Tracking of Stepwise Ablation of Persistent Atrial Fibrillation using Synchronization of nearby Electrogams

A Buttu[1], S Volorio[1], A Forclaz[2], P Pascale[2], SM Narayan[3], E Pruvot[2], JM Vesin[1]

[1]Applied Signal Processing Group, Swiss Federal Institute of Technology, Lausanne, Switzerland
[2]Department of Cardiology, University Hospital Center Vaudois, Lausanne, Switzerland
[3]University of California, San Diego, USA

Abstract

Intracardiac organization indices such as atrial fibrillation (AF) cycle length (AFCL) have been used to track the efficiency of stepwise catheter ablation (step-CA) of long-standing persistent AF (pers-AF), however, with limited success. The timing between nearby bipolar intracardiac electrograms (EGMs) reflects the spatial dynamics of wavelets during AF. The extent of synchronization between EGMs is an indirect measure of AF spatial organization. The synchronization between nearby EGMs during step-CA of pers-AF was evaluated using new indices based on the cross-correlation. The first one (spar(W)) quantifies the sparseness of the cross-correlation of local activation times. The second one (OI(W)) reflects the local concentration around the largest peak of the cross-correlation. By computing their relative evolution during step-CA until AF termination (AF-term), we found that OI(W) appeared superior to AFCL and spar(W) to track the effect of step-CA "en route" to AF-term.

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. Multiple parameters were developed to evaluate the dynamics of AF from intracardiac electrograms (EGMs) [2, 3]. AF cycle length (AFCL) measured from bipolar intracardiac EGMs has been recently used to assess AF organization during step-CA [4, 5]. Importantly, during step-CA, prolongation of AFCL predicted procedural AF termination (AF-term) [5]. The synchronization between nearby EGMs reflects the spatial coherence of activation wavefronts, and indirectly the number of AF wavelets [6]. The extent of spatial correlation of activation wavefronts during AF was first shown using the cross-correlation between multiple EGMs; its correlation decreased exponentially as a function of the distance between electrodes [7]. Recently, an index based on the corrected cross-conditional entropy evaluated the absence, but not the strength of the coupling between pairs of EGMs [8].

Our study is aimed at analyzing the synchronization between nearby bipolar recordings to assess the extent of spatial organization during step-CA. We briefly describe our method, and compare its performance to AFCL for the tracking of AF organization during step-CA "en route" to AF-term.

2. Methods

2.1. Patients and data acquisition

Patient population. The study group consisted of 6 consecutive patients with pers-AF (age 61 ± 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. Endocardial 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 pulmonary veins isolation (PVI), defragmentation of complex fractionated atrial EGMs (CFAEs), left atrium linear abla-

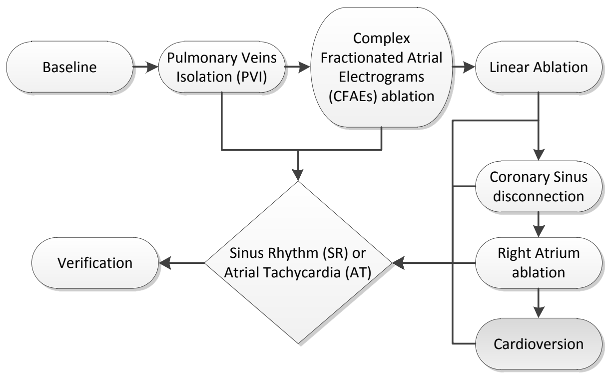

Figure 1. Step-CA ablation protocol.

tions, 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 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 (AT). Non terminated AF were cardioverted electrically.

2.2. Synchronization of bipolar electrograms

Bipolar EGMs were acquired from the proximal and distal dipoles of the quadripolar catheter placed into the RAA. The method detailed below is illustrated in Fig. 2. Signals were acquired at baseline during 10-sec.

1. **Local activation time (LAT).** LAT was defined as the maximum positive peak from each activation wave. Maximum positive peaks were detected using sliding 150 ms windows, and false detections were removed using temporal and amplitude information thresholding. LAT detection was performed separately on the distal (Fig. 2 top, cyan squares) and proximal (red circles) EGMs. Series of LATs were transformed in trains of impulsions on which the cross-correlation was computed.

2. **Cross-correlation of LATs.** The cross-correlation (W) between the distal and proximal trains of impulsions was computed. When the second spike train is a delayed version of the first one, the cross-correlation contains a large peak at a lag corresponding to the time delay between the two EGMs. This would correspond to the case where the two electrodes are excited by a unique periodic wavefront. For multiple wavefronts, the cross-correlation would present several peaks. The concentration of W thus reflects the local complexity of AF dynamics. In order to avoid the repetition of peaks due to the quasi periodic nature of the spike trains, the cross-correlation was only considered for lags between 0 and the mean AFCL.

2.3. Measurements of organization during AF

Two measurements of organization during AF were computed on W. The first one, spar(W), measures the sparseness of W. The notion of sparse coding refers to a framework for the representation of data vectors where most units take values close to zero while only a few take non-zero values. In this paper, we use a measure of sparseness presented in [9], which is based on the relationship between the L_1 norm and the L_2 norm:

$$spar(W) = \frac{\sqrt{N} - \left(\sum_{i=1}^{N} |w_i| / \sqrt{\sum_{i=1}^{N} w_i^2} \right)}{\sqrt{N} - 1} \qquad (1)$$

where N is the dimension of W. If the vector W contains a single-non zero element, spar(W) will be equal to 1, and to 0 if all components of W are equal.

