Comparison of three T-Wave Delineation Algorithms based on Wavelet Filterbank, Correlation and PCA

T Baas[1], F Gravenhorst[1], R Fischer[2], A Khawaja[2], O Dössel[1]

[1] Institute of Biomedical Engineering, Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany
[2] BIOSIGNA - Medical Diagnostics, Munich, Germany

Abstract

There is a large interest in analysing the QT-interval, as a prolonged QT-interval can cause the development of ventricular tachyarrhythmias such as Torsade de Pointes. One major part of QT-analysis is T-end detection. Three automatic T-end delineation methods based on wavelet filterbanks (WAM), correlation (CORM) and Principal Component Analysis PCA (PCAM) have been developed and applied to Physionet QT database.
All algorithms tested on Physionet QT database showed good results, while PCAM produced better results than WAM and CORM achieved best results. Standard deviation in sampling points (f_s=250Hz) have been 33.3 (WAM), 8.0 (PTDM) and 7.8 (CORM). It could be shown that WAM is prone to interference while CORM is the most stable method even under bad conditions. Furthermore it was possible to detect significant QT-prolongation caused by Moxifloxacin in Thorough QT Study # 2 using CORM. QT-prolongation is significantly correlated to blood plasma concentration of Moxifloxacin.

1. Introduction

QT-prolongation can cause the development of ventricular tachyarrhytmias such as Torsade de Pointes (TdP) and ventricular fibrillation often leading to cardiac death. QT-prolongation and TdP has been identified as a side effect of many commonly used medications [1]. Thus QT-analysis play a major role for pharmaceutical industries on their way to developing new drugs.
ICH E14 is a set of guidelines for clinical evaluation of QT/QTc interval prolongation and proarrhythmic potential for nonarrhythmic drugs [2]. The guidelines endorse manual QT measurement for "thorough QT/QTc studies" and highlight the need for further research before the use of fully automated methods can be accepted in these studies [3].
Automatic delineation of ECG signals is necessary for Holter ECG analyses. While R-peak delineation can be done very reliable and the following Q-point detection is straight forward, the identification of the T-wave boundaries is much more complex. A delineation algorithm has to handle the fact that the amplitude of the T-wave is low at the wave boundaries and often obscured by noise waves [4].
ICH E14 requests a further investigation on T_{end} delineation which was partly done in recent years. A short overview on important ECG delineation algorithms can be found in [5]. In 2006, Computers in Cardiology (CinC) presents the results of a challenge for measuring the QT-interval [3].
This work presents three different methods for T_{end} detection which all are fully automated. Validation is done using the physionet QT-database [6]. The method which shows the best result is additionally used to detect drug induced QT-prolongation in Thorough QT Study # 2 from THEW [7].

2. Methods

Three delineation methods are introduced. For T-wave delineation in a first step all algorithms need to detect the R-peaks. This is achieved by a wavelet based algorithm introduced in [8].

2.1. Wavelet based method (WAM)

First delineation algorithm evaluated in this study is a revised version of the wavelet based algorithm presented in [8]. To delineate the T-wave, a discrete wavelet transformation (DWT) of the original signal using the Haar wavelet is performed. The decomposition of the ECG signal into elementary building blocks that are well localized both in time and frequency, characterize the local regularity of signals [9]. DWT can be done very efficiently by applying a multi rate filterbank implementation which computes the approximation coefficients $c_k(l)$ and detail coefficients $d_k(l)$ for all k levels recursively.

The approximation coefficients $c_k(i)$ and detail coefficients $d_k(i)$ are equivalent to cascaded low- and band-

pass filters. As the T-wave is always located between two R-peaks, the detail coefficients of the corresponding RR-interval are used to delineate the T-wave. The sample frequency dependent level k_n, corresponding to a frequency range below 15Hz is used. The characteristics of the T-wave contribute a prominent signal in the detail coefficients of this level. A positive T-wave generates a minimum-maximum pair, while a negative one generates a maximum-minimum pair. To detect the peak values an amplitude threshold has to be calculated. It is calculated by the RMS of a sliding window with the length L.

$$T(n) = \sqrt{\frac{1}{L+1} \cdot \sum_{i=n-0.5L}^{n+0.5L} d^2_{n_{level}}(i)} \qquad (1)$$

Either way, the second significant extremal to consider is the one for the T_{end} detection. In particular, the signal within the first half of the interval between this extremal and the subsequent root is extracted. This is visualised in Figure 1.

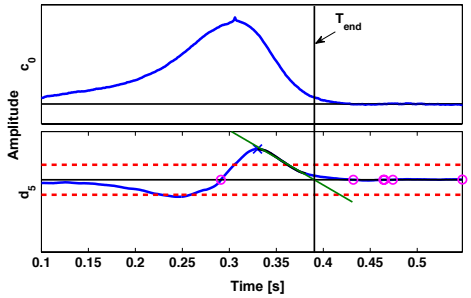

Figure 1. Top: original time domain signal, bottom: wavelet detail coefficients of level five, pink circles: roots, red dotted lines: RMS threshold, blue cross: second significant extreme values, green: least squares line, black vertical line: T_{end}.

