Termination of Atrial Fibrillation by Catheter Ablation can be Successfully Predicted from Baseline ECG

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Abstract

Several organization indices have been used to predict the outcome of stepwise catheter ablation (step-CA) in long-standing persistent atrial fibrillation (LS-pAF), however with limited success. Our study aims at developing innovative indices from baseline (BL) ECG (i.e before ablation) in order to predict the procedure outcome and the site of AF termination (AF-term) by step-CA. We report an adaptive method for tracking AF-term based on indices characterizing the relationship between harmonic components of atrial activity from the ECG. Our preliminary results suggest that adaptive measures of AF organization computed at BL perform better than classical indices for identifying patients whose AF will terminate during ablation within the left atrium only. These findings are indicative of a higher baseline organization in these patients.

1. Introduction

Atrial fibrillation (AF), the most common clinical arrhythmia, is associated with an increased risk of morbidity and mortality. Most AF triggers are located within the pulmonary veins (PV) and can be isolated by catheter ablation (CA)[1]. Sites with continuous high frequencies activities, described as complex fractionated electrograms (CFAEs [2]), and regions showing structural discontinuities in the left atrium (LA) are believed to be involved in AF maintenance [2]. CFAEs ablation throughout the atria could restore sinus rhythm (SR) in long-standing persistent AF (LS-pAF). Others reported the incremental benefit of linear ablations during LS-pAF CA over PV isolation (PVI) [3], and of stepwise CA (step-CA) on the AF organization (AF-org). The success rate of step-CA, however, appears limited as the organization and the amount of additional right atrium (RA) ablation required to achieve AF termination (AF-term) remain unknown. There is a strong interest in predicting procedural outcome from baseline ECG, and whether additional RA ablation is required for AF-term.

Our study is aimed at 1) developing innovative signal processing indices based on the surface ECG to quantify the level of AF-org, and 2) identifying patients in whom LS-pAF can be terminated by ablation within the LA.

2. Methods

2.1. Patients and data acquisition

Electrophysiological study. All patients had effective anticoagulation therapy for > 1 month. All antiarrhythmic drugs, except amiodarone and beta-blockers, were discontinued for ≥ 5 half-lives before the procedure which was performed under general anesthesia. A 3.5 mm cooled-tip ablation catheter was introduced via the right femoral vein. Chest lead V_6 was placed in the back (V_{6b}) of the patients to improve the recording of the antero-posterior activity of the atria [4]. Surface ECG was continuously recorded for off-line analysis at 2-kHz sampling rate (Axiom Sensis XP, Siemens). A database was constructed containing on average 11 ± 3 min of baseline recording per patient, segmented in epochs of 10-sec duration.

Ablation protocol. Fig. 1 describes the step-CA protocol which consisted in PVI, followed by CFAEs and LA linear ablation (roof and mitral isthmus). RA CFAEs and cavotricuspid isthmus linear ablation were performed if AF persisted. At the end of the procedure, the effectiveness of PVI and bidirectional conduction blocks across the lines was checked and completed when needed.

Procedural endpoint. The study endpoint was reached when AF-term into SR or AT. Non AF-term were cardioverted electrically.

Patient population. The study group consisted in 17 consecutive male patients with LS-pAF (59 ± 5 years, AF duration 7 ± 5 years that was sustained for 21 ± 13 months before ablation, and resistant to pharmacological and electrical cardioversion). Based on the clinical outcome of the procedure, the study population was divided into 3 groups:

- *Group 1: left terminated (LT).* Patients in whom AF was terminated into SR/AT during LA ablation (N = 11).

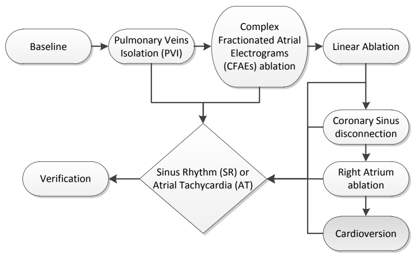

Figure 1. Step-CA ablation protocol.

