Compensation of Heart Rate Variation during Noninvasive Identification of Repolarization Changes

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Abstract*. Local repolarization changes in the myocardium can be noninvasively identified by an inverse solution using multichannel measurements of ECG potentials and QT integral maps in situation with and without changed repolarization. In this study, possible error of the inverse solution due to heart rate changes between the two measurements was analyzed on a model. Minimization of the error by compensation of QT interval changes was proposed. Four commonly used formulas for prediction of QT intervals from heart rates were compared on real measured data.*

Keywords: Body Surface ECG Potentials, Heart Rate Changes, QT Interval, Inverse Solution

1. Introduction

The ischemic heart disease arises as a consequence of decreased blood perfusion in the main coronary arteries. Early detection of starting ischemia allows its more effective medical treatment. Electrical activity of cardiac myocytes can be characterized by their action potentials (AP). Repolarization of a myocyte in the ventricular myocardium is practically independent of the activation sequence and can be described by an elementary integral generator (IG) over the whole cycle of ventricular activity (QT interval). During ischemia, AP amplitude and duration decrease and these changes can be represented by differences between IG's obtained from myocardium with and without ischemia. If the region with ischemia is reasonably small, these differences can be represented by single dipole generator. For known chest geometry and electrical properties, such generator can be assessed by inverse solution [1] from the surface map of differences between QT integrals:

$$DIQT = IQT_{ISCH} - IQT_{NORM} \qquad (1)$$

where IQT_{ISCH} and IQT_{NORM} are surface maps of QT integrals with and without ischemia, DIQT is surface map of differences between these two integrals.

In initial state, cardiac ischemia is not recognizable at rest conditions, but it can be induced by mental or pharmacological load or by exercise that is usually connected with increased heart rate (HR). As a consequence of changed HR, QT interval is also changed and values of IQT_{ISCH} and DIQT maps are influenced what can cause an error of the inverse solution. Therefore QT interval changes should be compensated. To avoid the difficulty with direct QT measurements [2] and compensation, a dependence of QT on HR can be used. In this study, several formulas describing this relation were tested on real ECG measurements.

2. Methods and material

Simulation of ischemia and its inverse identification

Body surface potentials (BSP) were simulated for a normal heart and for several cases of ischemia located subepicardially and subendocardially in three regions supplied by main coronary vessels. Cellular automaton and experimentally observed shapes and durations of

APs were employed to simulate the cardiac depolarization-repolarization. Boundary element method was used to compute BSP in 62 leads. For each lesion, DIQT maps representing the difference between normal and particular ischemic case were computed and together with information on torso geometry and conductivities were used for inverse identification of the best dipole representing the lesion. [1]. Error of the inverse solution was evaluated relatively to a representative dipole (RD) of the lesion obtained as the sum of dipolar moments of model elements in the ischemic region and placed at the centroid of the lesion.

Simulation of changed heart rate between two measurements and its compensation
In simulated IQT maps with and without ischemia manifestation, the same HR in signals was assumed. To analyze the influence of uncompensated HR changes on the inverse solution, changes of the QT_{ISCH} interval from 70% to 130% of the QT_{NORM} were simulated, QT_{NORM}=377 ms and HR_{NORM} = 75 heart beats per minute (BPM) were set for the normal case as the reference values. Changes of HR_{ISCH} from 38 to 165 BPM corresponded to these changes of QT_{ISCH}.

If no change of the QT duration due to ischemia is assumed, the simplest way to compensate the changed HR between the two measurements is to recalculate both *IQT* integrals in (1) to the same QT, e.g. for the QT_{NORM} during normal activation, using a compensation coefficient c_f and the compensated difference integral maps $DIQT_f$:

$$DIQT_f = c_f \,.\, IQT_{ISCH} - IQT_{NORM} \qquad (2)$$

$$c_f = QT_{NORM} / QT_{ISCH} \qquad (3)$$

Measured data and prediction of QT interval
Body surface potentials at 64 leads were measured in 9 patients suffering from heart diseases and in 3 healthy volunteers. All subjects underwent exercise test on supine ergometer with stepwise increasing load from 25 to 125 W. DIQT maps were computed from averaged ECGs at rest (before the exercise) and at load of 75W.

