A Novel P-wave Duration Estimation Method to Assess the Impact of the Hybrid Procedure for Atrial Fibrillation Ablation

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Abstract

Changes in P wave duration (PWD) following atrial fibrillation (AF) ablation have been described and may have diagnostic value. PWD is usually assessed manually from ECG. This study aimed at exploring a novel method for automated modeling of the P-wave and assessment of PWD. Moreover, it aimed at investigating the effect of hybrid procedure (HP) for AF treatment on PWD. P-wave modeling is achieved by means of a concatenation of two half-Gaussian functions, to account for potential left and right asymmetries in the P-wave morphology. When compared with a single Gaussian model, the method showed better fitting in terms of normalized mean square error (NMSE; 0.14±0.07 vs. 0.28±0.11, $p < 10^{-4}$*). When investigating the effect of HP on PWD, results showed that PWD was significantly decreased after procedure (111.49±23.29 ms vs. 96.27±30.28 ms,* $p = 0.0319$*). PWD pre-procedure, was significantly higher in persistent patients than in paroxysmal patients (126.85±15.50 ms vs. 106.70±23.82,* $p < 0.0272$*). Automated analysis of P-wave from ECG to extract PWD is possible. Results at 9 month follow-up suggest that selection of patients may be possible before procedure to individualize AF therapy.*

1. Introduction

Atrial fibrillation (AF) is known to be associated with an increased risk of mortality [1]. The current therapy of AF is still far from being satisfactory [2]. This is in part related to the progressive nature of the disease, which causes electro-structural changes in the atrial myocardium over time. Slowed conduction velocity in several regions with different refractory periods are believed to be the electrophysiological conditions provoking and maintaining AF [3]. This electrophysiological remodeling leads to increased stability of the AF substrate (in terms of incidence of conduction block and number of co-existing fibrillation waves), which reduces the success rate of any rhythm control therapy in AF. At an early stage of development of AF, those atrial conduction abnormalities have been shown to be reflected on the surface ECG in terms of prolonged and highly variable P-waves [3, 4]. As an intuitive consequence, the effect of specific treatments should reflect on P-wave morphology as well. With respect to catheter ablation procedures in particular, changes in P wave duration (PWD) have been described following AF ablation procedure and attempted to predict the arrhythmia recurrence [5]. Recurrence of AF after ablation tends to limit the success rate. Patient history of AF in terms of paroxysmal or persistent AF further affects this success rate [6, 7]. Hybrid procedure (HP) consists of combining a transvenous endocardial and thoracoscopic epicardial approach in a single procedure in order to overcomes shortcomings of standard ablation procedures (briefly, inability of creating transmural endo-epicardial block lines by solely epicardial or endocardial procedures) [8]. HP is effective in restoring sinus rhythm in patients with history of different types of AF. HP not only reduces PWD immediately after the procedure but also prevents AF recurrence over time. Finding suitable ways to estimate PWD noninvasively from conventional recording techniques (e.g. the standard 12-lead ECG) could provide an improved and more integrated diagnosis when combined with echocardiographic parameters (as dilated left atria) or AF type (paroxysmal, persistent), and help individualizing therapies by selecting the best candidates for HP.

Automated P-wave analysis has been investigated in several studies. Censi *et al.* proposed an approach based on Gaussian decomposition of the signal-averaged P-wave ECG. However, Corino *et al.* recently showed that there exist a beat-to-beat non-negligible variability in the P-wave morphology in healthy subjects, and suggested that this variability could be even more pronounced in patients affected by cardiac arrhythmias. This would potentially make analyses based on the signal-averaged P-wave inaccurate. As an alternative, these authors proposed a beat-to-beat analysis based on a single Gaussian model. Despite the valuable findings given by this approach, it does not take into account potential left and right asymmetries in the morphology of the P-wave. In this study, we present a beat-to-beat P-wave analysis based on a concatenation of two half-Gaussian functions, to account for those asymmetries. The method is first validated on a dataset composed by healthy subjects, and its performance compared with the single Gaussian model. The method is then applied to a dataset of patients who underwent HP to assess how effective HP is in restoring sinus rhythm in patients with different history of AF, by reducing PWD immediately following the procedure.

