MEASURING P-WAVE MORPHOLOGICAL VARIABILITY FOR AF-PRONE PATIENTS IDENTIFICATION

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Abstract: Atrial fibrillation is the most common arrhythmia encountered in clinical practice. Abnormal P-waves have been observed in patients prone to AF and the analysis of P-waves from surface electrocardiogram has been extensively used to identify patients prone to atrial arrhythmias. Measuring the temporal variability of P-waves, i.e., the variation over time of morphological characteristics of single P-waves, may represent a useful method for characterizing and predicting AF cases. In this paper, we propose a method for the statistical analysis of P-waves variability. It is based on the evaluation of the empirical distribution function of differences energy among normalized P-waves. The proposed method seems promising for capturing atrial anomalies and identifying patients prone to AF.

1 INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice (about 4.5 million people in the European Union): its prevalence is estimated between 0.4% and 1% in the whole population and increases with age (5% for patients older than 65 years and 8% for those older than 80 years). Although it is not a lethal disease, AF may increase mortality up to 2-fold, primarily because of embolic stroke. Indeed, the lack of coordinated atrial contraction leads to unusual fluid flow states through the atrium. These could favor the formation of thrombus at risk to embolize, especially after return to normal sinus rhythm.

When normal cardiac impulse travels through atrial myocardium, surface electrocardiogram (ECG) recordings show the P-wave. If atrial depolarization patterns differ from normal ones, P-waves may appear prolonged and highly variable. Indeed, slowed conduction velocity in several atrial regions together with different cell refractory periods are believed to be the electrophysiological conditions provoking and maintaining AF (Platonov et al., 2000).

Abnormal P-waves have been observed in AF-prone patients and the analysis of P-waves from surface ECG has been extensively used to identify patients prone to atrial arrhythmias, especially AF (Dilaveris et al., 1998; Darbar et al., 2002; Michelucci et al., 2002; Dilaveris and Gialafos, 2001).

In this context, P-wave analysis is usually performed following both the conventional 12-leads ECG approach and the three bipolar orthogonal leads one, used to determine the P-wave vector magnitude (Clavier et al., 2002; Klein et al., 1995; Jordaens et al., 1998; Dilaveris and Gialafos, 2002). Given the relatively low P-wave amplitude with respect to background noise, both approaches use signal averaging techniques to obtain a P-wave template. The analysis of P-wave template turned out to be useful in discriminating patients at risk of developing AF or with paroxymal AF. A typically considered parameter is the P-wave duration.

According to literature, the classical approach followed to study the relation between P-wave characteristics and AF is the analysis of P-wave templates. Nevertheless, following an approach similar to that used for T-waves in the analysis of ventricular repolarization (Pueyo et al., 2009), it could be worth investigating P-waves variability, i.e., the variation over time of morphological characteristics of P-waves. Indeed, as shown in Fig. 1 and Fig. 2, variability of P-waves morphology usually appears to be significantly higher in AF patients than in healthy controls. Hence, such an approach seems to be more suitable for investigating the complicated electrophysiological conditions believed to provoke and maintain AF.

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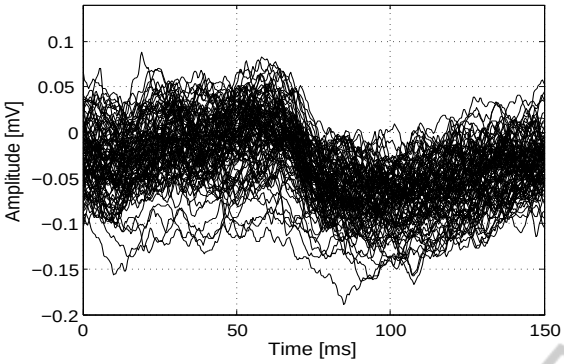

Figure 1: Butterfly plot of P-waves belonging to a patient prone to AF.

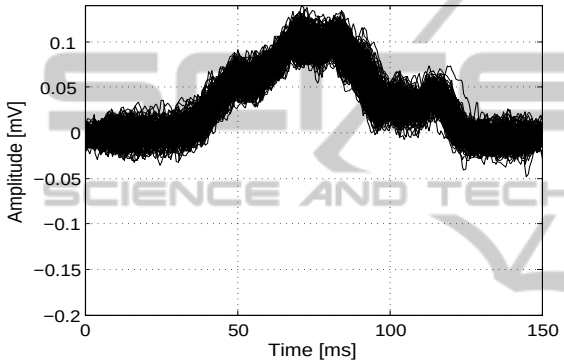

Figure 2: Butterfly plot of P-waves belonging to a healthy subject.

