Spatiotemporal Behaviour of High Dominant Frequency during Persistent Atrial Fibrillation

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Abstract

Atrial electrograms (EGMs) with high dominant frequency (DF) are believed to represent atrial substrates with periodic activation responsible for the maintenance of persistent atrial fibrillation (persAF). This study aimed to assess the DF spatiotemporal behavior using high density noncontact mapping in persAF. For 8 patients undergoing left atrial (LA) persAF ablation, 2048 noncontact virtual unipolar EGMs were simultaneously collected and after the removal of ventricular far-field activity, Fourier based spectral analysis was used to identify DF on each EGM. Atrial areas with the highest DF (HDF, DF ± 0.25 Hz) were delimited in each frame for all EGMs, creating HDF 'clouds'. Cumulative HDF clouds found at each frame were counted in the 3-D LA representation. To further assess the temporal stability of the cloud, the number of EGMs not hosting any HDF was determined for each window over time. The results show the number of occurrences of HDF clouds in the LA. The temporal behavior was analyzed by counting the number of positions on the 3-D representation of the LA not visited by HDF along time. Our results show HDF in persAF is not temporally stable and spatial distribution throughout the atria suggests the existence of driver regions with very rapid and regular activity maintaining AF. Therefore mapping the cumulative HDF might be an interesting strategy for ablation.

1. Introduction

Atrial fibrillation (AF) is the most common rhythm disorder seen in clinical practice. The complexity of electrograms (EGMs) obtained from intra-cardiac electrodes make signal analysis difficult in the time domain. Therefore changes in dominant frequency (DF) of the signals cannot be tracked since several time-consuming maps need to be generated [1] and also makes it harder to estimate the rate of atrial activation of signals during AF [2]. Therefore frequency domain analysis has been used to study the signals in depth. Spectral analysis has been used to find the DF of the signals in the regions of atria that may possibly host the origin of the AF trigger. This study aimed to assess the spatiotemporal behavior of the HDF using high density noncontact mapping in patients with persAF by mapping it cumulatively for each time window over the total period of the signal.

2. Methods

2.1. Patient characteristics

This study included 8 male persAF patients of age between 37-57 years old with AF duration of more than 9 months who underwent catheter ablation under the guidance of 3-Dimensional mapping system (Ensite 3000, 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, patients have been given heparin to reduce the risk of blood clots. Under fluoroscopic guidance, at His position and coronary sinus (CS) quadripolar catheter and steerable decapolar catheter were placed respectively via femoral access. Following the trans-septal puncture anticoagulant drugs was given and repeated doses were administered to maintain an activated clotting time 2-3 times more than control sample (300-350 seconds). Electro-anatomical mapping was performed in all patients to achieve detailed 3D 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 (EnSite 3000, St. Jude Medical, Inc.) and a conventional

deflectable mapping catheter.

2.3. Data acquisition and signal processing

Surface ECG was recorded for all the patients and band-pass filtered between 0.5 Hz and 50 Hz. The non-contact multi-electrode array also recorded the signals simultaneously from 2048 points along the endocardial surface of the LA and the virtual unipolar AF electrograms (VEGM) data were extracted from the system Ensite 3000 (St. Jude Medical, USA). All VEGMs were sampled at 1200 Hz band-pass filtered between 1 Hz and 150 Hz and analyzed offline using MATLAB (Mathworks, USA).

For 8 patients up to 38s of segments from each of the 16384 VEGMs were analyzed. Since the unipolar signals have a significant far field ventricular influence [3], initially a QRST subtraction in the VEGMs was applied to remove the ventricular influence using a method as previously described by Salinet et al. [4]. Fast Fourier Transform (FFT) with a Hamming window was then performed for every 4-second time window with 50% overlap (i.e. by moving the time window every two seconds) simultaneously for all the 2048 points in LA to find DF, the highest frequency component of the VEGM. Zero padding was also performed to increase the density of the frequency spectrum, thereby making the spectra smoother graphically. An overview of the methodology is provided in figure 1.

