Estimation of baroreflex sensitivity using pulse arrival time rather than systolic blood pressure measurement

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Abstract

Baroreflex sensitivity (BRS) is a parameter of the cardiovascular system that is reflected in changes in pulse interval (PI) and systolic blood pressure (SBP). BRS contains information about how the autonomic nervous system regulates hemodynamic homeostasis. Normally the beat-to-beat SBP measurement and the pulse interval measured from the electrocardiogram (ECG) are required to estimate the BRS. We investigated the possibility of measuring BRS in the absence of a beat-to-beat SBP measurement device. Pulse arrival time (PAT), defined as the time between the R-peak of the ECG and a single characteristic point on the pulse wave recorded from any arterial location was measured by photoplethysmography. By comparing the BRS obtained from conventional measurements with our method during controlled breathing, we confirmed again that PAT and SBP are closely correlated, with a correlation coefficient of -0.82 to -0.95. The coherence between SBP and PI at a respiration frequency of 0.07-0.12 Hz was similar to the coherence between PAT and PI. Although the ranges and units of measurement are different (ms/mmHg vs. ms/ms) for BRS measured conventionally and by our method, the correlation is very strong. Following further investigation under various conditions, BRS can be reliably estimated without the inconvenient and expensive beat-to-beat SBP measurement.

Key words : Baroreflex sensitivity, pulse arrival time, systolic blood pressure

I. INTRODUCTION

At present, there are no firm standards or protocols for the measurement or analysis of baroreflex sensitivity (BRS). Many reports suggest that BRS may be a risk factor for several cardiovascular diseases, such as congestive heart failure and myocardial infarction [1]. The definition of BRS as the slope of PI/SBP sequences includes only changes in pulse interval (PI) and systolic blood pressure (SBP). This relationship makes the BRS value more consistent than SBP or PI alone, which are single values in a single domain. The ratio of PI's and SBP's can be thought as the gain of the cardiac control system between the neural domain (heart rate control) and mechanical domain (pressure). BRS contains more information than heart rate variability (HRV), which mainly reflects the activity levels of the autonomic nervous system.

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Most BRS studies use noninvasive, continuous, beat-to-beat blood pressure signals to measure SBP, and electrocardiograms (ECG) to measure PI. Two well-known methods are used to calculate BRS from these measurements. The sequence technique makes calculations in time domain, and the spectral technique operates in the frequency domain [2]. Changes in BRS can be observed under several physiological conditions, such as postural changes from lying to standing, in head-up tilting, and with controlled breathing [3]. Estimations of BRS in either the time domain or the frequency domain methods require at least two signals, inter-pulse intervals (PI) in milliseconds and beat-to-beat systolic blood pressure in mmHg. PI is quite easy to measure and calculate from the ECG. To obtain beat-to-beat SBP time series noninvasively, volume compensation and tonometer methods have been used [4], but the instruments are complicated and expensive.

We assess the possibility of measuring BRS using pulse arrival time (PAT) without beat-to-beat measurement of SBP. Arterial stiffness, pulse wave velocity and pulse transit time are strongly correlated with SBP [5]. Using the pulse wave

(pressure or volume) at any arterial site recorded by photoplethysmography (PPG) and the time difference between the R-peak of ECG and any specific point in the PPG, it is simple to calculate the pulse arrival time (PAT) from the left ventricle to the measuring site as shown in Fig. 1. At higher values of SBP, the pulse wave velocity increases while PAT decreases, because this distance is fixed. Just as many factors are involved in blood pressure change, so there are many factors affecting PAT. Our experiment focused on the association between SBP, PAT, respiration, and heart rate. By recording ECG (PI) and beat-to-beat SBP and PAT simultaneously, we calculated and compared BRS values obtained by conventional methods and our technique.

