Peculiarities of Multivariate Analysis Based Methods for Detection and Evaluation of ECG T-wave Alternans

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***Abstract*—Two multivariate analysis methods based on Principal Component Analysis and Periodic Component Analysis designed for detection and evaluation of ECG T-wave alternans were tested on synthetic and clinical recordings in the aim to reveal their diagnostic features. Advanced data pre-processing including normalization of S-T,T segment duration by means of bicubic interpolation was used to increase methods reliability. Non-visible variations in shape of S-T,T segment were revealed by means of the methods in the recordings registered in severe cardiac situations. Results lead to the idea, that analysis of T-wave alternans could be used not only for prevention of critical cardiac situations, but give valuable additional diagnostic information about status of cardiologic patients during ordinary examination.**

***Index Terms*—Principal component analysis, periodic component analysis, ECG T-wave alternans.**

I. INTRODUCTION

The presence of electrocardiogram (ECG) T-wave alternans phenomena (TWA) in cases of severe arrhythmias and even sudden cardiac death was firstly reported in 1909 by Hering [1]. Visually detectable TWA in ECG recordings has been observed under various clinical conditions in association with severe arrhythmias, including acute myocardial ischemia, infarction, long QT-syndromes [2].

ECG T-wave alternans, observed as a beat-to-beat alternation in the morphology and amplitude of the ECG S-T segment or T wave, reflects variation of process of repolarisation of ventricles [3]. Heterogeneity of repolarisation causes conduction disorders also re-entry and other types of life-threatening arrhythmia [2]. During heterogeneity of repolarisation in the neighbouring areas of myocardial tissue process of repolarisation is not constant, but alternate every second heart beat.

Numerous studies have demonstrated diagnostical importance of checking of presence of TWA in patients with ischemic cardiomyopathy, while identifying patients at risk for sudden cardiac death [4], [5].

Currently there are a number of methods for the detection of this phenomenon. Methodology realized these methods have evolved over the last twenty years from visual ECG inspection based till computerized analytical methods for detection of non-visible TWA. Some methods give TWA estimates of alternans only in amplitude, measured in mV, others give nonlinear energy estimates obtained from spectral analysis. There are also methods based on multivariate analysis using truncated expansion of the signals and giving quantitative estimates of morphological changes in signal shape (eg. Principal Component Analysis (PCA), Karhunen Loeve Transform) [6]. Extraordinary event was "PhysioNet and Computers in Cardiology Challenge 2008" [7], when results of 23 newly elaborated methods were compared according to the results obtained analyzing 100 test recordings including clinical and simulated data. Quite recent multivariate analysis approach using Periodic Component Analysis (πCA) was published in [8]. The method shows quite high concordance of results analysing synthetic signals from PhysioNet Databank used in 2008 year event. However, authors provide only limited results of method testing with clinical recordings. Nevertheless, especially clinical usefulness or predictive value of results obtained by particular method should be the main estimate of quality of it. Gehi with co-authors [9] provides meta-analysis results about clinical usefulness of methods of detection and evaluation of TWA, rising hesitations: do existing methods reveal any incremental prognostic usefulness?

The aim of this work was to test and compare results of multivariate analysis based TWA detection and evaluation methods analysing real clinical recordings. We selected only multivariate analysis based methods for testing, because recent biophysical modelling, electrophysiological investigations [10] and detail analysis of clinical recordings in acute phase of myocardial infarction [11] revealed, that much more complex signal morphology changes then only

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alternans of amplitude could be found in clinical situations, where TWA phenomena is expected. We expected, that detail tests and comparison of performance of multivariate techniques will reveal informative estimates for characterization of patient status and outcome results. Diagnostic usefulness of the results obtained by the methods is also of great interest.

II. METHODS

Periodic component analysis based method for detection and evaluation of TWA described in [8] have shown impressive concordance with reference scores of TWA detection using PhysioNet databank (www.physionet.org) synthetic signals. However, authors provide only limited information about results, when analysing clinical recordings. It is expected, that analysing real clinical recordings method will face certain problems. The main problem is substantial changes in RR intervals and related changes in duration of S-T,T segment often found in ECG registered in critical situations, when results of analysis are of the greatest value. Empiric methods for normalization of duration of S-T,T segment are used since many years (Bazzet formula, or later modification of it by Sagie). We modified the method described by [8] introducing additional step in data pre-processing – time stretching of the ordinary ST-T interval to get normalized duration of all intervals. We used bicubic spline interpolation to stretch analysed Q-S-T,T segment, till its maximal cross-correlation with the template, constructed from the first 10 cardio cycles of the recording. The ratios of QT interval time stretch were close to the values reported by [12]. The periodic component analysis method described in [8] constructs the transformation $y'^{T}_{k} = w^{T} X'_{k}$, in the aim to maximize 2 heart beats periodicity in the analysed signal. Such measure of periodicity is the ratio of squared differences between original sequence of concatenated S-T,T segments $\boldsymbol{y'_k}$ and one cardio cycle right shifted sequence $\boldsymbol{y'_{k+m}}$

$$\varepsilon(w,m) = \frac{\sum_{k=0}^{K-1} \left\| y'_{k+m} - y'_{k} \right\|^2}{\sum_{k=0}^{K-1} \left\| y'_{k} \right\|^2}. \qquad (1)$$