2. Methods

2.1. Data and preprocessing

Two datasets were used in this study. The method validation dataset used was extracted from the PTB Diagnostic ECG Database available on Physionet (http://www.physionet.org/physiobank/database/ptbdb/). This included 51 recordings from healthy volunteers (mean age 44 ± 16 years; male/female: 38/13). Similarly to [9], two minutes recordings of X-Frank lead (sampled at 1000 Hz) were used. This dataset was used to test the quality of fit of the proposed method and to compare it with a standard fitting based on a Gaussian function [9]. The method was then applied to a clinical dataset including 35 patients who underwent HP (58 ± 10 years; males/females: 27/9; paroxysmal/persistent: 27/9). Inclusion criteria were: first ever ablation procedure, recognizable P-waves before and after the procedure (all patients converted to sinus rhythm after procedure), one minute ECG recording available. This dataset was analyzed to investigate the ability of the proposed method to describe changes in PWD following HP. One minute recordings of lead I (or II, in few cases where quality of lead I was poor; sampled at 1000 Hz) was used. All patients allowed a minimum follow-up of 9 months at the point of data collection. Signals in both datasets were preprocessed by applying a third-order zero-phase band-pass Chebyshev filter with frequency band between [0.5, 100] Hz to remove baseline wandering and high frequency noise. For each recording, the R-wave fiducial points were extracted using a Pan and Tompkins like algorithm [10]. P-waves were then segmented by manually looking for an optimal patient specific window starting from 300 ms before the R-wave. Each P-wave was then de-trended by means of linear interpolation. Unlike previous studies ([3, 9]) we avoided any P-wave exclusion criterion based on cross-correlation with an arbitrary reference P-wave. The impact of noise was reduced by removing outliers from the results at a post-processing stage.

2.2. P-wave Gaussian modeling

Each available P-wave segment (ECG segment likely containing a P-wave) was fitted by means of a concatenation of two half-Gaussian functions. This was done to account for potential left and right asymmetries in the P-wave morphology. Given the general expression of a Gaussian function:

$$f(x,\theta) = Ae^{-\frac{(x-\mu)^2}{2\sigma^2}} \tag{1}$$

defined by the mean μ, the standard deviation σ, and the amplitude A, the physical analogue of these parameters is [9]: the location of the P-wave maximum, a scalar multiple of the P-wave duration, and the P-wave amplitude, respectively. The parameter vector θ is defined as $\theta = [A\ \sigma]^T$. Potential asymmetries in the morphology of the P-wave might cause the estimate of the PWD by a scalar multiple of σ to be inaccurate. To avoid this, a first Gaussian function f_1 is estimated such as to maximize the fit with the left-half of the P-wave segment (from P-wave segment onset, P_{on}, to the location of the P-wave segment maximum, P_{max} (see Fig. 1a-b)). A second Gaussian function f_2 is then estimated to maximize the fit with the right-half of the P-wave segment (from P_{max} to the offset of the P-wave segment, P_{off} (see Fig. 1c)). Finally, a complete model of the P-wave is achieved by concatenating the left-half of f_1 with the right-half of f_2, giving f (Fig. 1d). PWD is then computed as PWD $= 2\sigma_1 + 2\sigma_2$. The factor 2 is chosen such that almost 50% of the area under each function is accounted for, at the same time excluding the tails of the Gaussian functions. This allows a more precise estimate of the PWD than using a single Gaussian function (as depicted in Fig. 1e, which gives a visual comparison of the estimated function f, thick solid line, and a model achieved by a single Gaussian function, thick dotted line). The estimation of the parameter vector θ is accomplished by means of the following optimization procedure. Eq. (1) is first linearized by applying a logarithmic transformation to both left and right members of the equation. After a few manipulations, the problem becomes:

$$\begin{aligned} \log y &= -\frac{1}{2\sigma^2}x^2 + \frac{1}{\sigma^2}\mu x + \log A - \frac{1}{2\sigma^2}\mu^2 \\ &= \alpha x^2 + \beta x + \gamma \end{aligned} \tag{2}$$

with

$$\alpha = -\frac{1}{2\sigma^2},\ \ \beta = \frac{1}{\sigma^2}\mu,\ \ \gamma = \log A - \frac{1}{2\sigma^2}\mu^2.$$

Additionally, both functions f_1 and f_2 are required to fulfill the following three constraints:

- the maximum of the P-wave must belong to the function;

