A New Robust T Wave Alternans Detector and its Threshold Optimization

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Abstract

The conventional spectral method is indeed a typical confidence interval computation that use normalized Fourier transform frequencies $F\{f\}$ at $f = 0.5$. In order to get a robust detector with respect to spikes due to single-frequency tone interference and to exploit the entire frequency band to reduce the variance we proposed new parameter called SMM $(F\{0.5\}/median(F\{]0.5, 0[\}))$.

The second stage of this work was to optimize the threshold selection by using a full Monte-Carlo simulation where alternans/no-alternans episodes of length 16 with magnitude of 2 were corrupted by a gaussian noise with different powers and a sines with different frequencies.

All the combinations of noise and frequency, repeated 500 times, were selected in order to compute a mean probability of detection (Pd) and mean false alarm probability (Pfa) for different thresholds. Imposing Pfa=0.05, we get the Pd for the t-test, matched pair t-test, GLRT, SM, SMM equal to 0.65, 0.68, 0.63, 0.75, 0.8, respectively. The optimized threshold is 2.05 for SMM and 3.6 for SM.

Study group consisted of 50 patients with ICD stimulated (ventricular) at 100bpm (age: 55.3 σ16.4; LVEF: 42.8 σ15.5). Two minutes recordings were analyzed. XYZ orthogonal lead system was used. The best performance was detected with use of SMM method in comparison with conventional spectral method. Positive TWA was detected when median of duration of all episodes above threshold was greater than 4.

1. Introduction

T wave alternans (TWA) detection is a well known issue because of the hypothesized relation between its occurrence and the risk of future cardiac failure. This phenomenon appears as a periodic pattern (ABABAB) considering consecutive segmented T waves. This pattern could be extracted for instance from the magnitude, the mean value, and so forth. Experimental conditions such as angioplasty, high rate pacing for ICD implanted patients, stress test are good candidates to elicit TWA phenomenon. It is expected that myocardial substrate condition that allows ventricular fibrillation genesis could facilitate the TWA phenomenon during repolarization. Hence, the presence of TWA during elicited or physiological changes of heart rate could be correlated to the risk of ventricular fibrillation episodes occurences [1][2].

All TWA detectors are constituted by a filter, usually nonlinear, followed by a decision rule based on a threshold crossing. They share the same pitfall that is the selection of the threshold for this detection decision. Unfortunately the optimal value for this threshold is not adapted to any kind of interference types and levels. These interferences are typically the gaussian or laplacian noise, periodic components and slow trends [3]. Among the TWA detectors, the conventional spectral method (CSM) [4] is a detector apart from others because the data are projected on a basis where the interferences are more efficiently processed. Indeed, this method is a typical confidence interval computation that use normalized Fourier transform frequencies $F\{f\}$ at $f = 0.5$. In [Ros], the detection is positive when:

$$\frac{F\{0.5\} - mean(F\{[0.45, 0.35]\})}{std(F\{[0.45, 0.35]\})} > 2.5 \qquad (1)$$

In this method, $F\{.\}$ stands for the mean of the magnitude of all the Fourier transforms calculated in signals composed of time correlated samples of consecutive T waves. The suggested length of the data to be transformed in the Fourier domain is 128 samples. This means that for shorter windows, e.g. 16 samples, the parameters should be modified otherwise the $mean$ operator would be applied on a single value. Shortening the window is meaningful when the TWA is variable during the recording and allows to track its dynamics. Among the well-known detectors such t-test [5], matched pair t-test [5], GLRT [6], none of them are really designed to be robust according to artifacts such trends and sinusoids. The Fourier domain provides a representation of the data where robustness can be improved because such artifacts affects only few frequency bins.

In this work, from the CSM methods we derived two filters for the TWA detection. These filters were compared to classical methods previously listed in a fully simulated context. Simulated interference such as noise and sines provided us ROC curves, allowing adapted threshold selection. The new filters performance were compared to the CSM on a set of 50 patients with ICD where it was shown that the ventricular fibrillation risk stratification can be addressed by TWA detection.

2. Methods

The problem of TWA detection is twofold. The first stage is to summarize the information conveyed by the T waves set in a sequence of values, named seq, that will be filtered. This information compression could be the average value, the maximal value, of each individual T wave. More complex decompositions such the SVD can be also applied [7]. Note that for the CSM the sequence of values to be processed is the mean of the magnitude of all the Fourier transforms of the time correlated T waves samples.

