Dominant Frequency and Organization Index for Substrate Identification of Persistent Atrial Fibrillation

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Abstract

The combined use of dominant frequency (DF) and organization index (OI) might help to identify atrial regions with organized, fast activation rates in persistent atrial fibrillation (persAF). We determined adaptive thresholds for DF and OI based on electrophysiological responses following AF substrate modification. 2048-channel electrograms (3206 EGMs, 30 s, EnSite Array) were analyzed from 10 persAF patients undergoing DF-guided ablation. After QRST subtraction, fast Fourier transform was used to calculate DF and OI. AF cycle length (AFCL) was measured before and after each ablation point (left atrium appendage). EGMs were grouped in two classes: collected at regions whose ablation resulted in AFCL increase (≥10 ms) and AFCL non-increase (<10 ms). Patient-specific z-score DF (DFz) and OI (OIz) were tested to separate the two classes (individually and AND-logic). Informedness (J), accuracy (Acc) and F1 score were used to assess classification performance. Best individual classifications were DFz=0.52 (J=0.16, Acc=65%, F1=0.41), and OIz=0.60 (J=0.19, Acc=70%, F1=0.40). Best AND-logic (DFz and OIz) classification was DFz=-0.52 and OIz=0.49 (J=0.23, Acc=71%, F1=0.43). DF and OI combination might help in the identification of patient-specific AF substrate to guide ablation in future clinical studies.

1. Introduction

Atrial fibrillation (AF) is the commonest cardiac arrhythmia in clinical practice, affecting 1-2% of the general population [1]. The loss of effective atrial contraction in AF patients may result in blood clots in the atria, which increases the risk of stroke five-fold [2]. Although catheter ablation techniques are widely applied to treat AF patients, the underlying pathophysiological mechanisms of persistent AF (persAF) remain unclear [3]. On the one hand, atrial regions hosting electrograms (EGMs) with fast activation rates and high dominant frequency (DF) might represent important sites for the maintenance of AF [4]. On the other hand, EGMs with fractionated activity might suggest tissue remodeling also participating in AF perpetuation [5]. Additionally, most studies consider single EGM-attribute maps for substrate-guided ablation – e.g., based either on DF or on complex fractionated EGMs [6]. Recent work has proposed a logical operator map that merges relevant electrophysiological features of the AF process in a single map [7]. The features investigated thus far are based on the time-domain.

The organization index (OI) calculated from the frequency domain helps to define the robustness of the DF to represent AF activation rate in EGMs [8], which can be used to identify AF drivers and guide ablation. The combined use of DF and OI might help to identify atrial regions with organized, fast activation rates. In the present work, we investigate individual thresholds for DF and OI, and their logical operator, for the classification of AF drivers based on electrophysiological responses following AF substrate modification.

2. Methods

2.1. Electrophysiological Study

Ten persAF patients (table 1) undergoing first time left atrial (LA) catheter ablation were enrolled. 30 s of LA noncontact electrograms (EGMs, Ensite Array, St Jude Medical) were exported to our Matlab platform to guide ablation targeting DF [9]. High DF regions in the LA were identified as previously described [10]. Four out of ten patients had AF terminations (3 flutter, 1 sinus rhythm) by high DF ablation before pulmonary veins isolation (PVI).

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Table 1. Clinical characteristics of patients.

	Median	Min	Max
Male (n)	10	-	-
On amiodarone (n)	2	-	-
Age (years)	57.8	36.1	76.4
Days in AF pre-procedure	219	132	848

2.1. Training Data Labelling

AF cycle lengths (AFCL) before and after ablating each atrial DF site (a cluster of lesion points defined by revisiting DF from 30 s data before ablation) were recorded in Labsystem™ Pro EP Recording System (Boston Scientific). Two classes of data were considered as labels: 1) AFCL increase (≥10 ms), 2) AFCL non-increase (<10 ms) [11]. Class 1 was considered as positive ablation results (Figure 1, left-hand side). In total, 3,206 nodes were ablated in all 10 patients: 947 (30%) AFCL-increase and 2,259 (70%) AFCL-non-increase.

2.2. Signal Pre-processing

The 30 s EGMs were sampled at 2034.5 Hz and then re-sampled to 512 Hz to reduce processing time and save storage using cubic interpolation method. Ventricular far-field activity present in the EGMs might appear as misleading frequency components on the atrial frequency spectrum, affecting the accuracy of DF identification, and QRST subtraction was performed as described in our previous work (middle panel Figure 1) [12, 13].

