

Dynamic Properties of QT Intervals

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Abstract

Five dynamic models of QT/RR coupling are tested on measurements of tilt table test at 19 healthy individuals. RMS of error signal (difference between measured and computed QT) and correlation coefficient (R) between error signal and RR are analyzed. Four models were based on weighted average of RR intervals - constant weighting, exponential weighting with linear dependency and nonlinear dependency and the new model given by exponential weighting, linear dependency and direct coupling with RR - MDCEXP. The fifth model was based on transfer function - MTRF. According to both parameters, RMS ($P < 0.001$), R ($P < 10^{-7}$) MDCEXP and MTRF are the best. Between MDCEXP and MTRF does not exist significant differences.

1. Introduction

Cardiac repolarization and depolarization is represented by the QT interval on the surface electrocardiogram. Understanding and defining the static and dynamic properties of QT are important tools in clinical practice and during drug testing [1-3]. QT interval for a given heart rate depends upon both the rate and the direction of the RR change. This dynamic dependency limits presently used QT analysis, but on the other hand represents important clinical information [4, 5]. The proper QT analysis should be based on a QT/RR coupling model which has a minimal number of parameters but effectively describes the static as well as the dynamic properties of QT/RR coupling, in particular the QT behavior after a sudden change of heart rate. Two backgrounds were used to describe QT/RR coupling: i) The models based on weighted averages of RR intervals preceding the $qt(i)$ interval [6,7]; ii) The model based on low order transfer function [8,9]. The models will be compared and discussed.

2. Methods

2.1. Models based on weighted averages of

RR intervals

The QT dependency on filtered RR (RRf) by FIR filter is assumed at these models. The RRf is given by:

$$rrf(i) = \sum_{j=-Ne+1}^0 w(j) \times rr(i+j) \quad \text{where } Ne \text{ is the number of weighting coefficients } w(j).$$

The weighting coefficients may be constant, $w(j) = 1/Ne$ or they may have the exponential shape [6, 7]. The used shape is: $w(j) = K \times \lambda \times (1 - \lambda)^{-j}$, where K is a normalization constant, given so that

$$\sum_{j=-N+1}^0 w(j) = 1 \quad \text{and } \lambda \text{ is a constant dependent on } Ne:$$

$$\lambda = \frac{2}{1 + Ne}. \quad \text{The linear or nonlinear dependency [6,7] is}$$

assumed between RRf and computed QT:

$$QTm = \beta + \alpha \times RRf \quad \text{or} \quad QTm = \beta + \alpha \times RRf^\gamma.$$

Where α , β and γ are fitted parameters together with Ne .

Four different types of models were tested:

- Constant weighting, linear dependency – MSUM
- Exponential weighting, linear dependency – MEXP
- Exponential weighting, nonlinear dependency – MEXP_NONL
- Exponential weighting, linear dependency between RRf and QTm, but with additive direct coupling between RR and QTm – MDCEXP

MDCEXP has not been published yet it is the extension of weighting models according to measured [10, 11] or computed [8, 9] shape of the step response. The computed QT (QTm) at this model is given by:

$$QTm = \beta + \alpha \times RRf + \gamma \times RR, \quad \text{where } RRf \text{ is filtered } RR \text{ like at the model MEXP and fitted parameters are: } \alpha, \beta, \gamma \text{ and } Ne.$$

2.2. Model based on transfer function

We have analyzed the order of the transfer function between RR and QT in [8] and the optimal transfer

function is:

$$H_{QTx/RRx}(z) = \frac{b_2 z^{-1} + b_3 z^{-2}}{1 + a_1 z^{-1}}$$

Computed QT with zero mean level ($QTxm$) is given by recursive relation:

$$qtxm(i) = b_2 rrx(i-1) + b_3 rrx(i-2) - a_1 qtxm(i-1)$$

where $rrx(i)$, $qtx(i)$, $qtxm(i)$ are i -th intervals of corresponding variables (RRx , QTx , $QTxm$) with zero-mean level, i.e. $RRx = RR - \text{mean}(RR)$, $QTx = QT - \text{mean}(QT)$, $QTm = QTxm + \text{mean}(QT)$. Fitted parameters are a_1 , b_2 , b_3 .

