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Beat to Beat Wavelet Variability in Atrial Fibrillation

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***Abstract*—Atrial fibrillation (AF) is a complex phenomenon, related with a multitude of factors, including the electrical properties of the atrial substrate. The purpose of this work is to present a method that highlights electrocardiographic differences between normal subjects and patients with paroxysmal AF episodes (PAF), potentially related with substrate differences. Vectorcardiography recordings are considered and, for each lead (X-Y-Z), on a beat by beat basis, a steady window before QRS, corresponding to the atrial activity, is analysed via continuous wavelet transform. Wavelet-based parameters are calculated and compared between the normal and AF group, with the beat to beat variation of wavelet energy as the most important feature showing a significantly higher variability in the AF group.**

I. Introduction

PAROXYSMAL atrial fibrillation (PAF) is the most common sustained cardiac arrhythmia [1], and it tends to become more persistent and more difficult to treat over time. PAF constitutes a situation that has often unknown causes and is also quite often unsuccessfully treated. It exhibits a very complex and difficult to understand pathophysiology, since various triggers and substrates interacting through different ways, leading to the development of reentrant circuits [2]. Its prevalence, the low regulation success, as well as the risks for stroke and cardiac diseases when the arrhythmia is unregulated, raise the need for new approaches towards a sophisticated treatment planning on a personalised basis. Among the difficulties in current approaches motivating this research is the fact that PAF constitutes a common cause of repeated admissions to hospital, while there is a lack of a definite cure for atrial fibrillation, i.e. catheter ablation is not always suitable, recurrence is possible after ablation, and medication therapy is questionable, with variable inter-subject effect.

It is thus evident that in depth understanding of the interplay among different functional and structural components of this complex phenomenon, and clarification of the arrhythmia mechanisms in different PAF populations remains critical for tailoring the correct treatment.

While computational models have proven useful in understanding the complex atrial mechanisms in PAF at various spatial scales [3], macroscopic analysis of the atria based on clinical ECG recordings remains one of the pillars for understanding and creating evidence as regards PAF.

In this scope, the duration and the morphology of P wave have been analyzed in various studies referring to atrial conduction disturbances. Prolongation of P wave, as measured in high resolution ECG, was found to be related to PAF [4]. Other studies have investigated the morphological characteristics of the traditional surface ECG or in the signal-averaged ECG, including spatial heterogeneity of P-wave morphology [5]. The presence of P-wave multiple deflections in PAF, potentially linked with an altered substrate and a modified atrial propagation, has been studied in [4] via wavelet analysis.

In order to fully investigate atrial phenomena, in terms of substrate instability, dynamical and non-stationary processes have to be considered, and analysis has to move beyond one beat or average beat analysis, towards beat to beat spatiotemporal analysis. P wave changes on a beat to beat basis have been analyzed via clustering techniques [6], to classify individuals into two groups: those who have a constant P wave morphology and those that suffer of beat-to-beat morphology changes. Beat-to-beat changes in normal population have been investigated in terms of time-domain modeling, and a morphological variability was found, independent of age or gender [7].

The present work proposes a methodology for the beat to beat wavelet analysis of atrial ECG activity in vectorcardiographic (VCG) recordings under sinus rhythm. Wavelet analysis is considered as a suitable methodology for the study of P-wave multiple deflections in PAF. The main advantages of the proposed methodology are:

a) low computational complexity and high robustness as regards the delineation of the region of interest,

b) a flexible framework allowing the investigation of beat to beat atrial activity in terms of average characteristics, overall statistical variations and beat to beat dynamics.

The application of the methodology in data from PAF subjects and controls of the same age reveals statistically significant higher temporal wavelet variability in PAF in the three orthogonal ECG leads (X-Y-Z), and a difference in the average activity.

II. Methology

A. Data and Preprocessing

VCG recordings (X-Y-Z leads), at 1000Hz, were used in

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this study. Two groups were considered: normal subjects at all ages and of both genders (Group N), and subjects who have a history of paroxysmal AF (Group A). For group N, the signals were obtained from Physionet's PTB Diagnostic ECG database, while for group A, signals were recorded at the 1st Cardiology Clinic of AHEPA University Hospital of Thessaloniki. Subjects were under no medication, for either group. Group N was subdivided in two subgroups, Ny and No, corresponding to younger and older patients, the latter age-matched with the group A. A total of 9,468 sinus rhythm beats, available in 3 leads (overall 3*9,468beats) were analyzed from 79 ECG recordings from all groups.