The second measure of organization is similar to the organization index (OI) first introduced by Everett et al. and defined as the ratio of the area of the dominant peak and its harmonic to the total area of the magnitude spectrum [2]. The cross-correlation W was smoothed with a Hamming window of length 9 (Fig. 2 bottom, green function). The area around the largest peak was divided by the sum of the components of W. We assume that a low OI(W) value is indicative of a weak dominance of the largest peak, and thus of a weak LAT synchronization. High OI(W) value is theoretically indicative of a single sharp dominant peak and of a high coupling between LATs.

Fig. 2 shows a spar(W) value of 0.8 indicating a relatively good sparseness of W. Note that most elements of W are 0 whereas only a few take significant values. The value of OI(W) (0.3) gives an indication of the shape of this distribution around its dominant peak. Interestingly, OI(W) has a small value, suggesting that most of the LATs were detected far from the dominant peak.

3. Results

Clinical results. The relative evolution (in $\%$) of the mean spar(W), OI(W) and RAA AFCL was compared between PVI *vs* and baseline, CFAEs *vs* and PVI and the last two steps preceding AF-term. Fig. 3 shows the statistics obtained from the distal and proximal RAA dipoles.

Following PVI, spar(W) and AFCL showed minor changes, while OI(W) displayed positive and negative variations as compared to baseline. Following CFAEs ablation, spar(W) and AFCL did not change, while OI(W)

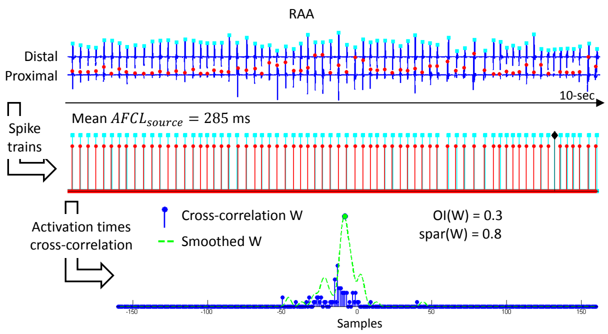

Figure 2. Method for synchronizing nearby bipolar EGMs. Top: distal and proximal bipolar EGMs acquired from the RAA. Cyan squares and red circles markers respectively indicate the LATs of the distal/proximal signals. Middle: distal and proximal train impulsions of LATs. The black diamond on the distal spike train corresponds to a LAT outside of the considered lags for the computation of the cross-correlation. Bottom: cross-correlation (blue, discrete sequence) and smoothed cross-correlation (green, dashed line).

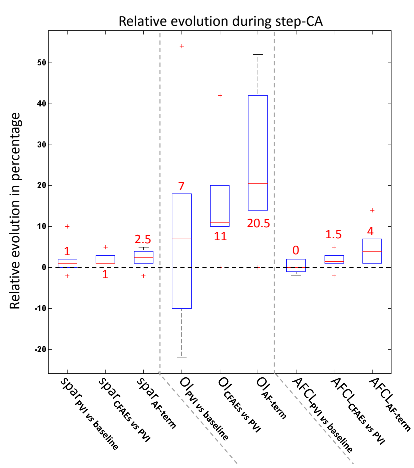

Figure 3. Boxplot of the relative evolution during step-CA. Median values are displayed.

showed significant variations that were only positive. Finally, OI(W) 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 OI(W) increased by $25 \pm 20\%$, while spar(W) and AFCL did not change ($2 \pm 2\%$ and $5 \pm 5\%$ respectively). Statistical comparisons were not performed due to the limited samples size.

4. Discussion

AF was originally considered as a disorganized process created by multiple random activation wavelets [10]. Using signal processing-based method, limited spatial correlation was observed during AF, that was decreasing exponentially as a function of the distance between electrodes [7]. Using an index based on a corrected cross-conditional entropy, Mainardi et al. developed a synchronization index that reliably characterized the absence, but not the strength of the coupling between pairs of adjacent EGMs [8]. In this study, we report new indices for quantifying the synchronization between pairs of nearby bipolar EGMs. The first one, spar(W), quantifies the sparseness of the cross-correlation vector. The second one, OI(W), is computed as the ratio between the area around the largest peak and the sum of the cross-correlation components. Our preliminary results show that OI(W) appears more sensitive than AFCL and spar(W) for estimating changes of AF dynamics during step-CA. Spar(W) reflects a global spread of the non-zero elements of the cross-correlation values and is therefore less sensitive to changes in the coupling of electrodes. OI(W) emphasizes the local concentration of non-zero values and shows greater variations. These results, however, must be corroborated with simulated data provided by a biophysical model of AF [11] in order to establish their significance.

5. Conclusions

In conclusion, indices based on the local distribution of time lags between nearby EGMs appear as promising parameters for tracking the organization during step-CA "en route" to AF-term and might help to titrate the amount of ablation required to restore long term SR. Theses methods, however, should be validated experimentally using computer simulations, but also on a larger population of ablated patients.

Acknowledgements

This study was supported by grant 205321_129876 from the Swiss National Foundation (SNF). The authors wish to thank Biosense Webster for their assistance.

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Address for correspondence:

Andrea Buttu
EPFL SCI STI JMV
ELD 234 (ELD building)
Station 11
1015 Lausanne - Switzerland.
E-mail address: andrea.buttu@epfl.ch