Investigating the Optimal Recording Duration for Summarising Spatiotemporal Behaviours of Long Lifespan Rotors Using Phase Mapping of Non-Contact Electrograms During Persistent Atrial Fibrillation

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Abstract

Understanding the spatiotemporal behaviour of 'rotors' in human atrial fibrillation (AF) is important for using them as targets for ablation. This study aims to track the spatiotemporal stability of rotors over 5 min time interval during persistent atrial fibrillation (PersAF). This study involved 10 PersAF patients, who underwent catheter ablation. 2048 non-contact virtual unipolar electrograms (VEGMs) were simultaneously collected and resampled at 512Hz, QRST interval removed and reconstructed using a sinusoidal wavelet fitting approach (Kuklik et al. Subsequent density maps of rotors were generated. The VEGM were divided into a total of 60 segments of different durations starting from 5s, 10s, 15s and so on. The segments were further divided into; group A ≤ 30 s, group B > 30, density maps of different time durations were compared with the full 300 s. Rotor density maps in segments recorded in group A differed significantly from group B, (CORR: group A 10 s = 0.47 ± 0.064 Vs. 30 s = 0.69 ± 0.067 Vs. group B 45 s = 0.76 ± 0.066 Vs. 60 s = 0.80 ± 0.063; P<0.0001). Rotor density maps for group B showed higher similarity and lower variation (0.88 ± 0.092) when compared to group A (0.53 ± 0.134). Our results suggest that time duration ≤ 30 s is not sufficient to detect/track spatiotemporal organization of rotors in PersAF patients.

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia seen in clinical practice. It affects more than 30 million individuals worldwide and increases the risk of stroke fivefold. Although the incidence is higher in the elderly, the burden of AF is found over the entire adult population with associated morbidity, mortality and healthcare costs [1]. The mechanisms that initiate and sustain AF are not yet well characterized. Successful catheter ablation of persistent atrial fibrillation (PersAF) in clinical practice is still a significant challenge, and the role of rotational activity (rotors) around the atria in sustaining AF is still debated, with studies suggesting that wavelet re-entries are mainly responsible for its maintenance. Furthermore, there have been fundamental differences between the studies on rotors in reporting their prevalence and spatiotemporal stability [2]. In contrast, in a clinical study (focal impulse and rotor modulation—FIRM) Narayan *et al.* [3], used a 64-electrode basket catheter (FIRMap™, Topera) with customized signal processing technique for detection of rotors and focal sources in human persAF and reported that rotors were present in approximately 90% of patients. Their results produced conflicting outcomes, however, due to the spatiotemporal complexities of the rotors and technical challenges in analyzing the intracardiac signals including fractionation, varying cycle lengths and complexities of activation patterns [4-5].

The main aim of this study is to use a phase mapping approach, to track the spatiotemporal stability of the rotors in persAF patients and provide further understanding of the length of time to record VEGMs signals needed to locate rotors during PersAF in human.

2. Materials and Methods

2.1 The Characterization of Enrolled Patients

This study recruited symptomatic PersAF patients (N = 10 Median age = 57.8 years, Min 36.1, Max76.4), who underwent left atrial (LA) catheter ablation for the first time guided by three-dimensional (3D) Non-contact mapping (NCM) using a multi-electrode array catheter (MEA) (EnSite Velocity, St Jude Medical). Ethics approval to conduct the study was obtained from the local ethics committee and all procedures were performed with informed consent.

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3. Electrophysiology Study

Prior to the electrophysiology (EP) study all antiarrhythmic drugs aside from amiodarone were halted. During the procedure, a quadripolar catheter and steerable decapolar catheter were advanced through the femoral vein and guided, until positioned in the coronary sinus (CS) and His position in the right atrium (RA) respectively. For all patients under fluoroscopic guidance, the single trans-septal puncture technique was used to access the LA, and then both a conventional deflectable mapping catheter and a high-density NCM MEA catheter were deployed in the LA. All patients were given heparin to maintain the activated clotting time ≥ 300 s. The 3D geometry of LA was reconstructed in real-time with catheter mapping (EnSite Velocity, St. Jude Medical), LA anatomical landmarks were annotated including Pulmonary Veins (PV), left atrial appendage (LAA), atrial roof, septum, anterior, posterior wall (PW), and mitral valve (MV). 2048 VEGMs with sampling frequency of 2034.5 Hz were simultaneously collected for 5 minutes, in addition to the 12-lead ECG. The data was transferred to a laptop and analysed using a research tool USURP-GUI developed by our research group (details in [5]). The area of interest High Dominant Frequency (HDF), was located and ablated [6], following this another 5 mins post-ablation data were recorded continuously for each patient, and then the MEA was removed and AF ablation using standard pulmonary vein isolation (PVI) procedure was performed.

3.1 Data Processing

The 5 min recording (2048 VEGMs with their associated 3D coordinates, and 12-lead ECG) were analysed offline using MATLAB (R2018a, MathWorks, USA). Signals were originally sampled at 2034.5 Hz and band-pass filtered (1-150 Hz) and then resampled at 512 Hz to reduce processing time. The surface ECG was band-pass filtered between (0.5-50 Hz). QRST subtraction was performed on the VEGMs to remove the far-field ventricular influence using the method developed by our group [7].