The second stage is the design of the filter adapted to the model of alternans and interference. In order to follow the same line than the CSM, the proposed filters were defined in the spectral domain. Because the range of frequencies suggested in [Ros] is not suitable for short length sequence we propose to use the modulus of the Fourier transform $F\{.\}$ of seq to define the spectral method (SM) filter:

$$SM = \frac{F\{0.5\} - mean(F\{]0.5, 0.25]\})}{std(F\{]0.5, 0.25]\})} \tag{2}$$

As for the CSM, this definition corresponds to a confidence interval calculation, under the assumption of gaussianity. However, when seq is contaminated by harmonic components, $F\{.\}$ exhibits spikes that makes the gaussianity assumption no more valid. Then, a second filter based on the median of $F\{.\}$ was defined as:

$$SMM = \frac{F\{0.5\}}{median(F\{]0.5, 0[\})} \tag{3}$$

The use of the median is meaningful when data are corrupted by outliers. Spectral spikes due to periodic components can be considered as the outliers in that case.

The performance of these filters, whose outputs are compared to a threshold for detection, were assessed with 500 simulated seq defined as:

$$seq_{1,i}(n) = (-1)^n + b_i(n) + c_i sin(\omega n); \quad n = 1 \cdots 16 \tag{4}$$

where it appears that the alternans sequence is corrupted by noise in addition to sine. Note that for low frequencies, because the length is 16 samples the sine could be equivalent to a trend and not seen as periodic. Gaussian noise sequences $b_i(n)$ were generated with different standard deviations σ_b = 0.1,0.3,0.5,0.7,1,1.5,2, the periodic pattern frequency is selected in the set $\omega(rad/s)$ = 0,0.1,0.3,0.5,0.7,1,1.7 and c_i is a gaussian random variable with $\sigma_c = 4$.

Indeed, for all possible values of the pair (σ_b, ω) a set of 500 positive sequences $seq_{1,i}$ ($i = 1 \cdots 500$) was generated. Negative sequences $seq_{0,i}$ were generated by using the model (4) where the alternans term has been removed.

Finally, adequate threshold was selected to compute the sensitivity and the specificity, alternatively the Pd and the Pfa, of the tested filters t-test [5], matched pair t-test [5], GLRT [6], SM and SMM. Unlike the SM and SMM, the three first filters were applied on the raw sequence and not on their Fourier transform.

In fig. 1 (only noise), fig. 2 (only sine), fig. 3 (noise and sine), the ROC curves of the filters are displayed in the interval $[2-10]\%$ in order to select the threshold corresponding to (1-specificity)=5%. This value corresponds to a risk of positively detecting 5 TWA sequences out of 100 when TWA is not present (probability of false alarm). It is clear that globally, SMM outperforms the other methods with this simulation model. It is worth noting that the two filters based on Fourier transform exhibit better performance in fig. 3 (noise and sine) where their optimized threshold is 2.05 and 3.6 respectively for SMM and SM. The corresponding sensitivities are 0.8 and 0.75 for the two filters and could be compared to 0.65, 0.68, 0.63 for the t-test, matched pair t-test and GLRT, respectively.

The behavior of pair t-test, t-test and GLRT detectors could be predicted because the requirements that support these detectors are not fulfilled. The two first assume that the data are gaussian and the last one relies on non adequate model according to the simulated one. This is evidenced in fig. 2 where only sine is considered as disturbances. Because SM and SMM outperform the others they will be selected for comparison with CSM in a real data case. Furthermore, they all share the property to work in the spectral domain.

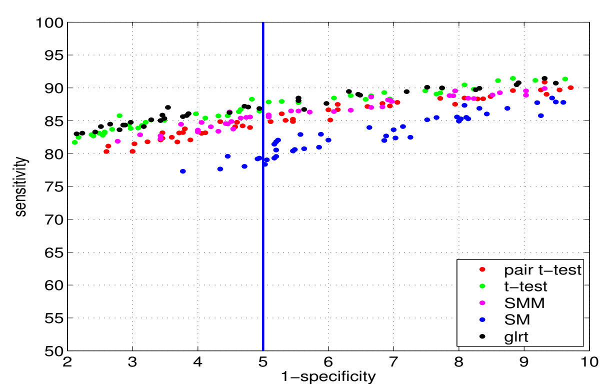

Figure 1. ROC curves of different filters in the range of (1-specificity) $[2-10]\%$. Only noise is added in the model