The aim of this work is to propose an approach to measure P-waves variability that could be effective in identifying AF prone patients.

2 METHOD

This section describes the strategy we have developed in order to measure P-waves variability within an ECG tracing of cardiac cycles.

2.1 Study Population

The study population consisted of 37 subjects, divided into 2 groups: 21 patients had a persistent form of atrial fibrillation and underwent electrical cardioversion (AF group); 16 subjects had no history of AF and have been considered as controls in this paper (control group). The AF group consists of 10 patients, who experienced at least another documented episode of AF within 3 months after cardioversion (AF relapse group), and 11 patients, who did not experience any documented AF episodes after cardioversion (no-AF relapse group). ECG was recorded for 5 minutes using a high resolution mapping system (Biosemi ActiveTwo, Amsterdam, Netherlands) with a sampling frequency of 2048 Hz, a resolution of 24-bit (about 30 nV LSB), and a bandwidth from DC to 400 Hz. For AF patients, ECG was recorded after successful cardioversion.

2.2 Pre-processing of P-waves

P-waves were first isolated according to the method proposed in a previous paper (Censi et al., 2007). After the detection of each R-wave, P-waves were extracted in a 200 ms-long window starting from 300 ms before the R-wave. Then, in order to remove baseline wander, a beat-by-beat linear piecewise interpolation was performed, selecting fiducial points from TP and PQ tracks of each beat for linear interpolation. Finally, ectopic atrial signals or P-waves with excessive noise were excluded by template matching of each P-wave as described in (Censi et al., 2007). The extracted P-waves are finite length sampled signals available in the following as vectors having the same size. P-waves from ECG II lead were considered.

2.3 Quantification of the Energy of P-waves Differences

P-waves selected during the above mentioned preprocessing phase are analyzed in order to define and characterize statistical indicators of AF phenomena based on P-waves morphological variability.

We denote by $\boldsymbol{p}_i$ the i-th segmented P-wave of the ECG tracing under analysis. Let us assume to have N of such waves each L samples long. In order to emphasize the morphological differences instead of absolute differences among waves, a unit-norm normalization is applied to each of them:

$$\hat{\boldsymbol{p}}_i = \frac{\boldsymbol{p}_i}{||\boldsymbol{p}_i||}.$$

Denote by $\varepsilon_{i,j}$ the energy of the difference between $\hat{\boldsymbol{p}}_i$ and $\hat{\boldsymbol{p}}_j$:

$$\varepsilon_{i,j} = ||\hat{\boldsymbol{p}}_i - \hat{\boldsymbol{p}}_j||^2.$$

In the following we consider the squared Euclidean norm:

$$\varepsilon_{i,j} = \sum_{k=1}^{L} \left[\hat{p}_{i,k} - \hat{p}_{j,k}\right]^2$$

where $\hat{p}_{i,k}$ is the k-th component of the vector $\hat{\boldsymbol{p}}_i$. However other norms revealing specific aspects of waves can be used.

The empirical cumulative distribution function of the differences energy among normalized P-waves is hence obtained as:

$$F_E(\varepsilon) = \frac{2}{N(N-1)} \sum_{i<j}^{N} \mathbf{1}_{\{\varepsilon_{i,j} \leq \varepsilon\}}$$

where $\mathbf{1}_{\{\cdot\}}$ denotes the indicator function of the set within brackets.

Although the empirical cumulative distribution function is rich of information about waves variability, the availability of descriptive parameters is also of interest. In the following we consider the sample mean and the sample variance of the differences energies as indicators:

$$\mu = \frac{2}{N(N-1)} \sum_{i<j}^{N} \varepsilon_{i,j}$$

$$\sigma^2 = \frac{2}{N(N-1)-2} \sum_{i<j}^{N} [\varepsilon_{i,j} - \mu]^2$$

3 RESULTS

Before ECG acquisition, AF patients underwent electrical cardioversion. In Fig.s 3, 4 and 5 we report the empirical cumulative distribution functions pertaining to controls, no-AF relapse group, and AF-relapse group, respectively. Each curve corresponds to a patient.

Fig. 3 shows the empirical cumulative distribution function of P-waves differences energy for patients belonging to the control group. All the functions exhibit similar behavior, with a high probability of having low differences among different P-waves. Conversely, Fig. 4 and Fig. 5 show the empirical cumulative distribution function of P-waves differences energy for AF patients. In this case the probability of significant differences among P-waves increases. This effect is considerably more evident in the case of AF relapse group. It is worth noting that the distribution functions of AF relapse group are significantly different from the corresponding functions pertaining to the control group. Moreover, considering the AF relapse and the no-AF relapse groups it is possible to appreciate differences in the distribution functions that allows same level of discrimination between the two groups.

