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POLISH ACADEMY OF SCIENCES

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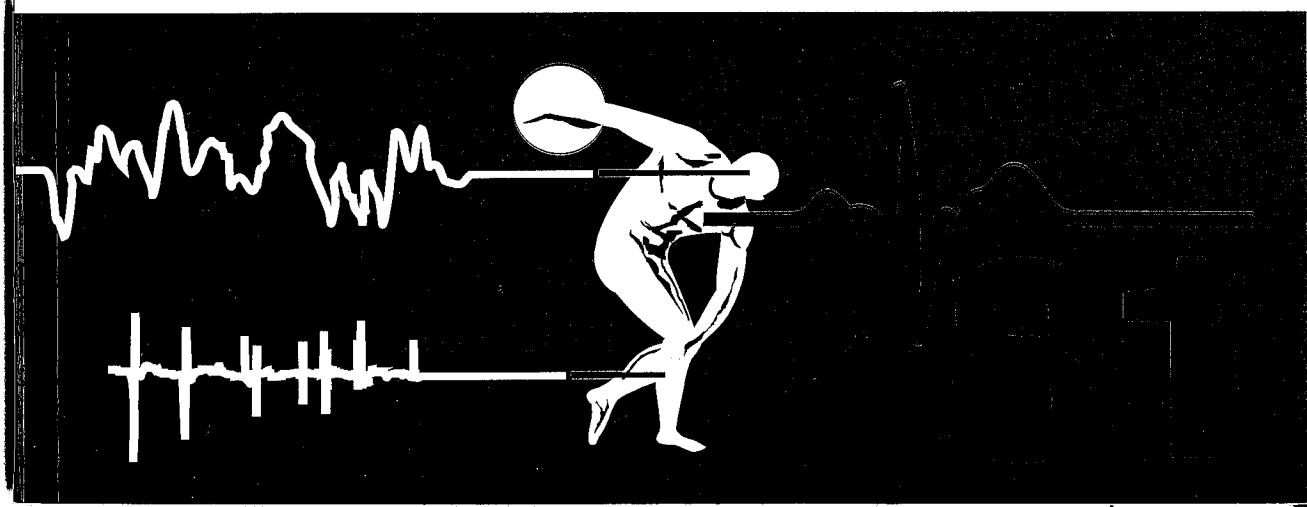
LECTURE NOTES OF THE ICB SEMINAR

VARIABILITY IN BIOMEDICAL SIGNALS

Warsaw, November 2008

Edited by: Roman Maniewski
Olivier Meste
Hervé Rix



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The ICB is a multi-national association of the Academies of Science and organizations interested in biocybernetics and health care through science and technology. The ICB acts in accordance with the Agreement about the establishment of the ICB as signed by its Parties. Membership to the ICB is opened, new members are admitted by applying in writing to the of President of Polish Academy of Sciences and signing the Agreement.
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- facilitation and encouragement of research and development;
- acquisition and dissemination of relevant information, including publication of scientific materials connected with ICB activities.

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The scientific program of the seminars includes the recent results of fundamental researches in physiological processes as well as the problems of new technology and design of bioartificial devices and systems for therapy, life support, clinical diagnosis and information processing.
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MULTILEAD ANALYSIS OF T WAVE ALTERNANS IN STRESS TEST

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Abstract

T-wave alternans (TWA) is considered as an index of susceptibility of sudden cardiac death. In this work, a TWA analysis has been performed on a set of stress test ECGs, comparing a novel multilead analysis scheme with a single-lead scheme. ECG signals belonging to healthy volunteers and ischemic patients have been analyzed. Results show that the multilead scheme provides a higher sensitivity to low-level alternans than the single-lead scheme. Furthermore, results obtained with the multilead scheme are significantly different in volunteer and ischemic groups, whereas results obtained with the single-lead scheme are not.

1. Introduction

T-wave alternans (TWA) is defined as a consistent fluctuation in the repolarization morphology on an every-other-beat basis, and is presently regarded as a promising index of susceptibility to sudden cardiac death (SCD) [1]. One of the main scenarios where TWA analysis is performed is in stress tests. TWA is a phenomenon partially related to heart rate, so TWA arises in patients at risk for SCD but also in healthy subjects at faster heart rates during stress tests. In practice, a cut-off point of 110 beats per minute (bpm) is considered to distinguish between normal and abnormal TWA [1].

Several methods exist to automatically detect and estimate TWA [2]. All of them work on a single-lead basis, and their major drawback is their low sensitivity to low-level alternans [1, 2]. In previous works [5,6], our group proposed a novel multilead analysis scheme that combines principal component analysis (PCA) with the existing Laplacian Likelihood Ratio (LLR) method [2,4], and evaluated its detection performance and its estimation accuracy with a simulation study.

