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Effect of using ECG derived respiration (EDR) signal in Linear Parametric QT-RR modeling

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***Abstract*— Linear parametric modeling techniques are widely used for modeling the short term QT-RR interaction to explore the factors (i.e. heart rate variability, Autonomic Nervous system) controlling ventricular repolarisation variability . Recent studies established that respiration also has important effect on the ventricular repolarisation process like it has on the heart rate variability. So for the clear understanding of cardiac regulations, respiration signal should be considered for modeling the QT-RR dynamics. Due to several problems in collecting original respiration signal using the traditional recording devices that measure the nasal air flow or abdominal or chest pressure, a lot of research has been done to extract respiration information from the ECG signal called the ECG derived respiration (EDR). In this study we verify the use of EDR signal as a surrogate of original respiratory signal in modeling QT-RR interaction. We collect 10 young subjects' ECG and respiration signal from Fantasia database. We developed linear parametric autoregressive model with multiple exogenous inputs with an autoregressive noise term and check the model performance by using original respiration and EDR signal and found statistically similar result. Our findings showed that EDR can be used as a surrogate of original respiration in QT-RR model for the better understanding of cardiac regulations in young healthy subjects.**

I. Introduction

Modeling the interaction between ventricular repolarisation (VR) and heart rate variability (HRV) has been done in many research studies to provide an insight of the control of autonomic nervous system (ANS) and the effect of other factors (i.e. drug effects, respiration, different pathology etc.) on the electrical conduction system of heart [1-5]. Analysis of ventricular repolarisation (denoted by QT interval) from surface ECG is very important since a small perturbation in this process could lead to lethal arrhythmias and sudden cardiac death (SCD) [3, 4]. QT interval variability is not only affected by the heart rate (inverse of RR interval of ECG) and heart rate adaptation (rate of change in QT with the change in RR), but also many other factors like genetic profiles, different pathological conditions, temperature, electrolyte imbalance in ion channels and more importantly the effect of autonomic nervous system (ANS) have significant effect on QT variability [4, 5]. Derivation of mathematical models describing QT-RR dynamic relation is a popular technique to identify the temporal dispersion of cardiac repolarisation process.

Respiration has an important effect on heart rate which is the modulation of autonomic input to the excitation of sinus node. Respiratory modulation of heart rate is termed as respiratory sinus arrhythmia (RSA) and it causes the increase in heart rate during inhalation and its decrease during exhalation of air. Hanson et *al.* [6] recently proposed that ventricular repolarisation process is also cyclically modulated by respiration. From multiple left and right ventricular endocardial recordings in healthy human heart, they observed that ventricular action potential duration varied with respiration cycle. So, for the better comprehension of ventricular repolarisation and heart rate interaction, respiration signal should be considered in developing the QT-RR model.

Porta et *al.* [1] have developed a dynamic linear parametric autoregressive model to represent the ventricular repolarisation variability dependency on heart rate and ANS control. The authors have developed a bivaritae model (RT-RR model) where they consider RT interval instead of QT interval as a representation of the ventricular repolarisation process due to the technical difficulty in T wave end detection. By considering the importance of QT interval in explaining the ventricular repolarisation process, Almeida et *al.*[5] have developed a modified QT-RR interaction model proposed by Porta et *al.*[1] by considering total QT interval instead of RT interval. Later the importance of inclusion of respiration in the model become obvious when Porta et *al.* [2] have presented a customized model of their previously proposed model by showing that, adding respiration as another input in addition to RR increases the predictability of the model.

Respiratory signal is normally collected by the use of spyrometer, pneumography, or plethysmography techniques. These methods are based on either the direct measurement of air flow in or out of the lung or by indirectly measure the body volume changes. Strain gauges or piezoelectric transducer devices are strapped to the chest or abdomen for recording the velocity and force of chest movement during respiration These recording procedures were not very much suited in ambulatory monitoring, overnight sleep studies to detect sleep apnea and in stress testing due to necessity of using bulky recording devices [7]. Moreover they affect the natural breathing and they sometime need conscious operation of the subjects which is not always possible in sleep studies and in continuous observation condition like in ambulatory ECG recording.

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Due to the importance of respiration in the cardiac regulation, various signal processing methods were developed to extract respiration information from the ECG signal called the ECG derived respiration (EDR) without the use of respiration recording devices used for monitoring breathing cycle [7, 8]. Many techniques were proposed in case of single lead and multi lead ECG signal which actually showed good performance for the representation of respiration information. In this paper, we test the hypothesis that EDR can be used as a surrogate respiration signal in modeling the short term QT-RR relation that can reduce the complexity involved in respiration signal collection.