TABLE I
DISTRIBUTION OF THE ANALYZED BEATS

Group	Beats	Samples	Mean Age	Males %	Mean Heart Rate	Duration (seconds)
No	2,974	24	53 ±9	70%	68±10	119±2
Ny	4,013	32	28 ±5	70%	65±11	118±4
A	2,481	23	53.5±7	61%	68±11	97±5

A preprocessing denoising procedure was applied in all the signals, including the removal of linear trend, a 50 Hz notch filter, and a high-pass Butterworth (1 Hz cut off frequency) for the removal of dc parameter. Subsequently, each beat was normalized with the absolute value of the respective R point, since the potential existence in the recording procedure of signals with different scales would lead to a bias or error in the following calculations.

B. Atrial Activity Analysis Window

In order to localize in each beat the part of the ECG which contains the atrial activity for further analysis, an additional preprocessing procedure was followed, aiming to locate the window within which the P wave is located, without insisting on finding the exact beginning and end of P wave.

First, the QRS points for each recording were extracted using the Ecgpuwave tool [8], which is an improved algorithm based on the algorithm of Pan and Tompkins [9] and is freely available in Physionet. In order to improve the exact positioning of R point, the final R point was defined as the instant the absolute value of the signal maximized within the time window [Re-200msec, Re+50msec], where Re is the R points as it is defined by the Ecgpuwave algorithm.

Additionally, medical experts marked a P wave in each one of the signals contained in the dataset, to be used as a reference template of P waves. Based on this template, the mean (meanPR) and the standard deviation (stdPR) of the distance between the end of these P waves and the R point were computed. The peak of the Q point was then defined as the instance when the value of the ECG is minimized within the time window [R-(meanPR+stdPR), R].

Furthermore, having localized the peak of the Q complexes, we defined the starting point of analysis time window in each beat as Q-250mesc, taking into account the statistical properties of abovementioned Pwave reference template, i.e. in all leads the P waves do not start before that time.

A final step was to exclude from the subsequent analysis the start of the Q complex. For that reason we calculated the mean (meanPQ) and the standard deviation (stdPQ) of the duration between the end of the P wave and the peak of the Q point, according to the reference template. Eventually, the atrial activity window segment to be later analyzed was defined to extend from Q-250mesc to Q-(meanPQ+STDPQ).

C. Wavelet Features

Continuous wavelet analysis was performed in the window of interest (defined in previous subsection), following equation 1.

$$X_w(a,b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} x(t) \psi^* \left(\frac{t-b}{a} \right) dt \qquad (1)$$

where x is a timeseries, ψ is the mother wavelet, α is the wavelet scale and b is the time translation parameter.

Three mother wavelet functions were tested. The first mother wavelet to be used was of the Symlets Wavelet Family and the order of the wavelet was chosen equal to 4 (Sym4). The second mother wavelet was of the Daubechies wavelet family and the order of the wavelet was equal to 4 (Db4). The last wavelet was the Morlet wavelet.

The three mother wavelet chosen have different properties. Daubechies wavelets are not symmetric, have highest number of vanishing moments for a given support width and are associated with minimum-phase filters. Daubechies wavelets are widely used in solving a broad range of problems, e.g. self-similarity properties of a signal or fractal problems, signal discontinuities, etc. Symlets are compactly supported wavelets with least asymmetry and highest number of vanishing moments for a given support width. The associated scaling filters are near linear-phase filters. Morlet wavelets are continuous and symmetric, with analytic definition as expressed in equation 2.

$$morl(x) = e^{\left(-x^2/2\right)} \cdot \cos(5x). \qquad (2)$$

They have been widely used in continuous wavelet transform analysis.

TABLE II
WAVELET SCALE BANDS AND FREQUENCY CORRESPONDENCE

Scale Band	Starting frequency	Ending frequency
S1	6 Hz	16 Hz
S2	16 Hz	25 Hz
S3	25 Hz	50 Hz
S4	50 Hz	100 Hz

The range of scales selected in our analysis corresponded to a frequency range of 6-100 Hz (according to the central frequencies of the mother wavelet), which is considered most relevant to the atrial activity. This frequency range was divided to 4 bands, as depicted in Table II.

As a next step, we computed the wavelet energy for each scale band, within the window of interest for each beat of each ECG signal. The following features were then

calculated and per scale band, and lead, for each subject:

a) WBmeanE (mean wavelet energy among beats). Having calculated the mean energy of the wavelet coefficients per beat, this variable is defined as the mean value of wavelet energies within a scale band.

b) WBcvE (coefficient of variation of wavelet energy among beats). For the calculation of this variable the standard deviation (WBstdE) of wavelet energy among beats is necessary. WBcvE is defined as the quotient of the above mentioned standard deviation to the mean energy (WBstdE/ WBmeanE) within a scale band.