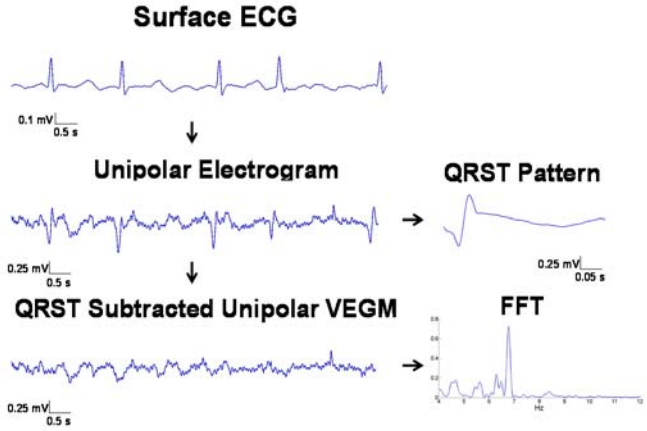

Figure 1. Demonstration ventricular far field influence removal from the VEGMs by subtracting QRST-intervals. The frequency spectrum is generated after spectral analysis (FFT). The top frame shows the surface ECG on which the QRST intervals are detected. The middle-left figure is one out of 2048 unipolar virtual electrogram (VEGM) collected from the endocardial surface of the LA. The middle-right frame is the QRST complex pattern obtained from the VEGM which is used as a template to remove the local ventricular activities in the atrial electrograms as shown in the bottom-left frame. Finally, the bottom-right frame is the frequency spectrum of the subtracted VEGM showing a single dominant frequency (DF) peak at 6.7 Hz.

2.4. Finding highest dominant frequency

DF was defined within the physiological range of 4 to 10 Hz. Highest DF (HDF) regions for each individual window were defined as any LA geometry node where the calculated DF was within ±0.25 Hz of the maximum DF measured for that window. This region is considered to represent regions maintaining the persAF arrhythmia and the area of HDF bounded by ±0.25 Hz forms a cloud which is assumed to represent the HDF activity for that region [5].

2.5. Spatiotemporal distribution of HDF

The number of times HDF occurring at each node of LA were counted for each patient in order to find the HDF density. In a more general mathematical sense, HDF density is a function *D(i)* that counts the number of observations that fall into each of the HDF areas. Thus, if we let n_j be the total number of windows and n_i be the total number of nodes, the HDF density *D(i)* is defined as

$$D(i) = \sum_{j=1}^{nj} I(i,j) \qquad (1)$$

Where i is the node number (i=1, 2, 3… n_i);
j is the window number (j =1, 2, 3…n_i);
I is the HDF density increment function;

$$I(i,j) = \begin{cases} 1 & \text{if in the HDF area} \\ 0 & \text{if not in the HDF area} \end{cases}$$

The total sum is taken over *I*, which represents the cumulative number of observations along time windows. Hence, it is upon this element that we focus our attention.

The atrial areas with HDF density were delimited in each frame for all 2048 VEGMs, such that the HDF clouds are overlapping at many sites. The number of times HDF clouds super-impose each other are recorded and represented in different colours since the number of times of overlapping are not the same. Representation of HDF clouds of the persAF is projected onto its 3D LA geometry as well as on a 2D map for better visualization.

To further assess the temporal stability of the HDF clouds, the number of VEGMs which did not host any HDF from the beginning of the mapping time was determined for every window by counting the number of nodes that did not contain HDF values in the first time

window and comparing with the subsequent one and repeating the comparisons with the following windows.

3. Results and discussion

3.1. Spatial distribution of HDF regions

Previous study suggested the use of center of gravity (CG) of the DF clouds and their trajectory to assess the spatio-temporal behavior of the atrial substrate [6]. In order to create the highest DF area trajectory map, Salinet et al. determined the CG for the DF cloud by averaging the coordinates of each one point in the cloud and weighting by their particular DF values. This CGs was acquired for every 4-second FFT window with 50% overlap over a 1 minute interval [6].

However, in some cases the CG seemed to be away from the HDF cloud's center as it is affected by each cloud's size, shape and their respective DF value as shown in the figure 2. Therefore it could lead to insignificant spatial distribution of DF activity if DF targeted ablation of persAF patients is performed. Hence, this study focuses on producing an area consisting of a collection of HDF clouds interpolated in distinctive colors that reflects average regional activity of DF.

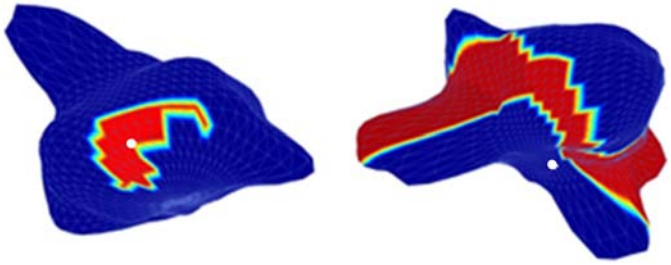

Figure 2. Location of CGs (white dots) in LA of two persAF patients obtained for a specific time window. In this case the CGs is located near the end and outside the DF cloud's boundaries respectively. The position of the CGs is not representing the true behavior of DF.

