Catheter Ablation Outcome Prediction in Persistent Atrial Fibrillation Based on Spatio-Temporal Complexity Measures of the Surface ECG

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Abstract

Radiofrequency catheter ablation (CA) is increasingly employed to treat atrial fibrillation (AF), yet selection of patients who would actually benefit from this therapy still remains an open issue. The present work introduces some non-invasive quantitative parameters to discriminate between successful and failing CA procedures by exploiting the spatial diversity of the 12-lead surface ECG. They are based on the normalized mean square error (NMSE) between consecutive atrial activity ECG signal segments and their rank-n approximations determined by principal component analysis. As opposed to the single-lead approach of previous works, we consider NMSE values computed on more than one lead. One such multilead-based parameter is able to distinguish between successful and failing ablations before performing the procedure with AUC=0.86, p value=$7 \cdot 10^{-5}$. This study demonstrates that the proposed multilead parameters can effectively predict CA outcome and potentially contribute to more accurate patient selection strategies for this AF therapy.

1. Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia. Even though it is not considered life-threatening, highly effective and safe therapies are still lacking. Several theories have been proposed to explain the origin and evolution of AF, so as to cure it by means of a systematic procedural protocol. This condition has been classically considered as the result of interactions between multiple wandering atrial wavelets [1, 2]. On the other hand, pulmonary veins (PVs) is known to be an important source of spontaneous electrical activity initiating AF [3]. Radiofrequency catheter ablation (CA) is increasingly used for treating persistent AF. Nevertheless, AF dynamics and in-depth heart electrical activity during the procedure are not completely known and are still the topic of intense research. CA is differently performed in clinical centres, according to patient's conditions and surgeon's evaluation. It follows that its effectiveness in suppressing AF and avoiding its recurrence is not guaranteed for all patients. As a consequence, there is an emerging tendency to attempt an a priori selection of patients who will actually experience a successful procedure. Several parameters have been proposed as potential predictors of CA outcome, both extracted from endocardial recordings and surface ECG [4, 5]. The present study investigates whether the atrial activity spatio-temporal organization can be exploited to describe AF dynamics during ablation and extract useful information for patient selection. Complexity observed on the ECG is supposed to be directly correlated to the number and interactions of atrial wavefronts [6]. Presence and evolution of organization modifications can help to distinguish between successful and failing procedures before their performance. Principal Component Analysis (PCA) allows quantification of AF complexity by taking spatial diversity of the surface 12-multilead surface ECG into account.

2. Methods

2.1. ECG data and acquisition

Surface ECG signals of 18 patients were examined in this study. They were all affected by persistent AF and underwent CA at the Cardiology Department of Princess Grace Hospital in Monaco, performed with the aid of Prucka Cardiolab and Biosense CARTO electrophysiology measurement systems. ECG signals were acquired by means of a standard 12-lead system. They were recorded at the beginning, after PV isolation and at the end of the CA procedure, at a sampling rate of 1 kHz. AF was terminated in 14 patients, either spontaneously obtained after the surgery or externally induced by electrical cardioversion or drug treatment. In this research, a short term success criterion has been adopted: AF is considered terminated if converted either to sinus rhythm or intermediate atrial tachycardia(s) within a 3-month blanking period.

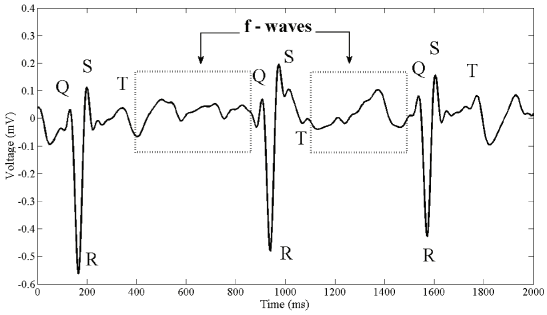

Figure 1: ECG recording on V_I during AF and its characteristic waves. Dotted boxes highlight TQ intervals forming the AA signal $\mathbf{Y}_{\mathrm{AA}}$ in Equation (1).