D. Statistical Analysis

The resulting feature set for analysis consisted of 2 features per band x 4 bands x 3 leads, per subject, i.e. WBcvE for the band S3 and in lead Y.

Initially, a statistical analysis took place between the groups No and Ny, i.e. normals of different age. In order to investigate the potential differences due to AF, between the two age matched groups No and A, a statistical analysis was performed for each feature.

Furthermore, the features generated by use of different mother wavelets were compared, in terms of better differentiating between normal and AF, i.e. least intra-class and biggest inter-class Mahalanobis distance. Further criterion employed were the ranking of features based on the area under curve (AUC) of the ROC for the division of the two groups and the number of features with statistically significant differences.

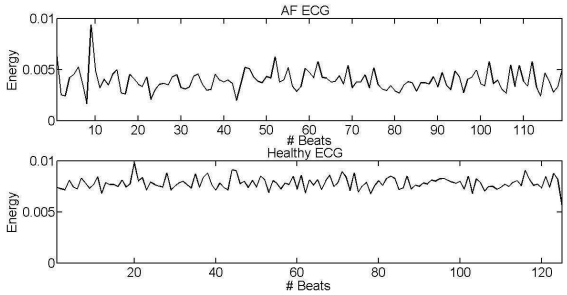

Fig. 1. Beat by beat wavelet energy for scale S3 and lead X. (top) AF subject, (bottom) healthy subject. The average value of the sequence is WBmeanE.

III. RESULTS

In Figure 1 the wavelet energy for scale S3 and lead X is depicted on a beat by beat basis, for the Daubechies mother wavelet, for a recording of group A and No respectively. No feature was found to have statistically significant differences between groups No and Ny, which is in agreement with a previous work employing model-based analysis [7].

With respect to the differences between groups No and A, the WBmeanE and the WBcvE were analysed for statistical differences between groups No and A, and the results are depicted in Tables III and IV, respectively.

TABLE III
STATISTICALLY SIGNIFICANT DIFFERENCES OF WBMEANE BETWEEN GROUPS NO AND A

Mother wavelet	Lead	Wavelet band	ttest p	No	A
Morlet	X	S2	0.0301	0.0448	0.0301
Morlet	X	S4	0.0056	0.001	0.000483

The results depicted in Table III show that only analysis with morlet wavelet detects statistically significant differences between the two groups. Specifically, in X-axis, mean energy is higher in group No than in A., especially in higher frequencies (S4: 50-10Hz). This is in agreement with previous findings [4], although the methodologies do not coincide (i.e. scale ranges and the number of beats analysed differ). Differences of opposite direction were found in Z-axis, however not statistically significant for this dataset.

TABLE IV
COMPARISON OF THE COEFFICIENT OF VARIATION WBCVE IN GROUPS NO AND A

Mother wavelet	Lead	Wavelet band	ttest p	Mean of WBcvE in No	Mean of WBcvE in A
Sym4	X	S1	0.0079	0.2012	0.4520
Sym4	X	S2	0.0026	0.2099	0.7227
Sym4	X	S3	$8.3159*10^{-004}$	0.2408	0.9526
Sym4	X	S4	$1.4752*10^{-004}$	0.2636	1.1263
Sym4	Y	S1	0.0264	0.2990	0.9327
Sym4	Y	S3	0.0342	0.5407	1.7291
Sym4	Y	S4	0.0022	0.4633	2.1802
Sym4	Z	S1	0.0072	0.1680	1.2481
Sym4	Z	S2	0.0079	0.1956	1.4370
Sym4	Z	S3	0.0011	0.2265	1.7468
Sym4	Z	S4	$2.8373*10^{-004}$	0.2619	2.0286
Db4	X	S1	0.0049	0.1872	0.4621
Db4	X	S2	0.0022	0.2127	0.7194
Db4	X	S3	$7.3298*10^{-004}$	0.2367	0.9762
Db4	X	S4	$1.1585*10^{-004}$	0.2624	1.1612
Db4	Y	S1	0.0189	0.2880	0.9467
Db4	Y	S3	0.0364	0.5433	1.4081
Db4	Y	S4	0.0032	0.4849	2.1712
Db4	Z	S1	0.0063	0.1699	1.2443
Db4	Z	S2	0.0077	0.1940	1.4513
Db4	Z	S3	0.0015	0.2288	1.7028
Db4	Z	S4	$2.4422*10^{-004}$	0.2641	2.0300
Morlet	X	S1	0.0046	0.1697	0.3756
Morlet	X	S2	$1.7768*10^{-004}$	0.2144	0.6606
Morlet	X	S3	$8.1964*10^{-004}$	0.2735	1.1167
Morlet	X	S4	$5.5443*10^{-005}$	0.2811	1.1933
Morlet	Y	S1	0.0345	0.3101	0.7984
Morlet	Y	S3	0.0241	0.5843	1.8666
Morlet	Y	S4	$5.8464*10^{-004}$	0.4320	2.3362
Morlet	Z	S1	0.0065	0.1740	1.1886
Morlet	Z	S2	0.0021	0.2332	1.8158
Morlet	Z	S3	$1.4354*10^{-004}$	0.2813	2.0779
Morlet	Z	S4	$1.3118*10^{-004}$	0.2905	2.2639

