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Lecture notes*

Sources of Variation in the QT Readings: What should you be Aware of?

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Abstract: *The QT interval is measured manually or automatically. In comparison with manual methods, the automated ones offer advantages in terms of absolute repeatability of measurements, immunity from errors related to observer fatigue, lack of attention, as well as efficiency and cost effectiveness that permits either more extensive and rigorous testing for the same cost as manual methods, or more rapid testing at lower cost. But a question arises: '**Can the QT interval be measured by fully automated methods with accuracy acceptable for clinical evaluations?**' We created a dataset of manually measured Q-onsets and T-ends for the PTB Diagnostic ECG Database. Further on we developed a fully automated method for QT measurements and forwarded it to PhysioNet/Computers in Cardiology Challenge, 2006. The manually measured dataset was then used as a 'gold standard' for assessment of the accuracy of the automated method. The current lecture notes summarize all our up to date publications on the QT measurements topic. Sources of variation in the QT readings are for the first time discussed by the authors.*

Keywords: *Electrocardiography, Q-onset and T-end delineation, QT measurement, PTB Diagnostic ECG database.*

Introduction

Why is it so important to have reliable tools to measure the QT interval correctly?

At the first place because there is a wide array of drugs that can cause QT prolongation and a large number of patients are exposed to them, with increasing age and multidrug therapy increasing the risk. Then there are several genetic disorders affecting the QT interval. Last but not least we must keep in mind that the clinical presentation of these electrophysiological changes can be the potentially fatal ventricular arrhythmia – Torsade de Pointes (TdP). A few words will be said to each of these conditions before referring to the technical aspects of QT interval measurement.

* Fifth annual meeting on QT Prolongation and Safety Pharmacology, Paris, France, 13-14 March, 2007

The most common in clinical practice is the so called acquired long QT syndrome (LQTS) – drug-induced QT interval prolongation. This can be observed in 1 to 10% of the patients treated with antiarrhythmic agents and much more rarely with other "noncardiovascular" drugs. A detailed and up-to-date list of all pharmacological agents known to cause a prolongation of the QT interval can be found at www.torsades.org and www.qtdrugs.org [20]. The long QT syndrome is an inherited disorder with prolonged ventricular repolarization, manifested with ventricular arrhythmias. A corrected QT interval (QTc) > 500 ms identifies patients with the highest risk of becoming symptomatic [16]. There are 10 different genetic subtypes known, with 3 of them the most common – LQT 1, 2, 3; LQT1 – mutation in the KCNQ1 or KvLQT1 gene, affecting potassium current I_{Ks}; LQT2 – mutation in KCNH2 (or HERG) gene, affecting potassium current I_{Kr}; LQT3 – mutation in SCN5A, encoding cardiac sodium channel [20].

A few words must be said also about the short QT syndrome (SQTS) – a relatively new clinical entity, discovered in 2000 [10] and characterized by abnormally short repolarization: QTc < 300 – 320 ms. Here the shortening of the QT interval is accompanied by T wave abnormalities. The disease is supposed to be highly lethal with an increased occurrence of atrial fibrillation and sudden cardiac death. It is of interest to note that all 3 SQTS genes (KCNH2, KCNQ1 and KCNJ2, affecting potassium currents I_{Kr}, I_{Ks} and I_{Kl} respectively) can cause also LQTS. The difference here is that instead of loss of function as is the case in LQTS, in SQTS patients there is a gain-in-function mutation [20].

It is important to say that before approval every new chemical entity requires estimation of its potential to prolong the QT interval. It must be kept in mind however that the prolongation of the QT interval is not a surrogate of ventricular arrhythmias, i.e. TdP and sudden cardiac death. Novel markers are immerging and are being widely tested; among them is also the QT interval dispersion which reflects the transmural dispersion or variability of depolarization and repolarization. It is measured as the difference of the maximal and minimal QT intervals on a 12-lead surface ECG and/or as the standard deviation between all 12 QT intervals.

QT measurements

The QT interval is measured manually or automatically. In comparison with manual methods, the automated ones offer advantages in terms of absolute repeatability of measurements, immunity from errors related to observer fatigue, lack of attention, as well as efficiency and cost effectiveness that permits either more extensive and rigorous testing for the same cost as manual methods, or more rapid testing at lower cost [12]. But a question arises: '**Can the QT interval be measured by fully automated methods with accuracy acceptable for clinical evaluations?**' In an attempt to answer the question the PhysioNet/Computers in Cardiology forwarded a Challenge in 2006 [12].

Manual QT measurements

Due to the fact that the manual delineation of the Q-onset and T-end is a very time consumable and tiresome task, it has a limited application. It is mostly used to establish a reference library, or 'gold standard' which will further be used for accuracy assessment of the different automated methods.

The Common Standard of Europe Working Party [17, 18] used a comprehensive interactive review process that was carried out by cardiologists from several institutes in Europe on highly amplified ECG tracings. In order to achieve convergence of the cardiologists'

markings and to correct the inter-observer differences the review process was assessed in 3 rounds.

We used the same method to create in 2006 [3] a reference dataset of manually measured QT intervals for the freely submitted in Internet Physikalisch-Technische Bundesanstalt (PTB) Diagnostic ECG Database. Four cardiologists and one biomedical engineer were engaged in the project. The reviewing rounds of the manual determination of the Q-onset and T-end are shown in Fig. 1.

