Individually Adaptable Automatic QT Detector

YC Chesnokov, D Nerukh, RC Glen

The Unilever Centre for Molecular Sciences Informatics, Department of Chemistry, University of Cambridge, Cambridge, UK

Abstract

The 7th Computers in Cardiology challenge presents the clinically important problem of developing and testing fully automated methods for measurement of the QT interval with clinically acceptable accuracy.

For this purpose a fully automated method was developed using time-frequency methods of continuous (CWT) and fast wavelet transforms (FWT). It consists of QRS detection and P, T wave boundaries identification which is implemented using consecutive ECG data filtering with CWT and FWT transforms. The frequency of the CWT transform can be adjusted for more precise identification of the T wave boundaries for an individual patient. A representative beat with a T wave is selected from an automatically annotated signal if it is not annotated as ectopic, noise or artefact.

The final score is the highest one in division three and second place in division two.

1. Introduction

The 7th Computers in Cardiology challenge introduced a question of great importance: fully automatic measurement of QT intervals with acceptable accuracy for clinical evaluations. The OT interval is the time required for both cardiac repolarisation and depolarization of ventricular tissue [1]. Ventricular repolarisation prolongation of the QT interval is associated with some severe adverse effects. Some people are born with a prolonged QT interval, but others have a prolonged QT interval induced by medicines that affect cardiac repolarisation [2]. QT prolongation predisposes the patient to a disorganised heart rhythm called Torsades de Pointes (TdP), which can degenerate into ventricular fibrillation and death [3]. Several valuable drugs have already been withdrawn from the market, or have had their use greatly restricted, because they can prolong the QT interval and are associated with a risk of sudden death [4]. To estimate the risk of very rare adverse events, pharmacoepidemiological studies require very large numbers. Furthermore, the events in question need to be clinically recognisable by doctors and adequately documented. Robust automated systems with a

clinically acceptable quality for QT interval measurement would be important in these studies [5].

A number of automatic QT annotation methods have been developed and are reported in the literature. There are some benefits from using automatic annotation compared to manual annotation. This approach is considerably faster and at a lower cost, not prone to errors due to human factors etc. However there is often a lack of agreement between manual and automatic QT interval determination. The relationship between the duration of cellular action potentials and the OT interval recorded at the body surface is very complex, therefore the QT interval is difficult to measure with precision. There is an inherent imprecision in identifying the end of the T wave due to an incomplete understanding of the recovery process and its projection onto the body surface. Significant variation both in the onset of the QRS complex and the end of the T wave among some ECG leads provides different QT values depending on the leads selected for measurement. The above problems do not appear to be solved by current automatic OT measurement techniques, which have been found to be less accurate in cardiac patients than in healthy controls [6].

2. Methods

The fully automated ECG annotation algorithm developed here consists of filtering the signal with continuous (CWT) and fast wavelet transforms (FWT).

Wavelet transforms offer simultaneous interpretation of the signal in time and frequency domains [7]. The CWT transform of the signal x(t) is defined as:

$$T(a,b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} x(t) \psi^*(\frac{t-b}{a}) dt \qquad (1)$$

where $\psi^*(t)$ is the complex conjugate of the analyzing wavelet function $\psi(t)$, a is the dilation parameter of the wavelet and b is the location parameter of the wavelet.

The scale parameter a, is inversely proportional to the frequency f, analyzed in the signal:

$$f \propto \frac{1}{a}$$
 (2)

To calculate the frequency f, analyzed by the wavelet computed on the scale a, for the signal sampled at sampling rate (SR) s, we need to introduce the constant of proportionality which includes SR of the signal. Using this constant of proportionality we will be able to analyze the signal sampled at particular SR. First we calculate the wavelet function $\psi(t)$ at a defined scale, a, and a location parameter b, equal to zero and assign it a sampling rate, s. Then we calculate the Fourier transform of $\psi(t)$. The peak of the Fourier frequency spectrum corresponds to the frequency f, which wavelet $\psi(t)$ analyzes in the signal on the scale a, and at a sampling rate s. Then the constant of proportionality f_{cs} for the wavelet $\psi(t)$ is calculated from the relation:

$$f = \frac{f_c s}{a} \tag{3}$$

For the CWT transform the Inverse wavelet was used:

$$\psi(x) = -xe^{\frac{-x^2}{2}} \qquad (4)$$

For the Inverse wavelet, $f_{\rm c}$ was calculated equal to 0.16.

