32nd Annual International Conference of the IEEE EMBS
Buenos Aires, Argentina, August 31 - September 4, 2010

Atrial Fibrillation Disorganization is Reduced by Catheter Ablation: A Standard ECG Study

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Abstract— **Selection of candidates to catheter ablation (CA) of long-lasting persistent atrial fibrillation (AF) is challenging, since success is not guaranteed. In this study, we put forward an automated method for noninvasively evaluating the reduction of the complexity of the AF organization following CA. Complexity is meant as the amount of disorganization observed on the ECG, supposed to be directly correlated to the number and interactions of atrial wavefronts. By means of PCA, the complexity of the AF organization is evaluated quantitatively from a 12-lead ECG recording. Preliminary results show that CA is able to reduce the complexity of AF organization in the atrial wavefront pattern propagation, despite the persistence of AF in most cases. This can be viewed as a first clinical validation of this parameter. Whether AF complexity and its reduction by CA are predictive of long-term outcome is thus still to be determined.**

I. INTRODUCTION

Atrial fibrillation (AF) severity increases together with time and consequent chronification, causing several electro-structural changes in the heart which may bring to hemo-dynamic complications, stroke, and thromboembolism, which is increased fivefold compared to healthy subjects. The time dependent impairing of the cardiac muscle due to AF is the reason why a specific treatment for this pathology still lacks nowadays. In relation to the duration of its episodes, AF is differently classified (as paroxysmal, persistent, or chronic), and differently treated [1]. Drug-resistant AFs can be treated with catheter ablation (CA) or electrical cardioversion. The use of ablation for treatment of persistent AF has been expanding. However, CA of long-lasting AF is a lengthy procedure, and inconsistent success rates have been reported by different centers offering the therapy [2], [3]. Thus, the most chronic patients need one or more cardioversions in order to re-establish and maintain normal cardiac functioning. Therefore, selection of candidates to CA of long-lasting persistent AF is challenging, in order to avoid useless and risky procedure. Indeed, even if most patients who undergo CA do not experience complications, some risks exist (mainly hemodynamic complications) [4].

The AF cycle length, measured from the left atrial appendage has been used as a predictor of procedure termination of persistent AF [5]. However, this can only be performed at the time of the procedure. Other studies have investigated the possibility to use noninvasive measurements of AF cycle length and fibrillatory wave amplitude from surface electrocardiogram (ECG) as variables predictive of a successful procedural and medium-term clinical outcome using sequential catheter approach in patients with persistent AF [6], [7]. They showed that both parameters are clinically useful pre-ablation tools for predicting patients in whom sinus rhythm can be restored by CA and maintained over time.

On the other hand, several studies have demonstrated the presence of a certain degree of local organization of the atrial activity (AA) during AF, which is inversely depending on the chronification of the pathology [8]. Moreover, the efficacy of the different treatments may also be influenced by the degree of organization in the AA [9]. Thus, AF chronification can be supposed to be inversely related to its organization degree, and the complexity of this organization can be investigated as predictive of CA of long-lasting persistent AF.

In this study, we put forward an automated method for noninvasively evaluating the reduction of the complexity of the AF organization following CA. Complexity is meant here as the amount of disorganization observed on the ECG, supposed to be directly correlated to the number and interactions of atrial wavefronts. The methodology presented here is similar to the one introduced in [10], but a clinical application of it is proposed in this study. By means of PCA, the complexity of the AF organization is evaluated quantitatively from a 12-lead ECG recording. PCA has been attested to be a valuable tool both for addressing diverse issues in ECG analysis [11], and for quantifying AA organization complexity in invasive recordings [12]. Effects of CA on the complexity of AF may be a first clinical validation of this parameter.

II. METHODS

A. Data and Acquisition System

A dataset composed of 27 patients was employed in this study (85% men, 60±8 years). All patients underwent CA of persistent AF. CA was performed with the CARTOsystem and included a circumferential pulmonary vein ablation, a roof line, a left atrial (LA) isthmus line and electrogram-based ablation of the LA. The acquisition system consisted of a standard 12-lead system. For each patient, a 10s ECG was recorded both before and after the CA procedure, before termination of AF obtained either spontaneously after CA or induced by electrical cardioversion. Signals were acquired at a sampling frequency of 977 Hz. AF was stopped by CA

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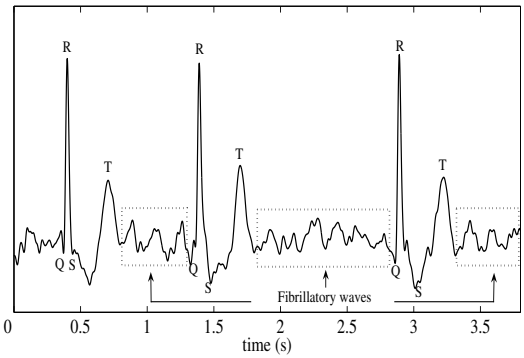

Fig. 1. Example of ECG recording during AF, showing the different cardiac waves. AA intervals of interest are highlighted by the dotted boxes. They are connected together to form the AA recording $\mathbf{Y}$.

in 15 patients. The remaining 12 patients needed electrical cardioversion.