3.2 Phase Analysis and Rotor Detection

There is a sequence of processing steps to be followed to convert VEGMs into phase maps. This study used the phase mapping approach reported by Kuklik *et al.* [8], The phase data can be extracted using Hilbert transform (eqn.1)[9], with the phase defined as the angle between the analytic signal and original signal, while the phase extracted using Kuklik *et al* uses the 'sinusoidal recomposition method', where the signal is represented as a sum of sinusoidal wavelets with amplitude proportional to the negative slope of the unipolar VEGMs (eqn.2).

$$\mathrm{H}(\mathcal{U})(t) = \frac{1}{\pi} P \int_{-\infty}^{\infty} \frac{\mathcal{U}(t)}{t-\tau} d\tau \qquad \text{(eqn.1)}$$

Here, applying Hilbert transform into function $\mathrm{H}(\mathcal{U})(t)$, where P is the Cauchy principal value of the integral, to allowing calculation of instantaneous phase as follows:

$$\varphi(t) = arctan\left(\frac{-\mathcal{U}(t)-\mathcal{U}^*}{H(\mathcal{U})-\mathcal{U}^*}\right) \qquad \text{(eqn.2)}$$

The method can be summarised in the following steps: (1) Recomposing the VEGMs from sinusoidal wavelets with amplitudes proportional to the negative slope of the electrogram using sinusoidal recomposition method, (2) applying the Hilbert transform on the recomposed sinusoids signals, followed by (3) calculating the instantaneous phase of each signal producing a phase map. Figure 2 (B) illustrates these different steps.

The PSs were automatically identified using an algorithm developed by our group based on topological charge method as described by Bray *et al*. 2001 [10]. The PS locations were determined where the phase progresses through a complete cycle from (– π to +π). The stable PSs are those tracked over time subject to threshold for distance and for time. In each time frame, the location of each PS was compared with its location in the previous frame, only PSs lasting over 100 ms were considered [11-12]. A rotor was defined as a stable PS, which persists for at least 100 ms with a spatial threshold of a 5-node distance between consecutive frames.

Rotor density maps were generated in 2D and 3D, in order to assess the spatiotemporal stability of the rotors. The VEGMs were divided into a total of 60 non-overlapping segments of different time durations starting from 5 s, 10 s, 15 s and so on, until the whole 300 s VEGM recording was covered. The results were represented into, group A ≤ 30 s and, group B > 30 s to investigate the minimum time duration required to track sustained rotors. Density maps of different time durations were compared with the full 300 s recording (figure 3 A), and Pearson's correlation (CORR) was used, in order to assess the similarity of the shorter time duration rotor density maps and the 300 s one.

3.3 Statistical Analysis

The statistical data were analyzed using Graphpad Prism (version 7.04 for Windows). The continuous variables with normal distribution were expressed as mean (± standard deviation). Wilcoxon matched-pairs signed-rank test was used to analysing nonparametric paired multiple data, while non-parametric unpaired data were analysed with Mann–Whitney test. A value of $P < 0.05$ was considered significant.

4. Results and Discussions

Figure1 summarizes the histogram of the rotors' lifespan in the LA over the 300 s of VEGM recording for

10 patients, Overall, as the time duration increased the number rotors detected gradually increased (5 s = 17.2 ± 8.8 *Vs*. 300 s = 998.3 ± 436.5, P< 0.05). This was observed in all patients, thereby, stating the dominance of rotors in sustaining this complex arrhythmia.

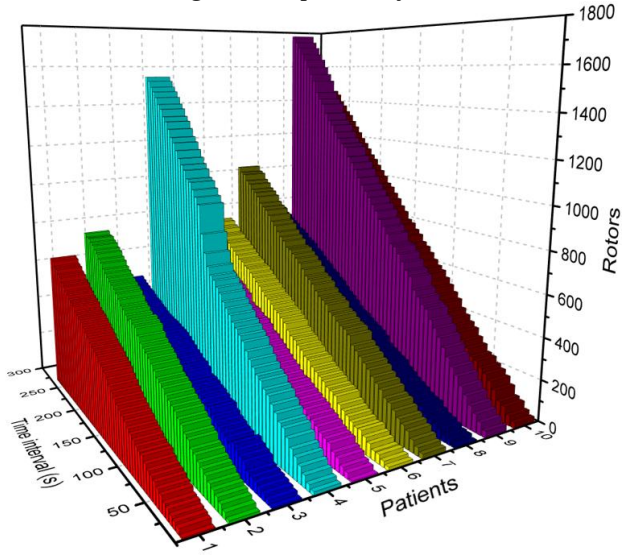

Figure 1: Histogram of rotors lifespan in the (LA) for 10 patients.

Whatever, electrophysiology mapping system is used to mapping AF, there is a debate in the literature with regards to the required time duration of VEGMs to be used detecting/tracking rotors. Several studies have used ≤ 10 s [13-15], while others used segments ≥ 30 s [2-16]. Thus, our results are expressed in two groups; group A ≤ 30 s and group B > 30 s. In order to investigate the time duration needed to produce a representative rotor density map, two time segments in each group were selected (group A 10 - 30 s, group B 45-60 s) to distinguish the difference of the spatiotemporal changes of rotors in each rotor density map in comparison with the rotor density maps of 300 s segment recording (gold standard).

