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Catheter ablation outcome prediction in persistent atrial fibrillation using weighted principal component analysis

Marianna Meo[a,*], Vicente Zarzoso[a], Olivier Meste[a], Decebal G. Latcu[b], Nadir Saoudi[b]

[a] Laboratoire d'Informatique, Signaux et Systèmes de Sophia Antipolis (I3S), Université Nice Sophia Antipolis, CNRS, France
[b] Service de Cardiologie, Centre Hospitalier Princesse Grace, Monaco

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ABSTRACT

Radiofrequency catheter ablation (CA) is increasingly employed to treat persistent atrial fibrillation (AF), yet selection of patients who would positively respond to this therapy is currently a critical problem. Several parameters of the surface 12-lead electrocardiogram (ECG) have been analyzed in previous works to predict AF termination by CA. Nevertheless, they are affected by some limitations, such as manual computation and the examination of a single ECG lead while neglecting contributions from other electrodes. AF spatio-temporal organization has been described on surface ECG by means of the normalized mean square error (NMSE) between consecutive atrial activity (AA) signal segments and their reduced-rank approximations based on principal component analysis (PCA). However, these features do not show to be correlated with CA outcome. In this study, such descriptors are adequately adapted and applied to CA outcome prediction. An NMSE index is put forward, computed over the set of eight linearly independent ECG leads after AA signal rank-1 approximations determined by weighted principal component analysis (WPCA). The final predictor is able to discriminate between successful (70.76 ± 17.74) and failing CA procedures (37.54 ± 20.01) before performing the ablation (p-value = 0.0013, AUC = 0.91). The proposed WPCA-based technique emphasizes the most descriptive components of AF electrophysiology by selectively enhancing contributions coming from the most representative ECG leads. Our investigation confirms that ECG spatial diversity exploitation in this WPCA-based framework not only endows the NMSE index with clinical value in the context of CA outcome prediction, but it also improves classification accuracy and increases robustness to ECG lead selection.

1. Introduction

Atrial fibrillation (AF) is a sustained cardiac arrhythmia characterized by rapid and disorganized atrial activations inducing a loss of atrial mechanical efficacy. Several theories have been suggested to explain AF electrophysiological mechanisms, so as to put forth a systematic procedural protocol for its treatment. AF activity has been first regarded as the result of interactions between multiple wandering atrial wavelets [1,2]. On the other hand, it is commonly acknowledged that pulmonary veins (PVs) significantly contribute to AF maintenance and evolution, especially in paroxysmal forms of this disease [3]. In spite of major advances in its treatment, AF remains a significant cause of cardiovascular morbidity and mortality, especially those arising from stroke and heart failure.

Radiofrequency catheter ablation (CA) has become the first-line strategy [4] for the treatment of this disease. However, as the precise pathophysiology of AF dynamics has not been completely clarified yet, it is still questionable whether CA effectively suppresses abnormal rhythm sources, and how it affects heart electrical substrate. Different CA techniques have been developed, yet none of them is widely considered as effective for the treatment of persistent AF. Their performance is still far from satisfactory, and they are less effective than equivalent procedures for paroxysmal AF. Since this cardiac interventional procedure is profoundly influenced by operator's experience and patient's health conditions, results reported by clinical centers are quite disparate and not easily comparable [5–7]. It follows that its efficacy in terminating AF and avoiding its recurrence is not guaranteed for all patients. This situation explains the increasing tendency to attempt an a priori selection of patients who can undergo CA and experience durable sinus rhythm (SR) restoration. Several parameters extracted from the surface ECG have been proposed as potential predictors of CA outcome [8,9]. For example, prolongation of atrial fibrillation cycle length (AFCL) can be associated with AF termination by CA [10]. In other studies [8], it has been argued that the higher the amplitude

* Corresponding author. Tel.: +33 492942741.
E-mail addresses: meo@i3s.unice.fr (M. Meo), zarzoso@i3s.unice.fr (V. Zarzoso), meste@i3s.unice.fr (O. Meste), dglatcu@yahoo.com (D.G. Latcu), nsaoudi@chpg.mc (N. Saoudi).

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of the fibrillatory waves (f-waves) observed on the surface ECG, the more likely procedural success.

In parallel, another line of research aims at noninvasive measures of AF spatio-temporal complexity, with the underlying assumptions that treatment modalities should be chosen and therapy outcome could be predicted on the basis of these measures. In [11], a noninvasive measure of AF organization is assessed by the normalized mean square error (NMSE) values between the atrial activity (AA) signal and its rank-3 approximations determined by principal component analysis (PCA) in lead V_1 [11]. This argument is supported by the hypothesis of a correlation between AF organization and the number and interactions of atrial wavefronts through the heart substrate. The choice of V_1 is justified by the fact that it presents the maximum atrial-to-ventricular amplitude ratio among all ECG leads [12]. In [13], CA performance was shown to influence AF spatio-temporal organization, and its effect can be quantified by variations in NMSE values.