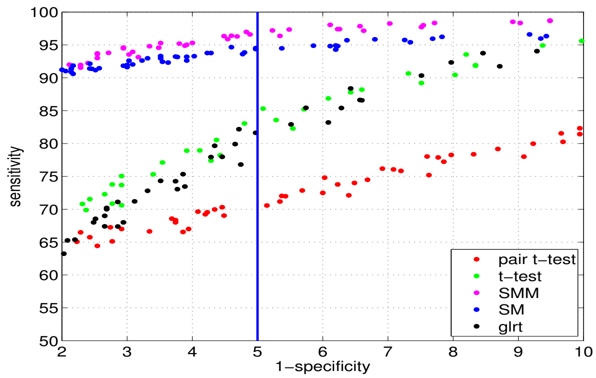

Figure 2. ROC curves of different filters in the range of (1-specificity) $[2-10]\%$. Only sine is added in the model

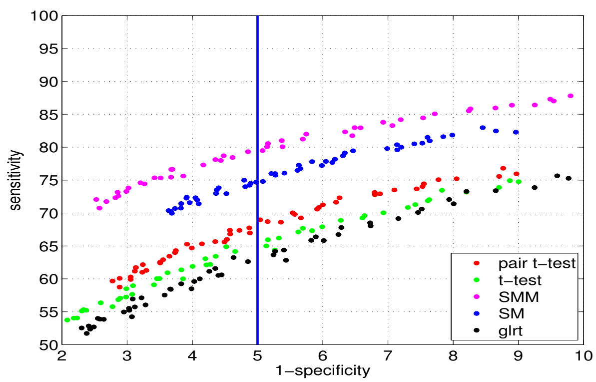

Figure 3. ROC curves of different filters in the range of (1-specificity) $[2-10]\%$. Noise and sine are added in the model. The thresholds corresponding to (1-specif)=5% are 2.28, 1.52, 2.05, 3.6, 1.07 for pair t-test, t-test, SMM, SM, GLRT, respectively.

3. Application

The study group consisted of 50 patients with ICD stimulated (ventricular) at 100bpm (age: 55.3 σ:16.4; LVEF: 42.8 σ:15.5). Two minutes recordings of XYZ orthogonal lead system were digitized with a sampling frequency equal to 2 kHz. After a QRS detection procedure, the T waves are segmented according to the classical definition of the T wave onset and offset. Ectopics beats were removed while preserving the alternans sequence. This will provide for each patient N ($N \gg 16$) segmented T waves with M samples for leads X, Y, Z, stored for TWA detection procedure. Information for each T wave will be computed by using the average over time of the T waves. This processing has the advantage to be less affected by misalignments of the T waves. Then, for each patient N data are at disposal for the three leads.

The processing of each lead is the following:

- Filter sequence from a sliding window of 16 values with SM and SMM
- Store filter output intervals > 3.6 and > 2.5 respectively for SM and SMM
- Compute the median value of the intervals length
- If this single value is greater than a final threshold (Th) then TWA detection is positive for the lead

Finally, if the detection is positive in at least one lead then the TWA is declared detected. One example of the output of the SMM filter applied to the Y lead is provided in fig. 5 (upper part) where it appears that the length of the interval crossing the threshold is about 10 beats.

In contrast to SM and SMM, CSM compute the average of Fourier transform instead of the Fourier transform of the average. In this case the sequence is 128 samples long that does not allow a sliding window processing. Then for each patient, CSM provides a single detection value for each lead. Similarly to SM and SMM if the detection is positive in at least one lead then the TWA is declared detected. Note that applied to the same data in fig. 5, CSM failed in detecting TWA.

Among the study group, 26 patients exhibited ventricular fibrillation (VF) episodes. It is expected to correlate these arrhythmia episodes with the detection of TWA elicited during ICD stimulation. This labeling allows the computation of the ROC curves for the SM, SMM and CSM detectors, using different values for Th. The two first are selected because their performances are better with simulated data and that they are based on Fourier transform. Also defined in the spectral domain, CSM is taken as the gold standard for the TWA detection. In fig. 4, the ROC curves are displayed for the three detectors.