In this work, the proposed multilead scheme is tested on real signals. Stress test ECGs belonging to healthy volunteers and ischemic patients are analyzed, and results are compared to those obtained with a single-lead scheme, which is the usual approach in clinical practice.

2. Data set

The ECGs of 136 patients referred to treadmill exercise test were recorded in the University Hospital Lozano Blesa of Zaragoza (Spain) [3]. 12-lead ECGs were digitally recorded at 1-KHz sampling rate. Subjects were classified in two groups:

Ischemic group: this group was composed of 79 patients with significant stenoses in at least one major coronary artery as shown by coronary angiography (gold standard).

Volunteer group: this group comprised 66 asymptomatic volunteers from the Spanish Army, who underwent an exercise test with negative results for coronary artery disease.

3. TWA analysis

Data were processed with two schemes based on the LLR method [2,4]: a multilead scheme based on PCA, and a single lead scheme.

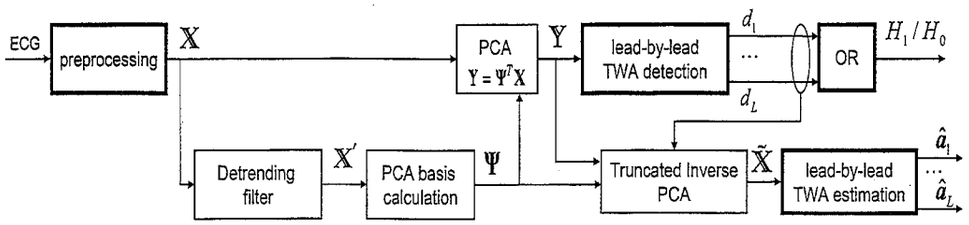

Fig. 1. Block diagram of the multilead scheme. The blocks in bold line are the ones used in the single-lead scheme. Note that in the single-lead scheme $\mathbf{Y} = \mathbf{X} = \tilde{\mathbf{X}}$

Both schemes are fully described in [5,6], and are summarized in the next subsections.

3.1. Multilead scheme

The block diagram of the multilead scheme is shown in Fig. 1. It consists of five stages: preprocessing, signal transformation with PCA, TWA detection, signal reconstruction and TWA estimation.

In the preprocessing stage, the multilead ECG signal is decimated to obtain a sampling frequency of 125 Hz, and low-pass filtered with a cut-off frequency of 20 Hz. Baseline wandering is removed using a cubic splines interpolation technique and ST-T segments are then extracted. Let K be the number of beats in the input signal, N the number of samples of each ST-T complex, and L the number of leads. For each beat k, ST-T complexes from all leads are put together into a matrix $\mathbf{X}_k$. Then, the $\mathbf{X}_k$ matrices are concatenated to form the data matrix $\mathbf{X}$.

PCA transformation is then performed as described in [5,6] to obtain the transformed data matrix $\mathbf{Y}$. After PCA transformation, TWA detection is carried out in every transformed lead (rows in $\mathbf{Y}$) by applying the Generalized Likelihood Ratio Test (GLRT) for Laplacian noise as proposed in [4]. To decide whether alternans is present or not, the resulting value of the test is compared to a threshold. The overall TWA detection is positive if TWA is detected at least in one transformed lead.

After TWA detection, a new signal $\tilde{\mathbf{X}}$ in the original lead set is reconstructed, considering only those transformed leads where TWA were detected. Then, the Maximum Likelihood Estimation (MLE) for Laplacian noise is applied to the reconstructed data as described in [4] to estimate the TWA waveform. On each lead, TWA amplitude is calculated as the root mean square (RMS) value across the estimated TWA waveform, and the final TWA amplitude is calculated as the maximum amplitude in the L leads.

3.2. Single-lead scheme

The single-lead scheme handles each lead independently throughout the process. It consists of the same preprocessing, TWA estimation and TWA detection stages as the multilead scheme, but without the intermediate PCA processing. The stages of the single-lead scheme are shown in bold in Fig. 1.

4. Results

Stress test records were processed with a sliding analysis window of $K = 128$ beats. Only the eight independent leads were considered. To set the same specificity for both analysis schemes, the detection threshold was determined from the records of the volunteer group, considering a probability of false alarm $P_{FA} = 0.01$. To do so, the assumption that no TWA should be found in volunteer records at heart rates below 110 bpm was made. Volunteer group signals were processed with each scheme, and for each scheme a threshold was calculated so that it was exceeded only by 1% of the GLRT values obtained before heart rate reached 110 bpm (false detections). Then, all records from both groups were processed with the resulting threshold values.

