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Extended summary

Comparison of methods for automatic identification of ECG T-wave alternans

Curriculum: Elettromagnetismo e Bioingegneria

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Date: 14-03-2011

Abstract. Microvolt T-wave alternans (TWA), consisting of every-other-beat changes in ECG T-wave morphology, is an index of susceptibility to malignant ventricular arrhythmias, requiring automatic techniques to be identified. Five of these, namely, fast-Fourier-transform spectral method (FFTSM), complex-demodulation method (CDM), modified-moving-average method (MMAM), Laplacian-likelihood-ratio method (LLRM) and adaptive-match-filter method (AMFM), were applied here to simulated and sample clinical data; the aim was to compare individual methods ability to properly identify TWA. The MMAM provided false-positive TWA when applied to simulated ECGs affected by amplitude variability or noise, but TWA. The FFTSM, the CDM and the LLRM showed limitations in the presence of time-varying TWA and T-waves misalignment. The AMFM resulted to accomplish the best compromise between the needs to avoid false-positive TWA and to detect and characterize true-positive TWA. Findings from our simulation approach were useful to explain different TWA levels measured by each competing methods applied to sample Holter ECGs from control-healthy subjects and acute-myocardial-infarction patients.

Keywords: signal processing of digital electrocardiogram, T-wave alternans, automatic identification techniques

1 Problem statement and objectives

1.1 T-wave alternans

T-wave alternans, consisting of 2:1 (or ABABAB…) changes in the amplitude, shape and sometimes polarity of the ECG T wave, has long been recognized as a marker of cardiac pathology in a wide variety of experimental and clinical situations [1,2]. Visible forms of TWA have been associated with life-threatening ventricular arrhythmias, like the ventricular fibrillation. In recent years, computerized analysis of digital ECG recordings proved the presence of subtle and non-visible TWA in experimental and clinical recordings [3]. These observations showed that TWA detection might serve as a clinically useful method to predict arrhythmic events and sudden cardiac death [3,4].

For the purpose of automatically detect and quantify TWA, a variety of algorithms have been proposed; among these, the fast-Fourier-transform spectral method (FFTSM) [5], the modified-moving-average method (MMAM) [6] (both available in commercial ECG machines), the complex demodulation method (CDM) [7], the Laplacian-likelihood-ratio method (LLRM) [8], and the adaptive match filter method (AMFM) [9].

The present study aims to compare performances of such methods by resorting to both simulation and clinical approaches. Simulated data were first evaluated in the ideal absence of interferences corrupting ECGs; successively, all methods were applied to non-ideal (presence of interferences) synthetic ECGs, in order to address the issue as to how, and at what extent, a TWA detection algorithm is affected by the imperfect outcome of real preprocessing. To demonstrate how results of this simulation approach may help interpretation of TWA levels detected from clinical data, the FFTSM, CDM, MMAM, LLRM, and the AMFM were applied to sample Holter ECGs from control-healthy (CH) subjects and acute-myocardial- infarction (AMI) patients.

2 Research planning and activities

Automatic methods for TWA identification. According to the FFTSM [5], beat-to-beat fluctuations in the electrocardiographic T-wave amplitude can be measured using a spectral approach. After aligning the ECG complexes, it calculates the spectral amplitude at 0.5 cpb of the cumulative power spectrum involving all the T-wave samples. This value, called "alternans peak", is compared to a threshold, and eventually used to estimate TWA amplitude. The CDM [7], at first, sequences areas of corresponding bins (groups of T-wave samples) from successive T-waves into time series areas. Each series is then modelled as a sinusoidal signal of frequency f_{TWA} (equal to half heart rate) and submitted to a complex demodulation (multiplication by a complex exponential at f_{TWA} and then application of a low-pass filter). The MMAM [6] recursively averages even and odd beats by applying some non linear constraints; TWA amplitude is then computed as the maximal absolute difference, in the T-wave segment, between modified moving averaged even and odd beats. The LLRM estimates TWA from the difference between each T-wave and the previous one in a sliding 32-beat ECG window centered on the analyzed beat [8]. The significance of the TWA estimation is provided by a generalized likelihood ratio test (GLRT), which verifies that estimated values are really due to TWA rather than to noise. The AMFM [9] filters the ECG signal by using an adaptive match filter designed as a 6^{th} order bidirectional

Butterworth pass-band filter, having the passing band 2·df_{TWA}=0.12 Hz wide and centered in f_{TWA}. The sinusoid amplitude of the filter-output signal provides a direct measure of TWA.