II. METHODS

A. Measurements

The ECG was recorded from the chest and abdomen, blood pressure by noninvasive beat-to-beat measurement from the wrist (left), and PPG from the middle finger (right hand). Typical signals are shown in Fig. 1. The analog blood pressure waveform (Tonometer, CBM-7000, Colin, Japan) was sampled and digitized. ECG electrodes (with an amplifier gain = 2000, band pass filtered between 0.05 and 35 Hz), PPG (bandpass filtered between 0.05 and 35 Hz), and a respiration belt transducer were attached, and the signals sampled using the MP150W (Biopac Co., USA) system. All signals were

sampled at 1000 Hz and analyzed with our own program with Matlab®. PI was calculated from the ECG R-peak and plotted with interpolation for analysis in the frequency domain. SBP was measured by detecting the local maximum value of the blood pressure wave. PAT was calculated by measuring the time difference between the ECG R-peak and the characteristic point in the PPG signal corresponding to each pulsation of the heart. The method of measurement for SBP, PI, and PAT is illustrated in Fig. 1. The characteristic point in this study was taken as the steepest ascending region in each systolic pulse of the PPG signal.

The measurements were made in two postures. Before measurement, the subject lay supine for 10 minutes to allow breathing to settle. Sound cues were used to help subjects control their breathing. The subject was requested to inspire during the higher tone and expire during the lower tone. After the adaptation period, the subject was required to breathe with a 10-second period using the sound cues. Ten minutes of data were collected with the subject supine, and then 10 minutes of data were collected with the subject standing. Throughout the measurements, the height of the sensor on the wrist and the height of PPG sensor were both kept level with the heart. Five male subjects participated in the study. The average age was 27.4 years (range 23-38 years), and the average weight was 81.8 kg (range 70.1 - 90.2 kg). None of the subjects had a history of cardiovascular disease.
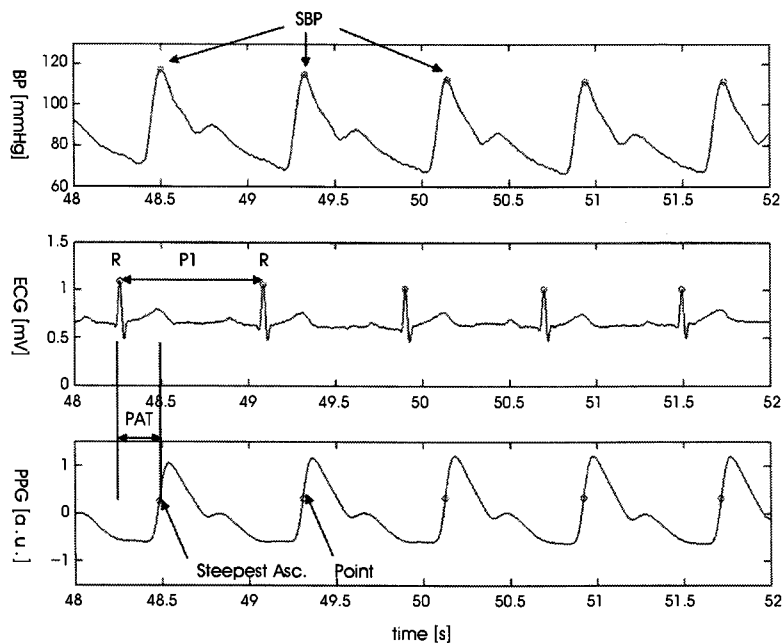

Fig. 1. The measurement of PI, SBP and pulse arrival time (PAT) from ECG R-peaks.

B. Analysis

Figure 2 shows the waveforms for PI(i), SBP(i), and PAT(i) for a 40-second period, where i represents the ith heartbeat. In the phenomena known as respiratory sinus arrhythmia [6] and pulsus paradoxus, PI and SBP oscillate with the cycle of breathing with a period, in this case, of about 10 seconds. PAT also fluctuates near the frequency as breathing with some phase lag. Our results confirm that PAT is inversely proportional to SBP [7].