According to [13] it could be rearranged into

$$\varepsilon(w,m) = \frac{w^{T} A_{X'}(m) w}{w^{T} R_{X'} w}, \qquad (2)$$

where $\boldsymbol{R}_{\mathrm{x}}$ is covariation matrix of the original sequence and $\boldsymbol{A}_{\mathrm{x}}$ is the covariation matrix of differences between original sequence and one cardio cycle right shifted sequence. The value of (2) is minimized by weight $\boldsymbol{w}$ determined by the generalized eigenvector corresponding to the smallest generalized eigenvalue of the matrix pair ($\boldsymbol{A}_{\mathrm{x}}$(m), $\boldsymbol{R}_{\mathrm{x}}$) [13], [14]. The columns of transformation matrix Ψ (generalized eigenvectors of matrix ($\boldsymbol{A}_{\mathrm{x}}$(m), $\boldsymbol{R}_{\mathrm{x}}$) are sorted according to the corresponding eigenvalues in ascending order of magnitude. So, transformation $Y = \Psi^{T} X$ gives the maximal periodic component in the first row of $\boldsymbol{Y}$. So, it is expected to get extracted TWA in the first transformed lead. As estimate of TWA we used energy of the signal represented by this first row estimated by its variance.

As second method, we used PCA based method for evaluation of TWA described in [15], which analyses extracted and time-normalized S-T,T segments ensemble after the same time stretching procedure as used in πCA case. Unlikely πCA or PCA based methods, described in [8], this method constructs a matrix not of continuous signal, but of concatenated arrays of samples redundantly representing S-T,T segments of one cardio cycle in all leads. PCA is used to reduce this dimensionality representing every vector $\boldsymbol{x}_{\mathrm{i}}$ (samples of ordinary ST-T complex) by linear combination of the principal components $\boldsymbol{\phi}_{\mathrm{k}}$ multiplied by coefficients $w_{i,\mathrm{k}}$

$$\mathbf{x}_i = \sum_{k=1}^{p} w_{i,k} \boldsymbol{\phi}_k . \qquad (3)$$

The variation of S-T,T complex shape is represented then by the variation of the coefficients one or at least few $w_{i,\mathrm{k}}$. Ten first coefficients were taken for further analysis due to our experience in detail described in [16]. Normalized estimate of power spectral density in detail described in [15] was used as quantitative estimate of TWA.

The methods were preliminary tested using synthetic ECG with added TWA. The test signal consisted of 10 generated cardio cycles. Each cardio cycle started with 25 samples long QRS complex obtained by means of bicubic interpolation between 5 reference points imitating average shape of real signal. It was followed by 350 samples long S-T,T complex generated using Gaussian Window function. Total length of cardio cycle was 375 samples. Six leads of synthetic ECG were produced randomly and independently varying scale of QRS and S-T,T complexes. T-wave alternans and random noise was added according to the recommendations described in [8]. Each S-T,T complex was modelled as

$$x_{k,l}(n) = s_l(n) + \frac{1}{2} a_l(n) \cdot (-1)^k + v_{k,l}(n), \qquad (4)$$

where $n = 0,...,N-1$, $s_l(n)$ is the average S-T,T complex, $a_l(n)$ is added voltage step with alternating polarity. $v_{k,l}(n)$ is random noise.

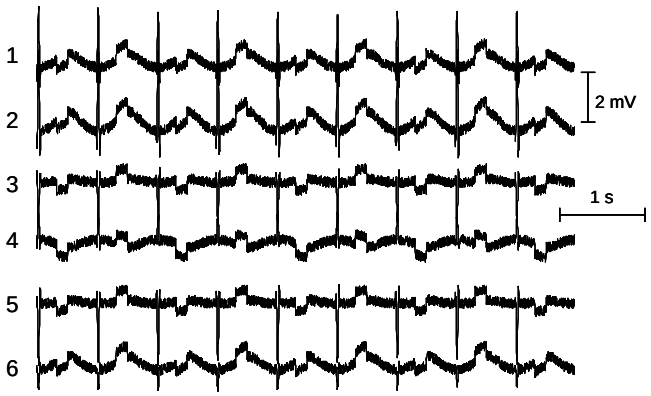

Fig. 1. Example of 6 leads of synthetic ECG with added TWA (beat-to-beat alternating voltage step in S-T,T segment) according to the model (4).