2.2. Atrial activity extraction

ECG signal filtering was first performed by means of a forth-order zero-phase Chebyshev bandpass filter with a -3 dB attenuation at 0.5 Hz and 30 Hz cut-off frequencies. The choice of this frequency band is motivated by AF dominant frequency typival values, ranging between 3 and 12 Hz. This stage was followed by ECG fiducial point detection. R wave time instants were located on lead V_1 by applying Pan-Tompkins' algorithm; Q wave onset and T wave offset were detected with an improved version of Woody's method. TQ interval segmentation, mean-centering and concatenation were finally carried out, yielding a signal representing atrial activity (AA) only, as illustrated in Fig. 1. This strategy allowed us to focus on the AA contribution to the surface ECG and to minimize the influence from other sources, e.g., ventricular activity and noise. According to this procedure, we build a matrix:

$$\mathbf{Y}_{\mathrm{AA}} = [\mathbf{y}_{\mathrm{AA}}(1) \cdots \mathbf{y}_{\mathrm{AA}}(N)] \in \mathbb{R}^{L \times N} \qquad (1)$$

where vector $\mathbf{y}_{\mathrm{AA}}(t) = [y_1(t), \ldots, y_L(t)]^T$ represents the multilead AA signal at the sample index t, L is the number of leads retained (e.g., $L = 12$ for the standard ECG), and N the number of samples of the AA signal $y_\ell(t)$ for each lead $\ell = 1, 2, \ldots, L$.

2.3. Principal component analysis

One well-known ECG signal property is its high spatial redundancy, i.e., the fact that the lead signals are correlated. Accordingly, one possible strategy to extract useful information is relying on the data compression and dimensionality reduction capabilities of PCA [6, 7]. Each AA multilead recording $\mathbf{Y}_{\mathrm{AA}}$ was divided into a fixed number S of equal-length segments. A reduced, representative set of L uncorrelated underlying sources $\mathbf{X}^{(s)}$, the so-called principal components (PCs), was extracted in each segment $s = 1, \cdots, S$ so that redundancy among them is minimized and the maximum variability (as described by variance) is retained by means of a linear, orthogonal transformation $\mathbf{Y}_{\mathrm{AA}}^{(s)} = \mathbf{M}^{(s)}\mathbf{X}^{(s)}$, $s = 1, \cdots, S$. Each column $\mathbf{m}_k$ of $\mathbf{M}^{(s)}$ is a principal direction and represents the relative spatial contribution of the kth PC to the ECG leads, so it can be considered as its spatial topography.

2.4. Atrial activity complexity

Even though a unified definition of AF organization is currently not available, the study in [7] highlights that AA complexity level can be estimated by investigating the descriptive power of the first few PCs, retaining most of the total variance. To this end, reconstruction of the original AA signal was attempted in [7] by using a fixed number n of spatial topographies in a reference segment. Mathematically, segment estimation $\hat{\mathbf{Y}}_n^{(s,r)}$ was computed for every segment $s, r = 1, \cdots, S, r \neq s$. The examined segment s has been projected on the n dominant spatial topographies $\mathbf{M}_n^{(r)}$ extracted from the mixing matrices computed in other segment r taken as a reference $\hat{\mathbf{Y}}_n^{(s,r)} = \mathbf{M}_n^{(r)}[{\mathbf{M}_n^{(r)}}^T\mathbf{M}_n^{(r)}]^{-1}{\mathbf{M}_n^{(r)}}^T\mathbf{Y}_{\mathrm{AA}}^{(s)}$. Reconstruction performance can be quantitatively evaluated by the Normalized Mean Square Error $\mathrm{NMSE}_\ell^{(s,r)}$ between the actual signal $y_\ell(t)^{(s)}(t)$ on the ℓth lead and its estimation $\hat{y}_{\ell,n}^{(s,r)}(t)$:

$$\mathrm{NMSE}_{\ell,\mathrm{n}}^{(\mathrm{s,r})} = \frac{\sum_{\mathrm{t}=1}^{\mathrm{N}} [\mathrm{y}_\ell{}^{(\mathrm{s})}(\mathrm{t}) - \hat{\mathrm{y}}_{\ell,\mathrm{n}}^{(\mathrm{s,r})}(\mathrm{t})]^2}{\sum_{\mathrm{t}=1}^{\mathrm{N}} [\mathrm{y}_\ell^{(\mathrm{s})}(\mathrm{t})]^2} \qquad (2)$$

with $\ell = 1, \cdots, L$. Experimental evidence shows that in most patients NMSE stops increasing and remains constant after a threshold value, generally about $S = 4$; hence, the choice of this value prior to signal decomposition. Moreover, it seemed reasonable to divide the AA recording into segments (at least $5 - 6$ seconds) long enough to analyze the AF pattern. This result also shows robustness of such an index to variations in the number of segments, whose value does not alter their discriminative power. It was expected that more organized AA waveforms needed fewer PCs [7] to be approximated with an adequate level of accuracy. Consequently, for sufficiently low values of n, it was remarked that the higher the NMSE value, the more disorganized the AA.

This previous study, however, considered a single lead to compute the NMSE in (2), neglecting contributions by other ECG leads. In particular, the choice of lead V_1 is motivated by the fact that it has the largest atrial-to-ventricular amplitude ratio [8]. Yet its proximity to the right atrial free wall may neglect useful information about other sites, in particular the left atrium and the PVs, which play a crucial role in AF initiation and maintenance [9]. This observation prompts us to consider other leads in order to yield a global overview of AA evolution.

To overcome these problems, we propose computing of the mean value $\mu_{\ell,n}$ and the standard deviation $\sigma_{\ell,n}$ of all

possible segment estimation error values from (2) for each lead ℓ. Index $\mu_{\ell,n}$ offers a global perspective of segment estimation performance, whereas $\sigma_{\ell,n}$ gives a measure of AF complexity variability along the recording, as well as a measure of uncertainty. Several parameter combinations were tested. We first defined the interlead NMSE weighted mean:

$$\overline{\mu_n} = \sum_{\ell=1}^{L} \sigma_{\ell,n}\mu_{\ell,n} \Big/ \sum_{\ell=1}^{L} \sigma_{\ell,n} \quad (3)$$

whose weights are represented by NMSE standard deviation values per lead; ECG leads exhibiting strong AF complexity intersegment variability have more weight, so they give the highest contribution. A further interpretation of $\sigma_{\ell,n}$ can be given in terms on uncertainty: low values of this parameter show a more stable reconstruction, whereas high values denote higher projection error probability. In the light of these considerations, the average $NMSE$ value associated with the lead having the lowest standard deviation was also tested as potential predictor:

$$\mu_n{}^{MIN\sigma} = \mu_{\ell,n} : \sigma_{\ell,n} = min\{\sigma_{\ell,n}, \ell = 1, \cdots, L\}. \quad (4)$$

Parameter n is set to 1 so as to verify if the only first spatial topography of the reference segment was sufficient to represent the whole signal, as it retains the highest percentage of overall signal variance among all principal directions. In other tests, $n = 3$ is assumed, as previous works in vectorcardiography stated that a three-orthogonal component system can guarantee a good reconstruction of heart electrical activity on the body surface [10].