LA regions with maximum overlapping of HDF clouds over time are shown in Figure 3. On an average for all the 8 persAF patients 65% (±19%) of the mapping time the HDF clouds were present at certain regions of the LA prior to ablation. In this study spatial sites, 'red' colour regions, are the sites considered stable and the 'blue' colour regions are considered as the sites with high variability with minimal DF values. HDF reoccurrence over a particular region in LA of persAF patient for a period of time suggests potential stable sources that may reflect mechanisms driving and maintaining the fibrillatory process of AF. With cumulative increase in the number of windows, the percentage of overlapping of HDF clouds and spatial extent of driver activities is observed more. Therefore cumulative plotting of HDF clouds over time shows that persAF is mechanistically sustained by individual drivers. Analysing its spatial behaviour would be helpful to locate the drivers and provide a detailed estimate for DF targeted ablation to reduce the sources maintaining persAF.

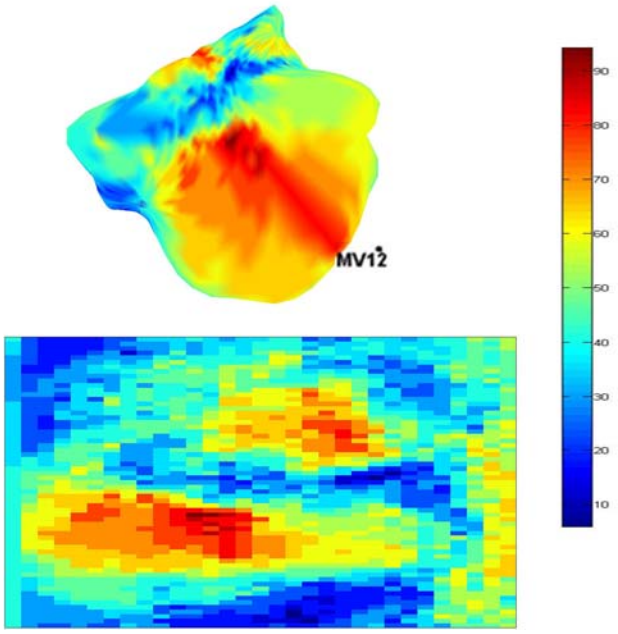

Figure 3. Representation of the cumulative HDF clouds stacked on the 3-D LA (Top) and 2-D spatial map of LA (Bottom). The map at the top appears smoother since it is interpolated and the spatial map at the bottom appears such as it shows the distribution of HDF density of the whole LA.

The percentage of frequency of occurrences of HDF clouds in the LA is represented by the colorbar. The HDF maps highlight the regions that remained spatially stable for a period of the mapping. In this case the cumulative mapping time of 38s represents the HDFs clouds and approximately 93% of the mapping time the HDF was present in the region illustrated in red color.

3.2. Temporal stability of HDF regions

To assess the temporal stability of the clouds, the number of VEGMs not hosting any HDF was determined for each window over time. The results showed that the number of nodes not visited by HDFs out of 2,048 nodes decreases with time in an exponential pattern and therefore logarithmic curves were fitted for each patient which gave an average time constant (τ) of 16.9 ± 11.2 seconds for all 8 persAF.

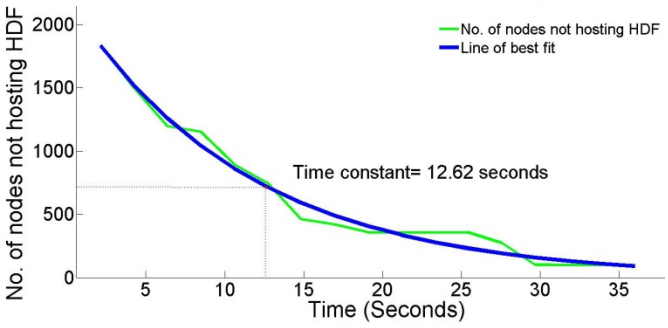

Figure 4. The resulting plot displays the number of nodes not visited by HDF (green) and the exponential fit (blue). It shows the temporal behavior of the HDFs of one persAF patient. The exponential fit has a time constant of 12.62 s in this case.

The temporal variability from the decay curves of the results proves to be a useful tool to describe AF content and offer a wider perspective about the movement of the HDF clouds therefore understanding that they are temporarily unstable.

4. Conclusion

AF is the most common sustained cardiac arrhythmia and can lead to stroke and heart failure, with increased mortality [7]. Despite in-depth research, the precise electrophysiological mechanisms of AF are still not well understood [7]. However analyzing the signals of the AF in frequency domain is a powerful tool to characterize spatial behavior of atrial activation rate in AF patients [8].

The results presented in the work suggest that despite of the unstable temporal nature of the HDFs, the reoccurrence of it in the same region shows their spatial distribution which provides further insight into potential regions sustaining persAF. This is important, if an ablation approach is considered based on DF analysis, since it uses dynamic 3D HDF maps that could improve ablation strategy for patients with persAF.

Acknowledgements

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