Dynamic Behavior of Rotors during Human Persistent Atrial Fibrillation as observed using Non-Contact Mapping

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Abstract

Rotors have been related to atrial fibrillation (AF) maintenance. We analyzed the behavior of rotors in persistent AF (persAF) utilizing a novel non-contact methodology and compared this to real time dominant frequency (DF) analysis.

2048 noncontact virtual unipolar atrial electrograms (VEGMs) were collected simultaneously (EnSite Array, St. Jude Medical) from 10 persAF patients (duration: 34 ± 25 months) undergoing left atrial (LA) ablation. After QRST-removal, FFT was used to identify the global DF of the LA (range 4 - 10 Hz; 1 s time-window; 50 % overlap; highest DF (HDF) (DF -0.25 Hz); up to 20 s/patient)**.** The organization index (OI) was measured and phase was found via Hilbert-transform.

Phase singularities (PSs) were tracked and were categorized according to their lifespan into short (lifespan <100 ms) and long lived (rotors) (lifespan ≥100 ms). A total of 4578 PSs were tracked. 5.05 % (IQR: 2.75 ~ 30.25 %) of the tracked PSs were long-lived and were observed in 11 % (IQR: 2.75 ~ 17.5 %) of the windows. The windows with rotors showed significantly higher HDF (mean ± SD, 8.0 ± 0.43 Hz vs 7.71 ± 0.50 Hz, $p< 0.0001$) and lower OI (0.76 ± 0.04 vs 0.79 ± 0.03, $p< 0.0001$) when compared with the short-lived PSs windows.

During persAF, the LA showed distinct behaviors as characterized by rotors. Often, no rotors were observed during sustained AF and, when present, the rotors continually switched between organized and disorganized behaviors. Long-lived rotors correlated with higher atrial rates. Our results suggest that rotors are not the sole perpetuating mechanism in persAF.

1. Introduction

Atrial Fibrillation (AF) is the most common arrhythmia and currently affects about 5 million people in the United States [1], and more than 0.5 million of people in the UK had AF in 1995 [2]. AF is a serious health concern and leads to increased morbidity and even mortality. The precise mechanisms that initiate and maintain human AF are not well understood. Previous studies in large animal hearts either failed to identify re-entry/spiral waves on the epicardium [3], or recorded only very short-lived re-entrant activity. However, many animal models and human fibrillation studies revealed AF is maintained by localized electrical rotors and focal sources [4, 5].

In a recent study [6], named CONFIRM (Conventional ablation with or without Focal Impulse and Rotor Modulation) trial, it was found that when these localized areas, which were usually about two sites in every patient, were targeted for ablation, AF terminated, or substantially slowed down (increase in AF cycle length) in about 86% of patients. In this study, we analyzed the behavior of rotors in persistent AF (persAF) utilizing a novel non-contact methodology and compared this to dominant frequency (DF) analysis. We also focused on rotor dynamics after DF guided ablation whether one or more 'leading rotors' are seen that could potentially sustain AF. We also evaluated whether the ablation revealed any significant anatomical differences in activation frequencies, AF organization, rotor location, and dynamics.

2. Methods

2.1. Patient characteristics

This study included 10 male (36.1-76.4 years old) persAF patients with AF duration ranging from 132 to

848 days, who underwent catheter ablation under the guidance of a 3D mapping system (Ensite Velocity, St. Jude Medical). The study was approved by the local ethics committee and all procedures were carried out after informed consent.

2.2. Electrophysiological study and electro-anatomical mapping

Prior to the electrophysiological study, all drugs except amiodarone were stopped. Under fluoroscopic guidance, a quadripolar catheter and steerable decapolar catheter were inserted via femoral vein. Following trans-septal puncture anticoagulant drugs were given and repeated doses were administered to maintain an activated clotting time between 300-350 seconds. Electro-anatomical mapping was performed in all patients to achieve detailed 3D left atrium (LA) geometry (which includes right superior, right inferior, left superior, and left inferior pulmonary veins, atrial roof, left atrial appendage [LAA], septum, lateral, anterior, floor, posterior and coronary sinus [CS]) with a noncontact multi-electrode array (MEA) catheter. After DF-guided ablation was performed, a post procedure recording was collected for up to 5 min. The MEA was removed followed by standard pulmonary vein isolation (PVI). In case this was insufficient to restore sinus rhythm, cardioversion was achieved by flecainide or internal defibrillation.

