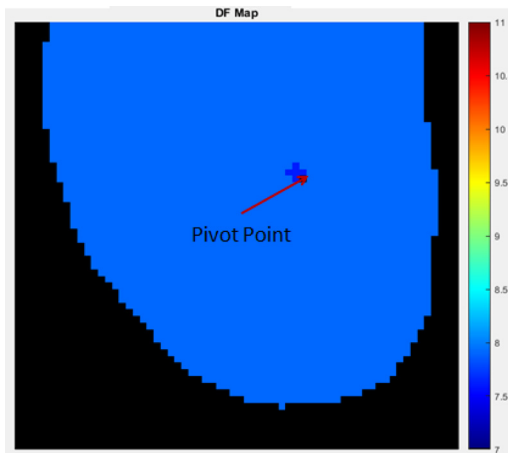

Fig. 2 Two-dimensional DF map showing uniform DF throughout the rotor zone. Pivot point is indicated by the arrow.

4 Interpretation

The optical mapping data with a single rotor have a single DF = 7.9 Hz, which was uniform throughout the DF map as expected and was unable to identify the rotor pivot point. The chaotic nature at the rotor pivot point yields more frequency components other than the DF, which are processed through the various weighted log normal filters that result in a frequency index different than DF which accurately identified the rotor pivot point as seen from the 2D i-MSF map in Fig. 3. The periphery of the rotor was expected to be uniform with the DF due to the less chaotic nature in this region compared to the pivot point and was slightly higher than DF at 9 Hz.

Fig. 3 Two-dimensional i-MSF map showing the correct identification of the rotor pivot point (see arrow)

In this work, high-resolution optical mapping data with stable rotor wave were used. The MSF approach demonstrates the feasibility to accurately identify the rotor pivot point taking into account the combined mechanistic and electrical properties of the rotor with various frequency components that are very different than the periphery.

Intra-atrial electrograms represent sparse data and challenges validation of new mapping approaches in addition to noise, misleading activation times, and phase information. MSF approach can overcome these limitations by capturing the intrinsic chaotic behavior of activation patterns characterized by the wide frequency spectrum at the rotor core given its complex spatiotemporal evolution. Further studies with multiple stable rotors and meandering rotor waves can demonstrate the efficacy of this approach in accurately identifying the pivot point of the rotors based on the multifrequency index. The preliminary results of this study motivate the application of this approach to raw intra-atrial electrograms from persistent AF patients to demonstrate its ability to identify active substrates that cause and maintain AF outside the PV region.

References

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