Simulated and clinical data for TWA analysis. A realistic, clean simulated ECG tracing was obtained as a 128-fold repetition of a single noiseless beat extracted from a real ECG [10]. In particular, we used a 0.75-s beat sampled at 200 samples per second. In the study concerning TWA analysis in the absence of noise, simulated ECG tracings, namely *NO_TWA* (absence of TWA but presence of T-wave variability), *S_TWA* (stationary TWA) and *TV_TWA* (TWA amplitude varying according to a sinusoidal pattern), were considered. Methods' reliability in the presence of interferences was evaluated by considering the following simulated tracings: *ELECTR_NOISE* (presence of physiological electrode motion noise, with amplitudes ranging from 0 to 0.1 mV), *PHYSIO_BASEL* (presence of physiological baseline wanderings with amplitudes ranging from 0 to 0.2 mV) and *T_SHIFT* (presence of 0 ± 20 ms T-wave misalignment). They were evaluated in the no-TWA case and in the presence of stationary TWA; errors were given as mean and standard deviation of ε = estimated TWA – simulated TWA. Methods were also applied to ECGs from twenty-five CH subjects and twenty-five AMI patients; mean and standard deviation of TWA values over each population were computed.

3 Analysis and discussion of main results

A graphical representation of the results obtained from ECG simulations in the absence of interferences is depicted in Figure 1. Results in the presence of interferences corrupting ECG tracings are provided in Figure 2 and Table 1. When analyzing no-TWA case, the FFTSM, LLRM, and AMFM always provided zero TWA level (Figs 1 and 2), while the MMAM identified a positive TWA in all conditions. Moreover, this method overestimated the TWA amplitude when applied to the tracing affected by both stationary TWA and physiological baseline. Altogether, the MMAM showed a tendency to ascribe to TWA ECG variability due to interferences; results from clinical data, shown in Table 2, confirm these findings. The CDM provided false-positive results in the *T_SHIFT* case: indeed, when TWA is absent but the bins are not perfectly aligned, a sinusoid at 0.5 cpb is detectable by the method and, therefore, wrongly attributed to TWA. Also the FFTSM and the LLRM are affected by the presence of T-waves misalignment: they did not detect the TWA

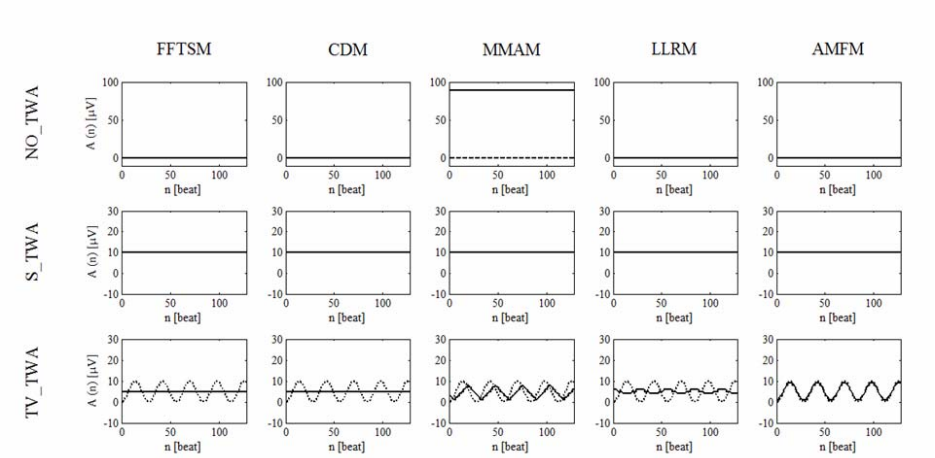

Figure 1. Simulated (solid line) and estimated (dotted line) TWA signals resulting from the analysis of ECGs not affected by interferences.

