# Morphological Study of Intracardiac Signals as a New Tool to Track the Efficiency of Stepwise Ablation of Persistent Atrial Fibrillation

A Buttu[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, however with limited success. The morphology of AF activation waves reflects the underlying activation patterns. Its temporal evolution is a local organization indicator that could be potentially used for tracking the efficiency of step-CA. We report a new method for characterizing the structure of the temporal evolution of activation wave morphology. Using recurrence plots, novel organization indices are proposed. By computing their relative evolution during the first step of ablation vs baseline, we found that these new parameters are superior to AFCL to track the effect of step-CA "en route" to AF termination.*

## 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) [2–4]. AF cycle length (AFCL) measured from bipolar intracardiac EGMs has been commonly used to assess AF organization during step-CA [5, 6]. Prolongation of AFCL has been observed during step-CA to predict procedural AF termination (AF-term). The morphology of bipolar AF activation waves reflects the local occurrence of various specific activation patterns. A method for quantifying the amount of organization from single bipolar EGMs during AF has been developed by Faes et al., in which a regularity index estimated the morphological similarity of intracardiac activation waves by computing an average of their thresholded pairwise distances over 4-sec epochs [3]. This regularity index, however, did not assess the temporal evolution of activation wave forms within this time frame.

Our study is aimed at analyzing the structural and temporal evolution of AF EGMs using recurrence plots (RPs). We briefly describe how these indices are computed, and compare their performance to AFCL in measuring 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 5 consecutive patients with pers-AF (age $60 \pm 4$ years, AF duration $16 \pm 10$ 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 electrograms (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

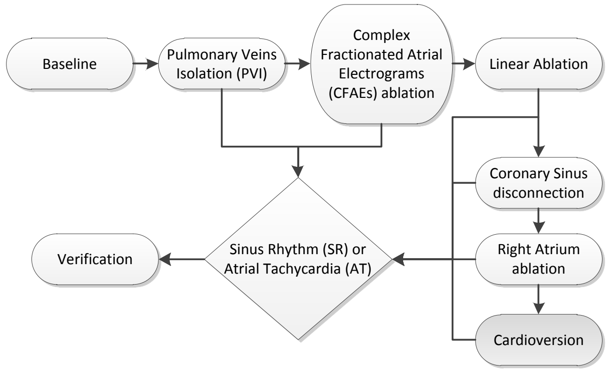


Figure 1. Step-CA ablation protocol.

(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. Activation times detection and alignment

Local activation waves were extracted from the bipolar recordings of 10-sec duration by detecting their maximum positive peaks using sliding windows of 150 ms. False detections were removed using temporal and amplitude thresholding. A window of 180 ms duration was centered around each maximum positive peak in order to extract the corresponding activation wave.

Local activation times were estimated by computing the activation wave barycenters [7]. A barycenter was defined as the sample dividing the local area of the modulus of the signal into two equal parts. A non-causal, finite impulse response, 90 coefficients filter was applied to the absolute value of each activation wave $w$:

$$s_w = \sum_{i=0}^{44} |w(t-i)| + \sum_{i=1}^{45} |w(t+i)| \qquad (1)$$

This filter performs a derivation followed by a low-pass operation. The barycenter $B_w$ was defined as the positive zero crossing of $s_w$. Finally, all activation waves were normalized and aligned with their barycenter.

## 2.3. Measurements of organization

**Distance.** Let $w_i$ and $w_j$ be two activation waves normalized and aligned on their barycenter for comparison. Their distance (or morphological dissimilarity [7]) is defined by:

$$d(w_i, w_j) = \arccos(w_i \cdot w_j) \qquad (2)$$

Low values of $d$ indicate a high similarity between the activation waves $w_i$ and $w_j$.

**Recurrence plots.** RP analysis has been introduced to graphically display recurring patterns in experimental time series [8]. Later on, RP-based parameters were proposed to quantify pattern recurrences [9].

