A New Method for ECG Tracking of Persistent Atrial Fibrillation Termination during Stepwise Ablation

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Abstract

Stepwise radiofrequency catheter ablation (step-CA) has become the treatment of choice for the restoration of sinus rhythm (SR) in patients with long-standing persistent atrial fibrillation (pers-AF). Its success rate appears limited as the amount of ablation to achieve long term SR is unknown. Multiple organization indexes (OIs) have been previously developed to track the organization of AF during step-CA, however, with limited success. We report an adaptive method for tracking AF termination (AF-term) based on OIs characterizing the relationship between harmonic components of atrial activity from the surface ECG of AF activity. By computing their relative evolution during the last two steps preceding AF-term, we found that the performance of our OIs was superior to classical indices to track the efficiency of step-CA "en route" to AF-term. Our preliminary results suggest that the gradual synchronization between the fundamental and its first harmonic of AF activity appears as a promising parameter for predicting AF-term during step-CA.

1. Introduction

Atrial fibrillation (AF), the most common clinical arrhythmia, is associated with an increased risk of morbidity and mortality. Stepwise radiofrequency catheter ablation (step-CA) has become the treatment of choice for the restoration of sinus rhythm (SR) in patients with persistent AF (pers-AF) [1]. Its success rate, however, appears limited as the amount of ablation to achieve long-term SR is unknown. Non-invasive characterization of AF dynamics can be performed from 12-lead ECG after QRS cancellation ([2]). AF cycle length (AFCL) measured from bipolar intracardiac recordings has been commonly used to assess AF organization during step-CA ([3, 4]). AFCL can also be computed non-invasively by analyzing the main frequency of the ECG f-waves [5]. Importantly, prolongation of AFCL has been observed during step-CA to predict procedural AF termination (AF-term) [3, 4]. However, in patients with pers-AF in whom AF continued despite pulmonary veins isolation (PVI), AFCL did not change during step-CA, while other indices based on large dipoles did [6]. We hypothesize that new organization indices (OIs) based on a global assessment of AF from the surface ECG improves the tracking of AF organization during step-CA as compared to intracardiac AFCL in patients with pers-AF.

2. Methods

2.1. Patients and data acquisition

Patient population. The study group consisted of 5 consecutive patients with pers-AF (age 60 ± 4 years, AF duration 16 ± 10 months) who successfully underwent step-CA. Pers-AF was defined as continuous AF lasting longer than 4 months, resistant to either pharmacological or electrical cardioversion.

Electrophysiological study. All patients had effective anticoagulation therapy for > 1 month. All antiarrhythmic drugs, with the exception of amiodarone and beta-blockers, were discontinued 5 half-lives before the procedure. The procedure was performed in general anesthesia. The following catheters were introduced via the right femoral vein: 1) a 3.5 mm cooled-tip ablation catheter for mapping and ablation, and 2) a quadripolar catheter into the right atrial appendage (RAA) for continuous monitoring. Surface ECG and endocardial electrograms (EGMs) were continuously monitored and recorded for off-line analysis at 2-kHz sampling rate (Axiom Sensis XP, Siemens).

Ablation protocol. Step-CA (Fig. 1) consisted in PVI, defragmentation of complex fractionated atrial EGMs (CFAEs), left atrium linear ablations, epicardial coronary sinus disconnection, ablation of right atrium CFAEs and linear ablation of the cavotricuspid isthmus.

After restoration of SR, verification of conduction block (PVI and lines) was performed, and additional ablations

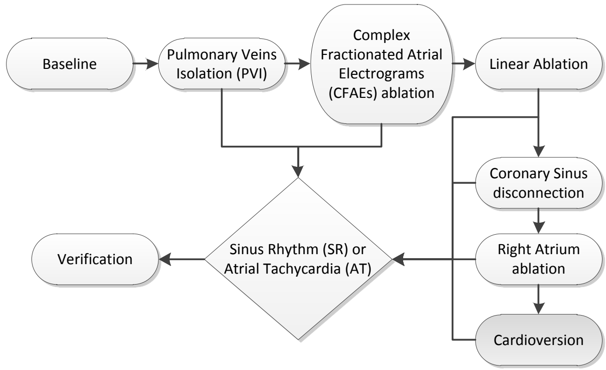

Figure 1. Step-CA ablation protocol.

were delivered to achieve a complete block when needed.

Procedural end point. The study endpoint was reached when AF was terminated into SR or atrial tachycardia. Non terminated AF were cardioverted electrically.

2.2. Signal processing

The ECG signals were downsampled to 50 Hz, as previous studies have shown that the atrial rate rarely goes above 10 Hz [7].

Ventricular activity subtraction. QRS complexes were canceled from 12-lead ECG recordings using the single-beat method [2].

Frequency analysis. The OI first introduced by Everett et al. was computed as the ratio of the area of the dominant peak and its harmonic to the total area of the magnitude spectrum ([8]). The first approach for characterizing AF using phase information was proposed in [9], where the fundamental frequency f_0 was determined by locating the largest peak in the interval from 3 to 12 Hz, and its fundamental and harmonic components extracted using linear, time-invariant bandpass filters centered around the identified spectral peaks. 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. But if the filter is too narrow, the oscillations may escape from the filter passband. If the filter is too large, the phase estimates 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 [10, 11]. 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.

2.2.1. 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:

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

The parameter β $(0 \ll \beta < 1)$ 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,

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

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 following cost function:

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

A tractable optimal solution is obtained by replacing the expectation with exponentially weighted average [12] which leads to the update:

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

where δ $(0 \ll \delta < 1)$ is a forgetting factor and the upper bar denotes the complex conjugate.

