Analytical approaches for analysis of intracardiac bipolar electrograms during atrial fibrillation

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Abstract. Atrial fibrillation is the most common type of cardiac arrhythmia encountered in clinical practice, in which heart muscles shows chaotic atrial depolarization and uncoordinated contraction. Underlying mechanisms of atrial fibrillation are incompletely understood and widely discussed in the scientific community. The abnormal electrical discharges in atrial repolarization is associated with localized drivers and multiple wavefronts that support the asynchronous heart rhythm. In this paper, a briefly overview of conventional techniques focus on mapping drivers of myocardial fibrillation and their application are discussed. We also introduce a novel mapping algorithm which is aimed to identity features of wavefront propagation and analyze the relative changes of generalized instantaneous dominant frequency calculated from intracardiac recordings. Our clinical trials showed that proposed algorithm provides insightful and useful information about triggered abnormal activity during atrial fibrillation, that potentially can be used for catheter ablation therapy.

1. Introduction

Atrial fibrillation (AF) is the most common type of cardiac arrhythmia encountered in clinical practice and a significant cause of hospitalization and morbidity. This pathology is caused by abnormal electrical discharges that generate chaotically atrial repolarization and lead to a rapid and irregular heart rhythm. In addition to being the most common cardiac rhythm disorder, AF has an increasing global prevalence and incidence. At present, it accounts for more than 35% of all hospital admissions for cardiac arrhythmias in the United States and clinical cases of AF is expected double in the next decades, progressing with the age and increasingly becoming a medical challenge [1].

Despite significant advances in this field, management options for AF remains limited as mechanisms that drive and maintain fibrillatory activity are elusive in the human heart. Pulmonary vein isolation (PVI) is the cornerstone of a catheter ablation for patients with paroxysmal AF. The organized driver hypothesis of AF has gained momentum recently, which suggests that persistent AF can be driven from localized sources outside the pulmonary veins and that limited ablation targeting these regions with successful outcome. The progression of paroxysmal AF to the persistent form is dependent on atrial remodeling and the formation of the arrhythmogenic substrate which leads to multiple repolarization wavefronts [2].

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The uncertainty about the mechanisms of myocardial fibrillation is due to limitations of currently available tools used to record intracardiac electrograms, such as limits in resolution and challenges in processing and interpreting the complex electrophysiological morphology of myocardial fibrillation. The application of analytical approaches for extraction time-frequency characteristics from recorded endocardial signals is deployed as powerful tool for detection the micro reentry circuits and mapping triggered activity, which can be potentially used for ablation therapy.

2. Materials and methods

In the clinical electrophysiological study (EPS), intracardiac bipolar electrograms are most commonly used method for analysis of atrial electrical activity [3]. Because of complex nature of AF, the recorded signals often appears chaotic and the organization patterns within signal can be difficult to appreciate from the raw recordings. The challenge of any analytical approach used to endocardial electrograms is to effectively translate disorganized signals into interpretable data about the nature of the wave front propagation and myocardial substrate sustaining fibrillation activity with using various information criteria. In this paper, we will briefly discuss some conventional techniques, which is used to process myocardial fibrillation data such as phase mapping, Shannon entropy and dominant frequency analysis. In addition, we also introduce a novel mapping algorithm to identity and represent features in wave front activation from intracardiac bipolar electrograms.

2.1. Phase mapping

Over the last two decades, there has been a lot of interest in the hypothesis that AF was sustained by organized driver in the form of self-perpetuated spiral waves or microrotors with interactions at a phase singularity point (PST) without a need for an anatomical obstacle. A phase singularity point resides at the core of a microrotor and represent an area without a definite phase that show continuous cycling in time and space dependent signal. The phase mapping is aimed to localize PST that exist as a core of a fibrillatory driver. Some clinical trials showed that mapping of atrial regions with PST might be critical step in fibrillation treatment with using of catheter ablation [4].

More recently, the techniques for phase mapping during AF have been proposed [5]. The calculation of phase characteristics from intracardiac electrograms is difficult due to several factors, such as non-sinusoidal and fractionated nature of recorded signals. Kuklik developed a phase mapping algorithm using sinusoidal decomposition in which the intracardiac signal is represented as a sum of harmonic wavelets with amplitude proportional the negative slope of the electrogram. This pre-processing algorithm generates a sinusoidal signal suitable for robust phase reconstruction using Hilbert transform. The tracking phase singularities from using data from clinical electrophysiological mapping allow to generate 3D reconstruction of atrial regions and to detect the microreentry circuits.