For a time series $x_i, i = 1, \cdots, N$, a RP is a $N \times N$ matrix, the element $(i, j)$ of which is the thresholded distance between $x_i$ and $x_j$:

$$R_{i,j}(\delta) = \begin{cases} 1 & : \|x_i - x_j\| \leq \delta \\ 0 & : \text{otherwise} \end{cases}, \qquad (3)$$

$$x_i \in \Re \;\; i, j = 1, \ldots, N$$

where $\delta$ is the threshold distance. When the RP is displayed, dots (recurrent points) correspond to pairs of time series elements that are close. Line segments parallel to the main diagonal correspond to similar sequences in time series. The following parameters are commonly used to quantify these recurrence features:

- Recurrence (REC): the proportion of recurrent points that measures the overall similarity between time series elements. It is equivalent to the regularity index in [3].
- Percentage of determinism (DET): measures the percentage of recurrent points forming line segments which are parallel to the main diagonal (the length of the lines being at least 2). Erratic time series give rise to no or very short segments, and thus low values of DET. Regular (such as quasi-periodic) time series give rise to longer segments and less isolated recurrent points, and, as a result, high values of DET.
- Entropy (ENT): Shannon entropy of the length distribution of segments parallel to the main diagonal. For irregular time series, the length distribution will be concentrated around the small values, resulting in small values of ENT.

In our study, $N$ was the number of activation waves, and the distance between elements was that defined by equation (2). The threshold $\delta$ was set empirically to $\pi/7$.

Fig. 2 illustrates the construction of an RP during AF from a 40-sec duration EGM acquired at baseline from the RAA catheter, and the corresponding RP parameters. The value of REC indicates that, on average, 29% of activation waves are morphologically similar. Interestingly, the value of DET suggests that more than half (54%) of these 29% are temporally forming a deterministic structure in activation waves temporal evolution.

**Significance of the RP parameters.** The RP parameters were used as organization indices (OIs), and their statistical significance was assessed using surrogate data and a one-sided rank-order test ($p < 0.05$) [10]. To test for the existence of a structure in the temporal evolution of activation waves morphology, surrogate time series were synthesized as random permutations of the original activation wave time series.

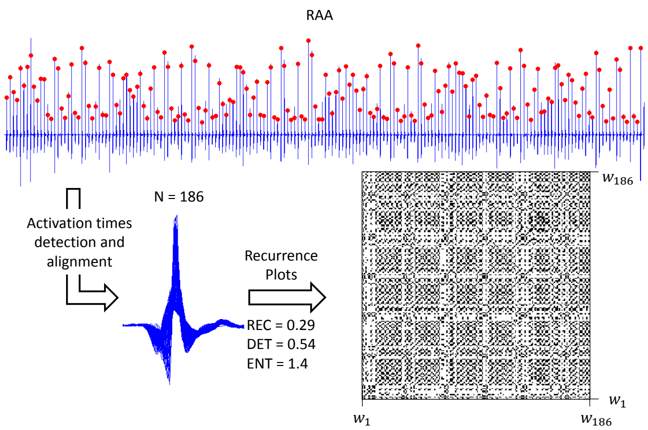


Figure 2. Example of a 40-sec signal acquired into the RAA (top) and EGM activation times (barycenters, red dots). Each activation wave was extracted and aligned (bottom left), and the corresponding RPs and parameters computed (bottom right). $w_i, i = 1, \cdots, N$, $N$: number of activation waves.

For a significance level set at $95\%$, the DET and ENT values obtained for the original time series should be larger than that for the 19 surrogate time series [10]. REC was not evaluated with surrogates as it is insensitive to temporal evolution.

## 3. Results

For each patient, a database was constructed containing 10-sec epochs in chronological order, but not necessarily consecutive as EGMs during ablation were discarded.

**Surrogate data.** Statistical significance of DET/ENT was observed on a large set of randomly selected files, indicating a deterministic structure in the temporal evolution of the morphology of the activation waves.

**Clinical results.** The RP parameters were compared to AFCL during step-CA until AF-term. Fig. 3 shows a representative example where the OIs were computed from the RAA bipolar EGMs. Each dot represents the mean value computed on a single 10-sec epoch. AF was terminated during CFAEs ablation (AT, red arrow). At baseline, the low mean REC value (0.25) suggested a weak morphological similarity and the low mean DET value a weak temporal organization (0.43). During PVI and CFAEs ablation, all RP parameters gradually increased, indicating a trend towards an increased similarity and temporal regularity of activation wavefronts. Importantly, AFCL did not change.

Finally, the relative evolution (in $\%$) of the mean RP parameters and AFCL were compared during PVI *vs* baseline conditions.

Fig. 4 shows relative changes in AFCL and RP parameters between baseline and PVI. Interestingly, AFCL did not change, while RP parameters estimated from the RAA revealed positive and negative variations after PVI suggestive of a greater sensitivity to the modification of the left atrial substrate by step-CA.