The FWT transform represents the signal at discrete frequency bands. The length of the calculated FWT spectrum is equal to the signal length. The analyzed signal is iteratively passed through high pass and low pass wavelet filters defined by numerical coefficients. The low pass and high pass iteration formulas are defined as:

$$s_{j+1,k} = \sum_{m}^{L} h_{m}^{*} s_{j,2k+m}$$
(5)
$$d_{j+1,k} = \sum_{m}^{L} g_{m}^{*} s_{j,2k+m}$$
(6)

where h* is the low pass and g* is the high pass filters for analysis, L is the length of the filter, s_j is the analyzed signal, s_{j+1} is the coarse grained signal, d_{j+1} is the high frequency band.

After a low pass iteration of the initial signal s_j for j=0, the sampling rate of the signal s_{j+1} becomes two times smaller. The high pass iteration produces a wavelet band d_{j+1} in the frequency range of SR/4–SR/2 Hz. Next the formulas 5 and 6 are applied again to the down sampled signal s_{j+1} .

To reconstruct the signal from its FWT spectrum the following relation is used:

$$s_{j-1,k} = 2\sum_{m} (h_{k-2m} s_{j,m} + g_{k-2m} d_{j,m})$$
(7)

where h is the low pass and g is the high pass filters for synthesis, s_{j-1} is the reconstructed signal, s_j is the coarse grained signal, d_j is the high frequency band.

The annotation algorithm is applied directly to the digitized ECG signal without prior denoising and provides precise results despite the presence of baseline wander, muscle artifacts and power line interference noise. Although identification of the T wave component in the parts of the signal contaminated with baseline wan-

der is poor compared to clean parts of the signal, for better annotation of the QT interval the signal should be base line corrected.

The first stage of the annotation procedure is the detection of QRS complexes.

First the ECG signal is transformed with CWT using an Inverse wavelet at a frequency of 12Hz. This amplifies the high frequency QRS part from the low frequency P, T waves and noise. Next the continuous wavelet spectrum of the ECG signal is filtered with an FWT transform using interpolation filters g, h, g^* , h^* [8]. The FWT frequency band below 30Hz is replaced with zeros thus removing the low frequency part of the ECG signal. The high frequency bands above 30Hz are denoised using a hard threshold formula [9]:

$$d_{j+1,k} = \begin{cases} d_{j+1,k}; |d_{j+1,k}| > p \\ 0; |d_{j+1,k}| (8)$$

where p is the threshold, $d_{j+1,k}$ is the high frequency band coefficient.

The threshold p is calculated for a 2 second window length for FWT high frequency bands using a MINIMAX formula:

$$p = \sigma(0.3936 + 0.1829\log(n)) \tag{9}$$

where σ is dispersion and n is the length of the 2 second window.

The reconstructed ECG signal after denoising contains only spikes with nonzero values at the location of QRS complexes. From this signal, the PQ junction and J point can be located as the boundaries of the spike. If the length of the spike is more or less than a predefined QRS length range it is annotated as noise and if the voltage is below a certain threshold, it is annotated as an artifact.

The next stage is the detection of the T wave. Every annotated heart beat of the original ECG signal beginning from the detected J point and extending to the possible longest duration of the T wave, which can be adjusted, is analyzed by the CWT at the 3 Hz frequency. The minimum and maximum of the CWT spectrum corresponds to the beginning and end points of the T wave and zero crossing to its center. Additional constraints are applied to detect the T wave duration and symmetry and to exclude probable erroneous results. The frequency of the CWT transform is varied between 1-3Hz to get a more precise annotation of the various sizes of the T wave. The same procedure is applied to detect the P wave in the PQ interval but the CWT transform is calculated on the 9Hz. The peaks of Q, R and S waves are identified in the annotated part of the ECG signal from the PQ junction to J point.

The presence of an ectopic beat is tested using 3 consecutive RR intervals: RR1, RR2 and RR3 [10]. The rules applied defined as:

 $1.15RR2_i < RR1_i \text{ and } 1.15RR2_i < RR3_i = true$ (10)

 $|RR1_i - RR2_i| < 0.3$ and $RR1_i < 0.8$ and $RR2_i < 0.8$

| and $RR3_i > 2.4*(RR1_i + RR2_i) = true$ | (11) |
|---|------|
| $ RR1_i - RR2_i < 0.3$ and $RR1_i < 0.8$ and $RR2_i < 0.8$ | 0.8 |
| and $RR3_i > 2.4*(RR2_i + RR3_i) = true$ | (12) |

If any of these rules is true, then the RR2 interval is identified as ectopic.