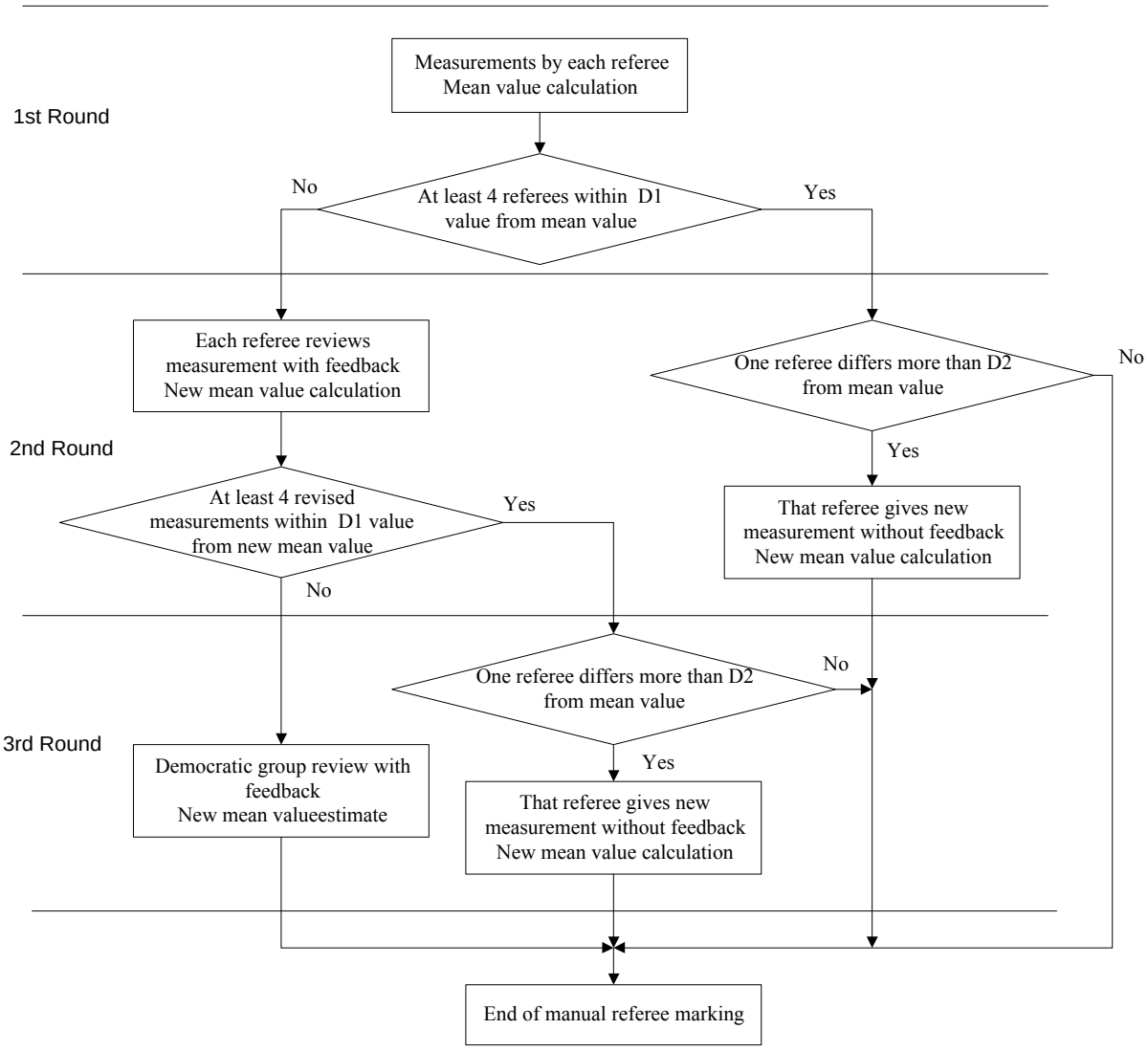

Fig. 1 Reviewing rounds in the manual determination of the Q-onset and T-end

The Q-onset and T-end thresholds used during the delineation are shown in Table 1.

Table 1. D1 and D2 thresholds in the measurements of the QRS onset and T-end

	Q-onset	T-end
D1 ms	6	26
D2 ms	8	36

In cases when more than one of the experts is outside the threshold D1, each referee receives feedback for a limited amount of time in the 2nd round. The referee is shown the mean value and the left-most and the right-most markings along with the respective person who has generated them (Fig. 2). Once shown and individually analyzed by each of the observers, all markings are hidden, and no further observations to the feedback is allowed.

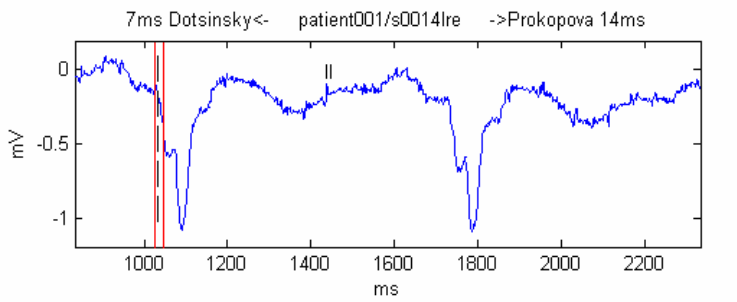

Fig. 2 Example of the feedback forwarded to all the referees during 2nd and 3rd rounds. The black vertical dashed line is the mean value. The red vertical lines denote the most left and the most right marks made by the observers, with their name and deviation from the median shown as a text at the top of the figure.

The mean and standard deviations of each referee after the 3rd round is presented in Table 2.

