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Morphological analysis of P-wave in patients prone to atrial fibrillation

F. Censi, G. Calcagnini, E. Mattei, R.P. Ricci, C. Ricci, A. Grammatico, M. Santini, P. Bartolini

Abstract— **Aim of this study was to present a P-wave model, based on a linear combination of Gaussian functions, to quantify morphological aspects of P- wave in patients prone to atrial fibrillation. Five minutes ECG recordings were performed in 25 patients with permanent dual chamber pacemakers set at 40/min in order to have spontaneous beats. ECG signals were acquired using a 32-lead mapping system for high-resolution biopotential measurement (ActiveTwo, Biosemi, The Netherlands, sample frequency 2 kHz, 24 bit resolution). Four healthy subjects were also recorded as a control group. Up to 8 Gaussian models have been computed for each averaged P-wave extracted from every lead. The P-wave morphology is then evaluated by the following parameters: best model orders @ Degrees of Freedom Adjusted R-Square (AdjRsq) =97.5%; minimum (σmin) and maximum (σmax) standard deviation of the gaussians included in the model, number of relative maxima and minima (max+min), and zeroes of the fit. Significant differences in the best model order were obtained between the control group and patients group. Accordingly, the number of relative maxima and minima was higher in the patient group. These parameters might all be markers of the fractionated electrical activity that characterizes paroxysmal AF patients in sinus rhythm.**

I. Introduction

P-wave morphology assessment has gained increasing interest to describe the mechanisms of atrial arrhythmias [1]. Morphological analysis of P-wave has been extensively used to assess inter-atrial conduction defects and abnormalities of the left and right atrium [1][2][3].

Changes in P-wave polarity as well as subtle differences in P-wave morphology are believed to reflect abnormal activation patterns in the atria [3][4]. Irregularities in the orthogonal P-wave morphology have been detected in AF patients and associated with local inter-atrial conduction delay [2]. Different shapes of P-wave have been shown to represent the presence or absence of an underlying pathophysiological condition in patients prone to AF attacks [4]. In the presence of a partial inter-atrial conduction block, P- wave shape changes have been demonstrated to depend on the direction of the activation wavefront [5]. The studies on P-wave morphology are usually performed by visual inspection of shape changes [5].

However, abnormalities of left or right atrium are likely reflected in subtle morphological changes beyond visual classification [3].

Aim of this study was to present a P-wave model, based on a linear combination of Gaussian functions, to numerically and automatically quantify morphological features of P- wave in patients with paroxysmal atrial fibrillation.

II. Methods and Materials

A. Experimental protocol

Twenty-five patients with permanent dual chamber pacemakers (AT500-Medtronic, Inc. Minneapolis, MN, USA) were recruited at S. Filippo Neri Hospital, Rome, Italy. The AT500 device combines the monitoring of atrial tachyarrhythmia with both intervention therapies and pace-termination therapies. Intervention therapies aim at suppressing atrial tachyarrhythmia trigger mechanisms by using 3 programmable pacing algorithms. In addition, 3 pace-termination algorithms recognize treatable atrial tachycardia and delivers antitachycardia pace-therapies to restore sinus rhythm.

The study population consisted of 12 females and 13 males, aged 73±8, affected by paroxysmal atrial fibrillation and bradycardia. Four healthy subjects, with no history or sign of cardiac disease, were recorded as a control group. Five minutes ECG recordings were performed for each subject, with the pacemaker programmed in VVI mode, (i.e. in single-chamber ventricular pacing mode) set at 40/min in order to have spontaneous beats.

ECG signals were acquired using a 32-lead mapping system for high-resolution biopotential measurement (ActiveTwo, Biosemi, The Netherlands), sample frequency 2 kHz, 24 bit resolution, 0-400 Hz bandwidth. The system is made of a battery powered AD box that digitizes the signals and transfers them to a PCI receiver on computer through fiber optic connection. The 32 leads guarantee spatial sampling on the body surface. The leads were strategically positioned as shown in Fig. 1, to allow accurate recordings of atrial signals. ECG recordings were acquired as single-ended signals, with respect to the common reference.

