Automated QT Interval Analysis on Diagnostic Electrocardiograms

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Abstract

In this study, we suggest a method for automatic measurement of the QT interval. The method derives from the standard technique of "selective beat averaging". To overcome those situations in which the templates are noisy as they arise from averaging only a small number of beats, two separate patterns were used: one for the QRS complex and the other for the T wave. The templates were carefully matched with the beats by cross-correlation, using an iterative refinement process.

The method was employed to automatically measure QT segments on the PTB Diagnostic ECG Database used for the 2006 Computers in Cardiology Challenge. A score in division 3 of 81.07 ms was obtained pointing out that the method needs further tuning and refinements. Excluding those beats for which the estimated QT values are outside the main physiological range (290-500 ms) a more promising tentative score of 41.62 ms might be obtained.

1. Introduction

The QT interval, e.g. the time elapsed between the Q onset and the end of the T wave, as measured on a standard diagnostic electrocardiogram, is typically employed to derive an indirect measure of the cardiac repolarization period. A prolonged cardiac repolarization was shown to be a prominent predictor of development of fatal cardiac arrhythmias [1][2] as it typically lead to fatal arrhythmias, like torsade de pointes. Among others, factors inducing prolonged QT intervals are: myocarditis [3][4], certain diseases in which electrolyte imbalance play a role, like hypocalcemia [4][5] and certain drugs (*e.g.* Quinidine, Sotalol) [6]. As pointed out by [6] "in the past decade, the single most common cause of the withdrawal or restriction of the use of drugs that have already been marketed has been the prolongation of the QT interval." It is no surprise then that a precise measure of the QT interval is fundamental for the diagnostic procedure of several diseases and for pharmaceutical trials.

The QT interval quantification is complicated by the fact that the repolarization period depends on the heart rate and it shortens when the frequency increases. Starting from the work of Bazett [7], several formulas have been proposed to model the QT/RR relationship, but as recently suggested such relation is highly individual [8]. A second possible approach is that of selecting a representative beat, a sort of median value, but the criteria underlying such choice are often subjective to the use of the measure envisioned by the physician.

The option to automatically measure the QT interval on long-term computerized ECG is today available on most commercial systems. Even so, manual measurements of QT intervals on ECG tracings are *de facto* the only generally accepted procedure for a quantitative evaluation. For example, the recently issued guidelines (ICH E14, [9]) for clinical evaluation of non-antiarrhythmic drugs, while calling for "thorough QT/QTc studies", endorse only manual QT interval measurements. This is possibly due to the lack of precision that automated methods shown in the past. Manual measurements bear though well-known limitations [10]: they are affected by the paper speed used to plot the electrocardiogram and by electrocardiogram gain (T amplitude); they vary with different readings and readers (on average up to 20 ms). Lastly, they need to be performed by a trained physician and they become unfeasible on long recordings where only a few indicative beats are thus taken into account.

Surely enough the availability of automatic procedures for the measurements of the QT interval *without* the intervention of the physician and with a precision similar to manual readings would foster new physiological researches on the ventricular repolarization period on long term Holter recordings and might also permit more exhaustive protocols during pharmacological and clinical trials. In this work we suggest such an algorithm which building over a standard technique, called "RR bin" or "selective beat averaging" [11] might be able to provide a reliable estimate of the QT interval. The method was tested on the PTB Diagnostic ECG Database which forms the testset of the 2006 PhysioNet/Computers in

Cardiology Challenge [12]. The database consists of 549 recordings of a couple of minutes each, collected from 294 subjects. For each record the 12 conventional leads and the 3 XYZ leads had been made available.

2. Methods

2.1. Preprocessing

The dataset did not contain annotations. Thus, each record was firstly processed for QRS detection using the freely available software ECGPUWAVE [13]. The routine also provided an estimate of the waveforms' boundaries which were used as starting point of the method described below. The choice was made just for convenience (the code was faster) and it could have been completely avoided using a fixed QT initial guess.

2.2. QT measurement

The ECG signal was first high-pass filtered to remove major baseline wander (5^{th} order Butterworth filter, cut off frequency 0.5 Hz).

Then local average patterns were built subject to the condition that the RR interval between successive beats did non change more than a specified threshold. In fact, as previously outlined, the QT interval changes with the heart rate; more importantly the QT length needs to adapt to the new pace when it changes and the process takes time. Building average patterns using only beats which are about at the same distance, it ensures that the QT measures might be taken in a portion of the ECG where QT adaptation already occurred (and measures are thus reproducible). Specifically the local patterns were built through successive refinement in an iterative process. First, within each ECG recording the groups of beat for which $|RR_{i+1}-RR_i|<30$ ms were located. Secondarily, for each group, two average patters, for the QRS and T waves respectively, were built. To produce the QRS pattern, which was 150 ms long, the beats were aligned 10 ms before the Q start (as obtained from the labeling software). A first guess of the position of the T end was obtained simply locating a point on the ECG 500 ms after the Q start. Also the T wave average pattern was built aligning the recording 200 ms before the T end and considering 250 ms of signal from there[1]. Then the Q start and T end of each beat were adjusted relatively to the average patterns selecting those time shifts which were maximizing the cross correlation between the single complex and the pattern. After each adjustment, before moving to the next beat, the average patterns were rebuilt. Once analyzed all the beats of each recording, each of these three major steps were repeated (starting from re-locating all the groups of beats with similar RR distance, as the adjustments of the Q starts might alter the number