Table 2. Mean and standard deviations of each referee after the 3rd round

	Q onset deviations [ms]		T end deviations [ms]	
	Mean	Standard	Mean	Standard
Referee 1	-0.76	±2.45	-2.45	±6.72
Referee 2	-0.11	±3.23	0.75	±7.62
Referee 3	0.81	±3.29	8.43	±7.88
Referee 4	0.34	±2.99	-7.59	±7.68
Referee 5	-0.29	±3.22	0.78	±10.24

We submitted an article to an Internet journal [3] and all the Q-onset and T-end referees' markings along with the mean value of the markings is freely available in Internet (http://www.biomedical-engineering-online.com/content/5/1/31).

All the experts participated in the PhysioNet / Computers in Cardiology Challenge 2006 for QT interval measurement, and one of the author of the present material was rewarded as 2nd best.

What should we be aware of?

There are several factors that highly influence the correct measurement of the QT interval:

- Accompanying noise;
- Low magnitude of the T wave;
- T wave having bidirectional waveform;
- Fussing U waves, etc.

Electromyographic noise

Example of recording contaminated with electromyographic noise is shown in Fig. 3. It is extremely difficult to delineate the Q-onset and T-end (see the 'red v' in the upper trace). It should be mentioned that the human brain has infinite resources and a trained cardiologist will always try to compensate the noise, looking at the nearby P-QRS-T intervals or at a simultaneously recorded another lead, which is almost impossible task for the automated methods.

Now let's see what we should mark if the ECG recording was not contaminated with electromyographic noise ('blue v' in the second trace). Let's superimpose the red and the blue marks. The small Q-peak of the QRS complex has been missed and the Q-onset error is +45 ms. The T-end error is -20 ms.

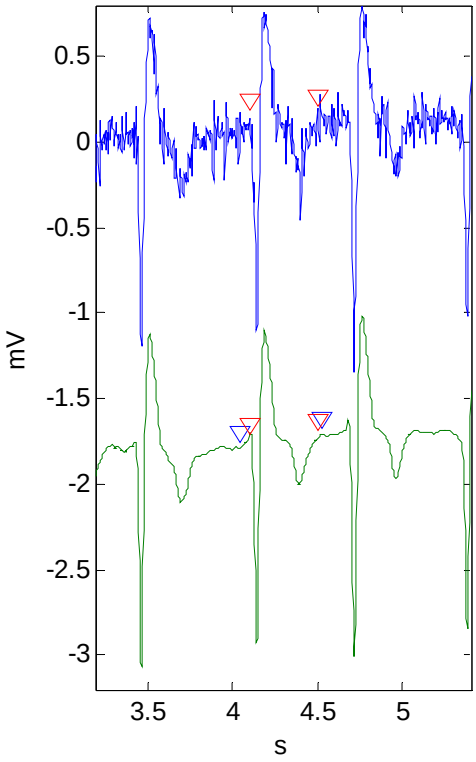

Fig. 3 Example of the electromyographic noise influence on the QT measurement

Mains interference

The power-line interference (50 Hz for Europe or 60 Hz for USA) is always accompanying the ECG recordings. Some ECG devices are optionally filtering this noise, but if the filtering methods are not enough sophisticated [11] they distort the ECG shape, decreasing the magnitude of the QRS complex and some T-waves of high amplitudes.

Example of an ECG contaminated with power-line interference is shown in Fig. 4. Q-onset and T-end delineation error of 20 ms for an alternating mains current of 50 Hz (or 16.7 ms for an alternating mains current of 60 Hz) should have always been expected (see the blue and the red arrows.

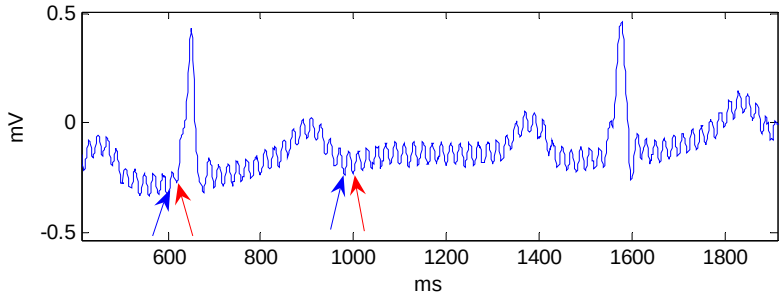

Fig. 4 Example of power-line interference accompanying the ECG recording. The blue and red arrows are demonstrating the error that can be done in the Q-onset and T-end delineations.

Baseline drift

This noise is due to respiration or any movement of the electrodes away from the contact area of the skin, leading to variations in the impedance between the electrodes and the skin. The

frequency of the baseline drift is 0.15-0.3 Hz and usually it is not influencing the correct QT measurements (Fig. 5).

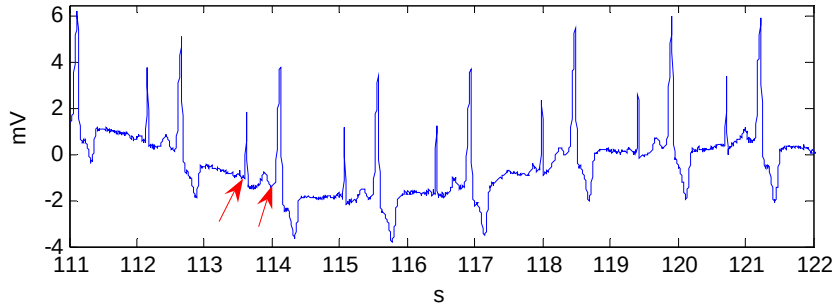

Fig. 5 The baseline drift noise is usually not influencing the correct QT measurements

Low magnitude of the T wave

The example presented in Fig. 6 shows that it is impossible (and better not do it) to mark the T-end in any of the peripheral leads I, II, III, aVR, aVL and aVF. T wave is clearly visible just from V1 to V4 of the precordial leads.

