Baroreflex Sensitivity Evaluation by Volterra Wiener Model and the Laguerre Expansion Technique

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Abstract

This paper presents a Volterra-Wiener model and the Laguerre expansion technique to analyze the changes in heart rate interval, as model's output to the corresponding changes in systolic arterial blood pressure, as model's input. This new technique can not only find the baroreflex sensitivity (BRS) but also can assess the nonlinear and dynamic behavior of baroreflex from the identified model parameters. The performance of this new technique was compared with the measurements by sequence technique (SEQ) and alpha coefficient technique (Alpha) in 5 normal and 11 hypertension subjects. The BRS of hypertension subjects was 4.4±2.0 ms/mmHg for SEQ, 4.6±1.9 ms/mmHg for Alpha, and 2.9±1.6 ms/mmHg for the new technique. For normal subjects, the BRS was 30.4±12.4 ms/mmHg for SEQ, 25.8±10.2 ms/mmHg for Alpha, and 17.5±7.7 ms/mmHg for the new technique. The proposed new technique yielded a reasonable lower BRS estimation than existing noninvasive BRS techniques.

1. Introduction

Baroreflex sensitivity (BRS) is an effective prognostic indicator in cardiology. For these years, many techniques have been applied in spontaneous BRS analysis including: (a) time-domain analysis - sequence technique [1] and cross-coefficient method (xBRS) [2], (b) frequency-domain analysis - alpha coefficient technique [3], transfer function technique [4], (c) model-based analysis - ARMA modelling technique [5], and (d) other ways - such as closed-loop Baselli model [6], the Z analysis [7]. Most of the above analysis use either systolic arterial blood pressure or average arterial blood pressure, either heart rate or RR interval as the analysis objects based on the framework of linearity. Compared with the invasive phenylephrine technique, these spontaneous BRS techniques can give correlated but probable higher BRS estimates.

There are evidences that the cardiovascular regulation mechanisms inherently exists a nonlinear dynamic interaction between arterial blood pressure and heart rate [8,9]. For noninvasively BRS estimation, we need to work further to find a more suitable and unrestrained nonlinear dynamic model which involves this dynamic nonlinearity. And this will definitely support more accurate BRS estimate and more physiological description about the baroreflex under estimated. To this aim, in this paper, we introduced a new technique for evaluating BRS noninvasively based on the Volterra-Wiener class of nonlinear model and the Laguerre expansion technique. By using the suitable selected Laguerre orthonormal bases, the model parameters obtained can be used to calculate BRS and other indexes concerning the baroreflex. Furthermore, the performance of this new technique was compared with the measurements by the sequence technique and the alpha coefficient technique.

2. Methods

2.1. Subjects, data recording and signal processing

Sixteen subjects were used in the study, including five healthy normal subjects (27±3 years, 3M/2F, all without cardiovascular disease or neuropathy history and not taking any medication) and eleven hypertension subjects (52±10 years, 8M/3F, all without taking any medication during past 2 weeks).

For each subject in resting supine position, the continuous electrocardiogram (ECG) and arterial blood pressure were acquired in 5 minutes at 1 kHz sampling rate using an instrument, and then beat-to-beat systolic arterial blood pressure (SBP) and R-R interval (RRI) time series were obtained using the programs in Matlab. After point by point checking and cubic spline interpolation, the new equally interval SBP and RRI were yielded. Accordingly, power spectra of SBP, RRI, ΔSBP, ΔRRI and coherence function were estimated using FFT based Welch's method (50% overlapping segments).

2.2. Nonlinear modeling of baroreflex

The arterial baroreflex is a key mechanism involved in blood pressure homeostasis and it can maintain a default setting of systolic arterial blood pressure in human body. In baroreflex regulation, acting as a nonlinear dynamic feedback control system, the controlled RRI would track the SBP step by step and then reveal corresponding changes between SBP and RRI. Thus, a reasonable choice for analyzing such profiles is the utilization of ΔSBP and ΔRRI accompanied with nonlinear SISO dynamic model. We adopted Volterra-Wiener model to describe such SISO nonlinear causal system. Under practical considerations of feasibility, the truncated discrete-time Volterra-Wiener model is used.

In this study, a second order Volterra-Wiener model was employed to relate the input ΔSBP and the output ΔRRI in the following manner:

$$\Delta RRI[n] = T\sum_{i=0}^{D_1-1} h_1[i]\Delta SBP[n-i] + T^2\sum_{i_1=0}^{D_2-1}\sum_{i_2=0}^{D_2-1} h_2[i_1,i_2]\Delta SBP[n-i_1]\Delta SBP[n-i_2] + \varepsilon[n] \quad (1)$$

Where n represents the discrete-time index, T denotes the sampling interval, h_k is the kth-order discrete-time Volterra kernel and D_k represents the memory depth of h_k. The choice of D_k depends on the length of available data. $\varepsilon[n]$ depicts the model error combination of measurement error and other contributions not accounted for by Volterra-Wiener model. Obviously, the Volterra kernels can completely describe the impact of the previous $\Delta SBP[n]$ and its historical $\Delta SBP[n-i]$ on the present $\Delta RRI[n]$ in Eq. (1). Owing to the nominal BRS is defined as the ratio of ΔRRI to ΔSBP and has unit in ms/mmHg, which aroused us the relationship between BRS and the first order Volterra kernel h_1. Accordingly we had defined BRS as the largest element of h_1 allowing for the potential baroreflex delay if $T=1$ in Eq. (1). In addition, the other elements of kernels could either be used as an assessment of the dynamic and nonlinearity of baroreflex or be involved into BRS evaluation according to the following proposed manner.