The transfer function model (MTRF) consists of 3 numerical parameters [a_1 , b_2 , b_3], that are used for computing QT parameters of physiological significance [8], described by the step response:

- Gain_L - gain of QT/RR coupling for low variability of RR. It corresponds to the QT steady state change at the unit change of RR;
- Gain_F - gain for fast variability of RR, it is the amplitude of QT change immediately after the unit change of RR;
- τ - the delay after which the step response has achieved 90% of the change needed to attain the new steady state value.

The QTc and QT variability independent of RR are also computed from numerical parameters.

2.3. Analyzed data

The healthy volunteers with no sign of heart disease (14 men, 5 women), underwent a tilt table test containing 3 stages - supine for 10 min, tilted for 10 min and supine again for 5 min. The average age was 42 ± 17 years (range: 23-72 years). The ECG was recorded with a 3 lead bedside system, model 90308, SpaceLabs, Inc., Redmond, WA, USA. The analog signals were sampled at 500 Hz. The signal with the maximal T wave was analyzed with our custom-designed software ScopeWin to obtain continuous series of RR and QT intervals. The QT interval duration was determined from the onset of the QRS wave to the end of the T wave, defined as the crossing between the isoelectric line and the tangent to the descending T wave. A semiautomatic method of QT detection was used. The results were visually reviewed and manually corrected in case of false automatic detection. If there was a doubt about the proper detection or if the accurate detection was not possible, the ECG part was marked as no detectable QT intervals.

3. Results

Two basic parameters were analyzed:

- Root mean square (RMS) of error signal, i.e. of difference between measured and computed QT;
- The Pearson correlation coefficient (R) between

error signal and RR intervals.

The results are in Tab. 1. The distribution of RMS over all subjects for different models is on Fig. 1. RMS level differs significantly over the subjects and the differences between the models are also presented. The RMS differences relative to MTRF model are on Fig. 2a and the differences relative to MEXP model are on Fig. 2b.

The Scheffé's method was used for the multiple comparisons of models. Statistical significance exists ($P < 0.001$) at RMS among MDCEXP or MTRF versus MEXP or MEXP_NONL or MSUM. Statistical significance does not exist between MDCEXP versus MTRF and MEXP versus MEXP_NONL. Statistical significance exists ($P < 10^{-7}$) in correlation coefficient among MDCEXP or MTRF versus MEXP or MEXP_NONL or MSUM.

Table 1. Mean level and standard deviation of RMS and Pearson correlation coefficient (R) over all subjects.

Model	RMS [ms]	R
MSUM	4.46±1.15	0.27±0.13
MEXP	4.18±1.08	0.28±0.13
MEXP_NONL	4.14±1.05	0.27±0.13
MDCEXP	3.77±1.03	0
MTRF	3.79±1.04	0.01±0.01

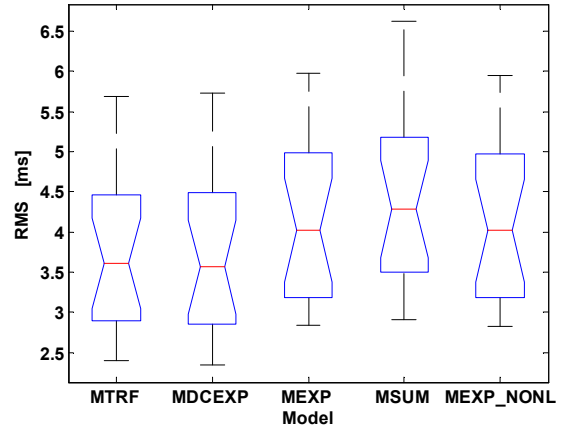
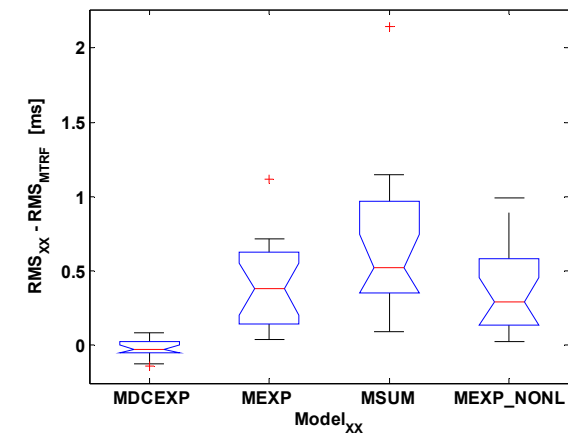


Figure 1. The distribution of RMS over all subjects for different models.