Subsequently, the coefficients for the straight line of the form:

$$f(x) = c_1 \cdot x + c_0 \qquad (2)$$

are determined that fit best to the extracted signal interval in a least squares sense. The zero-crossing of this line is considered as the position of T_{end}:

$$T_{end} = -\frac{c_0}{c_1} \qquad (3)$$

2.2. Correlation based method (CORM)

The second T_{end} delineation algorithm compared in this study is based on a correlation method [10]. First a template needs to be calculated. For that reason all RR-intervals are extracted. To avoid an influence of the next QRS-complex or an existing U-wave on the template, RR-intervals are shortened to 70% of their length by discarding the last 30%. Top of Figure 2 shows the result. To get a reliable patient specific template, all intervals influenced by artefacts and noise need to be detected as outliers. This can be done by using Hotelling's T^2. After performing a PCA, for each interval a variability score T^2 is calculated by the first three PCA Scores b and the variances α (eigenvalues):

$$T^2 = \frac{b_1^2}{\alpha_1} + \frac{b_2^2}{\alpha_2} + \frac{b_3^2}{\alpha_3} \qquad (4)$$

Signal intervals with T^2 higher than the mean are regarded as outliers. In a last step all intervals need to be vertically shifted and horizontal aligned. Bottom of Figure 2 shows the result.

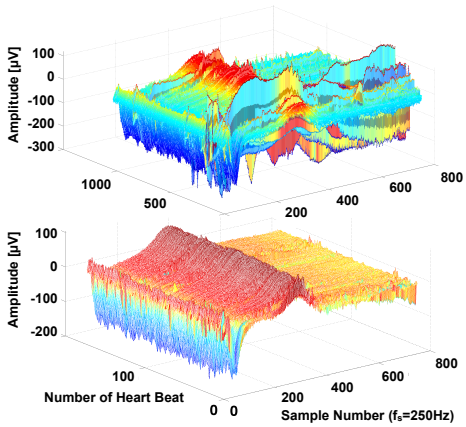

Figure 2. Top: original RR intervals after cutting of 30% at the end. Bottom: Horizontally and vertically aligned beats after identifying and ignoring outliers.

A template T-wave is calculated as the mean of the remaining aligned intervals. This template is finally marked using the wavelet method described previously. Figure 3 shows such a marked template.
After calculating the patient specific template, it can be used to detect T-waves in the ECG signal. First, all heart beats are split again into their RR-intervals. Regarding the template, for all further considerations only the part of the template between T_{on} and T_{end} is used. Several horizontally stretched versions of the template are generated. Stretch factors are limited by 0.88 and 1.13. Every heart beat's RR-interval y is correlated to a set of templates containing all combinations of available shift and stretch vectors. The pair of stretching and shifting values for which the correlation score is highest gives a good estimate of the T-wave position.
To further improve the accuracy of the T-wave position a refinement search is performed by applying a mean square

error (MSE) optimization. Keeping in mind, that the falling edge of the T-wave is most important, this part of the template gets a higher weight in MSE. The MSE score is calculated for scaled and shifted templates $t_{s,k}$ in a small range around the correlations estimation position:

$$MSE(s,k) = \frac{1}{N}\sum_{i=1}^{N} w_N(i) \cdot [y(i) - t_{s,k}(i)]^2 \qquad (5)$$

Due to its sensitivity to noise, changes of the shift and scale vectors by the MSE optimization are limited. The pair of stretching and shifting values (s_{best},k_{best}) for which $MSE(s,k)$ is lowest, provides the best T-wave position. Thus T_{end} is given by:

$$T_{end} = T_{end,Template} \cdot s_{best} + k_{best} \qquad (6)$$

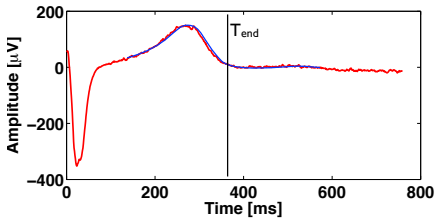

Figure 3. Shortened RR interval with T-wave (red) and template interval (blue) after correlation and refinement.

2.3. PCA based method (PCAM)

The third algorithm compared in this study is a PCA based method. This method works similar to the correlation method, but instead of using a correlation for computing the T-wave estimation a PCA is applied. For that reason, only the PCA based part of the algorithm is described.

Similar to the correlation method, s_{best} and k_{best} have to be found. To discover these heart beat dependent values, two PCAs, one for s_{best} and one for k_{best}, have to be carried out.

First a template for every scale factor s_x has to be calculated. Next a PCA is carried out. The PCA transforms the given data into a new coordinate system. The basis vectors of the new coordinate system are chosen in a way that they maximize the scores' variance. The order is determined according to the variance. Thus, the first few scores are supposed to represent the most significant differences between the observed templates. In this case, these scores are considered as uniquely indicating the T-wave's scaling.

All template signals that were extracted as described in section 2.2, are transformed into the new coordinate system. The scale factor of the template having the lowest distance in the first three dimensions to the heart beats signal interval represents s_{best} for that heart beat. Figure 6 shows the representation of the scaled templates in the first three dimensions of the coordinate system as blue cycles. A transformed heart beat of the ECG is shown as a green triangle.