The average of the slope between PI increments (or decrements) and SBP increments (or decrements) is the BRS value (units are ms/mmHg) in the sequence method. The slope between PI increment and PAT decrement is the alternative, new method to assess BRS, but the phase difference between PI and PAT signal is not consistent in all conditions. Therefore, we used the power spectrum method to compare the conventional method with the new method. As shown in Fig. 2, PIs are interpolated and sampled at 10 Hz to calculate the power spectrum between 0.07 and 0.12 Hz. The technique is almost the same as for low frequency power in the heart rate variability (HRV) analysis [8]. The power spectrum of the SBP signal was calculated in a similar way using an interpolation and re-sampling process and spectrum estimation with a nonparametric method. For time series of PI(t), let the power spectrum between 0.07 and 0.12 Hz be $POW_{PI}(f)$. In addition, from the re-sampled SBP time series SBP(t), the power spectrum at the same frequency range can be calculated as $POW_{SBP}(f)$. The α coefficient for the conventional method can be written as:

$$\alpha_c = \sqrt{\frac{POW_{PI}(f)}{POW_{SBP}(f)}} \qquad (1)$$

The coherence between PI(t) and SBP(t) was checked in this frequency range using the following equation, where $POW_{PI\_SBP}(f)$ is the cross power spectrum and $POW_{PI}(f)$ and $POW_{SBP}(f)$ represent the power spectrums of PI(t) and SBP(t), respectively.

$$C_{PI\&\,SBP}(f) = \frac{|POW_{PI\_SBP}(f)|^2}{POW_{PI}(f) \cdot POW_{SBP}(f)} \qquad (2)$$

The resampled time series of PAT(t), the power spectrum $POW_{PAT}(f)$ from 0.07 and 0.12 Hz can be calculated in a similar way, with the α coefficient of the suggested method written as:

$$\alpha_N = \sqrt{\frac{POW_{PI}(f)}{POW_{PAT}(f)}} \qquad (3)$$

We can evaluate the viability of our method by comparing the α coefficient and coherence from the conventional method with our method.[2] The power spectrum was estimated using the nonparametric method with a re-sampling frequency of 10 Hz after cubic interpolation. A Hanning window was used for five minutes of data.
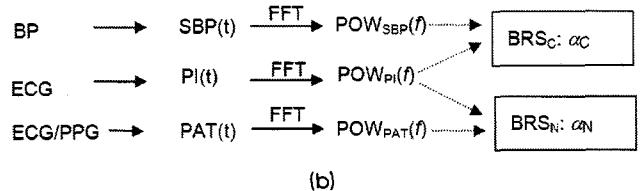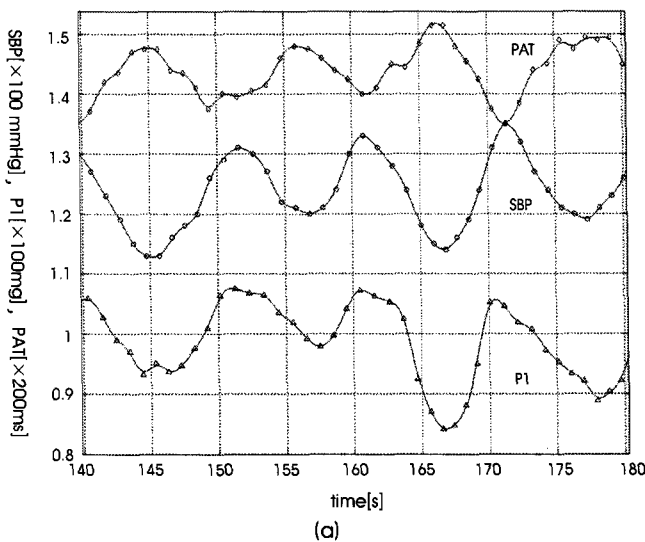