F. Censi, G. Calcagnini, E. Mattei, P. Bartolini are with the Istituto Superiore di Sanità, Roma, Italy (corresponding author: F. Censi, phone: +390649902028; fax +390649387079; email:censi@iss.it).

R.P. Ricci and M. Santini are with the Department of Cardiology, San Filippo Neri Hospital, Roma, Italy

C. Ricci is with the Department of Statistics, Probability and Applied Statistics, Univ. of Rome "La Sapienza", Italy

A. Grammatico is with Medtronic Italia, Roma, Italy

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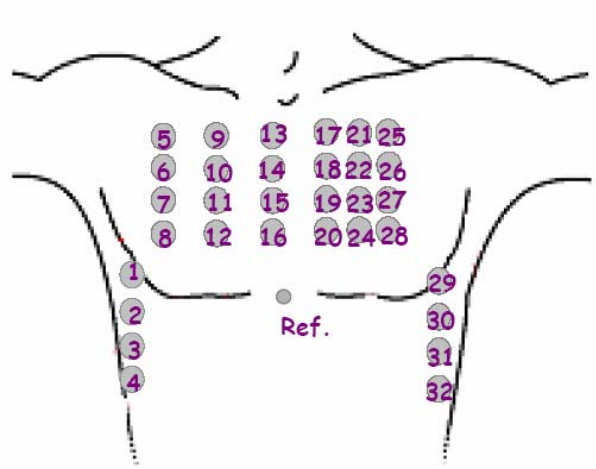


Fig 1. Electrode positioning scheme

B. P-wave pre-processing

Every lead signal was pre-processed and analysed to extract the average P-wave characteristic of the specific lead.

The first step is to detect P-waves from the acquired signals. P-waves are isolated considering 200ms windows triggered from the R wave of the QRS complexes. R-waves are detected using an algorithm similar to that proposed by Pan and Tompkins which actually acts as a high pass filter on the ECG signals, enhancing the high frequency QRS complexes [6].

Secondly, a beat-by-beat linear piecewise interpolation was used to remove baseline wander, on each P-wave.

Then, a coherent averaging procedure has been implemented. In order to take into account the variations in PR interval and/or the inaccuracy in R-wave detection, care had been paid to align the P-waves before the averaging procedure; particularly, P-waves were aligned according to the lag at which the cross-correlation function between the current averaged P-wave and each single P-wave shows its maximum [7].

C. The Gaussian function-based model

The morphological features of a wave can be quantified by counting the number of "bumps" (i.e. sequences of peaks and valleys) in the signal. To achieve this result, the average P-wave is reconstructed by a non linear least squares fitting $\hat{y}$ obtained as a linear combination of Gaussian functions:

$$\hat{y} = \sum_{i=1}^{n} a_i e^{\left[-\left(\frac{x-b_i}{c_i}\right)^2\right]}$$

where a_i is the coefficient of the linear combination, b_i represents the location of a peak (or valley) on the time axis, and c_i describes the width of the bump on the curve (distance between points on the curve at which the function reaches half its maximum value - Full Width at half maximum, FWHM).

The number of Gaussians (n) needed to fit the wave is chosen as *order* of the model and used as a descriptor of the wave shape. The parameters estimation is achieved iteratively by using a non linear least square method. Up to 8 Gaussian models are computed for each averaged P- wave extracted from every lead, i.e. from order 1 to order 8. The $(n-1)^{th}$ order model sets the initial conditions for the n^{th} order model. Order by order, the algorithm keeps trace of the previous peaks and the fitting improves. The goodness of fit is evaluated through the Degrees of Freedom adjusted R-square (AdjRsq), defined as:

$$AdjRsq = 1 - \frac{\sum_{k=1}^{N}(y_k - \hat{y}_k)^2 (N-1)}{\sum_{k=1}^{N}(y_k - \bar{y})^2 (v)}$$

where $\hat{y}$ is the P-wave estimated as the linear combination of Gaussian function, y is the original P-wave, $\bar{y}$ the mean value, N is the number of signal samples and ν is the residual degree of freedom. This statistic uses the R-square statistic, and adjusts it based on the residual degrees of freedom v. The residual degrees of freedom are given by the number N of samples of the signal minus the number of fitted coefficients. For all the averaged P-waves AdjRsq value≥99% can be achieved with an 8^{th} model order, however models that achieve an AdjRsq≥97.5% have been chosen as representative of the signal, thus assuming a remaining 2.5% proportion of unexplained variance as post-averaging residual noise.

