# Combination of Frequency and Phase to Characterise the Spatiotemporal Behaviour of Cardiac Waves during Persistent Atrial Fibrillation in Humans

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## Abstract

*The spatial distribution of atrial dominant frequency (DF), phase and phase singularity points (PSs) may reflect mechanisms driving and maintaining persistent atrial fibrillation (persAF). Here we developed an automatic algorithm that combines the three parameters and depicts the complex spatiotemporal patterns of fibrillation.*

*For 9 patients undergoing left atrial persAF ablation, noncontact virtual unipolar electrograms (VEGMs) were simultaneously collected using a balloon array (Ensite Velocity, St. Jude Medical). After removal of the far field ventricular influence, we used fast Fourier transform and Hilbert transform to detect the DF and phase of each VEGM. PSs are detected by finding the curl of the spatial phase gradient. DF along with phase and PSs were plotted for each window and the behaviour of the trajectory of HDF 'clouds' was observed.*

*Our results indicate that spatial and temporal organization correlating HDF and phase exists during persAF. Generating and analysing the maps of HDF and phase may prove helpful in understanding the spatial and temporal activation dynamics during persAF.*

## 1. Introduction

Atrial fibrillation (AF) is the most common supraventricular tachycardia and is characterised by disorganised atrial electrical activity and contraction. It appears in the electrocardiogram (ECG) as an aperiodic, irregular rhythm with absence of P waves and irregular R-R intervals, thereby outlining the complex electrical activations of the atria and its lack of coordination with the ventricles. Representation of atrial rate during AF has been expressed using the concept of dominant frequency (DF) [1]. Phase mapping has also been used as an effective approach to track the wave propagation during AF [2].

For paroxysmal AF (pAF, AF duration <7days), well-established treatment strategies have been developed, which show high success rates. During persistent AF (persAF), because of its complex states, suitable spatiotemporal complexity measurements are necessary for improving the analysis of DF and phase mapping. In this study, we evaluated the spatiotemporal relationships of parameters related to wave-dynamics of AF by combining DF, phase maps and PSs.

## 2. Methods

### 2.1. Patient characteristics

This study included 9 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 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, bottom, posterior and coronary sinus [CS]) with a noncontact multi-electrode array (MEA) catheter.

## 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 9 patients up to 30 s of segments were analysed. Since the unipolar signals have a significant far field ventricular influence [3], initially a QRST subtraction was applied to remove the ventricular influence using a method previously described by Salinet *et al* [4]. Power spectra were derived using Fast Fourier Transform (FFT) with a Hamming window for every 4 s time window with 87.5% overlap for all the 2048 points in 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. Highest dominant frequency

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. These regions are considered to represent sites maintaining the persAF arrhythmia. Therefore, the area of a HDF forms a 'cloud' which is assumed to represent the AF activity for that region [7]. In order to understand the HDF regions trajectory, the centre of gravity (CG) of the HDF clouds were determined by averaging the coordinates of each one node in the 'cloud' weighted by their DF values [8]. These CGs were acquired for every 4 s FFT window with 87.5% overlap over a 30 s interval.

## 2.5. Phase and phase singularity points

To obtain the phase we applied Hilbert transform to produce analytical signals from the unipolar signals obtained from the VEGMs collected from the persAF patients. PSs were located with the topological charge technique as described by Bray *et al* [5]. The PSs are identified as the points where there is a topological defect. This is done by finding the gradients of the spatial maps and integrating them over closed paths,

$$n_t = \frac{1}{2\pi}\oint_c \nabla\emptyset \cdot d\vec{l} \qquad (1)$$

Where,

$$\nabla\emptyset = gradient\ of\ the\ phase$$
$$c = closed\ path$$
$$\vec{l} = overall\ path$$

The sign of the integral corresponds to the chirality of the PS. This is the direction in which the associated wavefront circulates about the PS point (clockwise or counter-clockwise).

## 2.6. Combining highest DF, phase maps and PS points

To study the spatiotemporal relationship between PSs and HDF, we projected the PSs and HDF on phase maps (Fig.1), and investigated the PS distribution at the periphery of HDF sites *vs* non-HDF sites. In this study, for 30 s of recording we had 53 HDF windows and 2048 phase maps corresponding to each HDF. We counted the number of times the CGs of the initial and final HDF were in between PSs of opposite chirality. We only considered the propagation of HDF region when the transit of CG was at least 15 mm from its initial position.