II. DATA AND METHODS

A. Subjects

Simultaneously recorded ECG and respiration data sampled at 250 Hz of ten young healthy (Records f1y01 to f1y10) subjects were taken from the Fantasia database available at Physionet[10].120 minutes long ECG and respiration signals recorded in continuous supine position are available in that database. We collected approximately 10 min data from that 2 hour recordings for QT, RR and EDR series extraction and build the linear parametric autoregressive model. The selection criterion of the 10 min ECG segment from 120 min long data was less noisy ECG data so that from the ECGs, the QRS complex and T wave could be visibly detected.

B. ECG Analysis

ECG signal was first filtered with median filter to remove baseline wandering. The RR and QT interval series were formed by detecting the R wave peak, Q wave onset, T wave peak and T wave end from the ECG signal using the technique described in [11]. The T wave end or offset is found by searching for the point where the gradient of the T wave first changes its sign after the occurrence of T wave peak. This method of detecting the end of the T wave is similar to the maximum slope intercept method which defines the end of the T wave as the intercept between the isoelectric line with the tangent drawn through the maximum down slope of the T wave [11]. Ventricular repolarisation process is comprehensively described by QT interval rather than RT interval [5]. So in this study, QT interval was used for the representation of ventricular repolarisation variability instead of RT interval. We used both QT_{peak}(time interval between Q wave onset and T wave peak) and QT_{end} (time interval between Q wave onset and T wave peak) intervals to build and validate the model performance. The original respiration signal time series (RESP) for the model was formed by sampling the continuous respiratory signal at each R peak of the ECG (Figure 1).We also calculated the ECG derived respiration series using the R wave amplitude by the method described in. [12]. The QT, RR, Sampled respiration (RESP) and EDR time series data are linearly detrended before using as model input and output.

C. QT-RR model formation

We used 250 beats of the derived RR, QT(both QT_{peak} and QT_{end}), RESP and EDR time series for the formation of the autoregressive models with single and double exogenous inputs with an autoregressive noise term. We analyzed a bivariate ($ARX_{RR}AR$) and two trivarite ($ARX_{RR}X_{RES}AR$ and $ARX_{RR}X_{EDR}AR$) linear parametric models for our analysis using the methodology developed by Porta et *al.* [2]. RR and respiration signals (RESP and EDR) were used as the exogenous inputs in these models. The beat to beat time series are represented as $QT = \{QT(i), i = 1,2, \dots \dots N\}$, $RR = \{RR(i), i = 1,2, \dots \dots N\}$, $RESP = \{RESP(i), i = 1,2, \dots \dots N\}$, and $EDR = \{EDR(i), i = 1,2, \dots \dots N\}$. N is total number of beats counted for building the model, in this study N =250. The *i*th QT_{peak} or QT_{end} intervals followed the *i*th RR interval, thus directly linking the present QT interval with the preceding RR interv*al.* The *i*th respiratory sample $RESP(i)$ was taken in correspondence of the R-wave peak starting the *i*th RR interval.

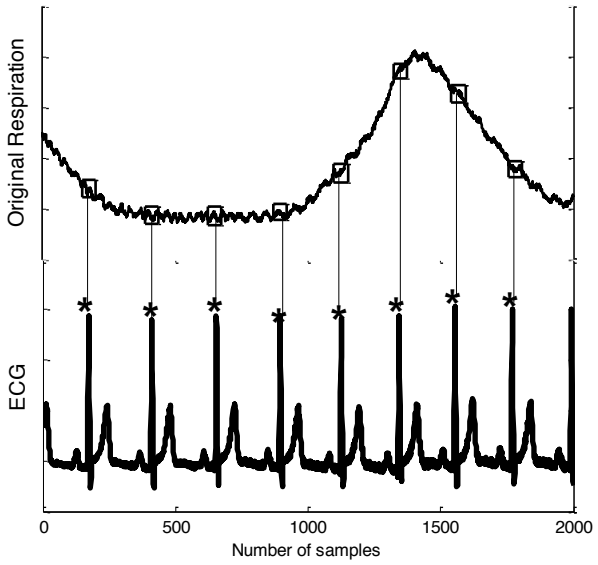

Figure 1. Sampling of the original respiration at every R wave peak of ECG for the RESP time series genaration. The squares on the respiration signal indicate the values taken for RESP time series formation which was taken at every R peak denoted by *.