B. ECG Preprocessing

Signals were processed by applying a third-order zero-phase high-pass Chebyshev filter with a -3 dB cut-off frequency at 0.5 Hz to remove baseline wandering due to physiologically irrelevant low frequency signal interference (< 1 Hz), like breathing influence [13]. That was followed by a third-order zero-phase low-pass Chebyshev filter with a -3 dB cut-off frequency at 100 Hz to remove high frequency noise, like myoelectric artifacts.

C. Atrial Activity Recordings

AA was analyzed by concatenating consecutive TQ intervals (from the end of the T wave to the beginning of the QRS complex) of 10s long ECG. For this purpose, the R wave peaks were detected, and the Q wave onset and T wave offset were properly segmented (see Fig. 1 for the definition of the different cardiac waves), and an AA signal was obtained by concatenating only the TQ segments. To this end, lead V1 was selected and the R wave instants detected using a Pan and Tompkins's QRS detection method [13]. Then, for each R wave instant, the corresponding QRS-T complex was segmented by defining a suitable window including it, and then removed. After QRS-T removal, each lead was visually inspected and parts of QRS-T complexes still present were further removed from all leads.

In this way, for each 12-lead ECG recording we obtained a 12-lead AA recording compactly represented by the $12 \times N$ matrix:

$$\mathbf{Y} = \begin{bmatrix} \mathbf{y}_1 \\ \vdots \\ \mathbf{y}_{12} \end{bmatrix}$$

where N is the number of samples of the concatenated TQ intervals, and the generic lead l is represented by a row vector:

$$\mathbf{y}_l = [y_l(1), \ldots, y_l(N)] \quad (1)$$

D. Principal Component Analysis

One manner to analyze the complex information contained in the ECG is to transform the original set of signals in a set of components by minimizing the redundancy among them [11]. This can be achieved by PCA. The derivation of principal components (PC) is based on the assumption that the signal $\mathbf{Y} \in \mathbb{R}^n$, the mean corrected observed signal, is a zero-mean random process being characterized by the correlation $\mathbf{R}_x = E\left[\mathbf{Y}\mathbf{Y}^{\mathrm{T}}\right]$, where symbol $(\cdot)^{\mathrm{T}}$ stands for the transpose operator. The PCs of $\mathbf{Y}$ result from applying an orthogonal linear transformation $\mathbf{M}$ to $\mathbf{Y}$, so that the elements of the PC vector $\mathbf{X}$, that is an estimate of the true vector of the unknown components, become mutually uncorrelated. Thus, the PCA of $\mathbf{Y}$ yields an estimate of the following noiseless model:

$$\mathbf{Y} = \mathbf{M}\mathbf{X} \Rightarrow \mathbf{X} = \left[\mathbf{M}^{\mathrm{T}}\mathbf{M}\right]^{-1}\mathbf{M}^{\mathrm{T}}\mathbf{Y} = \mathbf{M}^{\sharp}\mathbf{Y} \quad (2)$$

where $\mathbf{M}$ is the mixing matrix, and symbol $(\cdot)^{\sharp}$ stands for the pseudo-inverse operator. Even if the model in (2) is supposed to be noiseless, this model is usually employed in the presence of noise as well. In that case, the number of PCs generally matches the number of measured signals, and the last PCs are associated with noise. The *i*th column of $\mathbf{M}$ represents the source direction or spatial topography that links the *i*th component of $\mathbf{X}$ with the observed signals $\mathbf{Y}$. A spatial topography reflects the spatial pattern distribution of the relative potential field described by the associated PC onto the spatially-separated electrodes. PCA reduces the dataset of the observed signals to few representative PCs. The mixing matrix $\mathbf{M}$ can be obtained, e.g., from the singular value decomposition of the observation matrix $\mathbf{Y} = \mathbf{U}\mathbf{\Sigma}\mathbf{V}^{\mathbf{T}}$, where $\mathbf{M} = \mathbf{U}\mathbf{\Sigma}/\sqrt{N}$, with matrix $\mathbf{U}$ and $\mathbf{V}$ containing the left and right singular vectors of $\mathbf{Y}$, respectively, and matrix $\mathbf{\Sigma}$ being the diagonal matrix containing the singular values σ_i (≥ 0) at which each PC is associated. σ_i indicates how representative is the *i*th PC in the global data ensemble. The PCs are usually arranged so that the singular value sequence appears in a decreasing order, and it reflects some information regarding interlead variability. In fact, a fast fall-down is associated with a low spatial variability, while a slow fall-down indicates a large spatial variability. Hence, the ability of PCA to concentrate the original information in only few components gives an information about the complexity of the original data. Complexity is meant in this study as the amount of disorganization observed on the ECG, supposed to be directly correlated to the number and interactions of atrial wavefronts.