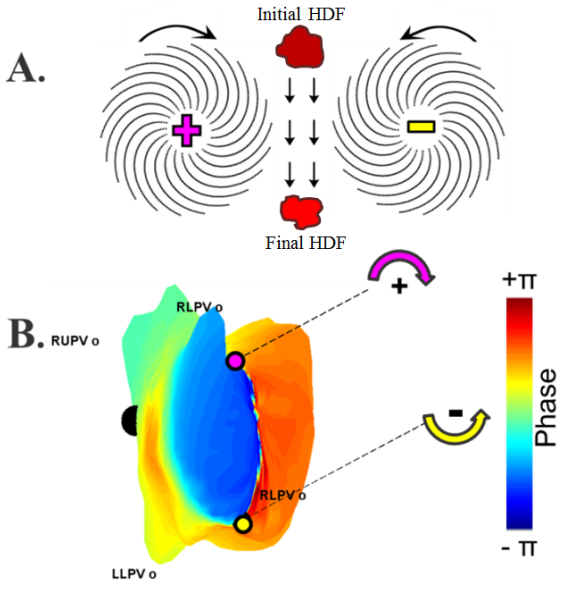


Figure 1- A. Schematic diagram defining the direction of PSs with opposite chirality. We examine the situations

when HDF channels through these PSs (arrows in the middle). B. 3D map of the left atrium showing the centre of a high DF area in black. The pink and yellow circles correspond to clockwise and counter-clockwise PSs respectively.

## 3. Results and discussion

To understand the spatiotemporal behaviour of cardiac waves during persAF we combined phase, PSs and HDF extracted from the VEGMs. By considering these simultaneously, spatiotemporal periodicity activities were noticed.

Several PSs have been observed throughout the LA. Many were seen to continuously appear and disappear with variable chirality and unstable spatial locations. This could be due to the meandering of rotors which causes the PSs to be located at various regions [6].

We compared spatiotemporal correlations of the PSs and HDF by representing each map as a 2D 64×32 lattice zone (Fig. 2A). PSs and HDF showed weak spatial correlation ($R = 0.063$, $P < 0.001$) and it was frequently observed that the PS points tended to be located around the boundary of the HDF areas rather than overlapping with them. This type of activity was observed in all patients (Fig. 2B).

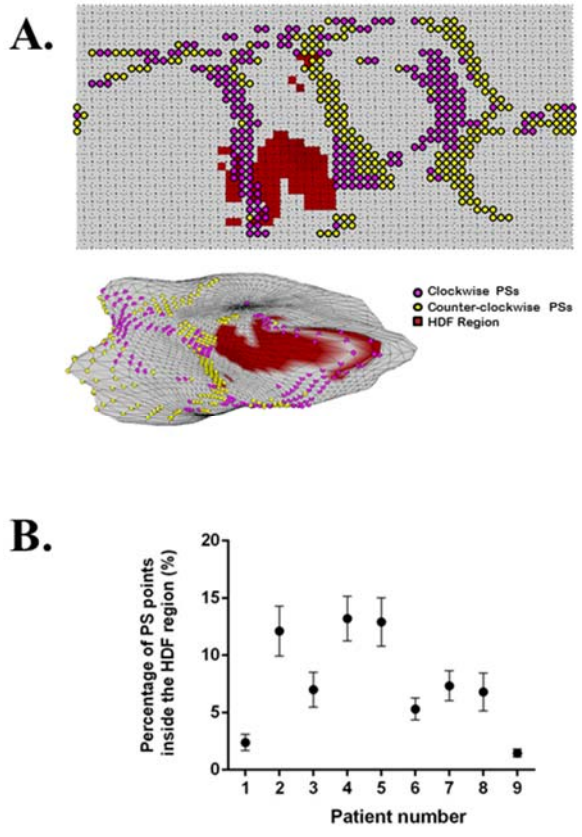


Figure 2- A. 2D and 3D views of spatiotemporal distributions of PSs and the HDF region for a single window. This map displays cumulative points of PSs in multiple time intervals during the corresponding period of the HDF. Maps of PSs are colour-coded as pink: clockwise; yellow: anti-clockwise, and HDF is represented in brown. B. Summary of the mean and standard error of the mean of percentage of PSs which overlap the HDF region for all the 9 patients.

Previously, we also reported regarding the stability of HDF in persAF and the study offered a wider perspective about the movement of the HDF 'clouds' illustrating that they are temporarily unstable [7]. In this study we focused more on understanding their movement. Our results suggest that the PSs might influence the spatiotemporal movement of HDF. The number of times PSs of opposite chirality appeared around the HDF was counted for all windows at the instant of time when the wave fronts of the two oppositely rotating wavelets propagate between the PSs (Fig. 3).