3. Statistical analysis and results

The parameters we put forward have been expressed as mean $\pm$ standard deviation. In our framework, each patient could belong either to the category ``AF termination''or ``non AF termination''according to the criterion explained in Sec. 2.1. Classification performance was assessed by computing the characteristic Receiver Operator Curve (ROC) parameters, namely, the Area Under Curve (AUC) and the p value under a confidence level α equal to 0.05. Firstly, Lilliefors' test was run to verify data normal distribution. Differences between successful and failing CA procedures were statistically determined by an unpaired Student's t-test if data data were sampled from a Gaussian distribution, a two-sample Kolmogorov-Smirnov test otherwise. Statistical analysis confidence level α was set to 0.05. Subscripts START, PV and END, concern data before CA, after PV ablation and after CA. Only statistically significant results are quoted in the sequel. Table 1 shows the above parameters we introduced are computed for each class, including p values of each unpaired test. Classification indices are reported in Table 2. As our investigation reveals in Fig. 2, classification outcome is profoundly influenced by interlead variability, and it can be

Table 1: Interpatient statistical analysis

	AF termination	AF non termination	p value
$(\overline{\mu_1})_{\text{START}}$	61.59 ± 16.52	83.86 ± 14.27	0.04
$(\mu_1{}^{MIN\sigma})_{\text{END}}$	35.78 ± 43.19	101.04 ± 1.24	0.04
$(\overline{\mu_3})_{\text{PV}}$	36.02 ± 18.17	46.44 ± 1.86	0.008
$(\mu_3{}^{MIN\sigma})_{\text{PV}}$	4.296 ± 3.399	15.09 ± 18.08	0.04

Table 2: CA outcome classification prediction performance

	AUC	p value
$(\overline{\mu_1})_{\text{START}}$	0.86	$7 \cdot 10^{-5}$
$(\mu_1{}^{MIN\sigma})_{\text{END}}$	0.86	$7 \cdot 10^{-5}$
$(\overline{\mu_3})_{\text{PV}}$	0.86	$7 \cdot 10^{-5}$
$(\mu_3{}^{MIN\sigma})_{\text{PV}}$	0.77	$1 \cdot 10^{-2}$

significantly different from a lead to another one. This evidence was confirmed by the computation of the NMSE mean value over segments for each patient and for each lead; output values were finally averaged over the whole database. Results in Fig. 3 highlight that mean NMSE strongly changes as a function of the electrode selected, and so does classification performance.

4. Discussion and conclusions

The discriminative power of the NMSE-dependent parameters presented in this work is corroborated by experimental results. The most relevant contribution is to demonstrate the superiority of multilead strategy over standard single-lead NMSE: the inspection of NMSE spatial distribution can provide a more complete outlook of AF evolution on the heart substrate. In Fig. 3 we can remark that mean NMSE value is strongly influenced by the choice of the lead. In addition, leads conventionally adopted for AA examination (e.g., V_1) are not necessarily suitable for its estimation, as they are characterized by higher projection error values. On the contrary, lead V_4 exhibits the most accurate predictive capability, probably because its location also reflects left-atrial activity. Hence, our proposal of some classifiers depending on NMSE values computed over several leads, so exploiting spatial relationships among them. As far as $(\overline{\mu_1})_{\text{START}}$ and $(\overline{\mu_3})_{\text{PV}}$ are concerned, every lead contribution is weighted in terms of spatio-temporal dispersion. On the other hand, if we examine $\mu_n{}^{MIN\sigma}$, we observe that variance can be exploited

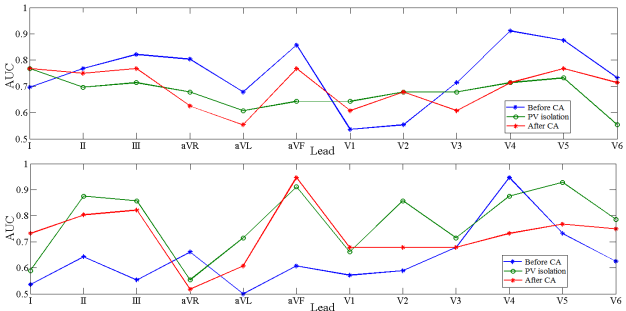

Figure 2: Classification performance of the AA single-lead NMSE as a function of the ECG lead selected according to the AUC criterion. (Top) $n = 1$; (Bottom) $n = 3$.