The determination of Volterra kernels h_k is a linear problem which can be done using least-squares minimization techniques. However, underlying the characteristic of nonstationary of arterial blood pressure and ECG signals, the length of available records was short. Thus it emerges the question that how to determine the element number of kernels with tradeoff between model accuracy and parameters compactness. Besides, various discrepancies between each estimated kernel values happened when using the least mean square error estimation criteria to fitting data. These issues could be improved by using Laguerre expansion technique. By Laguerre expansion technique, each of the unknown kernels h_k was expanded as the sum of several weighted orthonormal Laguerre basis functions. The Laguerre basis functions were found to be appropriate as a tradeoff between model accuracy and parameters compactness.

After some algebraic manipulation, Eq. (1) can be reformed as:

$$\Delta RRI[n] = T\sum_{j=0}^{J_1-1} c_j\phi_j[n] + T^2\sum_{j_1=0}^{J_2-1}\sum_{j_2=0}^{J_2-1} c_{j_1,j_2}\phi_{j_1}[n]\phi_{j_2}[n] + \varepsilon[n] \quad (2)$$

where $\phi_j[n]$ is the convolution of $\Delta SBP[n]$ and $La_j[n,p]$. $La_j[n,p]$ is the jth order Laguerre function, p is the scaling factor of Laguerre function and J_1, J_2 are the selected number of Laguerre functions used in h_1 and h_2 expansions, respectively. The determination of the new parameters c_k in Eq. (2) is also a linear problem similar to Eq. (1). By contrast, the number of the new parameters c_k needed to be estimated will diminish and the estimation stability of the follow-up estimated kernels h_k will also be affirmed according to our results.

Two major spectrum bands can be recognized from human cardiovascular variability series, which are generally used for BRS estimation: low frequency band (LF: 0.04-0.15 Hz) and high frequency band (HF: 0.15-0.4 Hz). However, a few researchers have recently reported that HF band reflects both baroreflex and non-baroreflex occurrences and thus suggested that the BRS evaluation should be restricted only to LF band [10]. In our proposed Volterra-Wiener model and the Laguerre expansion technique, termed VWL technique of BRS estimation thereafter, we restricted the scaling factor p ranging from 0.415 to 0.778 to ensure the model has the maximum response on LF band.

But the VWL technique also faces two problems: the decision of the scaling factor and coordination between model accuracy and parameters compactness. It draws a better compromise by the AIC (Akaike information criterion) guidelines as followed: searching for the optimum values of p and J_1, J_2 such that the following quantity is minimum.

$$N\log\left(\frac{\sum_{n}^{N}\left(y[n]-\hat{y}(n,p,J_1,J_2)\right)^2}{N}\right)+2N_c \quad (3)$$

where N denotes the length of the records, N_c is the number of c_k, $y[n]=\Delta RRI[n]$ and $\hat{y}[n,p,J_1,J_2]$ represents the predicted value of $\Delta RRI[n]$ at candidates of p,J_1,J_2. After gaining the best values of p,J_1,J_2, the kernels h_k can be obtained eventually.

2.3. Other descriptors about baroreflex

The relation between inter-beat ΔSBP and consequent inter-beat ΔRRI can be determined by Volterra kernels. With these quantities, not only the BRS can be estimated, but also other descriptors about nonlinear dynamic behavior of baroreflex can be provided. We have defined three descriptors about baroreflex – delay, memory depth and nonlinearity by followed way: (a) delay: the time index of maximum of h_1; (b) memory depth: the duration from beginning of the maximum of h_1 to the moment of 95% drops with the maximum of h_1; (c) nonlinearity: the ratio between 2-norm of h_1 and 2-norm of h_2.

2.4. Other BRS techniques for comparison

For comparison, we included results obtained with the sequence technique and the alpha coefficient technique. In the sequence technique, BRS was estimated by linear regression analysis of spontaneous sequences of three consecutive heart beats where changes in SBP and the associate next RRI had the same direction of changes, either up or down. In the alpha coefficient technique, estimate of BRS was obtained by averaging the root-squared ratio between RRI power spectrum and SBP power spectrum calculated in the LF band and HF band, provided that the coherence between SBP and RRI was greater than 0.5.