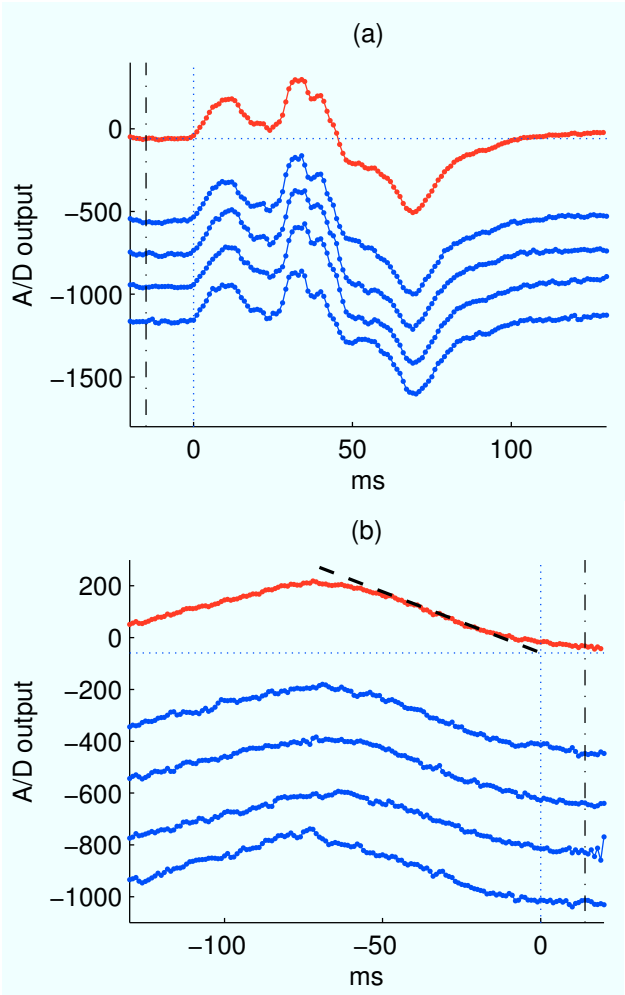

Figure 1. Using four beats for which $|RR_{i+1}-RR_i|<30$ the QRS (panel a) and T (panel b) average patterns were built (top lines; recording s0545_re). In both panels the horizontal dotted lines are the isoelectric levels identified following the standard the standard EN 60601-2-51. In panel b the dashed thick line is the tangent of maximum slope to the T complex. The T points is then obtained as the intersection between the tangent and the isoelectric level [14]. The dashed-dotted lines indicate the positions of the "Q start" and "T end" points respectively, on which the beats were aligned before averaging.

[1] Please note that what we call here "Q start" and "T end" are only conventional points on the ECG signal approximately located before the QRS wave and after the T wave respectively. A precise detection of the "proper" Q onset and T offset on each beat will be possible only using the reference points detected on the average patterns.

of beats belonging to each group). The iterative process was ended when the number of adjustments in a cycle was small or the number of cycles exceeded a threshold. To speed up the refinement process, instead of using a first T end guess located 500 ms from the Q start, we also employed the QT estimate provided by ECGPWAVE as specified in section 2.1. A couple of local average patterns obtained from a group of four beats are shown in figure 1.

Once adjusted the position of the two conventional points with respect to the average patterns and thus obtained patterns which reflected the morphology of each group more carefully, the Q onset and T offset were measured on the patterns themselves. The idea is that the averaging process reduces the intensity of the noise, which is in first approximation uncorrelated with the ECG signal, ensuring more precise measures. The isoelectric level was identified following the standard EN 60601-2-51:2005-06 as having duration of more than 6 ms and amplitudes not exceeding 20 μV for at least three samples. The Q onset was located at the end of the isoelectric level preceding the QRS complex. The T offset was instead detected using the Lepeschkin & Surawicz method [14] as the point at the intersection of the isoelectric level and the tangent of maximum slope to the T complex. The tangents were built using a local least squares approximation on short windows of 20 ms. Finally, individual QT measures might be obtained for each beat of the family adjusting the conventional Q start and T end points, as used to build the average patterns, with the offsets they show with respect to the patterns' Q onset and T offset. For example, if the T offset was detected on the average pattern to be 15 ms in front of the T start points on which the beats were aligned, each of the T start points might be moved of 15ms leading to an estimate of each T offset.