D. Model Equations

The equation of the bivariate QT-RR model is:

$$QT(i) = A_{QT-QT}(i) * QT(i) + B_{QT-RR}(i) * RR(i) + n(i) \quad (1)$$

And the equations of the trivariate QT-RR model including respiratory information are:

$$QT(i) = A_{QT-QT}(i) * QT(i) + B_{QT-RR}(i) * RR(i) + B_{QT-RESP}(i) * RESP(i) + n(i) \quad (2)$$

$$QT(i) = A_{QT-QT}(i) * QT(i) + B_{QT-RR}(i) * RR(i) + B_{QT-EDR}(i) * EDR(i) + n(i) \quad (3)$$

Where $RESP(i)$ is the sampled original respiratory signal and $EDR(i)$ is the respiratory information derived from ECG RR time series. The model performance was validated using both QT_{peak} and QT_{end} in $QT(i)$. The model equations indicate that it includes the QT variability due to RR, respiration independent of RR and other unknown inherent factors independent of RR and RESP, which was modeled by the noise term $n(i)$. A and B represent the model parameters which actually indicate the memory effect of QT, RR, and RESP that shows how a QT interval is affected by

the previous QT and RR intervals and other factors (i.e. respiration). The model parameters are identified using following equations:

$$A_{QT-QT}(z) = \sum_{k=1}^{p} a_{QT-QT}(k) * z^{-k} \quad (4)$$

$$B_{QT-RR}(z) = \sum_{k=0}^{p} b_{QT-RR}(k) * z^{-k} \quad (5)$$

$$B_{QT-RESP}(z) = \sum_{k=0}^{p} b_{QT-RESP}(k) * z^{-k} \quad (6)$$

$$B_{QT-EDR}(z) = \sum_{k=0}^{p} b_{QT-EDR}(k) * z^{-k} \quad (7)$$

The noise term is identified by the following equation:

$$n(i) = D_n(z) + w_n(i) \quad (8)$$

$$where\ D_n(z) = \sum_{k=1}^{p} d_n(k) * z^{-k}$$

and w_n is the zero mean white noise. z^{-k} is the k lag delay operator in z domain.. p is the number of the poles of the model transfer function or the model order which represents the model complexity for simulation. The larger the value of *p,* the more complex is the model to identify the interaction of the system parameters. Figure 2 shows the signals used for developing the model.

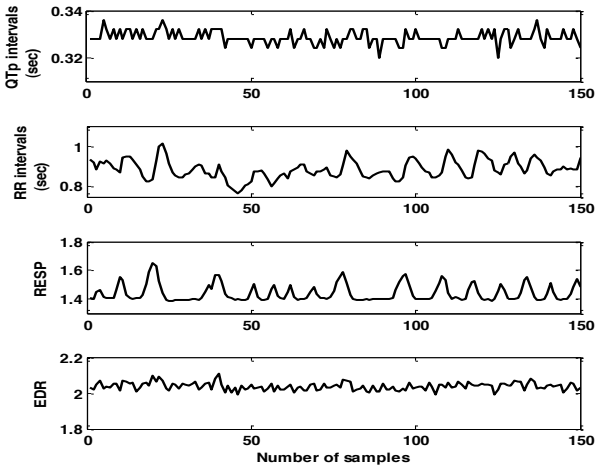

Figure 2. QT intervals,RR intervals, sampled original respiration and EDR signal of one subject used for QT-RR model development.

E. Model parameter identification and validation

Model parameter coefficients were calculated by Prediction error estimation method for linear models[13].This method uses a numerical optimization technique to minimize the weighted norm of prediction error which is defined as cost function. Same model order of p was considered for calculating the coefficients of the model transfer function for simplicity of model analysis. Model order was varied from 5 to 17 to find the best model order according to Akaike information criteria (AIC) [13]. Residual analysis was performed to check if the model passed the whiteness test and independence test to clarify that model residuals were not correlated with past input values. . The prediction capability of the model was determined by the value of goodness of fit of the derived model and it was calculated by measuring the Normalized Root Mean square Error (NRMSE) fit value. NRMSE computes the normalized error between the measured QT and one step ahead predicted QT form the model. All these analysis were done using system identification toolbox in MATLAB R2012a. Statistical tests were done using Wilcoxon Ranksum test and $p<0.01$ was considered significant.