E. Assessment of AA Organization

The degree of AA organization is investigated through the structure of the mixing matrices inferred from PCA of the AA signals $\mathbf{Y}$ generated as introduced in Section II-C. The data in $\mathbf{Y}$ are reprojected on the spatial topographies associated with the first 3 most significant PCs of $\mathbf{Y}$, stored in the first 3 columns of matrix $\mathbf{M}$. This projection can be

expressed as

$$\begin{aligned}\hat{\mathbf{Y}} &= \mathbf{M}_3\left[(\mathbf{M}_3)^{\mathrm{T}}\mathbf{M}_3\right]^{-1}(\mathbf{M}_3)^{\mathrm{T}}\mathbf{Y} \\ &= \mathbf{M}_3(\mathbf{M}_3)^{\sharp}\mathbf{Y} \end{aligned} \quad (3)$$

From this relationship, the normalized mean squared error (NMSE) between the actual data and their reconstruction from the 3 most significant topographies is computed. This error is computed on lead V1, as fibrillatory waves appear with higher amplitude compared with other leads [14], [15]:

$$\mathrm{NMSE}_3 = \frac{\sum_{i=1}^{N}(y_{V1}(i)-\hat{y}_{V1}(i))^2}{\sum_{i=1}^{N}(y_{V1}(i))^2} \quad (4)$$

where $\mathbf{y}_{V1}$ denotes the reference signal, actually measured on V1, $\hat{\mathbf{y}}_{V1}$ an estimate of it, and N their length. High values indicate notable differences between the original and reconstructed AA signals, while values close to zero are associated with very similar AA signals. This error measures the intra-patient differences between the actual data and their reconstruction obtained projecting the actual data on the subspace described by the 3 spatial topographies associated to the first 3 PCs. Thus, it assesses the accuracy with which the first 3 components are sufficient for reconstructing the whole data. We assume this measure is inversely proportional to the AF organization, and thus directly to the complexity of its organization. Indeed, it measures the residuum due to the non-dipolarity of the atrial electrical activations with respect to the dipolar model for normal cardiac activity. This residuum is thus calculated as the error in the reconstruction of the AA when using only its first 3 PCs since the more the AA resembles the healthy condition, the better it is expected to resemble the healthy cardiac wave description in a three-dimensional space, as claimed by the vectorcardiography. This justify the choice of reconstructing using only the first 3 PCs. Thus, signals characterized by low complexity are expected to be better reconstructed. Hence, the higher the complexity of the observed signal the higher the NMSE_3 of its reconstruction from 3 components. The NMSE_3 is calculated before (NMSE_3^{pre}) and after (NMSE_3^{post}) CA (or just before end of AF). The analysis of NMSE_3^{post} vs. NMSE_3^{pre} is expected to show a reduction in the complexity of the AF organization after CA, since complexity is expected to be decreased by this treatment. The relationship of NMSE_3^{pre} with the success of CA in terminating AF is also analyzed. Moreover, the intra-patient relationship of NMSE_3^{pre} with both the heart rate (HR) and the frequency of the AF estimated before CA is also analyzed. Significant relationships among these uncorrelated parameters could yield to a further improvement in CA outcome prediction. The frequency of the AF is assessed from lead V1 through a suitable procedure [16].

F. Statistical Analysis

Values of NMSE_3^{pre} and NMSE_3^{post} have been calculated for each patient. r-Pearson's correlation coefficient is calculated for each relation analyzed in the study. Statistical significances have been evaluated by means of Welch's t-test.

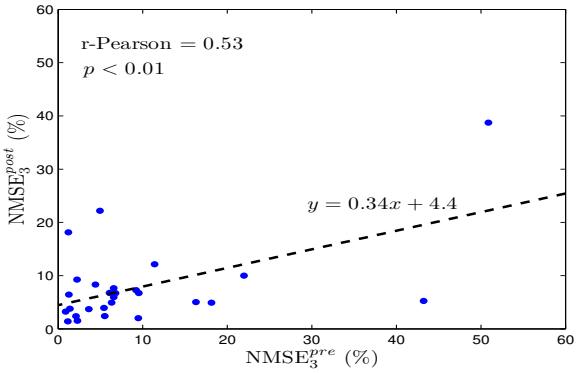

Fig. 2. Results of AF organization analysis. Analysis of NMSE_3^{post} vs. NMSE_3^{pre} is presented; the regression line equation and the values of the correlation coefficient r-Pearson and its significance p are also reported.