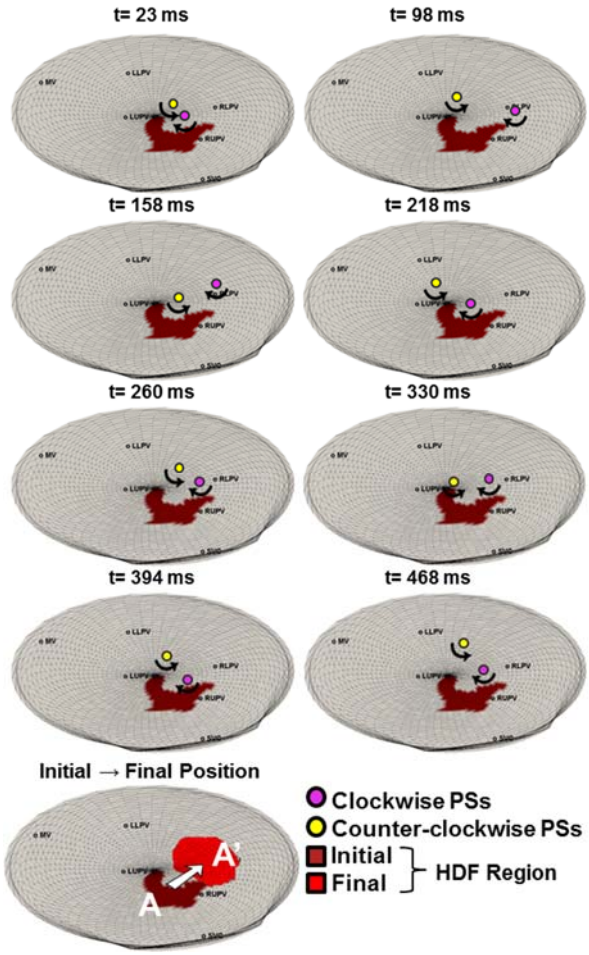


Figure 3. Sequence of images illustrating how PSs of opposite chirality appear spatially and their position in relation to the HDF and its propagation. Each frame shows the location of PSs (yellow and pink circles

indicate counter clockwise and clockwise chirality, respectively), and HDF (brown region). The arrows around the PSs help to indicate the direction of rotation (chirality) and the initial and final positions of HDF are denoted by A and A'.

For all the 9 patients, we analysed a total of 411 windows and PSs of opposite chirality were observed in all the windows. The HDF value of the LA ranged from 5.3 Hz to 7.7 Hz for this cohort of patients. Out of 411 windows, we observed HDF 'clouds' propagating in 293 windows (mean ± SD: 71.3 ± 10.7%). On average 13 (±9) times PSs of opposite signs were observed for each window that influenced the propagation of the HDF from current to the next window.

## 4. Conclusions

The results shown in this work provide a framework for helping to understand the complex dynamics of high frequency regions – represented by the HDF – with re-entry activation – represented by the PSs – in persAF. These propagating waves then travel across the atria giving rise to fibrillatory conduction and they seem to be related to the drift direction of the HDF 'clouds'. The wide range of HDFs in each patient suggests there are multiple wandering wavelets. Cumulative plotting of the HDFs along time would help identifying the potential stable sources of persAF [7] and analysing their spatial behaviour and its relation with the PSs would be helpful for understanding persAF activation and to guide ablation.

Studies have demonstrated that re-entrant drivers as well as atrial regions with high activation rates can be responsible for persAF maintenance. Therefore, understanding the relationship of phase and HDF is important.

Phase analysis of the VEGMs enables tracking the activation wave fronts simultaneously in the whole LA. Their spatial distribution and evolution in time provide insight into wave propagation dynamics and enable localization and tracking of PSs. Finding highest DF regions allows for the global identification of areas in the LA with rapid activations.

This study mapped the phase, PSs and HDF to study the dynamics and spatial behaviour of the VEGMs during persAF. It was observed that PSs are localized mainly around the HDF regions. It was also frequently observed the transit of HDF 'clouds' between rotors of opposite chirality.

Generating and analysing these spatiotemporal maps may prove helpful in understanding the spatial and temporal changes during AF and tracking the activation patterns dynamically. If we understand these we will be in a better position to establish ablation strategies based on these maps.


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