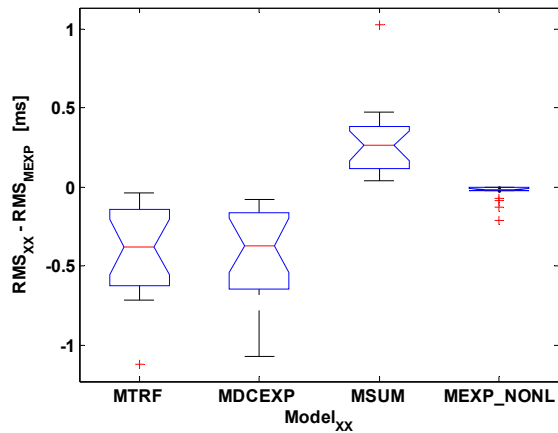
The step responses for the different models of one subject are on Fig. 3.

4. Discussion and conclusions

The models MEXP, MEXP_NONL and MSUM have significantly higher R and RMS than models MDCEXP



a)



b)

Figure 2. The RMS differences. a) relative to MTRF model b) relative to MEXP model.

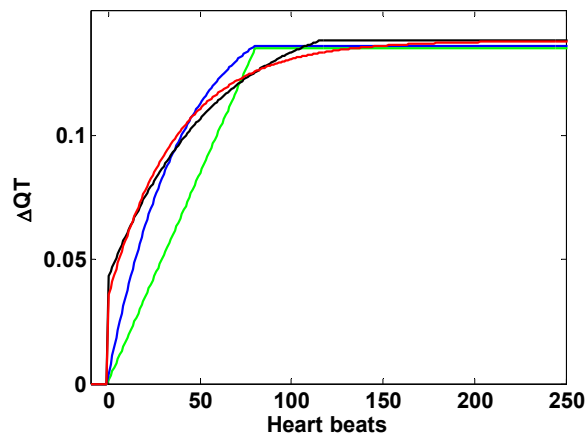


Figure 3. The computed step responses of one subject for the different models. Colors: MSUM-green, MEXP- blue, MDCEXP-black, MTRF - red.

and MTRF, i.e. some important QT parameter, as $Gain_F$, is missing in these models. The shapes of step responses differ both at start of step response and at final level of QT. The assumed nonlinearity at MEXP_NONL has not significant influence on RMS and R level. This partly corresponds with result in [6].

MTRF and MDCEXP models are the best according to both RMS and R. Comparing these models, MDCEXP has a bit lower (nearly not remarkable) RMS. This is given by sensitivity to irregular beats and corresponds with theory of stability of IIR filters and FIR filters. The correlation coefficient in MDCEXP is zero, comparing to very low level in MTRF. This corresponds to the theory that parameter γ fully eliminates the direct coupling. MDCEXP model is based on the known shape of step response. The background of MTRF is the control system theory, no assumptions are used and the shapes of analyzed step responses correspond with partial results [10, 11, 12]. Moreover, four parameters are optimized in MDCEXP, in comparison to three parameters in MTRF.

The transfer function model of QT/RR coupling is, according to our opinion, the best present model of QT/RR coupling. It doesn't use any questionable assumption about the shape of step response; it has only three optimized parameters. The resulting parameters ($Gain_L$, $Gain_F$, τ , QT_c and QT variability independent on RR) computed from model; represent the best full set of QT parameters in present. This model may help to finish the endless debates about the QT nonlinearity. The possible nonlinearity should be corrected after elimination of dynamic QT/RR coupling.

4.1. Limitations

The mathematical analysis and the models comparison are simple and clear. The clinical application has following limitations:

a) The analyzed data must be sufficiently long (20 min or more) with sufficient excitation of RR; otherwise the analyzed parameters are inaccurate. The excitation of RR must be defined, the QT parameters are not only subject specific but also excitation specific [1, 8]. The evaluation of parameters contribution may be done when the large set of measurements in heart disease patients and drugs measurements exists. The possible way may be an ECG international database as THEW [<http://thew-project.org/index.htm>].

b) The RR intervals must represent the continuous chain, without missing beats. The majority of QT intervals must be detected. Regarding the quality of the ECG data, this process may still present the problem [Computers in Cardiology Challenge 2006: QT Interval Measurement].

c) The QT duration and its dynamic properties are

analyzed in this article only; this QT behavior description has been tried to be solved by many for nearly one century already. Some other important clinical information may be given for example by the shape of T wave [13].

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