Recording modalities of phase mapping are typically limited in either resolution and coverage of mapping catheter. Jacquemet used statistical approaches to investigate the effects interelectrode spacing and rotor number and showed an increase in false positive PST detections with increasing distance from clinical catheters [6]. Accordingly, the phase mapping technique has limitations imposed with high spatiotemporal resolution, rotor guided ablation with tracking phase singularities as an adjunct to conventional PVI has not been proven to be beneficial in AF treatment.

2.2. Shannon entropy

Shannon entropy (SE) is a measure of uncertainty and unpredictability for appearance of some condition that applies to any numerical data. In the absence of information loss, entropy is numerically calculated as the smallest number of information bits coming from the data source. Thus, deterministic signals, for example, sinus rhythm on an ECG, have low arbitrary entropy whereas those that are more variable such as ventricular fibrillation on an ECG would have high entropy values. SE can be applied to analyze bipolar electrograms from different atrial regions to construct map with distribution of high and low entropy, organized drivers may be identified [7].
Shannon entropy for intracardiac signals is computed by binning the amplitude of the signal with predefined bin size with using the calculated relative probability of the signal falling in each amplitude bin:

\[ SE = \sum_{n=1}^{N} p_n \log_2 p_n \]  

(1)

The primary objective of this technique is to identify microreentrant circuits and drivers from recorded electrograms by analyzing of a SE spatial gradient. In animal AF studies, SE have been applied to mapping signals to show that higher SE values occurring at rotational core, whereas activation is more regular with lower SE. However, other studies have shown a contradicting relation between with a low SE at the core of fibrillation activity [8].

2.3. Dominant frequency analysis
Bipolar electrograms recorded from mapping catheter is non-stationary time series with complex morphological features. The hypothesis is that intracardiac signals has no identifiable cycle lengths due to amplitude and frequency changes. Therefore, the locations with the highest dominant frequency (DF) represent organized drivers. For mapping DF, the discrete time-sampled signal is transformed into the frequency domain using a discrete Fourier transform and relative power of each frequency is calculated. The dominant frequency is defined as the sinusoidal component with highest energy in the power spectrum:

\[ DF = \arg \max_f P(f) \]  

(2)

where \( P(f) \) is the power spectrum of recorded signal and \( f \) is the frequency in Hz.

The sites with higher DF compared to their surroundings have been postulated to be activity sources and localize to areas with sustaining rotational drivers in fibrillation [9]. Bipolar electrograms have been used to construct DF maps of the atrium with areas of maximal DF targeted for radiofrequency ablation. In control test designed to assess the efficiency of targeting high-frequency source ablation (HFSA) in AF, this approach was not superior to conventional treatment.

The problem of this approach is that DF maps in AF are spatiotemporally unstable and higher DF values are spurious result from wavefront collisions in areas remote from rotational circuits, calling into question feasibility of HFSA. To improve of informativeness of DF analysis target organization index (OI) is entered as mean power ratio of the DF and its harmonics (within 0.75 Hz window) to the total spectrum power [10]:

\[ R_{df} = \frac{P_{df}}{P} \]  

(3)

Areas of high PS clustering were found to correlate with areas of high OI and there was an increase in OI after circumferential pulmonary vein isolation (PVI). Although interest in DF guided ablation has waned, there might be a role in utilizing it with a more spatiotemporally stable methodology such as OI to identify substrate [11].

2.4. Novel mapping algorithm
In addition to conventional techniques, a novel mapping algorithm was developed to detect identifying features of electrical activation from intracardiac bipolar electrograms. Conventionally, the recorded bipolar signals from catheter electrodes is independently processed. Thus, application of classical approaches fail to investigate the relationship between simultaneously channels of mapping catheter and do not provide utility information about wavefront propagation during AF. The relative delays between the activation times (ATs) from adjacent electrodes affects arise due to slow conduction and rapidly
changes in impulse propagation at different atrial sites. The unorganized activations during AF are the result of rotating waves, abnormal local conduction and wavefront collision, which leads to wavefront breaks (WBs).