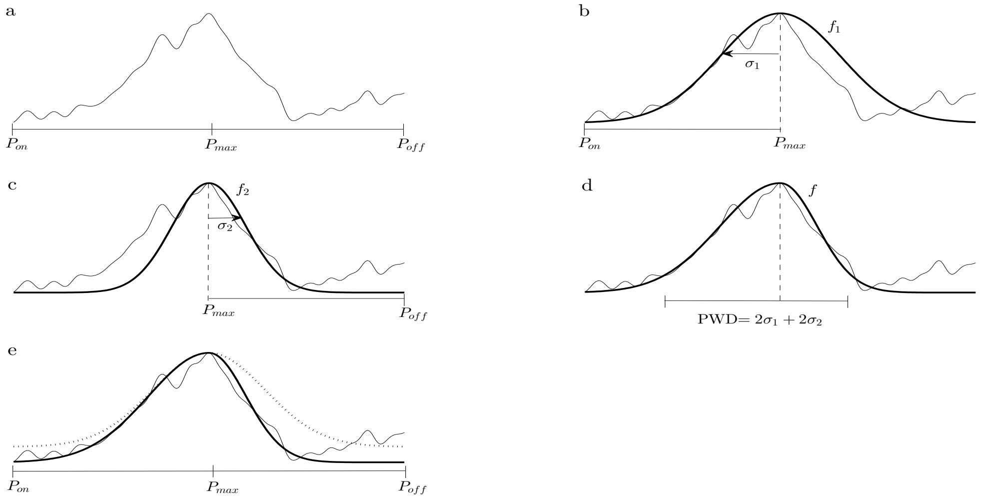

Figure 1. P-wave modeling based on a concatenation of two Gaussian functions; a: a P-wave from lead I; b: estimation of f_1 optimized on the interval $[P_{on}, P_{max}]$; c: estimation of f_2 optimized on the interval $[P_{max}, P_{off}]$; d: P-wave modeling achieved by concatenating the left-half of f_1 with the right-half of f_2, and corresponding estimate of the PWD by means of σ_1 and σ_2; e: comparison with a standard fitting by one Gaussian function (thick dotted line).

- the derivative of the function at the location of the P-wave maximum, P_{max}, must be zero;
- the function must pass through a second point optimally chosen to minimize the error between the function and the P-wave.

The optimization procedure is then based on constrained linear least squares. The aforementioned second point is selected by a grid search over a set of points. This set is different for f_1 and f_2. For f_1, the grid search is performed on the interval $[P_{on}, P_{max}]$, and the fit is evaluated on the same interval (and not over the whole P-wave). For f_2, the grid search is performed on the interval $[P_{max}, P_{off}]$, and the fit is evaluated on the same interval. The error between the function and the P-wave is evaluated by the normalized root mean squared error (NRMSE).

2.3. Statistical analysis

All data were analyzed by means of MATLAB, version R2013a (MathWorks, Natick, MA). All parameters are given as median±median absolute difference (MAD). Outliers were identified based on the interquartile range. Given the first and third quartile, Q_1 and Q_3, respectively, outliers were defined to be any observation outside the range $[Q_1 - 1.5(Q_3 - Q_1), Q_3 + 1.5(Q_3 - Q_1)]$. Outliers were removed to account for potentially noisy P-waves. To assess quality of fit, the new method was compared with a standard fitting based on a single Gaussian function in terms of NRMSE between each model and the original P-wave. Significant differences were tested by means of a Wilcoxon signed-rank test. For the experimental application, comparisons between different groups evaluated before or after the procedure were made using a Wilcoxon sum-rank test. Pre- versus post-procedure differences within the same group were analyzed using a Wilcoxon signed-rank test. Results were considered statistically significant at p<0.05.

3. Results

3.1. Method validation

The proposed method provided a more accurate fit of the P-waves in terms of NRMSE compared with a standard fitting based on one Gaussian function (0.14±0.07 vs. 0.28±0.11, $p < 10^{-4}$). Fig. 2 depicts a box-plot of the results of the two methods. This is also visually suggested by Fig. 1e.

These results finally suggest the proposed method is more suited for beat-to-beat P-wave modeling than a standard Gaussian model.

3.2. Effect of HP on PWD

Overall, PWD was significantly decreased after procedure (111.49±23.29 ms vs. 96.27±30.28 ms, $p = 0.0319$). PWD pre-procedure was significantly higher in persistent patients than in paroxysmal patients

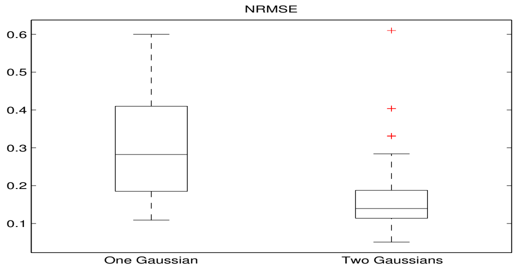

Figure 2. Boxplot from comparison of P-wave fitting by two half- or one Gaussian function.