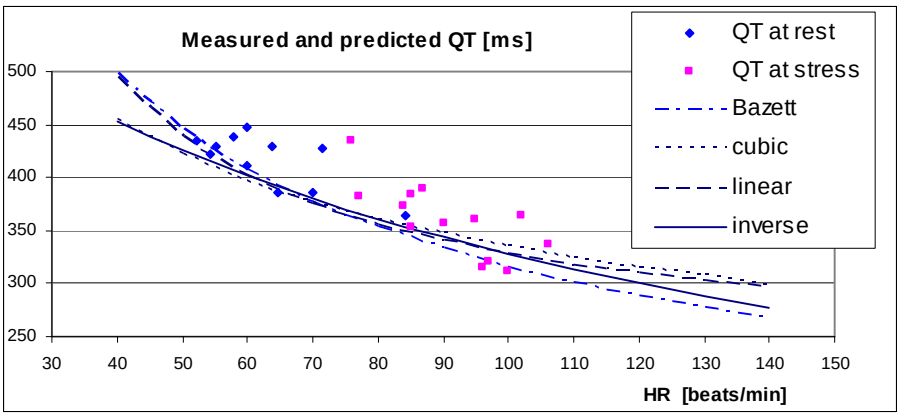

Fig.1. Relations between HR and QT intervals. Dots: QT intervals measured in 12 subjects at rest and during stress. Lines: Tested formulas for estimation of QT from HR or RR with parameters by [3].

ECG signals before the stress test were averaged during about 3 minutes and mean RR intervals were computed. During the load of 75 W, only 12 – 18 heart beats were averaged and HR was traced from the graphic protocol of load and HR. For individual subjects, HR before test varied from 44 to 84 BPM and during the load from 76 to 106 BPM; differences between HR before and during the stress were from 23 to 32 BPM (excluding two healthy

persons with differences 16 and 46 BPM). Instants of Q-onset and T-end were set manually, using graphs of averaged ECG signals in all leads and rms signal.

Because of the difficulties with direct QT measurements we proposed to use besides measured values of QT durations also their values predicted from the HR. Four formulas describing the dependence of QT duration on HR or on interval RR (RR=60/HR) were tested. The first formula is the well known formula QT = a1 / RR1/2 proposed by Bazett. Later on, alternative formulas were suggested and claimed to be more accurate: a cubic formula QT = a2 / RR1/3 (Fridericia), a linear formula QT = a3 + b3 RR and an inverse formula QT=1/(a4+ b4 HR) by Rautaharju [3]. Values of parameters obtained from large data sets [3] were implemented. Mean differences between measured and predicted QT were about 20-30 ms (up to 70 ms).

3. Results

Simulation of influence of QT interval changes on inverse identification of local ischemia
Uncompensated changes of QT_{ISCH} caused some errors of location and orientation of the inverse dipole. Mean and standard deviations (SD) of these errors are shown in Fig. 2.

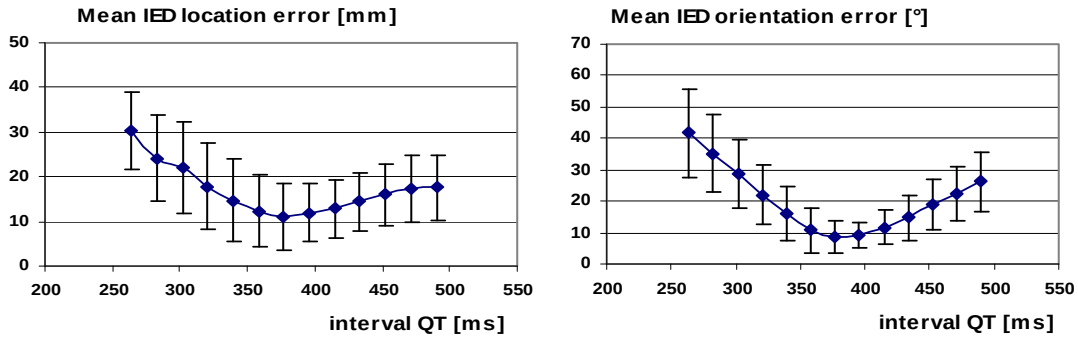

Fig.2. Simulated influence of uncompensated QT changes. The mean and standard deviation of the error of dipole location (left) and its orientation (right) for all simulated lesions.