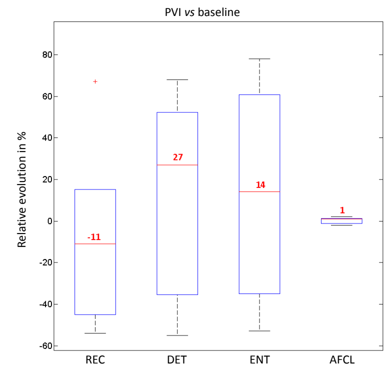


Figure 4. Boxplot of the relative evolution in percentage during PVI *vs* baseline.

## 4. Discussion and conclusions

AF was originally considered as a disorganized process created by multiple random activation wavelets [11]. Recently, using signal processing-based methods, some level of organization was identified [2] and demonstrated some correlation with the duration and severity of the underlying AF [2, 5, 6, 12]. The morphology of bipolar AF activation waves reflects the local occurrence of various specific activation patterns. Faes et al. introduced a regularity index which estimated the morphological similarity of intracardiac activation waves by computing an average of their thresholded distances over 4-sec epochs [3]. The temporal evolution within these 4-sec epochs, however, could not be evaluated. Our preliminary results extend these findings and show morphological similarity and determinism during AF within short time frames ($\approx$ 10 sec). Not only does our algorithm compute a regularity index (i.e. REC) similar to [3], but it also quantifies the deterministic structure of the temporal morphological evolution as reflected by the DET and ENT parameters. To our knowledge, this study is the first to show that modulation of the left atrial substrate by step-CA can induce structured morphological variations of activation waves within the RAA, while the AFCL remained unchanged. The pattern of changes (positive and negative), however, needs to be correlated with the outcome of the step-CA on a larger population. These measures appear as promising parameters to titrate the amount of ablation required to restore long term SR.

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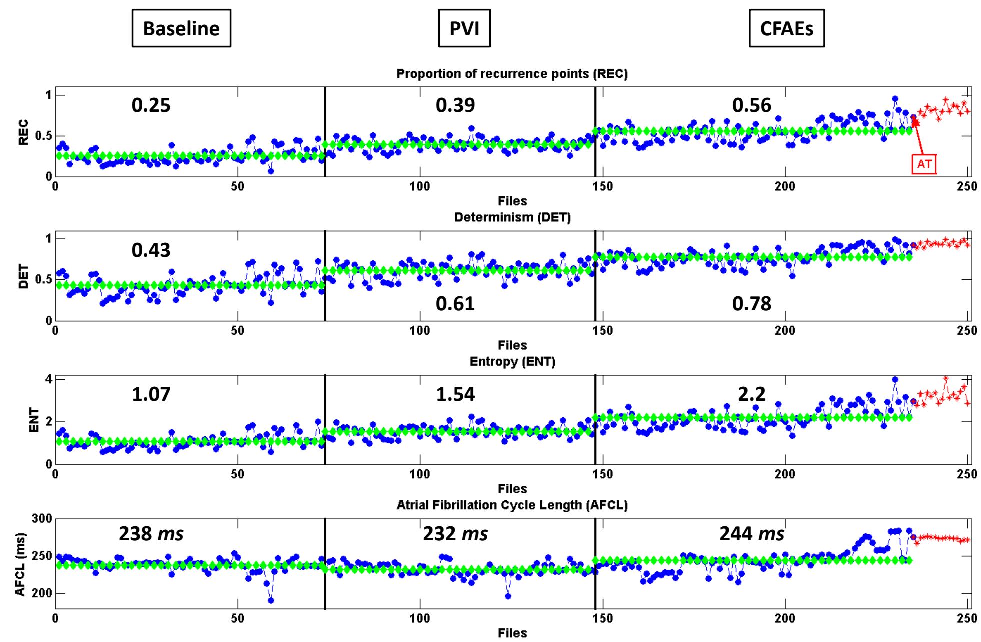


Figure 3. RP parameters during step-CA. AF terminated during CFAEs ablation. From top to bottom: REC, DET, ENT and AFCL. Green diamonds: mean values over each ablation step. Their values are also displayed. Red asterisks: AT. RP parameters, in particular DET and ENT, are more responsive to organization changes during PVI and CFAEs. Whereas AFCL is not.

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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