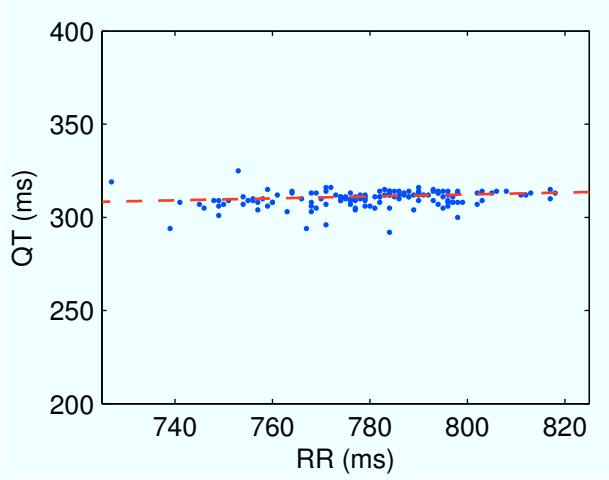

Figure 2. QT/RR relationship for recording s0398lre. Each point in the figure was obtained measuring the QT interval for the first beat of each group of similar beats, while the RR value was averaged within each group. The dashed line is the least squared linear interpolant.

3. Results

The method was employed to automatically measure QT segments on the 549 diagnostic ECG recordings which constitute the PTB Diagnostic ECG Database used for the 2006 Computers in Cardiology Challenge. The measures were performed on lead II, as required for the challenge. Moreover, it was required to provide a QT measurement for the first "representative beat" of the recording. We considered as "representative" the first beat of the first group of beats. In fact, if entering a group at the end of the refinement process such beat was guaranteed to be at least similar to a number of beat following it.

Due to low signal quality (2 cases) or to a high heart rate variability within the recording (which reduced the possibility to have groups of at least 2 beats with $|RR_{i+1}-RR_i|<30$ ms; 18 cases), for 20 recordings it was not possible to measure any QT segment. Of the remaining 529 cases, in 21 the value of QT estimated was below 290 ms, while in 54 cases, it was above 500 ms. When an estimated was falling outside the range (290, 500) ms we considered the value unreliable; but except for 7 cases, the others were nevertheless submitted for the competition.

A normalized score of 81.07 ms in division 3 was obtained. The score points out that the method needs further tuning and refining, but is also highly affected by the unreliable results obtained for 13% of the recordings. If we recomputed a hypothetical normalized score including only those records for which the results were into the physiological range 290-500 ms (454 cases), we would obtain a more promising value of 41.62 ms.

Figure 2 shows the relationship QT/RR for one of the recordings in the database and illustrates the pseudo-linear relationship among the repolarization period and the heart rate. For each of the group of beats identified by the algorithm a QT value was measured on the first beat of the group.

4. Discussion and conclusions

The method, using two different windows, permits to provide individual estimate for the QT interval of each beat. Moreover as the method is capable of handling small QT variations, it has been possible to increase the threshold for including beats in each group from 10 ms (a usual value in selective beat averaging techniques [11]) to 30 ms. While this might seem a minor point, there are

situations in which the patterns arise from averaging only a small number of beats, such as when, in short ECG segments, the noise level is not negligible, the heart rate variability high or many ectopic beats are present. In those situations taking the measures on the average patters is of little help unless we are able to increase the number of beats in the group. Therefore, the use of two separate patterns possibly increases the number of recording on which effectively using the technique.

Unfortunately, the technique we suggested proved capable of automatically refining the positions of Q onsets and T offsets in only a fraction of the total recordings (about 87%). When the recordings were highly corrupted by noise or the initial guess for the end of the T wave was misplaced, often the algorithm ended up misleadingly providing an estimate of the end of the P wave of the following beat (thus furnishing estimates for the QT interval far outside the physiological range). Obviously, for the sake of the competition, we could have substituted all the QT we knew were outside the physiological range (*e.g.* QT<290 ms and QT>500 ms) with a common physiologically-reasonable value, let's say 400 ms. As we verified after the competition was ended and the "gold standard" scores published, doing so our hypothetical score would have been of 44.63 ms, much closer to what we consider the true performances of our algorithm (see previous section). Nevertheless, we considered that such substitution, meaningful only for the competition, would have been of any scientific interest and we rather avoided it.

The method we suggested needs surely further work and a fine tuning. A multi-lead approach might be a possible improvement: applying the method on more than a lead could help to resolve those situations in which the QT value computed on the lead II was outside the physiological range. Also, a rough refinement of the initial guess for "T end" might help.

No matter how the method we proposed scored, we feel that the overall competition showed that it might be possible in the future to accept automated methods among those trusted to measure the QT interval from ECG recording, thus also ensuring a higher repeatability of measurements than today.

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