The next beat after the first in the annotated ECG signal is selected as representative for QT interval measurement if it is not annotated as noise, artifact, ectopic and not immediately followed the ectopic beat and contains an annotated T wave. Otherwise the next beat is tested for those conditions to be selected as representative.

3. **Results**

The QT interval was measured in lead II of the PTB Diagnostic ECG database containing 549 ECG records sampled at 1000Hz. The database contains various morphologies of the cardio cycle including myocardial infarction patients, cardiomyopathy and healthy controls. The representative beat was selected from the annotated signal and the QT interval was measured.

The first preliminary score achieved in division 2 of the competition was the highest one: 30.35. The following ECG records were excluded from the annotation for the first entry: s0476 re, s0488 re, s0489 re, s0542 re, s0544 re, s0549 re, s0553 re, s0555 re and s0556 re. The second score achieved was lower: 30.97 compared to the best in the automated division: 17.27. Subsequent entries were submitted to the challenge excluding only the annotation of the s0544 re file. These additional preliminary scores did not improve. To get better scores, the annotation was performed adjusting the frequency of the CWT transform of the T wave to resemble more closely to published QT intervals [11] measured by expert cardiologists for this challenge. The achieved score was 17.86, very close to best one 17.22 in the 2nd division. On the deadline day of the 4th of September we changed to the 3rd division with the same entry and got the best preliminary score. The final score is the best one in the 3rd division and second place in division 2.

4. Discussion and conclusions

A fully automated ECG annotation method is presented. It is fast and simple in implementation and the algorithm is applicable to a wide range of ECG cardio cycle morphologies and robust to various types of noise: baseline wander, muscle artefact and power line interference.

A number of methods are reported in the literature on the ECG annotation problem and compared to manual annotation. McLaughlin et al [12] tested four automatic QT interval measurement methods in post myocardial infarction patients, patients with arrhythmias and control subjects. They found that automatic QT measurement

techniques are less accurate in cardiac patients than in controls. Savelieva et al [13] carried out research to determine whether the automatic measurement of the OT interval is consistent with manual measurement in hypertrophic cardiomyopathy and normal subjects. They applied automatic methods that determine the T-wave end as the intersect of the least-squares-fit line around the tangent to the T-wave downslope with the isoelectric baseline. Manual measurements were obtained using a high-resolution digitizing board. They found that in patients with hypertrophic cardiomyopathy, the absolute values of the OT interval and OT dispersion were significantly higher than those in normal subjects (p < 0.0001). In both groups, the intra-subject variability of the QT interval was significantly lower with automatic than with manual measurement (p < 0.05). They conclude that the automatic QT interval measurements are more stable and reproducible than manual measurement. However, lack of agreement between manual and automatic measurements suggests that clinical experience gained with manual assessment cannot be applied blindly to data obtained from the automatic systems. Murray et al [14] compared manual and computer automated techniques for measuring QT dispersion. They used healthy, myocardial infarction and cardiac arrhythmias patients. They found that measurements of QT dispersion from small T waves increases measurement variability and reduces the potential for detecting clinical differences. Automatic measurement of QT dispersion gives different results from manual measurement, but can satisfactorily discriminate between normal and abnormal groups with good quality electrocardiograms. Vecchietti et al [15] compared QT interval and QT dispersion in ventricular ectopic beats with measurements from the preceding and immediately following sinus beats, and investigate differences between manual and automatic measurements. They used computer automated techniques to identify the end of the T wave by the intersection between the baseline and the slope of the T wave between 30% and 70% of peak amplitude [16] and manually measured intervals. Manual measurement resulted in greater QT values than automatic measurement. The ventricular ectopic beats resulted in an increase in the QT of the immediately following sinus beats. They conclude that the results confirm the need to interpret QT measurements with care in the presence of ectopic beats.

Different QT annotation methods are presented at the Computers in Cardiology 2006 conference including wavelet-based algorithms, which provide discrimination of the cardio cycle parameters in the time plane based on their frequency content. Using appropriate filtering to separate cardio components in a time-frequency plane and a set of rules to identify their boundaries, it is possible to develop fast algorithms, robust to noise and various morphologies of the cardio cycle waves.