Although the performances were not very high, the detection power assessed by the Area Under the Curve (AUC) is the best for SMM (AUC=0.69) and the worst is for CSM (AUC=0.5). This globally low AUC could be explained by the lack of real ground truth. In other words, it could be expected that patients suffering from VF should exhibit TWA but the presence of TWA doest not necessarily mean that VF will occur. This means that for a given level of sensitivity the specificity could be low.

According to the performance of CSM and the upper part of the example in fig. 5, it could be hypothesized that in such experiment TWA episodes are rarely long enough to make CSM efficient.

In addition, instantaneous analysis done by SMM is provided in fig. 5 (lower part). In contrast to the average in time of the T waves, the filter is applied on each time sample. So, the result is a matrix of filter outputs compared with the threshold. The corresponding elements where TWA is detected are plotted in red. It is clear that the localizations of the detected TWA are slightly different than in fig. 5 (upper part) and that they appears mostly in the first half of the T wave.

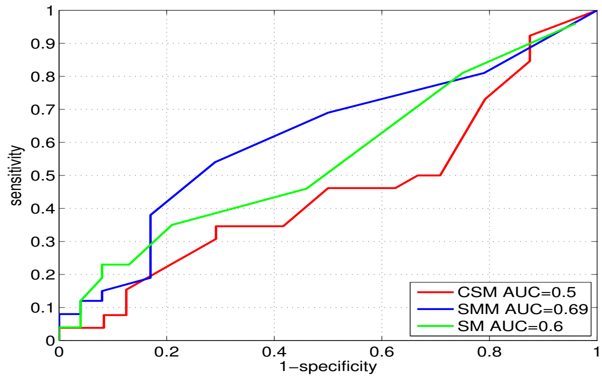

Figure 4. ROC curves for CSM, SMM, SM detectors using the three leads.

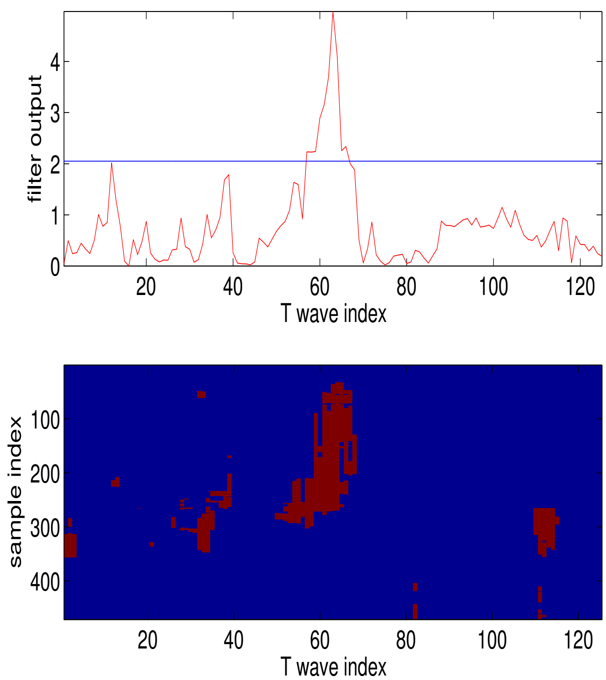

Figure 5. Upper part: SMM Filter output for a given patient (Y lead) where the sequence is the average in time of the T wave. Threshold is 2.05 (blue line). Lower part: SMM filter output for each time samples of the T waves (in red when > 2.05, in blue otherwise).

4. Conclusions

The classical spectral method is one gold standard for the TWA detection. This success could be explain by its robustness with respect to interferences not white but periodical. In this paper it has been shown that alternatives exist while using the spectral domain. In contrast to this method, the proposed tools are applicable to short time windows that allows the tracking of dynamic TWA episodes. Based on a fully simulated dataset, including different noise levels and frequencies of sinusoids, the proposed methods outperformed classical ones. In addition, optimal thresholds are provided for a given sensitivity. The improved spectral method has been applied to real data where it appears that the detection of TWA episodes correlated with the existence of ventricular fibrillation. Although this detection is not related to a very high specificity, the proposed method is an adequate tool compared to the classical spectral method. The poor performances of the classical spectral method could be explained by a dynamic TWA pattern where small durations and changes of phase may hinder accurate detections.

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