Spectral analysis was carried out on the EGMs following QRST subtraction by performing fast Fourier transform (FFT). A zero padding factor of 6 was applied when performing the FFT. A Hamming window was used to reduce the amplitude of the side lobes around the DF peak in the power spectrum. DF was defined as the frequency peak in the power spectrum within the physiological range of 4-10 Hz (right-hand side Figure 1). OI is defined as the ratio of the area of the DF peak (±0.375 Hz) together with its harmonics, and the total area of the power spectrum (up to 20 Hz). For each patient, z-score was calculated for both DF (DFz) and OI (OIz) in order to minimize inter-patient variability, accordingly:

$$Z = \frac{x - \mu}{\sigma} \qquad (01)$$

where x represents observed values, μ is the mean and σ the standard deviation of the sample.

2.3. Individual DF and OI Classifications

DFz and OIz were individually tested to separate the two classes (AFCL increase, AFCL non-increase). Each value found on DFz and OIz were tested as thresholds for classification. Higher values for DFz and OIz were assumed to correlate with AFCL-increase group.

2.4. DF and OI Logical Operator

A logical operator (AND-logic) was used to combine both DFz and OIz. Each value of DFz and OIz were tested as thresholds for crossed-classification. Higher values for DFz and OIz were assumed to correlate with AFCL-increase group.

2.5. Classification Performance

Best classification performance was defined as maximum Informedness (J). J is bound between -1 and 1, and it is defined based on the true positive rate (TPR) and true negative rate (TNR), as seen in the equation below:

$$J = TPR + TNR - 1 \qquad (02)$$

Informedness is preferred in the presence of class imbalance, which is the present case. In order to obtain high values of J, both TPR and TNR must be relatively high, meaning classification is more likely to be satisfactory for both classes – in other words, it must be an informed decision.

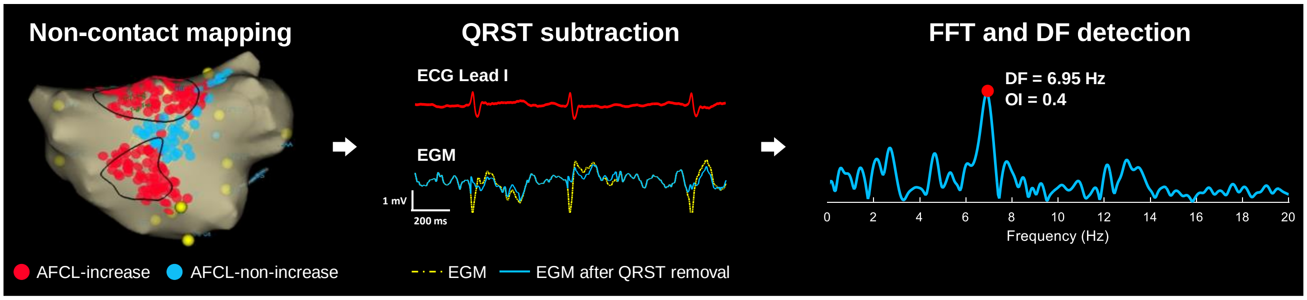

Figure 1. Left-hand side: LA regions where ablation resulted in AFCL increase (≥10 ms, red) and AFCL non-increase (<10 ms, blue). Middle panel: illustration of the QRST subtraction in noncontact EGMs. Right-hand side: frequency spectrum of a noncontact EGM following QRST subtraction estimated with FFT, with the annotated DF and OI (modified from [14]).

While J has been chosen as the main measure of classification performance, accuracy and F1 score were included as auxiliary measures of performance. Pearson correlation was also provided for optimal points of performance.

3. Results

3.1. Individual DF and OI Classifications

As illustrated in Figure 2, best individual classifications were achieved at DFz = 0.52 (J = 0.16, Acc = 65%, F1 = 0.41), and OIz = 0.60 (J = 0.19, Acc = 70%, F1 = 0.40). Correlation between predicted and true classes were 16% and 20%, respectively.