D. Quantification of morphological features

Since more than one gaussian function can be used by the model to cover steep portions of the signal, without really fitting a peak or valley, a better morphological description of the wave is obtained by evaluating the number of *maxima*, *minima* and *zeroes* of the extracted fit.

The P-wave morphology is then evaluated by the following parameters:

- model order @ AdjRsq≥97.5%;
- minimum (σ_{min}) standard deviation of the gaussians included in the mode;
- maximum (σ_{max}) standard deviation of the gaussians included in the model;
- number of relative maxima and minima (max+min);
- number of zero crossings of the model (zeros).

The gaussian fitting of two P-waves with different morphology is shown in figure 2.

The P- wave on the left achieves an AdjRsq = 98.93% with a second first order model (two gaussian functions),

while in the second case AdjRsq higher than 97.5% is only reached with a 6th order gaussian fit. Lower panel shows the values of the five pasrameters extracted from the Gaussian fit to quantify the morphological features.

E. Data representation

To compare the populations of controls and patients in spontaneous rhythm, 3 classes of risk have been defined, according to the number of AF episodes recorded by dual chamber pacemakers in the last 6 months preceding the acquisition:

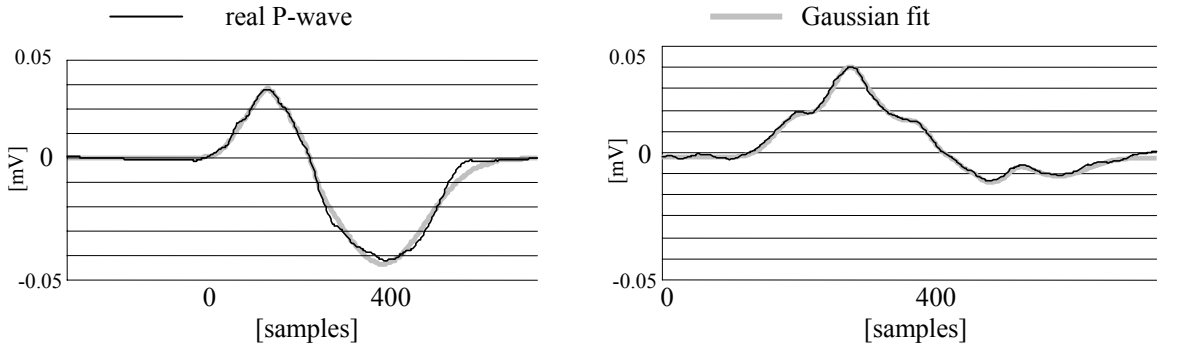
- class N: normal, no episodes and no risk associated, i.e. control subjects;
- class LR (low risk): number of episodes=0;
- class HR (high risk): number of episodes≥1.

III. RESULTS

Table I shows the results obtained by morphological analysis over the 3 risk classes. P-waves from the control group can be described by lower order models (2.7±0.2) compared to both LR (3.4±0.8) and HR patients (3.5±1.0) (N vs LR: $p<0.09$; N vs HR $p<0.05$), while morphological differences between LR and HR, evaluated in terms of model order, are not significant ($p<0.9$).The number of relative maxima and minima from the gaussian fit is slightly higher in HR class (4.2±1.2) compared to both LR (3.8±1.1) and N (3.1±0.4), however these differences are not significant (N vs LR: $p<0.3$; N vs. LR: $p<0.1$; LR vs HR: $p<0.3$). The number of zeroes, instead, is significantly increased in HR compared to LR (0.5±0.3 vs 0.8±0.3, $p<0.03$) but no particular differences are observed in the other cases.