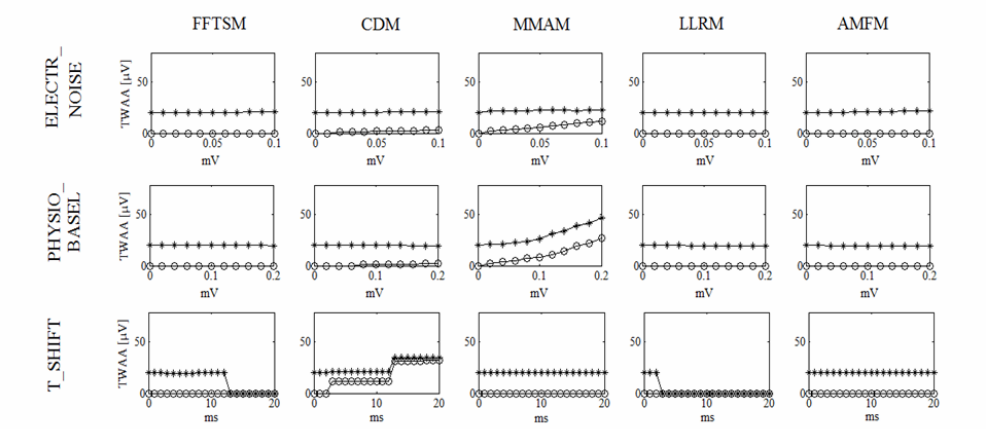

Figure 2. TWA-amplitude estimates from simulated tracings with no TWA (o) and stationary TWA (*), affected by interferences.

Table 1. TWA estimation errors obtained in the no-TWA case and in the presence of stationary TWA, when tracings were corrupted by interferences.

	ε_{FFTSM} (μV)	ε_{CDM} (μV)	ε_{MMAM} (μV)	ε_{LLRM} (μV)	ε_{AMFM} (μV)
No TWA					
ELECTR_NOISE	0±0	2±1	6±4	0±0	0±0
PHYSIO_BASEL	0±0	1±1	11±9	0±0	0±0
T_SHIFT	0±0	17±14	0±0	0±0	0±0
Stationary TWA					
ELECTR_NOISE	0±0	0±1	2±1	0±0	1±1
PHYSIO_BASEL	0±0	0±0	10±9	1±1	1±0
T_SHIFT	8±11	6±8	0±0	16±9	0±0

value in the presence of time shifts greater than 12 and 2 ms, respectively, because of an enhancement of the level of noise corrupting the signal. The noise-test algorithms involved in the two methods didn't even allow these methods to detect consistent TWA-level from clinical data (Table 2). The FFTSM and the CDM showed further limitations in identifying the non-stationary characters of the TWA phenomena (Fig. 1), the former assuming TWA to be stationary (constant in time), the latter including a low-pass filtering process in its algorithm. The MMAM was able to track the time course of TWA (Fig.1), while the LLRM provided a TWA-amplitude alternating signal, but having underestimated amplitude and opposite polarity with respect to the reference. Finally, the AMFM correctly identified TWA in all simulated cases (Figs 1 and 2, Table 1), thanks to its ability to filter out every ECG frequency component but the TWA one. Regarding to clinical data (Table 2), it provided TWA estimates with significant differences between CH and AMI groups, thus discriminating healthy subjects from patients at higher risk of cardiovascular diseases.

Table 2. Mean and standard deviation of TWA estimates over CH and AMI populations. *P<0.05 when comparing CH subjects vs. AMI patients with the t-test for normal distributions. In square brackets, number of subjects where methods detected non-zero TWA values.

	$\mathbf{TWA_{FFTSM}}$ (μV)	$\mathbf{TWA_{CDM}}$ (μV)	$\mathbf{TWA_{MMAM}}$ (μV)	$\mathbf{TWA_{LLRM}}$ (μV)	$\mathbf{TWA_{AMFM}}$ (μV)
Clinical Data					
CH SUBJECTS	0±1 [1]	4±2 [25]	25±16 [25]	0±1 [1]	5±1 [25]
AMI PATIENTS	0±0 [0]	6±3* [25]	40±15* [25]	1±3 [1]	8±2* [25]

4 Conclusions

Our simulation approach highlighted differences in TWA identification provided by the FFTSM, the CDM, the MMAM, the LLRM, and the AMFM both in the absence and in the presence of noise, baseline wanderings and T-waves misalignment. In particular, false-positive TWA values were detected by all techniques but the FFTSM, the LLRM and the AMFM, the last providing the most reliable quantification of time-varying TWA. Application of the five methods to CH-subjects and AMI-patients evidenced a discrepancy in that the FFTSM and the LLRM detected no more than one TWA case in each population (ascribed to their limited ability in identifying TWA in the presence of interferences), whereas the CDM, the MMAM, and the AMFM detected TWA in all CH-subjects and AMI-patients, with significantly lower TWA amplitude in the former group. In conclusion, the AMFM showed to achieve the best compromise between the requirement to avoid false-positive TWA and to identify TWA in different conditions.

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