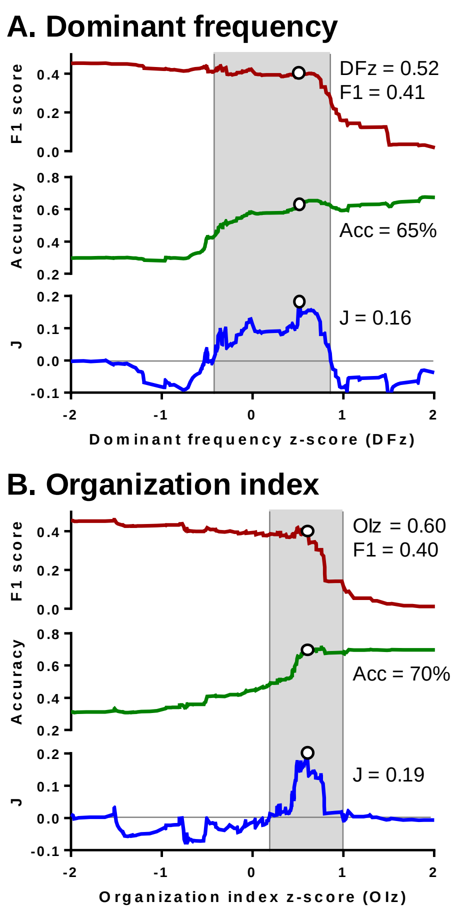

Figure 2. Informedness (J), accuracy (Acc) and F1 scores for different thresholds testing the individual classifications for DF (A) and OI (B). The white dots represent optimal thresholds. The grey regions highlight the region of interest for J>0.

3.2. DF and OI Logical Operator

Figure 3 illustrates the classification performance for the logical operator combining DFz and OI z (AND-logic). The best classification was achieved at DFz = -0.52 and OIz = 0.49 (J = 0.23, Acc = 71%, F1 = 0.43), with a correlation between predicted and true classes of 23%.

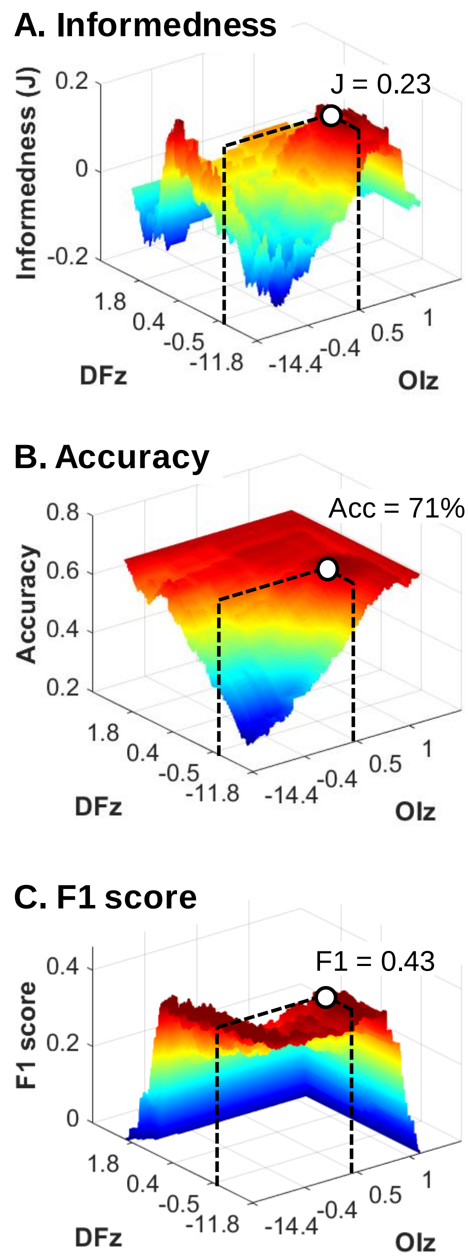

Figure 3. Informedness (A), accuracy (B) and F1 scores (C) for different thresholds testing the classifications for the logical operator combining DF and OI (AND-logic). The white dots represent optimal thresholds.

4. Discussion and Conclusions

We have previously used DF and OI to assess the impact of PVI on atrial substrate during persAF. We have shown that DF is significantly affected by PVI, while OI is overall unaffected [15]. In the present work, we are proposing a logical operator that combines the two frequency domain metrics for a more complete characterization of persAF substrate [7]. Additionally, we propose thresholds to both DF and OI that are adaptive to patient-specific characteristics through the calculation of z-scores.

Although the metrics have been assessed considering only AFCL changes before and after ablating each atrial sites, this represents the most important electrophysiological information consisting of a clinical 'ground truth' for AF substrate, which supports the relevance of our findings [16]. Accordingly, additional information such as anatomical sites and/or ranking of ablated sites would not provide additional data for the validation of the proposed method.

Interestingly, although the best classification performance was found with high OIz (0.49) and relatively low DFz (-0.52), a second peak performance was found at low OIz (-1.5) and high DFz (0.64) (Figure 3A). The first peak might represent highly organized EGMs. The second peak could suggest fractionated EGMs with very fast activation rates. Both regions, however, suggest combined thresholds efficient at discriminating atrial locations where ablation resulted in AF organization, illustrating the complex underlying pathophysiology of the arrhythmia and the importance of using both metrics to characterize persAF.

While DF and OI could be used individually to guide ablation, their combination might help in the identification of patient-specific AF substrate characterized by organized, fast activation rates to better guide ablation in future clinical studies.

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