- *Group 2: right terminated (RT).* Patients in whom AF was terminated into SR/AT during RA ablation (N = 2).
- *Group 3: not terminated (NT).* Patients in whom step-CA failed to terminate AF. SR was restored by electrical cardioversion at the end of the procedure (N = 4).

2.2. Signal processing

The ECG signals were downsampled to 50 Hz, as it has been shown that atrial rate rarely goes above 10 Hz [5].

Ventricular activity subtraction. QRS complexes were canceled from 12-lead ECG recordings using the single-beat method [6].

Frequency analysis. The organization index (OI) was computed as the ratio of the area of the dominant peak and its harmonic to the total area of the magnitude spectrum [7]. The first approach for characterizing AF using phase information was proposed in [8], where the fundamental and harmonic components of the largest peak were extracted using linear, time-invariant bandpass filters. Phase estimates were computed on a non-overlapping block-by-block basis. The phase relationship between the fundamental and the m^{th} harmonic was computed by subtracting the estimate of the fundamental from the estimated harmonic phase. Of note, for a perfectly regular oscillation, the harmonic frequencies are exact multiples of the fundamental one, while for irregular oscillations the expected harmonics largely deviate from the actual ones. If the filter is too narrow, the oscillations may escape from the filter passband and if the filter is too large, the phase estimates may become unreliable. Hence, a compromise must be made when setting the filter bandwidth, whose reliability may be affected by the large temporal variations of AF waveforms. We chose to circumvent this limitation by using adaptive bandpass filters.

The harmonic frequency tracking algorithm presented in this article is an extension of the single frequency tracker (SFT) we proposed previously [9, 10]. The adaptive algorithm is presented within the complex-valued signal framework. Reverting to real-valued data is always possible since the real part of the analytic representation is the original signal itself. In this article, the 1st harmonic component is considered to be the fundamental component.

Harmonic Frequency Tracking

In the SFT, the output signal, $y[n]$, is obtained by filtering the input signal $x[n]$ with a time-varying band-pass filter with transfer function:

$$H(z;\omega[n]) = \frac{1-\beta}{1-\beta e^{j\omega[n]}z^{-1}}. \quad (1)$$

The parameter $0 \ll \beta < 1$ controls the bandwidth and $\omega[n]$ is the current estimate of the instantaneous frequency that determines the central frequency of the filter. This filter has unit gain and zero phase at $\omega[n]$. The adaptive mechanism is based on the complex discrete oscillator equation,

$$c[n] = e^{j\omega_0}c[n-1], \quad (2)$$

which is satisfied for any cisoid at frequency ω_0. The estimation of the instantaneous frequency for the filtered signal $y[n]$ is performed by minimizing the cost function:

$$J[n] = \mathrm{E}\left\{\left|y[n] - e^{j\omega[n+1]}y[n-1]\right|^2\right\}. \quad (3)$$

A tractable optimal solution is obtained by replacing the expectation with exponentially weighted average [11] which leads to the update:

$$Q[n] = \delta Q[n-1] + (1-\delta)y[n]\bar{y}[n-1], \quad (4)$$
$$\omega[n+1] = \arg\{Q[n]\}, \quad (5)$$

where $0 \ll \delta < 1$ is a forgetting factor and the upper bar denotes the complex conjugate. The SFT is extended for extracting fundamental/harmonics by using one time-varying band-pass filter (1) for each harmonic component. An adaptive mechanism estimates the fundamental frequency from all the filtered components with a weighting procedure. The structure of the harmonic frequency tracker (HFT) is shown in Fig. 2. The input signal is composed of K cisoids with harmonic frequencies embedded with noise. Each harmonic component, $y_k[n]$, is extracted with a band-pass filter whose central frequency is an integer multiple of the current estimate of the fundamental frequency, $k\cdot\omega[n]$, $k = 1, 2, \ldots, K$. An instantaneous estimate of the fundamental frequency is obtained for each extracted component with the same approach as in the SFT:

$$Q_k[n] = \delta Q_k[n-1] + (1-\delta)y_k[n]\bar{y}_k[n-1], \quad (6)$$
$$\omega_k[n+1] = \arg\{Q_k[n]\}/k, \quad (7)$$

for $k = 1, 2, \ldots, K$. All the estimates are weighted in order to obtain a global value of the instantaneous fundamental frequency. This weighting procedure favors the components for which the discrete oscillator equation (2) is best satisfied [12]. The weights are computed by dividing an estimate of the band-pass filter output variance by an estimate of the cost function (3) yielding a scale-independent

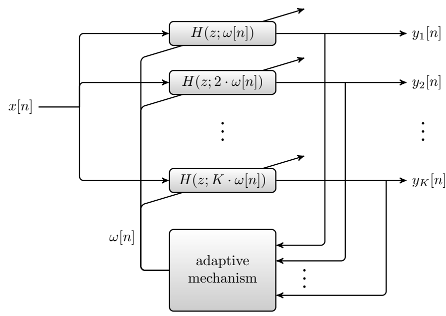

Figure 2. Structure of the harmonic frequency tracking algorithm: $x[n]$ is the input signal, $y_k[n]$ are the filtered output signals, and $\omega[n]$ is the estimated fundamental instantaneous frequency.

scheme. The cost function and variance instantaneous estimates are computed with exponentially weighted averages:

$$\hat{J}_k[n] = \delta\hat{J}_k[n-1] + (1-\delta)\big|y_k[n] - e^{jk\omega[n]}y_k[n-1]\big|^2,$$
$$\hat{S}_k[n] = \delta\hat{S}_k[n-1] + (1-\delta)\big|y_k[n]\big|^2,$$

for $k = 1, 2, \ldots, K$, where δ is the same forgetting factor as the one used in (4). The weights are defined as follows,

$$W_k[n] = \frac{\hat{S}_k[n]/\hat{J}_k[n]}{\sum_{l=1}^{K}\hat{S}_l[n]/\hat{J}_l[n]}, \tag{8}$$

for $k = 1, 2, \ldots, K$. Finally, the global estimate of the instantaneous fundamental frequency is given by

$$\omega[n+1] = \sum_{k=1}^{K} W_k[n]\omega_k[n]. \tag{9}$$

Measurements of organization

AF cycle length (AFCL). After QRST cancellation [6], spectra based on 10-sec epochs from ECG chest leads were computed with Welch's method. The dominant frequency (DF) was estimated as the frequency of the largest peak between 3 and 15 Hz in the power spectral density estimated of each lead. ECG AFCL was then computed as the inverse of the DF. Mean ECG AFCL was calculated for each patient within 10-sec epochs for chest leads V_1 and V_{6b}.

Organization index (OI). The OI [7] is computed as the ratio of the power in a 1 Hz band centered on the dominant peak to the total power in the spectrum.

Adaptive Organization Index (AOI). The AOI was computed as the ratio between the power of the extracted components and the total power of the signal. The AOI quantifies the amount of oscillations within AF waves.

Phase Difference (PD). The difference between the phases of two oscillations is an indicator of their synchronization. The PD between the 1st harmonic and higher harmonic components extracted with HFT was used as a measure of complexity. The 2nd harmonic phase component was divided by 2. After computation of the PD, its slope was locally estimated by fitting a polynomial of degree one to sliding windows of odd length $L = 101$. The variance of the local slope of the PD was computed in order to assess the complexity of the underlying AF signal. Small PD values indicate more organized oscillations and a higher spatial AF-org.