2.3. Data acquisition and signal processing

Surface ECG was recorded and band-pass filtered between 0.5 Hz and 50 Hz for all the patients. The non-contact MEA (Ensite Velocity, St. Jude Medical, USA) recorded 2048 points of AF VEGMs simultaneously from the endocardial surface of the LA. All VEGMs were resampled at 512 Hz, band-pass filtered between 1 Hz and 100 Hz and analysed offline using MATLAB (Mathworks, USA).

For all 10 patients up to 20 s of segments were analysed. Since the unipolar signals can have a significant far field ventricular component, a QRST subtraction was applied to remove the ventricular influence using a method previously described by Salinet *et al.* [7]. Power spectra were derived using Fast Fourier Transform (FFT) with a Hamming window for every 1 s long time window with 50% overlap for all the 2048 points in the LA to find the DF, defined as the frequency component with highest power in the frequency range between 4 and 10 Hz. Zero padding was used to increase the density of the frequency spectrum, making it smoother.

2.4. Spectral analysis, phase, phase singularities and rotor tracking

Previous publications have described DF and phase singularity (PS) analysis in detail [8]. Highest DF (HDF) regions for each individual window were defined as LA geometry nodes where DF was within 0.25 Hz of the highest DF measured for that window. The organization index (OI) was also measured.

Phase videos were created by Hilbert transform and PS detection was performed. We used spatiotemporal 'thresholds' to track PSs. A maximum spatial ($\Delta dmax \leq 3$ nodes) and temporal separation ($\Delta tmax \leq 10$ ms) between detected PS was set. As a result of the tracking algorithm implementation, analysis of PS was more accurate and robust against losses of detection in short periods of time, for tracking long standing rotors.

PS lifespan was obtained for each PS (Figure 1) as the temporal difference between these two temporal points and for those PS lasting ≥ 100 ms (rotors), we calculated the density of rotors (defined as number of rotors arising per surface unit). The density of PSs and also PSs appearing at any instant were obtained to help the visualization of the complexity of the PSs clustering/appearance. This analysis was performed on both pre- and post-ablation data.

3. Results and discussion

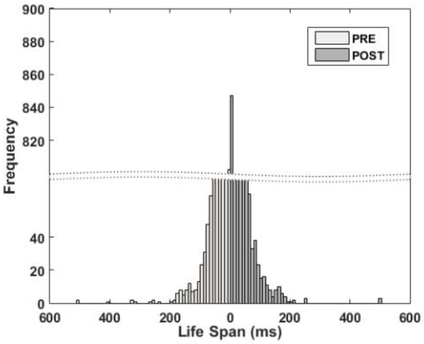

Figure 1. Analysis of lifespan of PSs during persAF in ms for both pre-/post ablation data.

Figure 1 shows the PSs lifespan for both pre-/post-ablation data of all the 10 persAF patients. For all the patients, prior to ablation, a total of 4578 PSs were tracked over 20 s interval of time. Rotors were observed in 9 out of the 10 patients and on average, 5.05 % (IQR: 2.75 ~ 30.25 %) of the tracked PSs were classified as rotors (Figure 2) and were seen in 11 % (IQR: 2.75 ~ 17.5 %) of the windows.

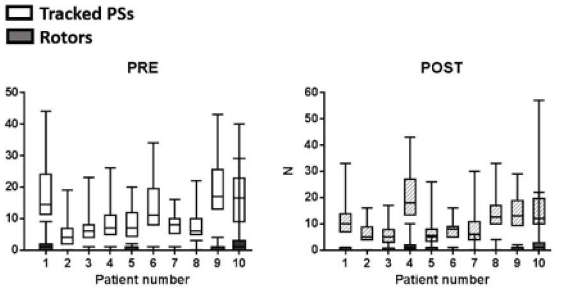

Figure 2. Comparison of number of tracked PSs and rotors observed in each patient for both pre-/post-ablation data.

