# SOFTWARE FOR HEART RATE VARIABILITY AND QT INTERVAL VARIABILITY ANALYSIS

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**Abstract: Regulated by the intrinsic automaticity of the sinoatrial node and the modulating influence of the autonomic nervous system, the electrocardiografic waves show each one some beat to beat variability. The analysis of this variability can be fundamental in cardiovascular diagnosis; the R-R time series may provide essential information for the determination of hidden cardiopathy and the Q-T series have been proposed as marker of sudden death risk. The purpose of this study was the software implementation to analyse this variability. Its implementation has been divided into two processes: ECG signal pre-processing and HRV and QTV processing. ECG signal pre-processing comprises all steps from the original ECG signal to the tachogram generation: the ECG signal is sampled at 240 samples/second, filtered and interpolated to ~1000 samples/second; RR and QT series are detected (using wavelet transform) and resampled to 1 sample/second to generate the intervals time series. Signal edition by the user is allowed making possible to correct any error in RR or QT interval detection. HRV and QTV processing include time and frequency domain measures and nonlinear Poincaré plot, performed on periods of 5 minutes ECG recordings. The implemented software tool has allowed RR and QT variability studies in different areas.**

## Introduction

The Autonomic Nervous System (ANS) regulates the internal organs activity to support body homeostasis as a whole. Thus, autonomic tone can be either increased or decreased to modulate the activity of specific tissues, such as the heart [1].

Heart rate variability (HRV) is a noninvasive electrocardiographic marker reflecting the activity of the sympathetic and vagal components of the ANS on the sinus node in the heart. In a normal heart with an integer ANS, there will be continuous physiological variations of the sinus cycles reflecting a balanced sympatho-vagal state and normal HRV. In a diseased heart, the changes in activity in the fibers of the ANS and in the local neural regulation will contribute to the resulting sympatho-vagal imbalance reflected by a diminished HRV [2].

In 1996 a Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology defined and established standards of measurement, physiological interpretation and clinical use of HRV [3]. Time domain indices, geometric measures and frequency domain indices constitute nowadays the standard clinically used parameters.

Time domain analysis refers to statistics that are derived directly from the measurement of the normal-to-normal (N-N) intervals and statistics calculated from the differences between successive N-N intervals (Table 1).

Table 1: Time domain measures of heart rate variability recommended for short-time recordings

| Indices | Unit | Definition |
|---|---|---|
| SDNN | ms | Standard deviation of normal RR intervals |
| RMSSD | ms | Root mean square of successive RR intervals difference |
| pNN50 | % | Percent of difference between adjacent RR intervals that are greater than 50 ms |

Frequency domain (Power Spectral Density) analysis describes the periodic oscillations of the heart rate signal decomposed at different frequencies and amplitudes, and provides information on the amount of their relative intensity (termed variance or power) in the heart's sinus rhythm [3, 4]. The power spectrum consists of frequency bands ranging from 0 to 0.5 Hz. Short-term spectral recordings (e.g. five minutes) are characterised by the VLF (very Low Frequency, 0.0005 to 0.04 Hz), LF (Low Frequency, 0.04 to 0.15 Hz) and HF (High Frequency, 0.15 to 0.4 Hz) components, while long-term recordings include a ULF (Ultra Low Frequency, 0 to 0.0005 Hz) component in addition to the three others. The HF component is generally defined as a marker of vagal modulation. This component is mediated by the respiration and thus determined by the frequency of breathing. The LF component is modulated by both the sympathetic and parasympathetic nervous systems. In practical terms, an increase of the LF component has been generally considered to be a consequence of sympathetic activity. The LF/HF ratio reflects the global sympatho-vagal


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balance and can be used as a measure of this balance. ULF and VLF are spectral components with very low oscillations. The ULF component might reflect circadian and neuroendocrine rhythms and the VLF component long period rhythms [3].