We took the clinical recordings from "PhysioNet/Computers in Cardiology Challenge 2008"

Databank (www.physionet.org/challenge). It contains one hundred ECG recordings sampled at 500 Hz with 16-bit resolution. Number of the leads in the recordings was 2, 3, and 12. The recordings are from patients with certain risk factors for sudden cardiac death. The control recordings from healthy volunteers are given together with synthetic signals, containing calibrated amplitudes of T-wave alternans. Each record lasts approximately 2 minutes.

Signal pre-processing starts with the detection of fiducial point of each cardio cycle – peak of ECG R-wave. Advanced two steps R-wave peak time point determination method was necessary to achieve sufficient accuracy. After preliminary detection, using high-pass filtered ECG signal, final adjustment of exact position of fiducial point was achieved finding maximal cross-correlation of the sliding in time R-wave template with the ECG signal. R-wave template we constructed from first 5 cardio cycles of the recording and updated after every processed cardio cycle. The component of the baseline wander was calculated by the means of bicubic spline interpolation between reference points – 10 consequent samples from the interval between the end of T-wave of preceding cardio cycle and beginning of P-wave of current cardio cycle. The component of the baseline wander was reconstructed and subtracted from the original ECG signal in each lead. For details see [15].

III. RESULTS

Both methods were giving concordant results, when analysing the synthetic signals. Examples of both methods results are given in Fig. 2. Three top traces, marked PCA, show the values of the coefficients of first three eigenvectors of the covariation matrix. Beat to beat alternans in coefficient of the first eigenvector reflects added TWA. Six lower traces, marked πCA, represent rows of the matrix $\boldsymbol{Y}$ – result of πCA. Added TWA is concentrated in the first row of this matrix. Example of results of analysis of clinical recordings from PhysioNet databank is shown on Fig. 3. High TWA reference rank 80 having recording containing visually non-detectable TWA is shown on panel A. Clearly visible alterations in shape of S-T,T segment were revealed in the first raw of matrix $\boldsymbol{Y}$ by means of πCA (see panel B). Vertical lines on this graph delimit concatenated excerpts from every cardio cycle. Quantitative estimates of shape of S-T,T segments – coefficients of first three eigenvectors of covariation matrix, obtained by means of PCA shown below, are also changing in concordance with the first raw of the matrix $\boldsymbol{Y}$. TWA estimates obtained by means of both methods – variance of the first raw of matrix $\boldsymbol{Y}$ of πCA and spectral estimate, obtained by means of PCA, together with reference ranks of the recordings given in PhysioNet databank are shown in Fig. 4. Overall correlation of the TWA estimates with reference ranks given in PhysioNet, unfortunately, was non-significant. However, these reference ranks are obtained as the cooperative result of all algorithms – participants of the event; therefore, it is not a "Golden Standard". Interestingly some significant ranks are given even for recordings from healthy persons of normal sinus rhythm groups. Nevertheless results analysing recordings from "St. Petersburg Institute of Cardiological Technics 12-lead Arrhythmia Database" PCA results comply with the reference ranks showing significant Kendall tau rank correlation coefficient 0.592 ($p = 0.036$). Results of πCA in this case did not show significant correlation.

TWA episodes were mostly expected in "Sudden Cardiac Death Holter Database". Six out of 10 recordings have significant reference rank given by PhysioNet. Results of PCA method showed TWA positive results in 8 out of 10 recordings. πCA method did not show any significant results because of limited amount (only 2) of leads in the recordings.

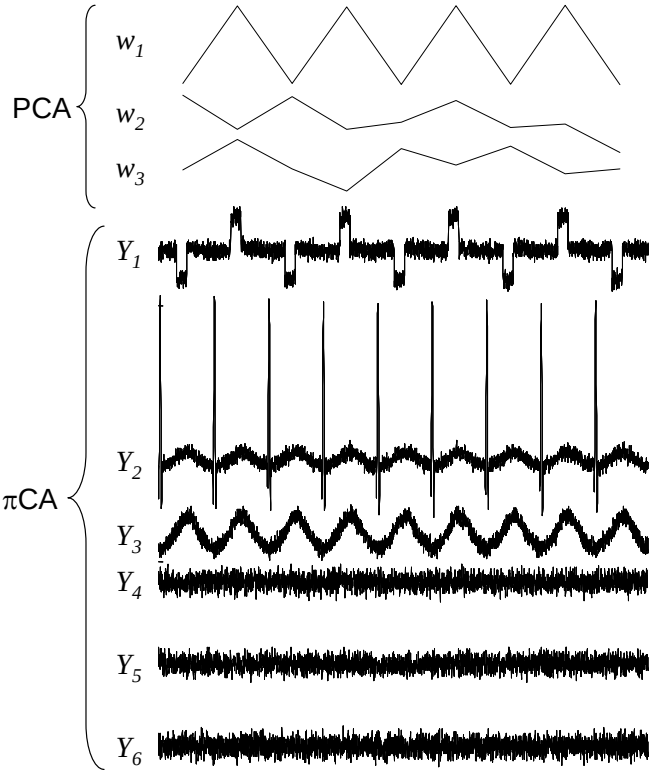

Fig. 2. Result of PCA and πCA performed on synthetic signal presented in Fig.1. PCA: coefficients of first three eigenvectors of covariation matrix. πCA: first rows of matrix $\boldsymbol{Y}$ – result of periodic component analysis.