After DF guided ablation, the total number of tracked PSs for all patients did not change significantly (n= 4358), however, the number of rotors increased and on average, for all 9 patients, 6.34 % (IQR: 11 ~ 29.25 %) of the tracked PSs were rotors (Figure 2). These rotors were seen in 12.67 % (IQR: 6.5 ~ 16.5 %) of windows when tracked over the same time interval.

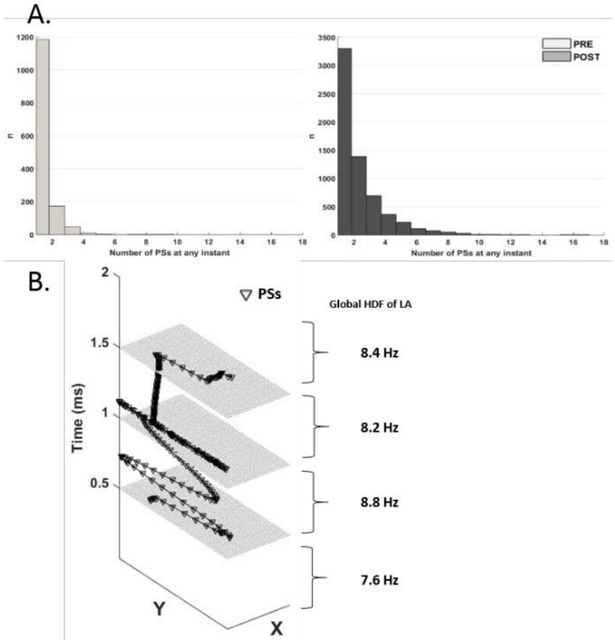

Figure 3. **A.** Number of PSs at any one instant. Interestingly, up to maximum of 9 and 16 PSs were observed in pre-/post-ablation data respectively. B. Complex PSs clustering for one patient during 1 - 1.5 s interval. Presence of rotor coincided with higher atrial activity.

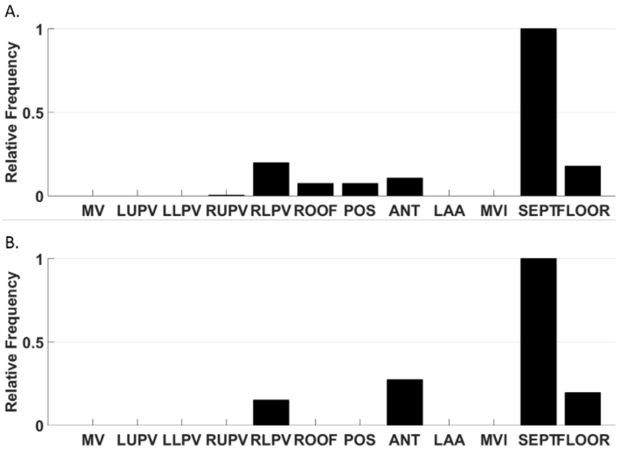

Figure 4. Incidence of rotors – before and after ablation – in the different LA regions, namely: MV, PVs, roof, posterior wall, anterior wall, LAA, MVI, septum and floor.

The number of PSs observed at any instant (pre- / post-ablation) are shown in Figure 3A. From our results, in 98.61 % and 93.86% of the time no PSs were observed in pre-/ post- ablation data respectively. A maximum of 9 and 16 PSs were also detected at any instant in pre-/post-ablation data respectively. As a result, complex clustering of PSs were seen in some instances when the several PSs (within 3 nodes of each PS) were detected close to each other. From figure 3B complex PSs clustering for one patient during 1- 1.5 s interval can be seen. In order to check if the rotors appeared in the similar region of the LA or not, the rotor density maps for all the 9 patients have been studied.

Although very few rotors had long life spans, their dynamic behavior tended to be consistent over time in the similar anatomical regions. From our results, rotors were observed in several regions, with the septum having the highest incidence, followed by the RLPV, floor, anterior wall, roof and posterior wall and RUPV (Figure 4A). Kumagai *et al.* [9] concluded that unstable reentrant circuits, principally involving the septum, appeared to be important for the maintenance of AF.