Nonlinear methods are based on the chaos theory and fractals. Chaos describes natural systems in a different way because it can account for nature's randomness and nonperiodicity. Perhaps the theory of chaos may help in better understanding HR dynamics, taking into account that the healthy heartbeat is slightly irregular and to some extent chaotic. Among many tools for the studies of nonlinear dynamics of heart rate, the return map or delay map of RR intervals deserves special attention because the return map has been applied to many clinical studies of heart rate variability [5, 6, 7]. The return map is the plot that displays the relationship between a point and its consecutive point in a time series.

Studies have shown that left ventricular hypertrophy associated with arterial hypertension is a risk factor for sudden death. In recent years attention has focused on a predictive index of sudden death based on temporal dispersion of the QT interval (1), namely the QT Variability Index (QTVI) [8]. In subjects with structural myocardial disease, an increased QTVI is correlated with malignant ventricular arrhythmias. One of the distinctive characteristics of this marker is its dependence on RR interval variability. Low RR variability is itself another marker of sudden death [3].

The electrocardiogram (ECG) is extensively used as low cost tool to provide information about the heart performance. The time interval between consecutive R waves in the ECG (tachogram) is the simplest cardiovascular signal to obtain HRV [3], as well as, the time intervals between Q and T waves to get QTV.

Therefore, the study of the ECG signal and its intrinsic variability can be a powerful tool to assess the integrity of the cardiovascular system [2]. This paper describes the development of a system for HRV and QTV analysis to evaluate heart autonomic modulation and provides tools to assess its integrity.

$$QTVI = \log_{10}\left(\frac{QT_v / QT_m^2}{RR_v / RR_m^2}\right) \qquad (1)$$

**Materials and Methods**

This first version was developed in Borland® Delphi 7.0 and the Data Base used for data storage was MySQL®.

The Figure 1 show the block diagram of the software developed.

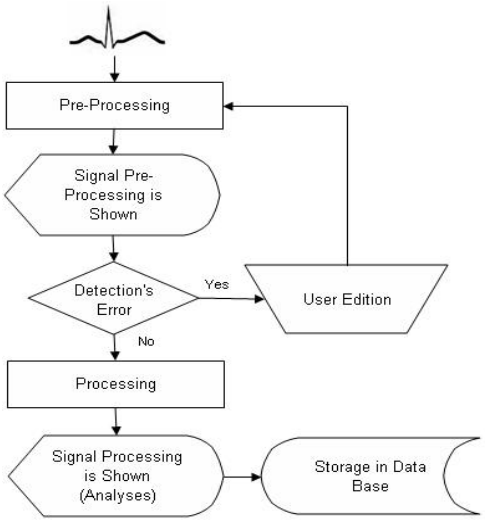


Figure 1: Block Diagram of the software developed.

The purpose is take on input originals ECG signals and return on output indices that quantify the HRV and QTV analysis. The software implementation was divided into two main processes as follows:

- **Signal Pre-Processing**

The signal pre-processing module is the start-up of the system. It receives the original signal and prepares to show the time series that represent intervals between R waves (heart beats) and Q-T waves (total time of both ventricular depolarization and repolarization). Thus, the six module steps are:

1. ECG signal acquisition: it was made through of the WinDaq/Lite® Chart Recorder Software using a A/D converter of 10 bits. ECG signal was recorded from a lead II on five minutes and digitized at 240 samples/second [9].
2. Signal filtering: a simple type of low pass filter (five-term average filter) was used to smooth out high-frequency variations of the signal that could cause errors during processing.
3. Signal interpolation: following the Guidelines [3] that a minimum sampling frequency of 250 samples/second for accurate HRV analysis, a data interpolation is made in the system. Therefore, the sampling frequency changes linearly from 240 to 960 samples/second, becoming possible a higher precision in the identification of signal parameters.
4. Continuous Wavelet Transform (CWT): an algorithm based on wavelet transform was developed for detecting ECG characteristic points. The chosen wavelet was a first derivative of a Gaussian function [10, 11]. The scales used, based on the spectral characteristics of the ECG signal, were 4 for QRS complex and 8 for and QT interval identifications.
5. Signal waves and interval detection: the wavelet transform application results in a signal with parameters of waves start/end and peaks


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characterized for positive maximum-negative minimum pairs and zero-crossing between the set of modulus maximum, respectively [12]. Search algorithms were used to pinpoint the signal parameters through these characteristics found with the CWT application. The pertinent waves and intervals in this study were: Q, R, S and T waves; R-R and Q-T intervals.