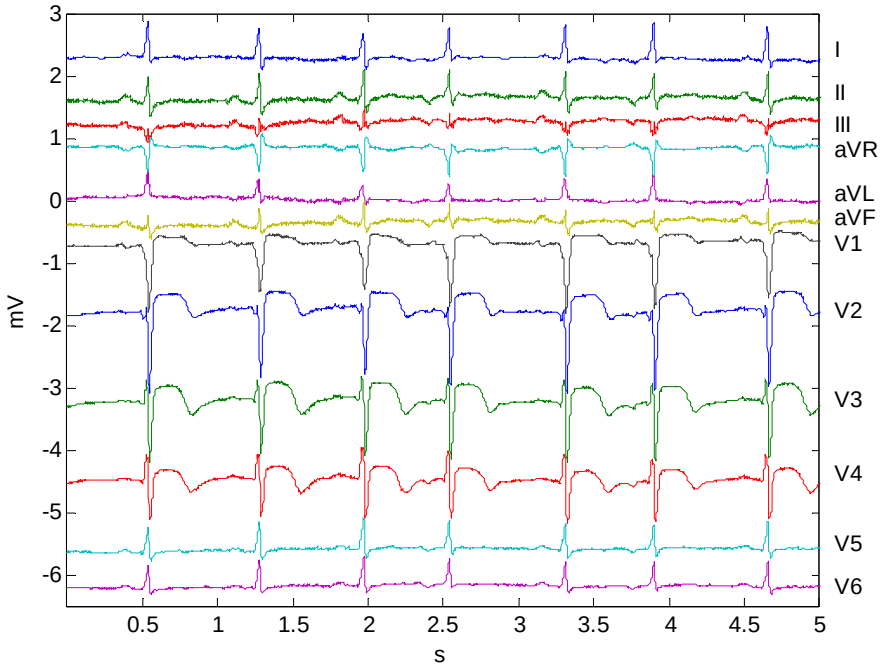

Fig. 6. Absence of T-wave in leads I, II, III, aVR, aVL, aVF, V5 and V6

Several works by Murray et al. are devoted to errors in the manual measurement of the QT intervals [13, 14, 15]. The authors have shown that longer QT intervals are reported by the experts with increase of the amplification gain (8 ms for any doubling of the gain) and at slower paper speed (11 ms going from 100 mm/s to 50 mm/s) [13]. The highest mean difference reported of the Q-onset among four cardiologists was 6.7 ms at a gain of 5 mm/mV, which decreased to 3.2 ms at a gain of 10 mm/mV [14]. Faber et al. [8] claimed that the paper speed, but not the amplifier gain, has more effect on manual QT measurement.

T-wave having bidirectional waveform and Fussing U-waves

If the T-wave morphology is normal, the T-end is identified when the descending limb returns to the baseline. In case of T-wave with T1 and T2 phases, the T-wave offset is identified at the time when T2 returns to baseline (Fig. 7).

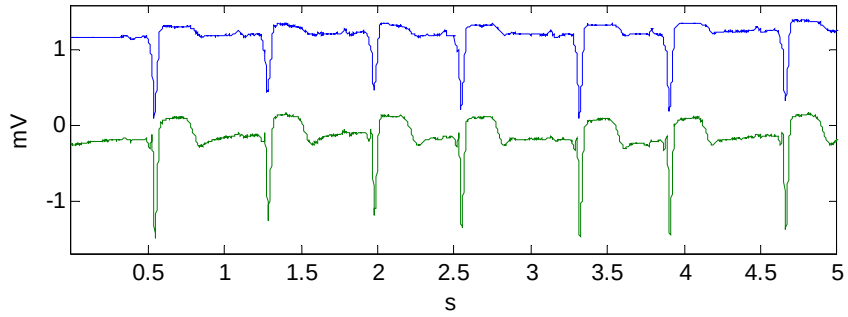

Fig. 7 Example of a biphasic T-wave having a very low magnitude in the 2nd phase (T2) in the upper lead. To determine the T-end correctly it is better to correlate it with the lower lead.

When the T wave is followed by a U-wave (Fig. 8), or when a second low-amplitude repolarization wave interrupts the terminal portion of the larger T wave (no matter whether it should be categorized as biphasic T-wave or a U-wave), the end of repolarization should be measured at the final return to baseline in both cases [9].

The manual T-end delineation introduces a large degree of subjectivity, particularly when biphasic T waves are present or when large U waves interrupt the return of the T wave to the baseline. It is even more difficult for computer analysis because it requires the definition of two symmetric thresholds, within which T or U wave potentials return to baseline.

At any case it is better to correlate the end of repolarization with another simultaneously recorded lead, as it is shown in Fig. 7 and Fig. 8.

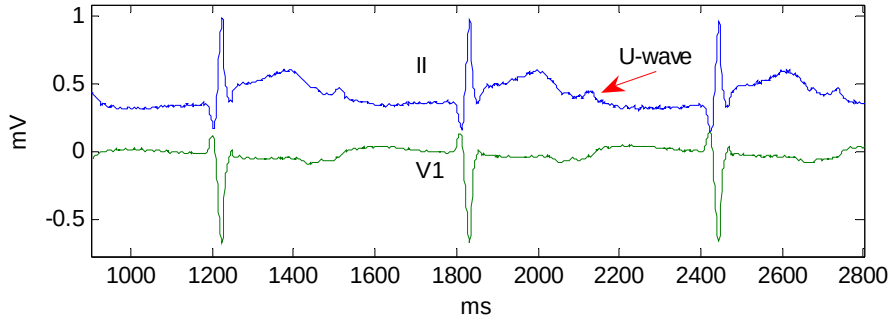

Fig. 8 Example of a U-wave in lead II. Its inclusion in the repolarization phase is better is better done after comparing it with another simultaneously recorded lead (V1 in this case).