The results for all patients showed that the rotor density maps of group A had lower correlation (mean ± SD: 10 s = 0.47 ± 0.064. *vs* 30 s = 0.69 ± 0.067, *P<0.0001*), when compared with the gold standard, while for group B had higher correlation (mean ± SD: 45 s = 0.76 ± 0.066, *vs* 60 s = 0.80 ± 0.063, *P<0.0001*) in comparison with the density map using the 300 s – long segment.

Figure 2 shows the rotor density maps in 3D for one patient. From the figure, it can be noticed that the 3D maps produced using the time duration (10 s up to 30 s) (left maps) do not represent the actual spatiotemporal behaviour of rotors when compared with the gold standard rotor density map (Centrale map). Consequently, this may lead to misinterpretation of rotors' locations and targeting of false rotors. Therefore, time duration of 30 s or less are not adequate for producing maps representing the dynamics of rotors. In group B (right-hand side figure 2A) the location of the regions that host sustained rotors seemed to be consistent over the time duration and correlate better with the full 300 s map (centre).

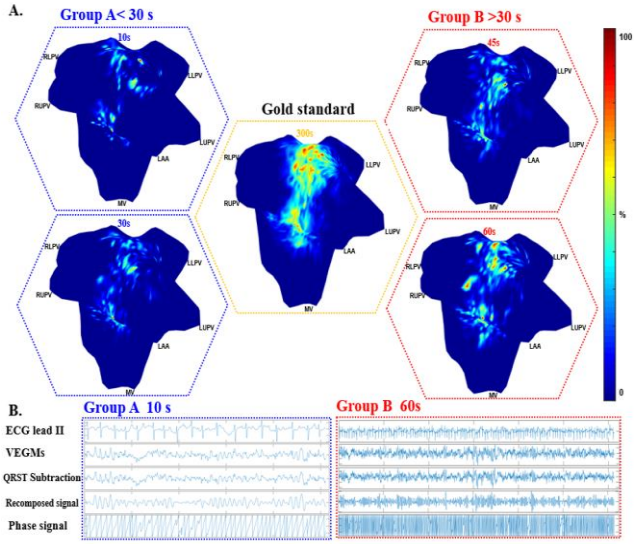

Figure 2(A), a comparison of rotor density maps for group A (10 s, 30 s) and group B (45 s, 60 s) against the full-length density map 300 s for one patient. The similarity results for group A were (CORR: 45%, 64%) *Vs*. group B (CORR: 76%, 80%). The colour bar indicates the region hosting sustained rotors for each density map. (B), an example of phase reconstruction of VEGMs of group A (10 s segment), and group B (60 s segment): starting with ECG lead II recording, original VEGMs recording followed by its subtracted version (after QRST subtraction) and finally, its recomposed signal (sum of sinusoidal wavelets) from which the corresponding instantaneous phase signal was calculated.

From the results in figure 3 (A), for all patients using the similarity index CORR. the rotor density maps of group A showing the similarity of 45 – 64 % respectively, when compared to 300 s recording. Thus time duration ≤ 30 s is not sufficient to characterize the spatiotemporal behaviour of rotors and identifying the atrial regions that host the majority of rotors activities. The maps obtained from 60 s segment were much better correlated to the map using 300 s recording with similarity of 80 %. Figure 3 (B) shows a decreasing trend in the standard deviation for all patients, with P<0.0001 presenting significant difference between the groups. Therefore 60 s is adequate to locate rotors.

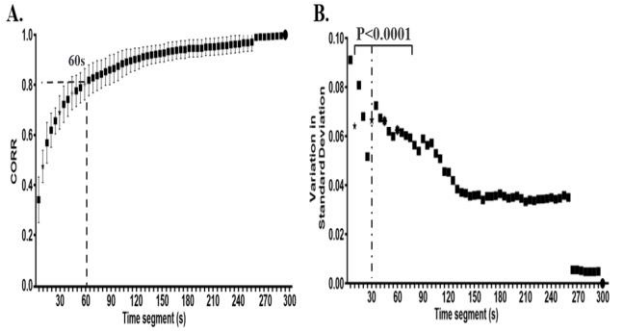

Figure 3: (A), Correlation coefficients CORR for 10 patients within the 60 s segments of VEGMs, (B) illustrates the drop standard deviation for 10 patients over the whole recorded segments as the length of data used increases.

5. Conclusions

Tracking the stable drivers (rotors) can provide a clear picture of the characteristics of complex arrhythmias during AF. However, rotor-based ablation for persAF remains an ongoing debate, due to the lack of stability of spatiotemporal rotors' behaviour. Thus, the time duration of the VEGMs used for phase mapping has a significant effect on the identification of rotors. Our results suggest that VEGMs' duration $\leq$ 30 s is not long enough to characterise rotors in PersAF patients, and time duration of 60 s is our recommendation for identifying them.

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