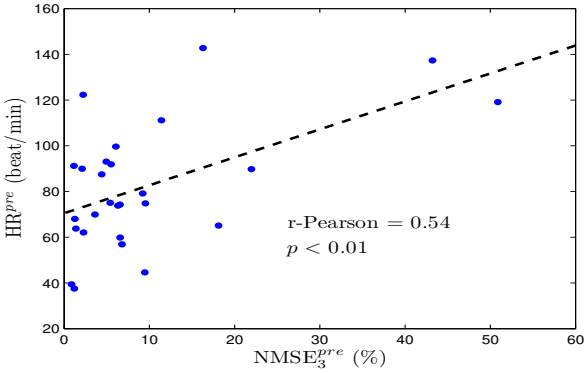

Fig. 3. Results of the analysis NMSE_3^{pre} vs. HR^{pre}; values of the correlation coefficient r-Pearson and its significance p are also reported.

III. RESULTS

The results of the analysis of NMSE_3^{post} vs. NMSE_3^{pre} are presented in Fig. 2. The analysis showed a significant reduction in the complexity of AF after CA (r-Pearson=0.53, p<0.01), underlined by the slope (< 1) of the regression line, despite the persistence of AF in most cases. This result is in line with the idea that complexity is expected to be decreased by CA. No significant correlation was found between NMSE_3^{pre} and the success of CA, and between NMSE_3^{pre} and NMSE_3^{post}.

Fig. 3 shows the significant positive correlation found between HR estimated before CA (HR^{pre}) and NMSE_3^{pre} (r-Pearson=0.54, p<0.01). No significant correlation was found between NMSE_3^{pre} and the frequency of the AF.

IV. DISCUSSION AND CONCLUSIONS

Success of CA of long-lasting persistent AF is difficult is not guaranteed. Thus, selection of candidates to CA is challenging. This work puts forward an automated method for noninvasively evaluating the reduction of the disorganization of the AF following CA, evaluated in terms of

complexity of the differently interacting atrial wavefronts. Two are the main results of this study. Firstly, the significant correlation between complexity evaluated before and after CA showed that AF disorganization is generally reduced by CA. That is, CA is able to increase organization in the AA wavefront pattern propagation, as reasonably expected, despite the persistence of AF in most cases. Secondly, the significant correlation between complexity and HR suggests that different independent parameters can combine to yield an improvement in CA outcome prediction.

CA outcome prediction through noninvasive recordings has been already considered [5], [6], [7]. Particularly, the possibility to use noninvasive measurements of AF cycle length and fibrillatory wave amplitude from ECG as variables predictive of the success of CA and of medium-term clinical outcome has been investigated [6], [7]. AF cycle length and fibrillatory wave amplitude were shown to be clinically useful predicting pre-ablation tools. However, one limitation related to these measures is that they are manually provided, and that the related findings are only relevant when AF cycle length can be calculated, that means, when unambiguous fibrillatory waves on lead V1 not fused with the QRS-T complexes could be visually detected. Moreover, the fact that these measures are based on just few leads (V1, I, II) prevents the exploitation of the spatial diversity of multi-lead ECGs and might not be always representative of the voltages that can be recorded from the whole body surface. Conversely, the parameter complexity proposed in this study is provided in an automated way, it eases the requirement of observing unambiguous fibrillatory waves, and it exploits all the spatial diversity offered by multi-lead ECG recordings.

One limitation of this study is the lack of comparisons with both [6] and [7]. Still, there is a lack of knowledge about the pharmacological treatments the patients underwent before CA, and thus about possible influences of them on the presented results. Correlation can be highly influenced by a few samples far from the mean that may be outliers. In this particular case the correlations underlined between NMSE_3^{pre} and NMSE_3^{post}, and between HR^{pre} and NMSE_3^{pre} may be supposed to be dependent on the few samples with high NMSE.

Finally, even if this study did not show any significant correlation between the complexity of the AF organization evaluated before CA and its success, results showed that CA reduces the complexity of AF analyzed on surface ECG, suggesting that a possible relation is still to be discovered. Further research should assess whether a significant correlation between complexity and CA outcome can be noninvasively highlighted. This will justify the follow up of the patients who underwent CA to analyze whether AF complexity and its reduction by CA are predictive of long-term outcome, in order to select "good" patients for CA, so as to partly contribute to the question of the selection of the most suitable therapy for AF in each patient.

V. ACKNOWLEDGMENTS

The work of Pietro Bonizzi is supported by the EU by a Marie-Curie Fellowship (EST-SIGNAL program: http://est-signal.i3s.unice.fr) under contract No MEST-CT-2005-021175.

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