IV. DISCUSSION

Standard approaches for P-wave analysis deal mainly with the analysis of the P-wave duration. However, there is the lack of good and accepted definitions of P-wave onset and offset, whose determination cannot be automatic and has a high interobserved variability. Morphological analysis of P-wave has recently gained interest, although it is a more complicated way to assess the signal. Indeed, different P-wave morphologies reflect different atrial activation patterns and could identify conduction deflects [4]. In this study a P-wave model was presented to numerically and automatically quantify, beyond visual inspection, morphological aspects of P- wave in AF patients.



Best order: 2
Zeros: 1
Max+min:2
σ_{max}*: 53.53*
σ_{min}*: 30.69*

Best order: 6
Zeros: 1
Max+min:4
σ_{max}*: 53.78*
σ_{min}*: 23.20*

Fig. 2. Gaussian fit of two P-waves with different morphology. Upper panel – left: two Gaussian functions fit the P-wave with AdjRsq =98.93%. Upper panel – right: AdjRsq higher than 97.5% is only reached by a 6th order model. Lower panel: values of the five parameters extracted from the Gaussian fit to quantify the morphological features.

TABLE I.

	N	LR	HR	population *p*-value	N vs. LR *p*-value	N vs. HR *p*-value	LR vs. HR *p*-value
best model order	2.7±0.2	3.4±0.8	3.5±1.0	0.1	0.09	0.05	0.9
zeroes	0.7±0.3	0.5±0.3	0.8±0.3	0.08	0.4	0.4	0.03
Max+min	3.1±0.4	3.8±1.1	4.2±1.2	0.2	0.3	0.1	0.3
Sigma_max	46.8±6.7	50.8±6.2	51.0±10.2	0.4	0.2	0.2	0.9
Sigma_min	24.5±2.2	22.2±10.7	23.5±9.6	0.5	0.2	0.6	0.5

Results for the morphological analysis expressed as mean values ± standard deviations and p-value obtained according to the statistical analysis explained in the text.

The model is based on a gaussian fit of averaged P-wave. Up to eight gaussian functions have been linearly combined to describe the waveform, and the number of gaussians that explain 97.5% of the signal variance is automatically selected as representative of that specific wave. The fit in a way acts as a filter that eliminates high frequency noise. The parameters chosen synthesise the main morphological characteristics of the original waveforms: the order of the model is the the number of gaussians required; the number of maxima and minima provides information on the number of 'bumps' included in the waveform; the number of zeros accounts for the phase changes of the P-wave. Mean values of these parameters over the 32 leads have been considered. Significant differences in the best model order were obtained between the control group and patients group. Accordingly, the number of relative maxima and minima was higher in the patient group. Also, the number of zeros succeeded to discriminate between the two classes of high risk and low risk patients. These parameters might all be markers of the fractionated electrical activity that characterises paroxysmal AF patients in sinus rhythm. P-waves in control group, as expected from visual inspection, appear smoother than those from AF patients. To our knowledge, no previous studies have performed a similar analysis in paroxysmal AF patients, thus no comparisons are possible. Gang and colleagues have recently proposed some complex morphological descriptors of the P- wave for prediction of AF risk in post-CABG patients based on singular value decomposition of the ECG signal [3]. These descriptors take into account global shape abnormalities and dissimilarities between shapes in individual leads. These parameters increased in AF patients, showing morphological alterations in this group, but failed to independently predict postoperative AF. A polynomial representation of P-wave was implemented by Clavier and colleagues, who developed a method for automatic analysis of the P-wave based on the use of a hidden Markov model and wavelets transformation [8]. A polynomial interpolation can only partially represent details in P- wave morphology that are thought to reflect the atrial conduction abnormalities, and degrees higher than the fourth generate waveforms that do not have a limited temporal extension, characteristic that is indeed preserved by a linear combination of gaussians. In addition, the gaussian functions-based model of P- wave proposed in this study has the great advantage of being independent on the definition of P- wave boundaries, thus it can provide useful information in AF risk assessment.

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