3. Results

Measures of organization. Fig. 3 displays an example of atrial activity from lead V_1 after QRST cancellation (top) and the resulting AOI (middle) and PD (bottom) parameters. Note the progressive organization (red dashed square) of the ECG signal reflected as a gradual increase in AOI

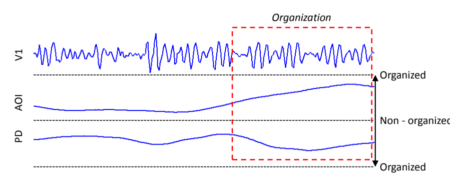

Figure 3. Example of OI parameters. Top: V_1 devoid of ventricular activity. Middle: AOI. Bottom: PD.

Clinical results. Fig. 4 reports the box plot of the organization indices for chest leads V_1 (panel A) and V_{6b} (panel B) that best discriminated LT from RT and NT patients. Only significant results/leads are shown.

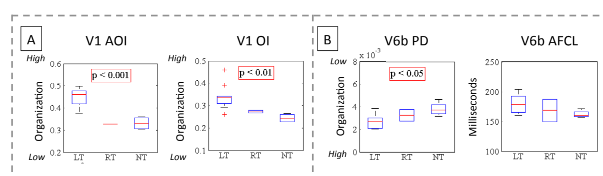

Figure 4. Distribution of the different organization indices. Panel A: chest lead V_1. Panel B: dorsal lead V_{6b}.

Importantly, AOI and PD improved the separation between groups compared to AFCL and OI. The OI from lead V_1 revealed a higher AF-org for the LT group, with some overlap with the RT group as well, while the AOI improved the separation.

Interestingly, the PD distribution was significantly different between the three groups when measured on lead V_{6b}. A significant gradient of AF-org on V_{6b} is observed from LT, being the most organized, to RT showing an intermediate pattern and to NT, the least organized.

4. Discussion and conclusion

Previous studies have reported that RA activity during AF is a major contributor to the fibrillatory waves (f-waves) recorded from chest lead V_1 [13], while posterior leads best correlated with LA activity [4], suggesting that RA and LA contributions during AF can be independently determined using specific regions of the thorax.

Non-invasive characterization of AF dynamics can be performed from 12-lead ECG after QRS cancellation [6]. AFCL measured from bipolar intracardiac recordings is commonly used to assess AF-org during step-CA [3, 13]. It has been shown that patients with longer baseline ECG AFCL have a better outcome compared to patients with shorter AFCL after single LA ablation [13]. In LS-pAF, some patients may benefit from bi-atrial ablation [14]. Rostock et al. found that the baseline intracardiac AFCL was the strongest predictor of procedural success, but the authors did not report whether this parameter helped to distinct single from bi-atrial AF-term. [14].

Several methods based on AF harmonics components have been developed for the assessment of AF-org [7, 8]. It has been shown that the intracardiac OI was more predictive of AF-term than the mean DF [15]. Another approach characterized AF based on phase information [8]. Using linear, time-invariant bandpass filters, the atrial activity was divided into fundamental and harmonic components from which a phase relationship was extracted. This approach, however, is restricted to relatively organized AF; for disorganized AF, the estimate may become unreliable.

In pers-AF, the f-waves may strongly vary over time, which renders both methods unreliable for the tracking of rapid variations, [**?**, 8]. Our algorithm is able to extract two parameters that are complementary: the AOI as an estimation of the temporal evolution of AF oscillations and the PD as a quantification of AF regularity between the fundamental and harmonic components. Patients showing at baseline a more regular AF oscillations on lead V_1 as well as a higher regularity between fundamental and harmonic components on a posterior lead are more likely to experience AF-term during ablation of the LA only. Conversely, patients for whom bi-atrial ablation was necessary present a lower AF-org at baseline.

The quantification of the coupling between the fundamental and its first harmonic of AF activity measured from the ECG is an important feature for characterizing AF-org and for discerning patients who successfully need single atrial from bi-atrial ablation. Our findings are indicative of a higher baseline AF-org in LT patients, which could be used to select candidates for AF-term by step-CA.

Acknowledgements

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