Automatic QT measurement

Automatic QT measurement with reasonable accuracy has been a difficult task, approached since the first attempts at computerised electrocardiogram interpretation. While the manual methods for QT measurements can somehow manage (compromising the accuracy) with the noise that accompanies the ECG, it is absolutely impossible for the automatic QT measurements to handle the noise. Attention should be paid to the filtering procedures integrated into the automatic QT measuring algorithms [19]. After high-pass filtering,

increasing level of noise is shifting the onsets and offsets of most programs outward. Programs analyzing an averaged beat show significantly less variability than programs which measure every complex or a selected beat.

Signal preprocessing for automatic QT measurement

The ECG signals are preprocessed suppressing power-line interference, EMG (electromyographic) noise, and baseline drift, according to our previously published investigations of the Q-onset [5] and T-end localization [6]:

- Moving averaging of samples in one period of the power-line interference. This filter is meant to eliminate the power-line interference. Its frequency response has a first zero at the interference frequency 50 Hz (60 Hz);
- A smoothing procedure for EMG noise suppression is applied [4, 5]. It uses the least squares approximation method, applied for defining the weighting coefficients. The mathematical description of the process is:

$$Y_i = \frac{1}{N}\sum_{j=-n}^{j=n} C_j X_{i+j},$$

where ***Y*** and ***X*** represent the signal after and before approximation respectively, ***n*** is the length of the approximation interval at both sides of a sample, C_j are weighted approximation coefficients, and ***N*** is a normalization coefficient. The procedure is applied on $2n+1$ samples. We are working with approximation interval of 31 ms. The approximation coefficients are:

$Cj = 3n^2+3n-1-5j^2,$

and the normalization coefficient is:

$$N = \frac{(2n+1)(4n^2+4n-3)}{3}$$

The QT delineation noise immunity of the power-line interference and electromyographic noise suppression procedures is shown in Fig. 9. Noise-free QRS complex is presented in Fig. 9a, with manually marked Q-onset and T-end. An EMG noise is added to the ECG and presented in Fig. 9b. Interference of 50 Hz with amplitude of about 12% of the QRS magnitude is also added and shown in Fig. 9c. The ECG contaminated with the electromyographic noise and the 50 Hz interference is processed by the moving averaging procedure and then by least squares approximation procedure and the result is presented in Fig. 9d. The same marks for the Q-onset and T-end of Fig. 9a are superimposed on the processed ECG in Fig. 9d. As seen, they are correct also for the processed ECG, thus proving that the preprocessing is not affecting the appropriate delineation.

It has to be noted, that the preprocessing procedures decrease slightly the QRS amplitude, as seen comparing Fig. 9a and Fig. 9d, and should be used only for time-related delineations, but not in case of magnitude-related analysis.

- High-pass recursive filter for drift suppression [7]. The phase characteristic of this filter is linear and the phase distortions introduced in forward time direction are cancelled by a second-pass backward application. The high-pass recursive filter is given by the formula:

$Y_n = C_1(X_n - X_{n-1})+C_2Y_{n-1},$

where Y_n is the filtered samples' sequence, X_n is the samples' sequence of the original signal and n is the consecutive number of samples. The constants C_1 и C_2 are calculated by the formulae:

$$C_1 = \frac{1}{1+tan(F_c \pi T)} \qquad C_2 = \frac{1-tan(F_c \pi T)}{1+tan(F_c \pi T)},$$

where T is the sampling period and F_c = **0.64 Hz** is the chosen cut-off frequency.

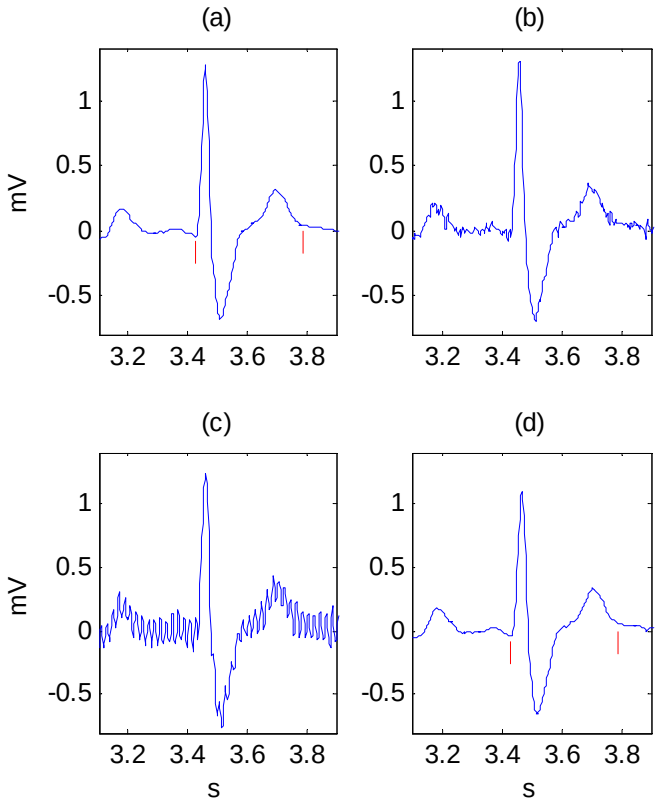

Fig. 9 QT delineation noise immunity of the power-line interference and electromyographic noise suppression procedures. (a) Noise-free QRS complex with marked Q-onset and T-end; (b) EMG noise added to the ECG; (c) ECG + EMG noise + 50 Hz interference; (d) Processed signal with the same Q-onset and T-end markings as in (a).