(126.85±15.50 ms vs. 106.70±23.82, $p = 0.0272$). Associations of P-wave changes with recurrence of AF at 9 month follow-up were analyzed for all patients (30 in sinus rhythm; 5 showing AF recurrence). Pre- vs. post-procedure PWD decrease was significant for patients without recurrence (117.39±21.99 ms vs. 97.12±29.79 ms, $p = 0.0407$). Relation between AF recurrence and AF type is summarised in Table 1. A χ^2 test (with Yates' correction) on this contingency table did not give any significant relation between type of AF and 9-month recurrence. For completeness, all analyses were repeated on PWDs estimated using the single Gaussian model. None of the previous analysis was significant for this model.

Table 1. Relation between AF type and AF recurrence at 9 months.

	No AF recurrence	AF recurrence
Paroxysmal AF	22	4
Persistent AF	8	1

4. Conclusion

Automated analysis of P-wave from ECG to extract PWD is possible. A novel technique to model P-waves based on a concatenation of two half-Gaussian functions was presented, which accounts for left and right asymmetries in the P-wave morphology, allowing for a more accurate estimate of PWD. When applied to a dataset of patients who underwent HP, the analysis showed that PWD was significantly reduced by HP. Pre-procedure PWD was significantly higher in persistent than paroxysmal patients, while there was no difference after the procedure. At 9-month follow up, 86% of the patients were in sinus rhythm. These results highlight the effectiveness of HP in treating patients with different history of AF, and suggest that selection of patients may be possible before procedure to individualize AF therapy. A new study with a larger dataset is needed to confirm these findings.

References

[1] Camm AJ, Kirchhof P, Lip GYH, Schotten U, Savelieva I, Ernst S, et al. Guidelines for the management of atrial fibrillation: the task force for the management of atrial fibrillation of the european society of cardiology (esc). Europace 2010;12:1360–1420.

[2] Kirchhof P, Breithardt G, Aliot E, Al Khatib S, Apostolakis S, Auricchio A, et al. Personalized management of atrial fibrillation: Proceedings from the fourth atrial fibrillation competence network/european heart rhythm association consensus conference. Europace 2013;15(11):1540–56.

[3] Censi F, Calcagnini G, Ricci C, Ricci RP, Santini M, Grammatico A, Bartolini P. P-wave morphology assessment by a gaussian functions-based model in atrial fibrillation patients. IEEE Trans Biomed Eng 2007;54(4):663–72.

[4] Platonov PG, Carlson J, Ingemansson MP, Roijer A, Hansson A, Chireikin LV, Olsson SB. Detection of inter-atrial conduction defects with unfiltered signal-averaged P-wave ECG in patients with lone atrial fibrillation. Europace 2000; 2:32–41.

[5] Blanche C, Tran N, Rigamonti F, Burri H, Zimmermann M. Value of P-wave signal averaging to predict atrial fibrillation recurrences after pulmonary vein isolation. Europace 2013;15:198–204.

[6] Caldwell J, Koppikar S, Barake W, Redfearn D, Michael K, Simpson C, Hopman W, Baranchuk A. Prolonged P-wave duration is associated with atrial fibrillation recurrence after successful pulmonary vein isolation for paroxysmal atrial fibrillation. Journal of interventional cardiac electrophysiology 2013;39(2):131–8.

[7] Bunch T, Day JD. Achieving favorable very long-term outcomes after catheter ablation for atrial fibrillation: an exciting adventure or delusional quest? Journal of cardiovascular electrophysiology 2011;22:1215–1216.

[8] Pison L, La Meir M, van Opstal J, Blaauw Y, Maessen J, Crijns HJ. Hybrid thoracoscopic surgical and transvenous catheter ablation of atrial fibrillation. Journal of the American College of Cardiology 2012;60:54–61.

[9] Corino VDA, Chouvarda I, Maglaveras N, Mainardi L. A beat-to-beat P wave analysis in healthy population. In In Computers in Cardiology 2010. Belfast: IEEE Computer Society Press, volume 37. 2010; 553–556.

[10] Pan J, Tompkins WJ. A real-time QRS detection algorithm. IEEE Trans Biomed Eng 1985;32:230–236.

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