IV. DISCUSSION

Visually non-detectable TWA in clinical recordings, revealed by means of multivariate analysis methods, was much more complicated in shape as used in synthetic recordings. Therefore some methods – PhysioNet Challenge participants, showing good concordance with known amplitude in synthetic signals failed in clinical recordings. Another problem in testing and validation of methods is absence of reference clinical recordings. So, we can only expect presence of TWA in the recordings made in known severe cases. Testing of correlation of detected TWA with other clinical parameters related with dangerous clinical situations can reveal methods predictive power. Results of PCA based method showed good correlation with Left Ventricular Ejection Fraction and rehospitalization of patient within 6 months [11]. However it was not possible to test πCA based method using these recordings containing only one lead. The method requires at least 3 or more leads. This feature significantly limits the usage of it, but modern ECG monitoring systems usually register more than 3 leads. Anyway, testing of these two multivariate analysis methods

revealed new features of the TWA phenomena. It should be treated not only as alternans in amplitude of T-wave, but as variation of it shape. Therefore only multivariate analysis based methods can give informative estimates of such variation.

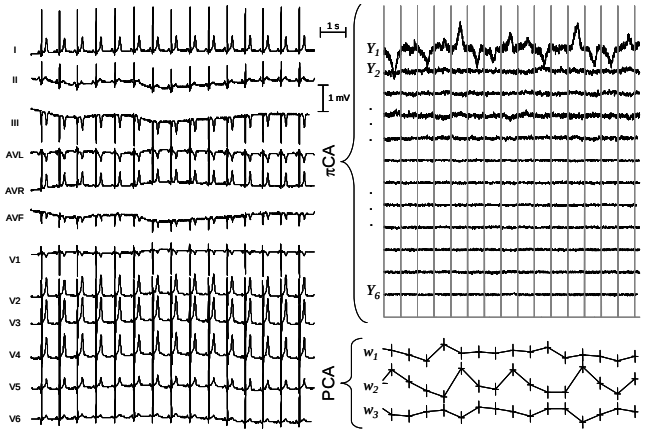

Fig. 3. Results of PCA and πCA performed on clinical recording from PhysioNet Databank, having high TWA reference score 80: a – excerpt of ECG with no clearly visible TWA; b – shape variations of S-T,T segment revealed by means of πCA on the first row of matrix $\boldsymbol{Y}$ and quantitative estimates of S-T,T segment shape – coefficients of first three eigenvectors – the result of PCA.

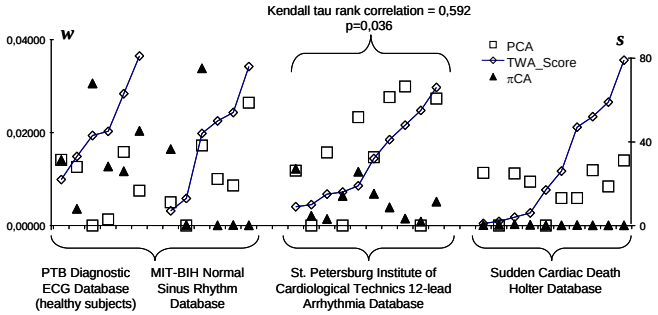

Fig. 4. TWA estimates, obtained by means of tested methods: πCA – $\boldsymbol{s}$ (variance of first raw of matrix $\boldsymbol{Y}$) and PCA – $\boldsymbol{w}$ (spectral estimate of coefficients of first eigenvectors) together with reference ranks of the recordings given in PhysioNet. "PTB Diagnostic ECG Database (healthy subjects)" and "MIT-BIH Normal Sinus Rhythm Database" groups of recordings where no TWA episodes were expected. "St. Petersburg Institute of Cardiological Technics 12-lead Arrhythmia Database" and "Sudden Cardiac Death Holter Database" – groups where TWA episodes were highly expected.

V. CONCLUSIONS

Multivariate analysis based methods for detection and evaluation of TWA can reveal new features of the phenomena and could be used for monitoring of heart activity in severe cardiac situations in aim to prevent sudden cardiac death.

Promising results of multivariate analysis based methods testing lead to the idea that such analysis tool could provide cardiologists with valuable additional diagnostic information not only in critical cases, but in ordinary examination of cardiologic patients.

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