Delineation of the time interval for Q-onset search

An 'isoelectric' (flat or of low slope) segment is searched in the interval from the highest peak of the complex (QRS_P, Fig. 10a) to 120 ms backwards on the time axis. The segment is found if all successive differences in 20 ms interval between adjacent samples are less than a preset value Crit and the difference between the end-samples of the 20 ms interval is less than 4Crit. The value of the Crit is dependent on the QRS magnitude:

Crit = 0.02(maxQRS - minQRS).

The rightmost point of the searched interval (Q_R) is found where a peak or a slope (whichever occurs first) is detected to the right of Q_L. Looking for a peak we analyze three 10 ms equidistant samples. Differences between the middle and the two adjacent ones are considered. A peak is found if both differences are with the same sign and higher than 3Crit. A slope is detected by analysis of 9 samples, equally spaced by 2 ms. Differences between successive samples are formed. A slope is found if the 8 differences have same sign and their

absolute values are higher than 4Crit. The midpoint of the slope or the peak is set as the rightmost point of the searched interval.

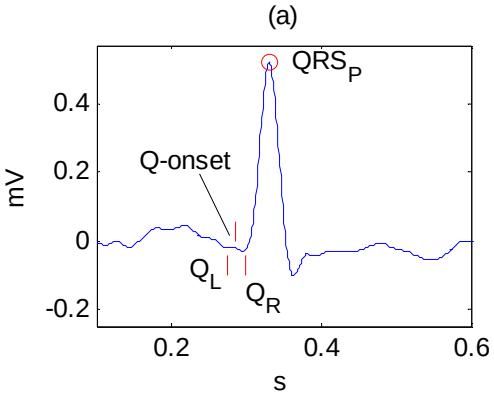

Fig. 10a Automatic detection of the Q-onset

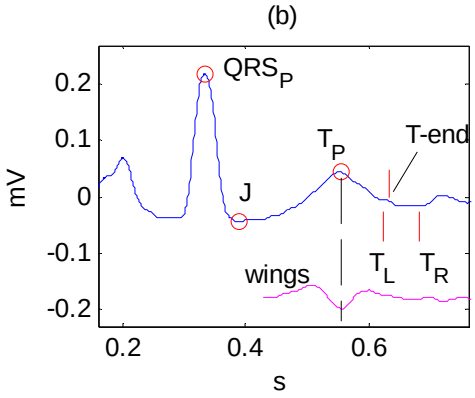

Fig. 10b Automatic detection of the T-end

The leftmost sample of this segment (***Q_L***), Fig. 10a is set as the leftmost point of the searched time interval.

Delineation of the time interval for T-wave end search

QRS-offset point ***J*** (Fig. 10b) is searched to the right of the QRS_P, repeating the described above criteria for Q_L search.

Two adjacent segments forming 'wings' are defined, each segment being of 40 ms length:

$W_1 = D_{i-40ms} - D_i \qquad W_2 = D_i - D_{i+40ms}$

where ***D*** are the corresponding signal samples.

The 'wings' function (***W = W₁W₂***) in the interval from ***J*** to ***J + QTc* - 100 ms** *is* shown in Fig. 10b (lower trace). ***QTc*** is calculated by the well known equation of Bazett. The minimum of 'wings' corresponds to the T-wave peak T_P, no matter if the T-wave is positive or negative.

The steepest slope (***T_S***) is searched as a maximum of the ***W*** in the interval from ***T_P*** to ***T_p* + 0.2*QTc*.**

The right sample of the search interval ***T_R*** (Fig. 10b) is sought as an absolute minimum of the ***W*** in the interval from the point of the steepest slope to ***T_P* + 0.2*QTc*.**

The left sample of the search interval ***T_L*** (Fig. 10b) is obtained as a point where the amplitude of the T-wave is **0.8(*T_p* - *T_R*)**.

Q-onset and T-end detection

Our method for automatic detection of Q-onset and T-end (Figs. 10a and 10b) is based on the minimum value of the angle between two segments having a common mid point and equal lengths of 10 ms. The minimum of the angle is searched in the defined time intervals delineated separately for the Q-onset and T-end.

If no T-wave in lead II can be observed or its magnitude is less than 0.06 mV (normally more than 20% of all the recordings), our algorithm localizes the search interval in the precordial lead V2, and then performs the T-end measurement in lead II.

Our method for automatic delineation of the Q-onset, T-end and QT measurement has won the second best place in the PhysioNet/Computers in Cardiology Challenge 2006 [12]. It has been published in [1, 2].

Results

All 548 recordings of the PTB Diagnostic ECG Database have been processed. The automatic Q-onset and T-end delineation was performed only on lead II, and on the same heart beat, as chosen by the reference dataset [7].

Mean value and standard deviation of the automated method compared with the 'gold standard' of the reference dataset of Q-onset, T-end and QT interval [7] are given in Table 3 for 95% and for 100% of all the recordings.

Table 3. Mean value ± Standard deviation of the automatic algorithm compared with the 'gold standard' of manually measured Q-onset, T-end and QT interval. Results are presented for 95% and for 100% of all the recordings.

	Mean ± Standard deviation [ms]	
	95% of recordings	100% of recordings
Q-onset	-0.08 ± 2.71	0.46 ± 4.84
T-end	5.10 ± 9.22	1.28 ± 16.75
QT interval	4.40 ± 9.93	0.83 ± 16.67

Histograms of deviations between the markings of the automatic algorithm compared with the 'gold standard' of manually measured Q-onset, T-end and QT interval are presented in Figs. 11, 12 and 13 respectively. Subplots (a) for all of the figures are for 95% of the recordings, while subplots (b) are for 100% of the recordings. The 'gold standard' is marked by long vertical line, the deviation of the algorithm's mean value is depicted by the short vertical line, and the upper horizontal green bar is presenting the algorithm's Standard deviation.