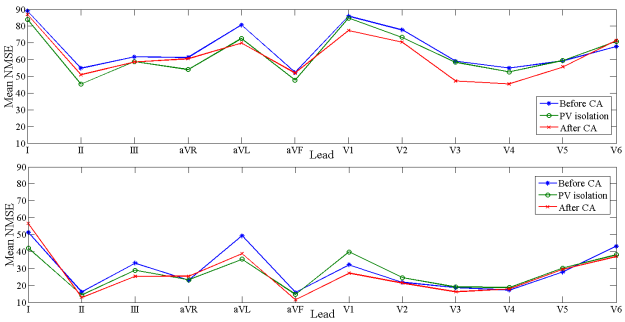

Figure 3: AA Single-lead NMSE as a function of the ECG lead selected. (Top) $n = 1$; (Bottom) $n = 3$.

as a lead selector: it detects the electrode where the signal shows the lowest complexity and is likely to yield the most accurate signal estimation. Actually, it is worth noting that NMSE inter-segment variance can quantify the spatio-temporal degree of repetitiveness of the AA wavefront pattern: the higher NMSE dispersion among segments, the more complex and disorganized AA. PCA capability of representing AA by compressing its content into very few PCs is also confirmed, as the novel parameters are expressed as a function of projections of the input signal over 1 or 3 maximum-variance PCs. Moreover, the existence of a relationship between AF organization and surgical actions is proved by statistically significant tests in several steps of the procedure. Special consideration should be paid to PV isolation role during CA performance. Actually, our results may suggest that a process of atrial remodelling is triggered when electrically disconnecting these sites from the rest of the heart. This could explain the radical changes of heart substrate with respect to moments before the ablation, reflected by significant variations in some of our quantitative descriptors. In conclusion, this study demonstrates that AA organization and spatial variability typical of the multilead surface ECG can be used to predict CA outcome by means of PCA an appropriate selection of ECG leads.

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References

[1] Konings K, Kirchhof C, Smeets Jea. High-density mapping of electrically induced atrial fibrillation in humans. Circulation 1994;89:1665–1680.

[2] Moe G. On the multiple wavelet hypothesis of atrial fibrillation. Arch Int Pharmacodyn Ther 1962;140:183–188.

[3] Jaïs P, Haissaguerre M, Shah Dea. A focal source of atrial fibrillation treated by discrete radiofrequency ablation. Circulation 1997;95:572–576.

[4] Nault I, Lellouche N, Matsuo Sea. Clinical value of fibrillatory wave amplitude on surface ECG in patients with persistent atrial fibrillation. J Interv Card Electrophysiol Oct. 2009;26(1):11–19.

[5] Bollmann A, Husser D, Mainardi Lea. Analysis of surface electrocardiograms in atrial fibrillation: techniques, research, and clinical applications. Europace Nov. 2006; 8(11):911–926.

[6] Bonizzi P, Meste O, Zarzoso V, Latcu DG, Popescu I, Ricard P, Saoudi N. Atrial fibrillation disorganization is reduced by catheter ablation: A standard ECG study. In Proc. IEEE EMBS 2010. 2010; 5286–5289.

[7] Bonizzi P, Guillem MS, Climent AM, Millet J, Zarzoso V, Castells F, Meste O. Noninvasive assessment of the complexity and stationarity of the atrial wavefront patterns during atrial fibrillation. IEEE Trans Biomed Eng 2010; 57(9):2147–2157.

[8] Petrutiu S, N.g. J, Nijm Gea. Atrial fibrillation and waveform characterization ;25(6):24–30.

[9] Haïssaguerre M, Jaïs P, Shah Dea. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998;339:659–65.

[10] Ghista D, Acharya U, Nagenthiran T. Frontal plane vectorcardiograms: Theory and graphics visualization of cardiac health status. J Med Syst Aug 2010;34(4):445–458.

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