Nevertheless, such parameters are affected by several shortcomings. In the first place, some classical ECG-based descriptors are manually computed [8,10], so they are subject to operators' subjectivity and thus prone to errors. Furthermore, as most of them are measured in only one ECG lead, they do not account for information that may be provided by other electrodes. Indeed, ECG analysis is not always straightforward, and visual inspection does not capture AF features underlying the whole ensemble of leads; hence, the limitations of classical single-lead techniques, which do not fully exploit multilead ECG spatial diversity. However, AF spatio-temporal complexity as defined in [11] has not been shown to correlate with CA outcome.

Our investigation focuses on the potential application of the spatio-temporal organization of AA measured on the standard ECG by the NMSE index as a tool to discriminate between successful and failing CA procedures before applying the therapy. Contributions provided from the eight independent ECG leads are expressed in terms on NMSE between successive segments of the actual AA signal and their rank-1 approximations computed by weighted principal component analysis (WPCA), and they are finally combined in a single parameter capable of predicting long-term CA outcome. Thanks to this decomposition, the spatial variability of the standard ECG is taken into account, and the most significant ECG leads are also automatically enhanced by assigning different weights to data based on their estimated relevance.

2. Methods

2.1. Characteristics and acquisition modalities of the persistent-AF database

Twenty patients (19 males, 60 ± 11 years) with a median persistent AF episode duration of 4.5 months (2–84) were enrolled in the present study. They all 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. They all gave their informed consent. Surface 12-lead ECG recordings were acquired at the beginning of the procedure, at a sampling rate of 1 kHz. An example of the signal recorded on the lead V_1 for one of the patients is shown in Fig. 1. CA was accomplished according to the sequential stepwise protocol [14], whose major actions consist in 1) circumferential PV isolation, 2) fragmented potentials' ablation, and 3) non-PV triggers, roof line and mitral isthmus line right atrial ablation.

The most recent HRS Expert Consensus Statement guidelines for CA trials [14] recommend that immediately after CA performance, there is a three-month "blanking period" during which any fibrillatory episodes are not regarded as symptoms of AF recurrence, but as a physiological reaction during recovery from CA. After this blanking period, if the patient remains free of arrhythmia recurrences, procedural AF termination is considered effectively accomplished.

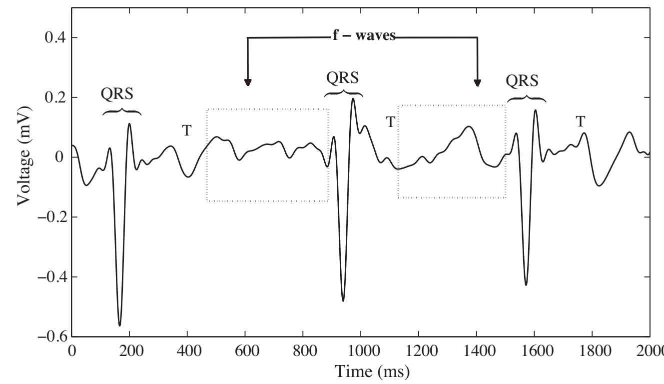

Fig. 1. Example of ECG recording during AF and its characteristic waves. Boxes highlight TQ intervals which are concatenated to form the AA signal $\mathbf{Y}_{AA}$ in Eq. (1).

Procedural success is defined as freedom from ECG/Holter documented sustained AF recurrence (>30 s) during follow-up, after the 3-month blanking period. Immediately after performing CA, AF can be converted either directly to SR or to intermediate tachyarrhythmia, exclusively by ablation or after an electrical cardioversion. For its clinical interest, a long-term criterion is adopted in our investigation to distinguish between successful and ineffective CA procedures. In our experimental framework, after a median follow-up of 9.5 months, CA was successfully accomplished in $n_S = 13$ out of $n_P = 20$ patients (65%), whereas $n_F = 7$ procedures were not effective. A follow-up of m months was available at the time of our analysis, where m ranged between 4 and 19 months depending on the patient.

Some patients received a pharmacological treatment subsequent to CA procedure, mainly amiodarone (for some patients, solatol and flecaine). Three patients underwent a second ablation. In this case, only ECG signals related to the first procedure are taken into account in our study. As opposed to previous studies [8,9], termination of AF during CA was not achieved in all patients. Nevertheless, this is not detrimental to our analysis, since AF termination by CA is not predictive of long-term outcome [15], which is the event with clinical interest.

2.2. ECG preprocessing and atrial activity segmentation

A fourth-order zero-phase Chebyshev type II bandpass filter with −3 dB attenuation band between 0.5 Hz and 30 Hz has been applied to standard ECG recordings of our database, whose length is about 1 min. This preprocessing stage allows AF content enhancement, whose dominant frequency typically ranges between 3 and 12 Hz, as well as removal of baseline wandering and high frequency noise such as myoelectric artifacts and 50 Hz power line interference. Automatic detection of ECG fiducial points is then accomplished, in order to segment TQ intervals. R wave time instants are detected on lead V_1 using the Pan–Tompkins' algorithm [16]. Then, Q wave onset is defined 40 ms before the subsequent R wave, this being the typical duration of this wave in these conditions (an abnormal Q wave denotes presence of infarct). Finally, T wave offset is identified with an improved version of Woody's method and automatically computed after visual inspection and selection of the lead exhibiting the most visible T waves (in general, V_2 and V_3) [17]. Such intervals are finally mean-corrected and