6. In this part, the output of this process is shown graphically and in tables representing the measured intervals.

Before the start-up of the next processes it is allowed that the user can edit and correct the ECG signal characteristics that by chance had shown error in the automatic detection.

- **HRV and QTV Processing**

The HRV and QTV processing are setup in the same time. It is allowed that the user select the more appropriate tools for each case. In agreement with the Guidelines for HRV assessment of short-term recordings [3] and with the described indices for the QTV [13], the following measurement indices were derived:

- HRV analysis: time domain indices (SDNN, RMSSD and pNN50); frequency domain indices (VLF, LF and HF); nonlinear indices – RRI[n] X RRI[n+1] – (pearson coefficient, slope and Y-intercept);
- QTV analysis: time domain indices (QTc and QTVI); frequency domain indices (VLF, LF and HF); non-linear indices – RRI[n] X QTc[n] – (pearson coefficient, slope and Y-intercept).

In the frequency domain analysis the power spectrum for the HRV and QTV is calculated with a parametric method based on autoregressive time series modelling. The modified covariance method with order 18 was used to compute the estimate of the AR model parameters [14, 15].

The study of nonlinear dynamics was made with Poincaré graphic tool. The Pearson coefficient, slope and Y-interception indices were used to characterise and quantify the Poincaré plot that displays the relationship between a point and its consecutive point in a time series.

**Results**

The Figures 2, 3, and 4 show some screens of the developed system.

The main screen (Figure 2) shows all the functions implemented in the system. Configuration options such as language, layout's colours, login of each user and help files are also show in this screen.

The screen shown in Figure 3 allows the user to edit and correct ECG signal parameters and RR time series that have presented detection errors.

The screen of the system that comprises the HRV and QTV analyses results is shows in Figure 4. The user decides how the results are output, just clicking in the wished option.

The database of the system was developed for the storage of all the required indices and to allow the patient evolution analysis during the following up clinical evaluations. The user may choose what data to save as well as to select a structure to print the reports.

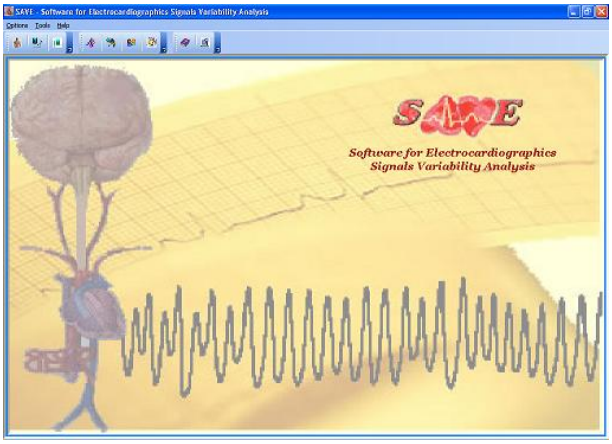


Figure 2: Main screen of the system.

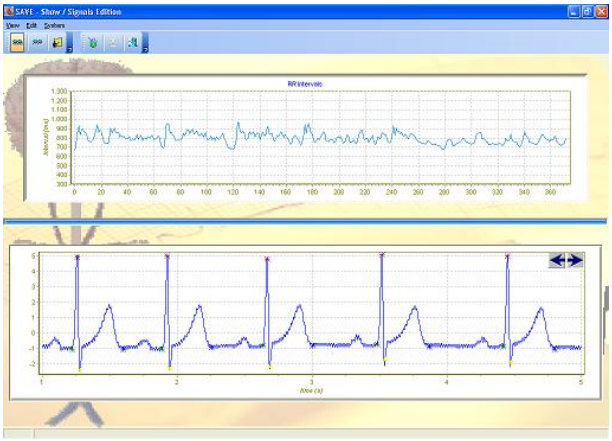

Figure 3: Screen where the ECG signal parameters and RR time series may be edited.