Although DF guided ablation did not affect the number of rotors significantly, in particular, a significant reduction ($p < 0.0001$) in the number of rotors were more evident in the RUPV, roof and posterior wall and interestingly with highest incidence in the septum (Figure 4B). Our results suggest that, over the 20 s interval, there was evidence of anatomical determinism in all the 9 patients who frequently re-formed at the same anatomical location, although there was dynamic movement of the rotor to other near regions.

Other researches [3] on fibrillation also stated, a possible location of the mother rotor is at the region where the posterior free wall intersects with the septum.

They concluded that region is the fastest activating region which gives rise to activation fronts that is leading to fibrillation. Though our results contradict the presence of any persistent or leading rotor, interestingly the windows with rotor(s) coincided with higher atrial activity, HDF (mean ± SD, 8.0 ± 0.43 Hz vs 7.71 ± 0.50 Hz, $p < 0.0001$) and lower OI (0.76 ± 0.04 vs 0.79 ± 0.03, $p < 0.0001$) when compared with the short lived PSs windows (Figure 5).

Without the application of band pass filtering at the range of DF, PSs were observed at every recorded time period. Band pass filtering at the HDF removes the activity at other frequencies and thereby identifies PSs within a relatively narrow frequency. This limits the detection of other potential PSs which might contribute/reflect the true dynamic nature of the disease. Thus it can be understood that emphasizing the sensitivity of such techniques can bring an effect on tracking PSs and thereby on tracking rotors as well. Therefore, the phenomenon of rotors, i.e., whether they are active drivers of fibrillation or simply represent a passive phenomenon is still unclear. Studies have also shown that, structural remodeling of the heart has been shown to interfere with rotor behavior [10]. This, along with our results supports the idea that, rotors solely are not the dominant mechanism in persAF, however, presence of any intermittent or spatially stable rotors contributes to the multiple components in the frequency spectra (lower OI), i.e., more chaotic electrograms. Therefore, the presence of multiple sources is one important cause of multiple peaks in the frequency spectra during persAF.

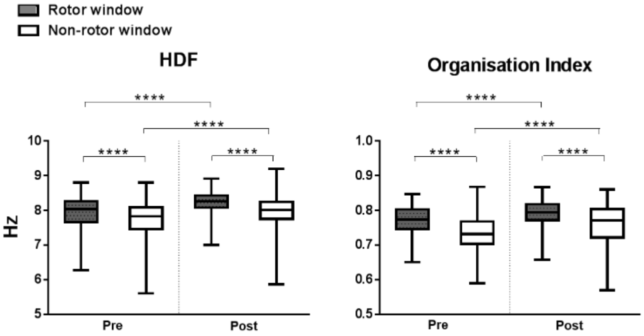

Figure 5. Relationship of HDF and OI with the PS life span. The HDF during the presence of a rotor presented higher value, lower standard deviation and lower organization index.

4. Conclusions

PersAF is being recognized increasingly as a deterministic process resulting from multiple mechanisms such as rapidly firing foci and fibrillatory conduction rather than a fundamentally turbulent and self-sustaining process. As observed using non-contact mapping, in persAF patients, over 20 s interval of time, rotors were seen only rarely (11 % of the time) . When appeared, they continually switched between organized and disorganized behaviors. DF guided ablation did not have a significant effect on the number of tracked PSs (pre vs post, n= 4578 vs 4358), however, the number of rotors increased (pre vs post, average: 5.05 % vs 6.34 %). Although very few rotors had long life spans (both pre-/ post- ablation), their dynamic behavior tended to be consistent over time in the similar anatomical regions with the septum appearing to be the most visited region during AF. Rotors also tend to appear whenever HDF is higher and OI is lower thereby leading to higher atrial rate as well as chaotic electrograms

The correlation between sites of HDF and rotor regions was not assessed in this study. Future work includes studying the relationship between these sites as well as understanding the role of high-frequency areas in driving and sustaining AF.

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