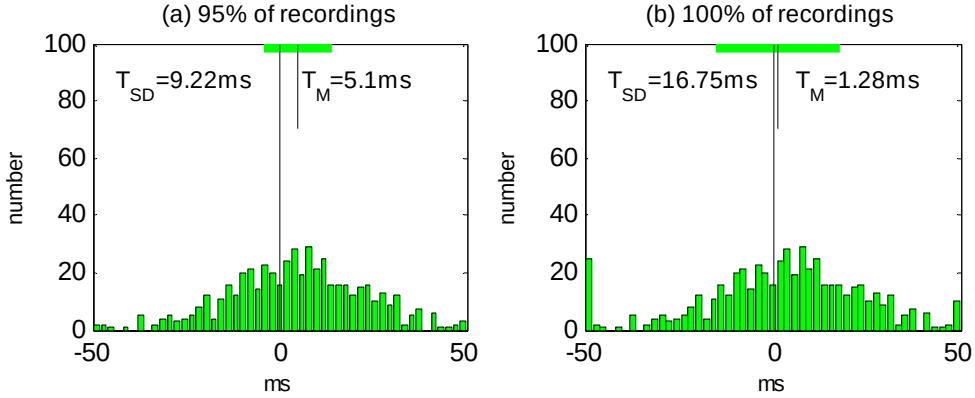

Fig. 11 Histograms of T-end deviations between the markings of the automatic algorithm compared with the 'gold standard' of manually measured T-end (a) for 95% of the recordings, (b) for 100% of the recordings. The deviation of the algorithm's mean value $\boldsymbol{T_M}$ is depicted by the small vertical line, and the upper horizontal green bar is presenting the Standard deviation $\boldsymbol{T_{SD}}$.

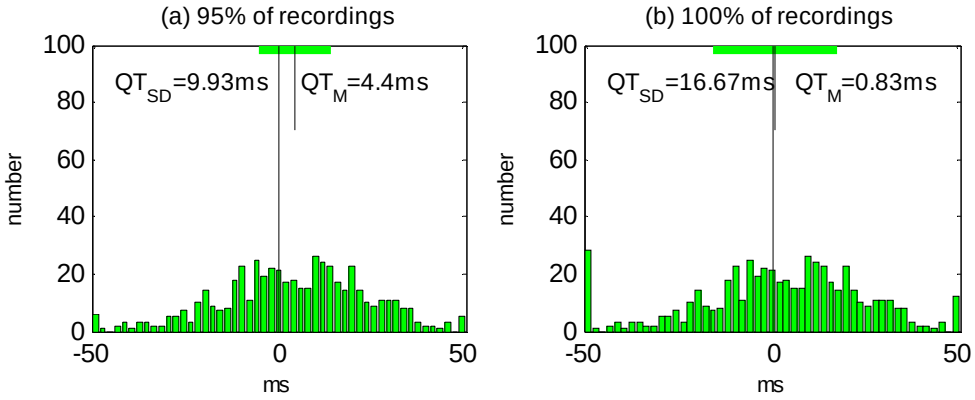

Fig. 12 Histograms of QT deviations between the markings of the automatic algorithm compared with the 'gold standard' of manually measured QT (a) for 95% of the recordings, (b) for 100% of the recordings. The deviation of the algorithm's mean value $\boldsymbol{QT_M}$ is depicted by the small vertical line, and the upper horizontal green bar is presenting the Standard deviation $\boldsymbol{QT_{SD}}$.

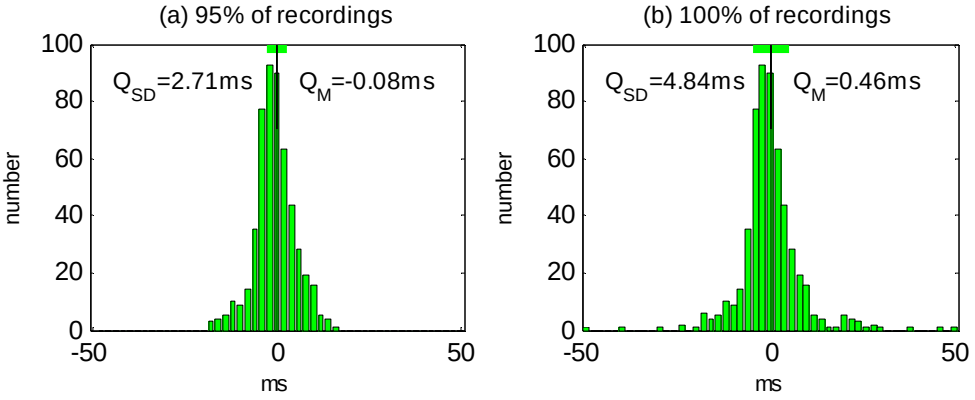

Fig. 13 Histograms of Q-onset deviations between the markings of the automatic algorithm compared with the 'gold standard' of manually measured Q-onset (a) for 95% of the recordings, (b) for 100% of the recordings. The deviation of the algorithm's mean value $\boldsymbol{Q_M}$ is depicted by the small vertical line, and the upper horizontal green bar is presenting the Standard deviation $\boldsymbol{Q_{SD}}$.

Conclusion

Our method for fully automatic QT measurements won the second best place in the Physionet/Computers in cardiology challenge 2006 [12].