The morphological features of recorded intracardiac electrograms assume that for atrial sites with clear wavefront propagation the local activation peaks from different electrodes occur very close to each other. However, for the areas where a WB occurs due to regions with slow conduction, the delays between adjacent electrodes increase and asynchronous peaks occur during a longer time interval. Therefore, the generalized signal has a multiple small peaks which include local time segment with high frequency. Our assumption is that the features of instantaneous dominant frequency (IDF) from spatially separated channels reflects disorganization of electrical impulse propagation. Consequently, the detection of significant variation of generalized IDF with short-time Fourier transform (STFT) allows to identify wavefront breaks (WBs). We developed computationally efficient algorithm to estimate local AT and quantify atrial regional wavefront discontinuities from bipolar intracardiac signals.

To obtain the power spectrum with STFT the recorded signal is divided into time sections with duration and overlapping ratio 90%. The use of STFT allows to determine the frequency characteristics of local segments and it changes over time. Additionally, the mean amplitude is removed and the Hamming window is applied for each segment before power spectrum calculation. Then, the preprocessed signals of all catheter electrodes are averaged to one signal. The following two-sided finite impulse response filter is used to smooth the generalized signal and remove high-frequency components corresponding to WBs.

Finally, generalized IDF is calculated using the equation:

$$GIDF(t) = \arg \max_k \int P_k(f, t, T)$$  \hspace{1cm} (4)$$

where $P_k(f, t, T)$ is the power spectrum from k-th bipolar electrode and $f$ is the frequency in Hz.

The selection of the time window length $T$ determines the accuracy of the extracted GIDF and enables to identify WBs. The high value for $T$ improves the frequency resolution and degrades the time resolution thus obscuring transient WB events. We select time window length $T$ to be equal 0.5 sec, this value is smaller than the common value that used for conventional dominant frequency analysis [12]. We define WB as any relative drop in calculated GIDF curve which is more than 2 Hz and lasts longer than 50 msec.

3. Clinical study

Data were collected from patients with persistent and paroxysmal AF attending for diagnostic electrophysiological studies with catheter ablation. The study was conducted in the department of interventional cardiology of Main Military Clinical Hospital named after N.N. Burdenko. The left atrium

Figure 1. The map of recording points for intracardiac bipolar electrograms.
was mapped with using Carto 3 navigation system and high-definition bipolar catheter (Navistar, Biosense Webster) with 3.5 mm inter-electrode distance. The intracardiac bipolar electrograms from 13 patients (average age 60.7±8.9 years, 7 male, 5 paroxysmal, 8 persistent) with duration of 10 seconds were recorded with sampling frequency 1500 Hz. The map of 28 recording points from different left atrial sites is on figure 1. Due to artifacts after the onset of the pacing pulses in catheter, the first 10 milliseconds of the recorded signal were removed from analysis. For noise and powerline interference removal the Butterworth bandpass filter with 3-80 Hz and notched filter with 60 Hz is used, respectively.

![Figure 2](image.png)

**Figure 2.** Example of calculated GIDF for random patient with persistent AF.

As we discussed earlier, study of the spatial distribution of the WB might provide clinically important insight regarding putative sources of the AF. The detection a significant drops in GIDF curve from collected bipolar electrograms allows to identity features of wavefront propagation. Example of calculated GIDF for random patient with persistent AF at different recording points is shown on figure 2. Regions with WBs can potentially be a putative driving source of AF and, therefore, might be a good candidate site for the ablation. Offline data analysis was performed with custom-made software based on Matlab (Mathworks, Inc., USA). The median GIDF for 5 paroxysmal and 8 persistent patients was 5.87 and 5.14 Hz, respectively.

For considering feasibility and efficacy of the proposed algorithm we conduct pilot clinical trials characterize a WB and establish its relationship to the DF and ablation outcomes. Our results showed, that selective catheter ablation for atrial sites with WB allows to restore sinus heart rhythm in 5 out of 13 patients. It should be also mentioned, that for 6 patients sites with significant drops in GIDF curve were not detected. This fact can be associated with a limited spatial resolution and location of recording points. Moreover, bipolar intracardiac electrograms were collected exclusively from the left atrium, and the right atrium during AF is not represented in these data.

### 4. Conclusion

The discontinuity of wavefront propagation during WBs in AF patients might be the results of rotating waves, local conduction block and wavefront collision. We introduced the novel mapping algorithm which is aimed to identity features of wavefront propagation and analyze the relative variation of generalized instantaneous dominant frequency calculated from intracardiac recordings. The analysis of wavefront propagation can be insightful map to characterize and differentiate signal complexity leading to a more informed choice of ablation target when combined with conventional mapping techniques. Further work is needed to characterize a WB and establish correlation relationship with ablation outcomes.

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