Our methods includes those advantages. The consecutive application of CWT and FWT transforms separates noise and P, T waves from the QRS complex. This provides better results compared to one stage filtering of the QRS complex with only FWT or CWT transforms, if P and T waves are of high amplitude. Different wavelets and wavelet filters were tried to achieve better precision of the QRS complex location: Mexican hat, Gaussian derivatives, Daubechies, coiflets and biorthogonal. Inverse wavelet and interpolation filters provided better time localization of the QRS complex boundaries. CWT transforms at 3 Hz of the T wave provides inherent denoising. This is essential in precise detection of the T wave end, since it might be corrupted with muscle artifact noise. The main advantage of the method is that it can be adjusted by varying the CWT transform frequency in the range of 1-3 Hz to particular T wave morphologies with clinically accepted precision which resulted in improvement of our score. This is crucial in solving the problem of disagreement between manual and automated annotation methods. Clinicians can define clinically acceptable T wave ends for particular patient's cardio cycle morphology and the frequency of the CWT transform providing that precision can be selected. Fig. 1 shows annotation of one beat for the record s0010 re where the T wave was transformed on 3.5 Hz. Fig 2 shows annotation of one beat for the record s0010 re where the T wave was transformed on 2.5 Hz.



Figure 1. T wave annotation with CWT transform on



Figure 2. T wave annotation with CWT transform on 2.5 Hz

Comparing Fig. 2 with Fig. 1 we can see that the lower frequency of the CWT transform provides a longer QT interval. This provides an easily adaptable method for particular T wave morphologies without excessive computational effort.

Acknowledgements

This work is supported by the Medical Research

Council grant Ref. G0401505.

References

- Moody GB, Koch H, Steinhoff U. The Physio-Net/Computers in Cardiology Challenge 2006: QT Interval Measurement. Computers in Cardiology 3006;33.
- [2] Sala M. et al. Antidepressants: their effects on cardiac channels, QT prolongation and Torsades de Pointes. Curr Opin Investig Drugs 2006;7(3):256-63.
- [3] Vohra J. Drug-induced prolonged repolarisation (acquired long QT syndrome) arrhythmias. Heart Lung Circ 2003;12: 85-9.
- [4] Friberg LE et al. Pharmacokinetic-pharmacodynamic modeling of QT interval prolongation following citalopram overdoses. Br J Clin Pharmacol 2006;61(2):177-90.
- [5] Jane R et al. Evaluation of an automatic threshold based detector of waveform limits in Holter ECG with the QT database. Computers in Cardiology 1997;24:295-298.
- [6] Kautzner J. QT Interval Measurements Cardiac Electrophysiology Review 2002;6(3):273-277.
- [7] Addison PS. Wavelet transforms and the ECG: a review. Physiol Meas 2005;26:155-199.
- [8] Wavelet interpolation filters. http://www.ann.jussieu.fr/~koutchmy/filters/plots/indexawf .htm
- [9] Chen SW, Chen HC, Chan HL. A real-time QRS detection method based on moving-averaging incorporating with wavelet denoising. Comput Methods Programs Biomed 2006;82(3):187-95.
- [10] Tsipouras MG, Fotiadis DI, Sideris D. An arrhythmia classification system based on the RR-interval signal. Artificial Intelligence in Medicine (2005);33:237-250.
- [11] Christov I. et al. Dataset of manually measured QT intervals in electrocardiogram. BioMed Eng Online 2006;5(31).
- [12] McLaughlin NB, Campbell RW, Murray A. Accuracy of four automatic QT measurement techniques in cardiac patients and healthy subjects. Heart 1996;76(5):422-6.
- [13] Savelieva I et al. Agreement and reproducibility of automatic versus manual measurement of QT interval and QT dispersion. Am J Cardiol 1998;81(4):471-7.
- [14] Murray A, McLaughlin NB, Campbell RW. Measuring QT dispersion: man versus machine. Heart 1997;77(6):539-42.
- [15] Vecchietti S, Langley P, Severi S, Cavalcanti S, Murray A. Effect of premature ventricular beats on manual and automatic repolarization measurements. J Electrocardiol 2004;37(3):181-9.
- [16] Langley P, Murray A. Comparison of manual and automatic QT dispersion measurements in clinical groups. Computers Cardiol 2001;28:1645.

Address for correspondence

Yuriy Chesnokov

The Unilever Centre for Molecular Sciences Informatics, Department of Chemistry, Cambridge University, Cambridge, CB2 1EW, UK

yc274@cam.ac.uk