It can be definitely said that some automated methods are possessing acceptable accuracy for clinical evaluations. Further more, combining objectively the strengths of varied approaches, as it is done in 'Meta-6' algorithm [12], accuracy close to the experts' measurements can be obtained.

Summary

✓ The manual QT measurement made by experts has better accuracy and is used as a 'gold standard' for assessment of the accuracy of the automatic methods. The standard deviations of the experts are:

Q-onset	from ±2.45 ms to ± 3.23 ms
T-end	from ±6.72 ms to ±10.24 ms

- ✓ Automated methods for QT measurements offer advantages in terms of absolute repeatability of measurements, immunity from errors related to observer fatigue, lack of attention, as well as efficiency and cost effectiveness that permit either more extensive and rigorous testing for the same cost as manual methods, or more rapid testing at lower cost. The standard deviations of our method as compared with the 'gold standard' of the experts' markings are:

  Q-onset ±2.71 ms
  T-end ±9.22 ms
- ✓ Noise contaminating the ECGs is decreasing the accuracy of manual QT measurement and is fatal for the fully automatic methods.
- ✓ Signal preprocessing aiming at noise reduction should be performed with special and sophisticated filtering procedures, ensuring best preservation of the ECG wave borders.

References

1. Christov I., I. Simova (2006). Fully Automated Method for QT Interval Measurement in ECG, Computers in Cardiology, 33, 321-324, http://cinc.mit.edu/archives/2006/pdf/0321.pdf
2. Christov I., I. Simova (2007). Q-onset and T-end Delineation: Assessment of the Performance of an Automated Method with the Use of a Reference Database, Physiological Measurement, 28 (2), 213-221.
3. Christov I., I. Dotsinsky, I. Simova, R. Prokopova, E. Trendafilova, S. Naydenov (2006). Dataset of Manually Measured QT Intervals in the Electrocardiogram, Biomedical Engineering Online, 5 (31), 1-8, http://www.biomedical-engineering-online.com/content/5/1/31
4. Christov I., I. K. Daskalov (1999). Filtering of Electromyogram Artifacts from the Electrocardiogram, Medical Engineering & Physics, 21, 731-736
5. Daskalov I. K., I. I. Christov (1999). Electrocardiogram Signal Preprocessing for Automatic Detection of QRS Boundaries, Medical Engineering & Physics, 21, 37-44.
6. Daskalov I. K., I. I. Christov (1999). Automatic Detection of the Electrocardiogram T-Wave End, Medical & Biological Engineering & Computing, 37, 348-353.
7. Daskalov I. K., I. A. Dotsinsky, I. I. Christov (1998). Developments in ECG Acquisition Preprocessing Parameter Measurement and Recording, IEEE Engineering in Medicine & Biology, 17, 50-58.
8. Faber T. S., J. Kautzner, M. Zehender, A. J. Camm, M. Malik (2001). Impact of Electrocardiogram Recording Format on QT Interval Measurement and QT Dispersion Assessment, Pacing and Clinical Electrophysiology, 24 (12), 1739-1747.
9. Goldenberg I., A.J. Moss, W. Zareba (2006). QT Interval: How to Measure it and what is "Normal", Journal of Cardiovascular Electrophysiology, 17 (3), 333-336.
10. Gussak I., P. Brugada, J. Brugada et al. (2000). Idiopathic Short QT Interval: A New Clinical Syndrome?, Cardiology, 94, 99-102.
11. Levkov Ch., G. Mihov, R. Ivanov, I. Daskalov, I. Christov, I. Dotsinsky (2005). Removal of Power-line Interference from the ECG: A review of the Subtraction Procedure, Biomedical Engineering Online, 4 (50), 1-18, http://www.biomedical-engineering-online.com/content/4/1/50
12. Moody G. B., H. Koch, U. Steinhoff (2006). The PhysioNet/Computers in Cardiology Challenge 2006 QT Interval Measurement, Computers in Cardiology, 33, 313-316, http://cinc.mit.edu/archives/2006/pdf/0313.pdf.
13. Murray A., N. B. McLaughlin, J. P. Bourke, J. C. Doig, S. S. Furniss, R. W. Campbell (1994). Errors in Manual Measurement of QT Intervals, British Heart Journal, 71 (4), 386-390.

14. Murray A., N. B. McLaughlin (1995). Variation in the Identification of Q Wave Initiation and its Contribution to QT Measurement, Physiological Measurement, 16 (1), 39-42.
15. Murray A., N. B. McLaughlin, R. W. Campbell (1997). Measuring QT Dispersion: Man Versus Machine, Heart, 77 (6), 539-542.
16. Priori S.G., P.J. Schwarz, K. Napolitano et al. (2003). Risk Stratification in the Long QT Syndrome, New England Journal of Medicine, 348, 1866-1874.
17. The CSE Working Party (1985). Recommendations for Measurement Standards in Quantitative Electrocardiography, European Heart Journal, 6, 815-825.
18. Willems J. L., P. Arnaud, J. H. van Bemmel, P. J. Bourdillon et al. (1985). Assessment of the Performance of Electrocardiographic Computer Programs with the use of a Reference Data Base, Circulation, 71 (3), 523-534.
19. Willems J. L., C. Zywietz, P. Arnaud, J. H. van Bemmel, R. Degani, P. W. Macfarlane (1987). Influence of Noise on Wave Boundary Recognition by ECG Measurement Programs. Recommendations for preprocessing, Computers and Biomedical Research, 20 (6), 543-562.
20. Zipes D., A. Camm, M. Borggrefe et al. (2006). ACC/AHA/ESC 2006 Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death, Europace, 8, 746-837.