Following the same approach, a coordinate transformation which results in shift-sensitive coefficients k_{best} has to be found.

3. Results

To compare the quality of the three delineation methods introduced before, the Physionet QT database [6] is used. In this database, T_{end} is manually marked by an expert. ECG records were sampled at 250Hz. In total a number of 2647 heart beats have been considered. To validate the acquired results, the difference in number of samples between the experts reference and the algorithms were chosen. Standard deviation (SD) is smallest for the CORM. PCAMs SD was little higher, while WAMs SD was significantly higher.

Mean error was smallest for PCAM and a little higher for CORM. WAM was again significantly higher. Table 1 shows the exact values.

Table 1. Comparison of T_{end} detection algorithms

Value	PCAM	CORM	WAM
mean error	-1.8462	-1.9804	6.2862
standard deviation of error	8.0053	7.7751	33.3356
detection rate ($e < 100ms$)	97,65%	97,54%	77,22%

Figure 4 shows a histogram built from the results of all three methods. Again the difference to the reference annotations is considered. CORM has detected most T_{end} in a range of ± 5 sample points ($\pm 20ms$) around expert marks. Again PCAM is second, while WAM marked fewest heart beats in this interval. Detection rate was measured considering all T_{end} in a range of 25 sample points (100ms) around the reference marks as detected. Again PCAM and CORM performed significant better than WAM.

To further confirm the results, CORM was successfully used to detect drug induced QT prolongation in Thorough QT Study # 2 from THEW [7]. Figure 5 shows the results for two patients.

4. Discussion and conclusions

One major problem in T_{end} delineation is the missing golden standard. Comparing automatically generated de-

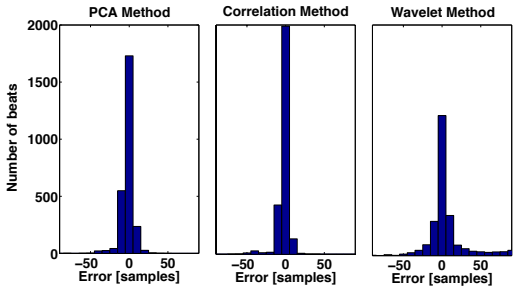

Figure 4. Comparison of T_{end} detection algorithms. Histogram on the differences between expert annotations and delineation by the algorithms.

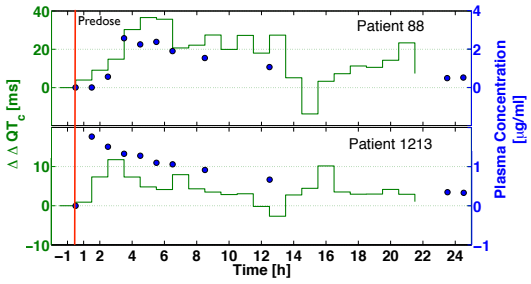

Figure 5. QT-prolongation caused by Moxifloxacin for two patients in THEW studie. Green line: difference of $QT_{c,Bazett1h}$ for placebo and Moxifloxacin measurement, blue dots: Moxifloxacin plasma concentration, red line: medicine administered.

lineations to expert annotations is a possible validation method, but introduces the problem of beat to beat deviation in handmade ECG delineation.

Both, PCAM and CORM showed very good results. It turned out that there is a major drawback in using PCAM instead of CORM. The two coordinate transformations used for the identification of s_{best} and k_{best} are not perfectly independent. As Figure 6 shows, it is not always possible to distinguish between scale and shift scores of the PCA.

CORM was successfully used to identify known QT-prolongation caused by Moxifloxacin, as shown in Figure 5. As the QT-prolongation correlates to the blood concentration of Moxifloxacin CORM to work very reliable in Holter ECG analysis.

WAM showed problems in intervals with artefacts and noisy signals. It seems that this method is not well suited for T-wave delineation in noisy signals. On the other hand this method works very reliable in signal intervals having no artefacts, noise or extreme baseline wander. For that reason WAM is used to delineate the template in COEM and PCAM, as the template represents a 'clean' patient specific T-wave.

In total this study showed that CORM offers a reliable and efficient way for T-wave delineation in ECG signals. It is suitable for QT-analysis, as the detection of QT-prolongation of 5ms is possible.

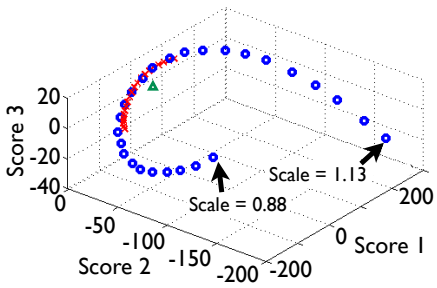

Figure 6. Scale sensitive coordinate system with both, scaled (blue cycles) and shifted (red crosses) templates representation. Green mark is a heart beat.

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Address for correspondence:

Tobias Baas

Institute of Biomed. Eng. Karlsruhe Insititute of Technology

Kaiserstrasse 12, 76131 Karlsruhe, Germany

tobias.baas@kit.edu