Minimal mean location and orientation errors represented the error of the inverse method itself were observed for QT_{ISCH}=QT_{REF} = 377 ms (11mm and 9° respectively). Little changes of the interval QT_{ISCH} of about 5% (corresponding to HR changes between 64 and 87 BPM) caused very small increase of the mean dipole location error up to 12 mm and the mean dipole orientation error up to 12°. Changes of QT_{ISCH} to 264 ms (0.7 of QT_{NORM}) caused a considerable increase of the mean error of dipole location of up to 30 mm and error of orientation up to 41°. For some individual lesions the errors were far higher.

Testing of formulas for prediction of QT intervals from measured data

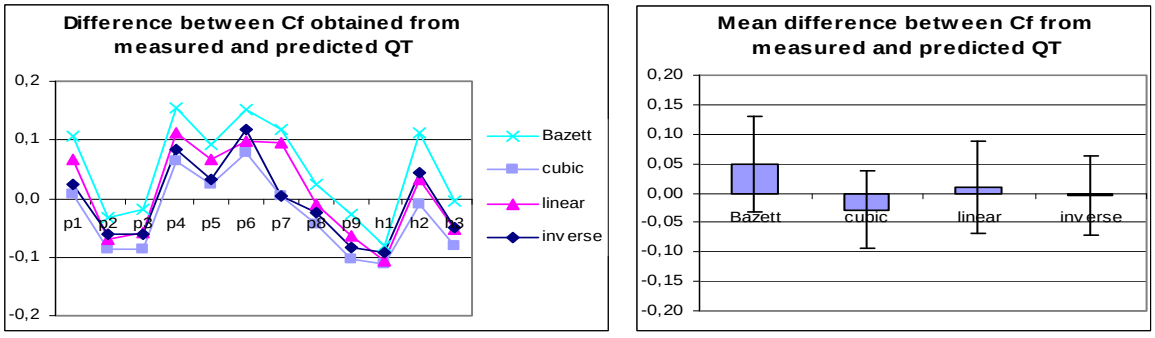

Fig. 3. Differences of c_f coefficients obtained from predicted and measured QT intervals for 4 tested formulas. Left: Individual values for 12 subjects. Right: means and standard deviations of values.

All 4 formulas slightly underestimated measured QT durations (Fig. 1). But for $DIQT_f$ maps and for the inverse solution precision of the c_f coefficient is more important than the QT value itself. Differences between c_f coefficients from measured and predicted values of QT for tested 12 subjects and 4 formulas are shown in Fig. 3 left; mean and SD for 4 formulas are shown in Fig.3 right. The minimum mean value was observed for inverse formula; the minimum SD for cubic and inverse formulas (Fig.3 left).

4. Discussion and Conclusions

Influence of HR variations and connected QT interval changes on the inverse identification of an ischemic lesion was simulated on a model. Simulation results revealed that it is desirable to compensate QT changes above 5%. It corresponds to HR changes of about 12 BPM. High changes of HR significantly influenced the inverse solution.

For real data, HR changes of up to 46 BPM were observed between situations at rest and during exercise. Simple compensation of related changes of QT duration was proposed. In previous study, selection of the formula appeared as more important than selection of its parameters for c_f computation. [4]. Four formulas for prediction of QT interval were tested on 12 subjects and gave moderate differences between predicted and measured QT intervals. When measured and predicted compensation coefficients c_f were compared, inverse formula gave the best results; the worst results were obtained from the formula of Bazett (in agreement with [3]).

However, differences between measured and predicted QT intervals in several individual cases exceeded 5% and corresponding differences of c_f were out of the 0.05 limits (Fig. 2 left) that ensure acceptable error of the inverse identification. To improve the QT prediction, HR stability during each measurement should be checked and interval of averaging should be selected so that HR before and during the period is relatively invariable (for example at the end of the load). Particular heart cycle can be included into the averaged data only if the whole QT pattern falls into prescribed boundaries.

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