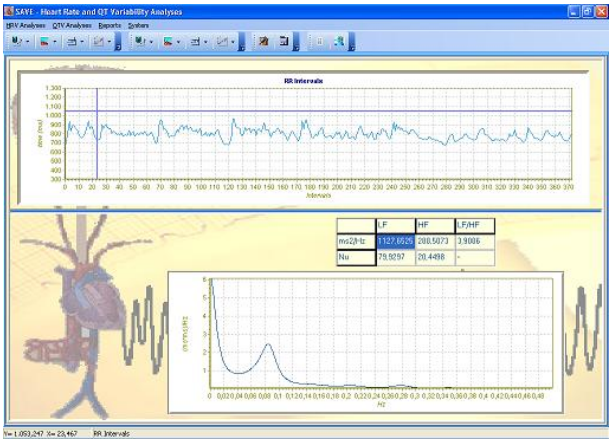

Figure 4: Screen of HRV and QTV analysis.


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All the methodologies and tools of the system are being tested in some applications aiming the software validation, were processed ECG signals of diabetic subjects with and without diabetic autonomic neuropathy.

- **Diabetic Autonomic Neuropathy**

Diabetic Autonomic Neuropathy (NAD) is a serious complication that can happen with diabetic patients. It is a frequent cause of morbidity and mortality among individuals with Diabetes Mellitus and is characterised by neurological degeneration affecting the small nerve fibres of the parasympathetic and sympathetic branches of the autonomic nervous system. Diabetic subjects with NAD show lower SDNN, RMSSD, and R-R interval and higher LF/HF and pearson coefficient than diabetic subjects without NAD [16, 17].

The Table 2 shows the calculated HRV and QTV indices (mean ± SD, n=5) of diabetic patients with and without NAD (W and WO, respectively). Results were considered statistically significant if $p<0.05$ using Mann-Whitney test.

Table 2: HRV and QTV indices of diabetic subjects with (W) and without (WO) diabetic autonomic neuropathy. Values are displayed as mean ± SD, n=5.

| | Indices | Unit | WO | W | p |
|---|---|---|---|---|---|
| **HRV** | SDNN | ms | 52±6 | 20.41±7 | <0.04 |
| | RMSSD | ms | 50.82±15 | 7.77±0.5 | <0.01 |
| | RR | ms | 970±150 | 835±67 | <0.01 |
| | LF/HF | - | 0.63±0.2 | 1.86±0.9 | 0.4 |
| | ρ | - | 0.51±0.2 | 0.88±0.06 | <0.01 |
| **QTV** | QT | ms | 371±42 | 370±32 | 0.8 |
| | QTc | ms | 377±17 | 406±41 | 0.3 |
| | QTVI | - | 0.25±0.18 | 1.34±0.11 | <0.01 |
| | LF/HF | - | 0.41±0.02 | 0.41±0.08 | 0.4 |
| | ρ | - | -0.03±0.01 | 0.06±0.01 | <0.01 |

HRV and QTV analysis combined were able to discriminate between patients with (W) and without (WO) autonomic neuropathy.

## Discussion

The autonomic reflexes are fundamental for the heart regulation. If altered it may cause cardiac arrhythmias and sudden death. Joint linear and non-linear techniques as carried out in this system bring about higher confiability to make a diagnostic or prognostic of patients' cardiovascular status.

Heart rate variability has gained importance because is a non-invasive and low cost technique that make possible to assess the ANS state through of sympatho-vagal relation and as well as to evaluate the cardiovascular condition.

The system was developed aiming to be suitable for use in several clinical applications allowing a better analysis of RR and QT variability and to establish its association with disease.

In the simple study realized just to test the developed tools were obtained results coherent with those found in the literature for similar case study. As expected, the results of HRV and QTV analysis in diabetic patients with NAD show significant differences compared to patients without NAD [15, 16].

## Conclusions

From the preliminary results we believe that the developed software is satisfying the original objectives, since it allows a robust set of methodologies to analyze RR and QT variability.

The use of digital signal processing techniques together with computational technologies becomes a powerful tool to support the understanding of the dynamic process between health and illness.

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