3. Results

Figure 1 depicts the box and whisker plots of estimated BRS of normal and hypertension subjects via three different techniques – SEQ technique, Alpha technique and the proposed VWL technique. In Figure 1, the BRS of hypertension subjects is 4.4±2.0 ms/mmHg for SEQ, 4.6±1.9 ms/mmHg for Alpha, and 2.9±1.6 ms/mmHg for the new VWL technique. For normal subjects, the BRS is 30.4±12.4 ms/mmHg for SEQ, 25.8±10.2 ms/mmHg for Alpha, and 17.5±7.7 ms/mmHg for the new VWL technique.

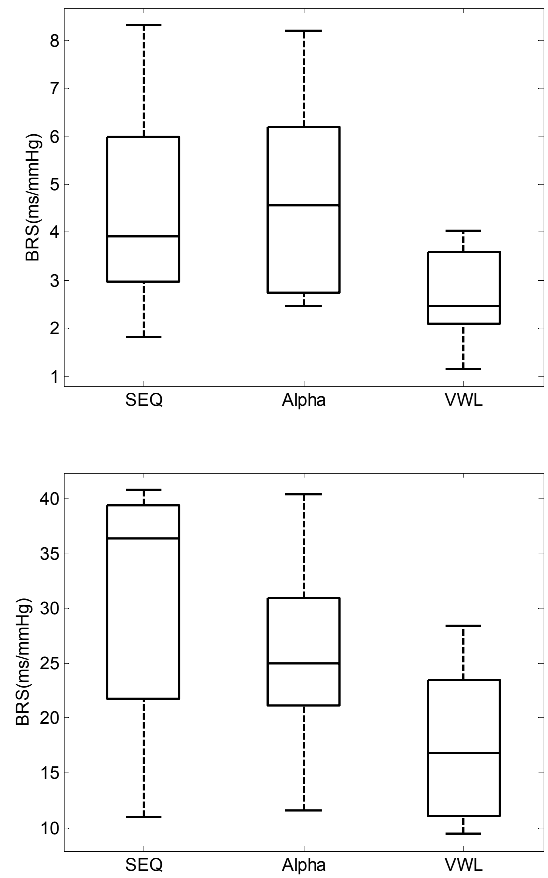

Figure 1. Comparison among BRS estimates using three techniques for normal and hypertension subjects at rest. Top panel: hypertension subjects, bottom panel: normal subjects. SEQ: sequence technique, Alpha: alpha coefficient technique, VWL: Volterra-Wiener model with Laguerre expansion technique.

The three descriptors of baroreflex are demonstrated in Table 1. The possible baroreflex delay between blood pressure and heart interval was identified, and has higher value in hypertension subjects. In addition, the baroreflex seems also to be with longer system memory depth and less nonlinearity in hypertension subjects.

Table 1. The baroreflex descriptors in normal and hypertension subjects

	normal	hypertension
Delay (sec)	1~2	1~5
Memory depth (sec)	9±4.5	18±7.1
Nonlinearity (%)	6.5±7.6	4.7±4.2

Table 2 demonstrates various BRS estimation results reported in the literatures concerning the difference between invasive phenylephrine method and noninvasive spontaneous BRS techniques with subjects suffered from cardiovascular or other diseases. All values are mean±SD

Table 2. Estimates of BRS by phenylephrine method (Phe) , sequence technique (SEQ) and alpha coefficient technique (Alpha) presented in literatures (unit in ms/mmHg)

	Phe	SEQ	Alpha
Nollo et al. [11]	6.43±4.73	12.56±7.06	
Lipman et al. [12]	7.62±4.42	10.44±6.98	11.10±4.37
Hartikainen et al. [13]	5.1±4.3	7.1±6.5	
Pitzalis et al. [14]	10.57±7	11.55±8	12.56±9

4. Discussion and conclusions

Up to date, although still controversial, the most accepted gold standard technique to measure BRS has been the phenylephrine method. Refer to Table 2, all results indicated that the phenylephrine method gives lower BRS estimates than that of the sequence technique and the alpha coefficient technique for 10%~50%. In this study, our new technique also yields a reasonable lower BRS estimates than that of the sequence technique and the alpha coefficient technique, which consistent with the cognition that the BRS is overestimated by many existing noninvasive BRS techniques. In addition, based on Gribbin et al. [15], the VWL technique can obtain comparable results in normal subjects.

This paper proposed a new spontaneous BRS analysis technique which can produce BRS estimate and other descriptors about baroreflex without extra constrains compared with the sequence technique and the alpha coefficient technique. The technique implicitly considers the effect of probable baroreflex delay. It is similar to the cross-correlation method which takes into account the delay between SBP and RRI when applied to BRS estimation. In the future, we need to make more data analysis to verify the effectiveness of this new technique. Moreover, because the way of least-squared fitting and AIC protocol decide the estimation accuracy, these parts need to be improved to enhance the robustness of present new BRS estimation technique.

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