The extension of the SFT for extracting fundamental/harmonics consists in 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. In this case, 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, $k \cdot \omega[n]$, $k = 1, 2, \ldots, K$.

First, an instantaneous estimate of the fundamental frequency is obtained for each extracted component with the

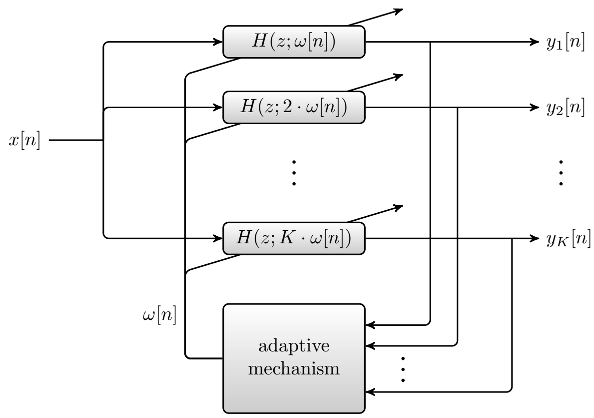

Figure 2. Structure of the harmonic frequency tracking algorithm: $x[n]$ is the input signal, $y_k[n]$ are the filtered output signals, and $\omega[n]$ is the estimated fundamental instantaneous frequency.

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 $k = 1, 2, \ldots, K$. Then, all the estimates are weighted in order to obtain a global estimate of the instantaneous fundamental frequency. This weighting procedure favors the components for which the discrete oscillator equation (2) is best satisfied [13]. The weights are computed by dividing an estimate of the band-pass filter output variance by an estimate of the cost function (3) so as to yield a scale-independent scheme. The cost function and variance instantaneous estimates are computed with exponentially weighted averages:

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

$$\hat{S}_k[n] = \delta \hat{S}_k[n-1] + (1-\delta)\left|y_k[n]\right|^2,$$

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,

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

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

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

2.2.2. Measurements of organization

Adaptive organization index. An adaptive OI (AOI) was computed as the ratio between the power of the extracted components and the total power of the signal. This complexity measure quantifies the amount of oscillations in AF waves.

Phase difference. The difference between the phases of two oscillations is an indicator of their synchronization. In this study, we used the phase difference (PD) between the 1^{st} harmonic and higher harmonic components extracted with HFT as a measure of complexity. The phase of the 2^{nd} harmonic component was divided by 2 to ensure that both quantities were comparable. After computation of the phase difference, 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 phase difference was computed in order to assess the complexity of the underlying AF signal. Small values of this parameter indicate more organized oscillations, and thus a higher spatial organization.

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 of the ECG signal reflected as a gradual increase in AOI and decrease in PD.

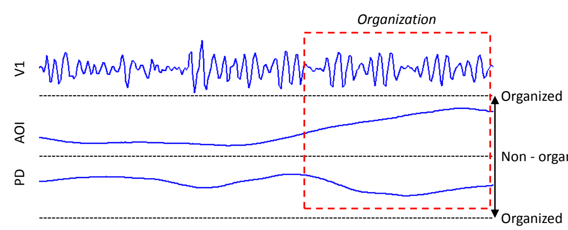

Figure 3. Example of OI parameters. Top: V_1 devoid of ventricular activity. Middle: AOI. Bottom: PD.

Clinical results. The evolution in percentage during the last two steps preceding AF-term of the mean AOI and PD were computed and compared to that of mean RAA AFCL and OI [8]. Fig. 4 shows the statistics obtained from ECG lead V_1. PD appeared more sensitive than the other indices for the tracking of AF organization "en route" to AF-term. The comparison between the last two steps preceding AF-term showed that PD decreased by $38 \pm 21\%$, AOI increased by $16 \pm 15\%$ and OI by $15 \pm 14\%$, while RAA AFCL did not change $(4.8 \pm 5.4\%)$.

4. Discussion and conclusions

Multiple methods based on AF harmonic components have been developed for the assessment of AF complexity ([8, 9]). The intracardiac OI first introduced by Everett et al. [8] has been used to optimize the success of AF cardioversion. Takahashi et al. [14] recently showed that

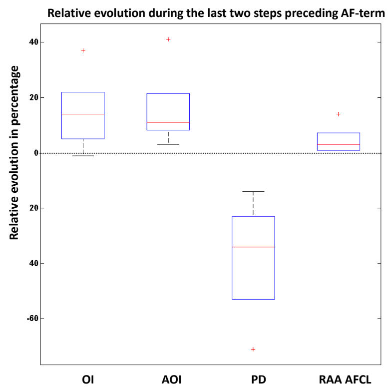

Figure 4. Boxplot of the relative evolution in percentage .

the intracardiac OI was more predictive of AF-term than the mean dominant frequency. Another approach characterized AF based on phase information [9]. 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 fibrillatory waveforms may strongly vary over time, which renders both methods unreliable for the tracking of rapid variations, [9, 14]. 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. In our study, both AOI and PD successfully estimated the AF dynamics from the surface ECG and efficiently tracked AF organization during step-CA. Importantly, both PD and AOI improved the short term prediction of AF-term in contrast to intracardiac AFCL. These results are in line with Forclaz et al. [6] who showed that, after exclusion of patients who converted into SR during PVI, AFCL did not predict AF-term , while global indices based on large dipoles did. Our results corroborate these findings as our new indices are based on the surface ECG and rely on a global characterization of AF complexity.

In conclusion, our preliminary results suggest that the gradual coupling between the fundamental and its first harmonic of AF activity is an important feature of AF organization "en route" to AF-term by step-CA. These new indexes might help to titrate the amount of ablation required to restore long term SR, but deserved clinical validation on a broader population.

Acknowledgments

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