III. RESULTS AND DISCUSSIONS

The goodness of fit values of all developed models is shown in Table 1. Prediction capability, measured by goodness of fit, was found better for all the models derived with QT_{peak} as output variable than QT_{end} . This finding is aligned with the results reported by Porta et *al.*[2]. The model predictability increases significantly when respiration information (RESP or EDR) was added as an exogenous input in comparison to the results found from the model developed using only QT and RR signals. This enhancement in prediction was found for both models having QTpeak and QTend as output variables. The trivariate models ($ARX_{RR}X_{RESP}AR$ and $ARX_{RR}X_{EDR}AR$), which had RESP or EDR signals as respiration signal input along with QT and RR, showed statistically similar goodness of fit values (Table 1). The goodness of fit of the models predicting QTpeak dymaics having original respiration signal (median: 0.62) and EDR (median: 0.60) were found to be almost same.

TABLE I. COMPARISON OF GOODNESS OF FIT VALUES OF THE MODELS

Goodness of fit of the models			
QT dynamics	$ARX_{RR}AR$	$ARX_{RR}X_{RESP}AR$	$ARX_{RR}X_{EDR}AR$
QT_{end}	0.41(0.39-0.45)	0.57(0.55-0.6)	0.55(0.52-0.58)
QT_{peak}	0.48(0.45-0.51)	0.62(0.58-0.64)	0.60(0.55-0.64)

values are shown as Median(First to Third Quartile)

The Box-Whiskers (BW) plot in Figure 3 shows the median and interquartile range of goodness of fit values for all subjects for each model. From Figure 3, it is obvious that the models having respiration information show significantly better performance than the model formed from using QT-RR only. Moreover, there is no statistically significant difference in model predictability whether it has original respiration or EDR as a model input.

The investigation of cardiac regulation from only a single lead ECG necessitates the exploration of effect of respiration using EDR. EDR is an established technique in sleep studies for respiratory rate and apnea detection [8, 9]. Another study on ambulatory single lead ECG recording for cardiac monitoring showed that EDR in different stages of daily activity gave similar performance like the original respiration signal recorded using traditional methods [7]. Besides, QT-RR models are widely used for exploring the internal dynamics of ventricular repolarisation process [4, 5] and the effect of respiration on cardiac regulation is also established by many research studies [6]. Therefore, the addition of the effect of respiration improves the identification of cardiac dynamics represented by the interaction of QT and RR [2]. Use of EDR in place of original respiration, to the author's knowledge is the first effort to validate the performance of

QT-RR dynamics model with respiration information. The results of our work justify that EDR could be used as a surrogate of respiration signal for QT-RR modeling of healthy young subject. More exploration is needed to validate the use of EDR in different physiological (age, gender etc) and experimental (body postures where respiratory pattern is altered) conditions.

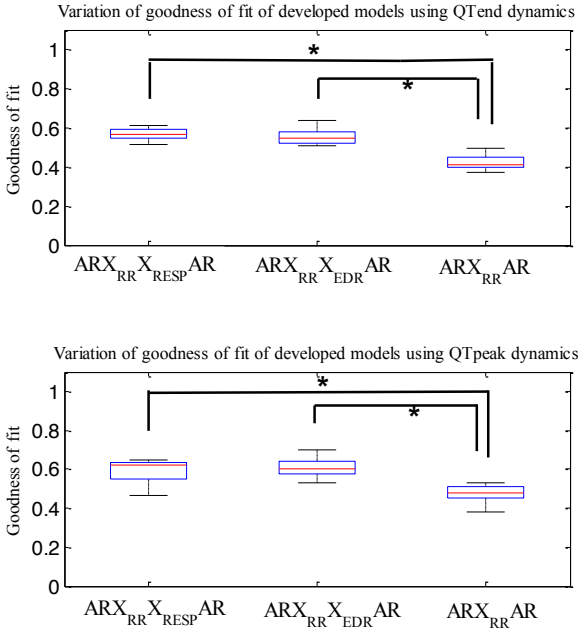

Figure 3. Box whiskers plots showing the variation of goodness of fit in the developed models.* indicates goodness of fit is significantly different between two models with $p<0.005$.

In this study, models used for the analysis were developed using the ECG and respiration data continuously recorded at the supine resting position of the subjects. Porta et al.[2] performed multivariate parametric spectral decomposition of their derived model to understand the dependency of QT variability on the model input parameters. Their findings indicated that in resting condition the influence of respiration on the QT variability is not very significant unlike the effect of RR whose effect on QT variability is dominant. However, the inclusion of respiratory information (RESP) in their model increases the goodness of fit significantly which might prove the presence of respiratory modulation on the ventricular repolarisation [2]. This supports the findings of our study where inclusion of respiration (RESP or EDR) improves the model predictability for supine resting condition. Further study is required to consolidate the findings.

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