The analysis of WBcvE (see Table IV) reveals that the atrial signals in group No are more stable in time, as regards wavelet energy in all leads. In group A, the coefficient of variation of the wavelet coefficients is higher than in No, and especially in the leads X and Z there are statistically significant differences in all the scale bands. It is characteristic that in the Z lead the WBcvE of the Group A is 10 times greater than that of group No. Furthermore,

statistically significant differences in WBcvE are found for all mother wavelets, being more evident for morlet wavelet.

With respect to comparison among mother wavelets, it is evident that the results based on the three options are not very distant. The intra and inter class Mahalanobis distance for each WBcvE feature (produced by MANOVA analysis in matlab) are depicted in Table V. The same table holds the outcome of ranking based on the AUC criterion, i.e. after sorting the WBcvE features based on their AUC value, the percentage of the first 12 features belonging to each mother wavelet category. The total number of statistically significant features (WBmeanE and WBcvE) is depicted in the last column of Table V. Taking into account the contribution of all these criteria (in a 'voting' sense), Morlet wavelet seems to have an overall slightly better performance than the other two mother wavelets, in terms of discrimination between the two classes in focus.

TABLE V
COMPARISON OF THE THREE MOTHER WAVELET PERFORMANCE. BEST PER CRITERION (COLUMN) IN BOLD.

Mother wavelet	WBcvE				All stat. sign. features
	Inter-class	Intra-class		AUC ranking	
		Group No	Group A		
Sym4	6.94	4.61± 8.54	30.22± **21.09**	3/12	11
Db4	6.74	**4.18**± 8.62	31.33± 21.77	4/12	11
Morlet	**7.04**	4.67± **7.74**	**30.05**± 22.69	**5/12**	**13**

IV. DISCUSSION

A new methodology is proposed for the analysis of normal and pathologic atrial activity on a beat by beat basis, that is based on three pillars: a) the safe detection of an atrial activity window, without 'promising' an accurate Pwave detector, b) wavelet analysis in each beat, c) overall features expressing the average behavior and the variation among beats. The choice of mother wavelet is tackled, and based on the performance of three mother wavelets, the Morlet function is considered the best choice.

Beat to beat wavelet analysis has been previously proposed in the context of ECG analysis [10, 11, 12], as regards QRS and late potential analysis, linking the temporal variability with substrate instability. The application of beat by beat analysis to atrial activity is an innovative approach.

The proposed methodology is able to show differences between normal subjects and PAF-prone patients of same age, especially in terms of coefficient of variation, and secondarily in mean energy, while no differences are found in between the younger and older normals. Mean wavelet energy differences in PAF suggest potential changes in conduction pathways [4]. Increased coefficient of variation in all axes in PAF suggests a potential difference in the electrical substrate. Both findings have to be subjected to extended medical assessment that might potentially lead to new indicators of vulnerability to AF, based on macroscopic markers, also alleviating the limitations of the current study related to the use of data from two different databases.

The quantitative measures of the current study could be further employed towards assessing the success of treatment options, either pharmacological therapy or ablation, via quantitative criteria. Further studies could be of interest, towards studying AF subgroups with different frequency of AF recurrences, potentially leading to a more effective intervention in cases of highly recurrent patients.

V. CONCLUSION

The beat-to-beat wavelet analysis of atrial activity can successfully identify atrial conduction characteristics that associate with the development of PAF. The recognition of these abnormalities can lead us to the better understanding of the arrhythmiogenic substrate and subsequently to a more effective intervention.

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