Results are shown in Table 1. The first row shows the total number of records of each group, and the number of records where one or more TWA episodes were detected. For each episode three parameters were calculated: the maximum TWA amplitude in the episode V_{max} *(μV)*, the duration D *(s)*, and the onset heart rate HR_o *(bpm)*. For each group, the mean value and the standard deviation of these parameters were calculated in two ways: considering all the episodes (second row), and considering the episodes detected exclusively by one scheme and not by the other (third row). In Table 2, results were recalculated considering only the episodes detected before the heart rate reached 110 bpm in the stress test.

Differences in the number of records with TWA were evaluated with the Fisher's exact test; differences in mean values of V_{max}, D and HR_o were evaluated with the Mann-Whitney U test. A p-value < 0.05 was considered significant.

Table 1. Results of TWA analysis in stress test data, calculated considering all episodes regardless of when they are detected. (P_{FA} = 0.01 for the two schemes). Data expressed as (mean ± one standard deviation). †indicates a significant difference between volunteer and ischemic groups; ‡indicates a significant difference between multilead and single-lead schemes

			MULTILEAD		SINGLE-LEAD	
			volunteer	ischemic	volunteer	ischemic
Detection	*# records*		66	70	66	70
	# records with TWA		26	27	19	20
	% records with TWA		39.39	38.57	28.79	28.57
TWA characteristics	all episodes detected by each scheme	V_{max} *(μV)*	85±114‡	95±128	133±133‡	135±146
		D *(s)*	26±26	48±59	29±24	51±39
		HR_o *(bpm)*	124±30†	106±20†	121±30†	105±20†
		# episodes	38	33	26	22
	episodes detected by one scheme and not by the other	V_{max} *(μV)*	21±15†‡	37±22†	52±35‡	66±35
		D *(s)*	7±7	30±71	17±16	18±21
		HR_o *(bpm)*	127±27†	107±19†	112±7	105±18
		# episodes	17	18	5	7

Table 2. Results of TWA analysis in stress test data, calculated considering the episodes detected before heart rate reaches 110 bpm (P_{FA} = 0.01 for the two schemes). Data expressed as (mean ± one standard deviation). †indicates a significant difference in the number of records with TWA in volunteer and ischemic groups

			MULTILEAD		SINGLE-LEAD	
			volunteer	ischemic	volunteer	ischemic
Detection		*# records*	66	70	66	70
		# records with TWA	6†	14†	6	12
		% records with TWA	9.09†	20.00†	9.09	17.14
TWA characteristics	all episodes detected by each scheme	V_{max} (μV)	72±58	108±109	83±72	134±120
		$\mathcal{D}$ (*s*)	36±30	49±42	31±28	58±44
		HR_o (*bpm*)	90±13	92±10	95±11	94±9
		# episodes	8	15	6	11
	episodes detected by one cheme and not by the other	V_{max} (μV)	42±33	50±19	30	78±72
		$\mathcal{D}$ (*s*)	31±31	14±11	1	8±1
		HR_o (*bpm*)	83±11	90±13	94	101±0
		# episodes	3	6	1	2

5. Discussion and conclusions

As shown in Table I, the number of records where TWA is detected is greater with the multilead scheme in both groups. Since the specificity of both schemes is the same, this means that the sensitivity of this scheme is higher than with the single-lead scheme.

When considering the episodes detected only by the multilead scheme, episodes from volunteers have significantly lower amplitude than episodes from ischemics, and they appear at a higher HR_o. These differences are not significant with the single-lead scheme. In volunteers, episodes detected only by the multilead scheme have significantly lower amplitude than episodes detected only by the single-lead scheme, and a higher HR_o; this suggests that the multilead scheme detects low amplitude episodes near the peak effort that the single-lead scheme cannot detect.

The percentage of records with TWA is similar in volunteer and ischemic groups, both with the multilead scheme (39% and 38%) and with the single-lead scheme (28 % in both groups). This can be due to the fact that volunteers reach a higher peak heart rate during the test. To distinguish between groups according to the risk of SCD, it is necessary to analyze only the results obtained before the heart rate reaches 110 bpm (Table 2). Indeed, when interval before 110 bpm is considered, the percentage of records with TWA is higher in the ischemic group. This difference is significant only with the multilead scheme. Differences in amplitude and duration are not significant due to the low number of detections.

In conclusion, results show that the multilead scheme provides a higher sensitivity to low-level alternans than the single-lead scheme. Furthermore, results obtained with the multilead scheme are significantly different in volunteer and ischemic groups, whereas results obtained with the single-lead scheme are not.

Acknowledgements

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