The joint analysis of sample mean and sample variance confirms the difference between the control group and the AF patients groups. Fig. 6 shows the log-log plot of the pair sample mean and sample variance, namely (μ, σ^2), for each patient. We can distinguish two regions: (i) low values region and (ii) high values region. In the low values region both mean and variance of the differences energy is small. This region identifies controls and, hence, patients without AF problems. Conversely, the high values region identifies AF patients belonging to the AF relapse group. In this figure, control group results to be well separated from AF-relapse group. No-AF relapse group turns out to be characterized by intermediate values with respect to other groups. The

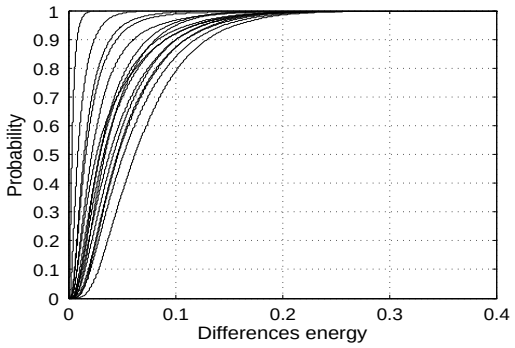

Figure 3: Controls: empirical cumulative distribution function of P-waves differences energy.

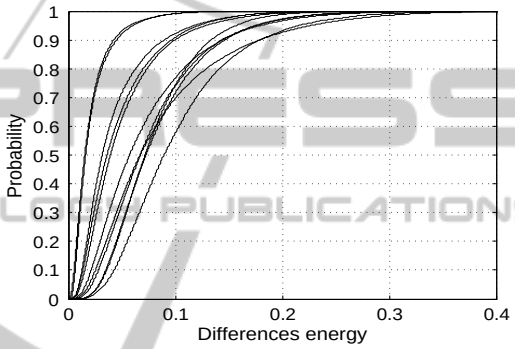

Figure 4: AF patients (no-AF relapse group): empirical cumulative distribution function of P-waves differences energy.

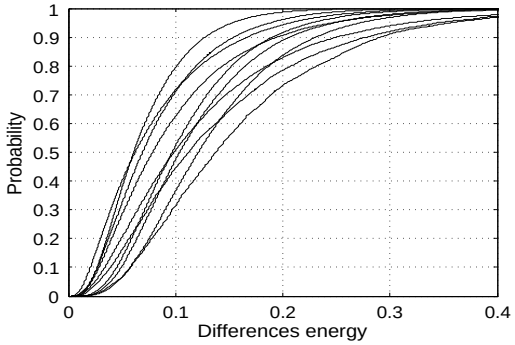

Figure 5: AF patients (AF relapse group): empirical cumulative distribution function of P-waves differences energy.

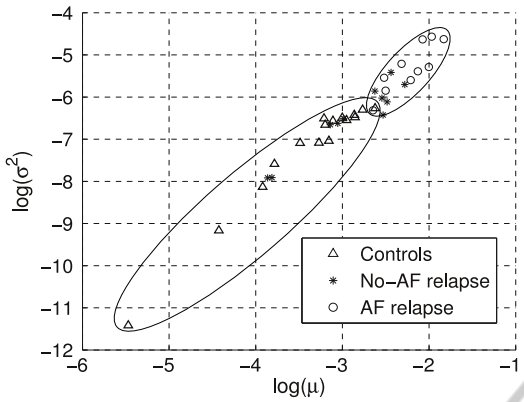

Figure 6: Sample mean and sample variance of differences energy for AF group and control group.

proposed method seems able to discriminate between healthy and AF patients. In this regard it could be of help in identifying AF-prone patients.

4 CONCLUSIONS

The availability of methods for measuring P-waves variability over time represents a useful tool to deeply understand the mechanisms underlying the atrial electrical substrate, and may help in identifying patients with substrates predisposing to AF. Indeed, the P-wave variability is related to the dispersion of atrial refractory period. In this paper, we propose a method to measure such variability. It is based on the computation of the empirical cumulative distribution function of the differences energy among normalized P-waves. The proposed method is able to discriminate between AF patients and control subjects. This fact is highlighted by the joint analysis of estimated statistical parameters such as the sample mean and the sample variance of differences energy. It is worth noting that the proposed method exhibits some ability even in discriminating between patients who experienced AF relapse from patients who did not. In conclusion, the analysis of the empirical distribution function of differences energy among normalized P-waves seems promising for capturing atrial anomalies and identifying patients prone to AF.

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