Fig. 2. (a) A 40-second sample of measurements. PI, SBP and PAT oscillate with respiratory movements. Triangles represent the instant of the R-peak; circles represent the SBP from the blood pressure waveform, and diamonds represent the steepest ascending regions of PPG. (b) This diagram illustrates the flow of signal processing used to calculate BRS in the conventional way, and in our method.
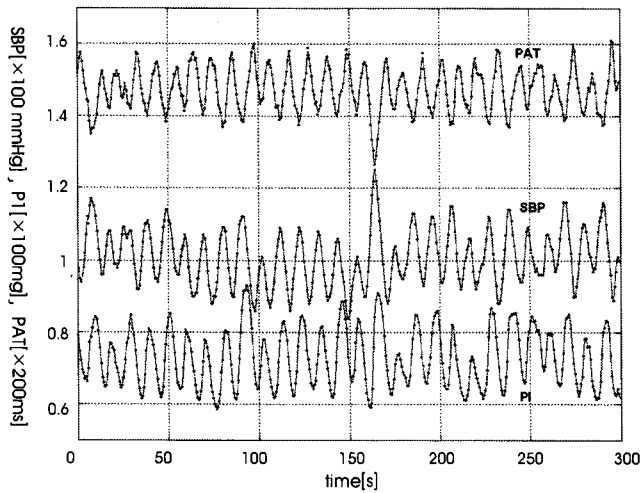
Fig. 3. PI(t), SBP(t) and PAT(t) for 300 seconds in one subject. PAT is inversely proportional to SBP
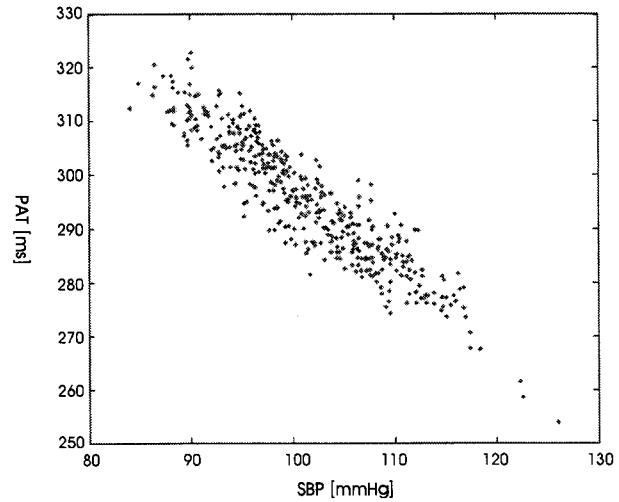

Fig. 4. Correlation plot between SBP and PAT for the data in Fig. 3. The correlation coefficient is -0.83.

III. RESULTS

Figure 3 shows the preprocessed PI(t) signal obtained from the ECG, the SBP(t) from tonometer measurements and the PAT(t) obtained from PPG and ECG over a five-minute period. The subject was required to breathe to the sound-cue rhythm. Note that the three signals oscillate in time with respiration. The variation in PI in this case was closely related to the respiratory sinus arrhythmia. The SBP oscillation is related to the pulsus paradoxus, caused by changes in thoracic pressure from breathing movements. PAT is inversely proportional to SBP, as can be seen in this figure (the top and middle signals). The phase difference between these signals is always approximately 180 degrees.

Figure 4 shows the correlation plot for the SBP and PAT data shown in Fig. 3. The correlation coefficient is -0.83. As there are many other factors affecting SBP and PAT, this relationship is valid only over a short time, and cannot be generalized to other subjects, or to other conditions in the same subject. This plot shows that BRS analysis is possible over a short period using either SBP or PAT.

The coherence between PI and SBP should be checked before performing the spectral analysis, and the value should exceed 0.5. The coherence between these signals at around the respiration frequency (0.07 Hz $< f < 0.12$ Hz) was calculated using equations (2). The results are summarized in Table 1. The coherence value between PI and SBP is similar to the coherence value between PI and PAT. This is further evidence that PAT can be used to assess BRS instead of SBP.

It is not possible from these preliminary results to determine the stochastic relationship between BRSc (the conventional calculation) and BRSN (the new calculation). Fig. 5 shows that

Table 1. BRS values and coherence between supine and standing postures.

Posture		S1	S2	S3	S4	S5
Supine	BRSc (a_C)	23.16	18.35	26.57	25.90	8.01
	BRSN (a_N)	10.36	8.21	11.00	9.85	9.87
	CPI&SBP	0.78	0.77	0.88	0.75	0.89
	CPI&PAT	0.74	0.76	0.82	0.76	0.88
Standing	BRSc (a_c)	11.20	10.90	8.88	9.92	4.20
	BRSN (a_N)	8.47	6.45	7.56	6.21	5.69
	CPI&SBP	0.88	0.84	0.77	0.55	0.87
	CPI&PAT	0.65	0.87	0.75	0.51	0.88

Note: BRSc is the a value from the conventional spectral technique using PI and SBP. BRSN is calculated from PI and PAT without SBP. CPI&SBP represents the coherence value between PI and SBP, CPI&PAT represents the coherence value between PI and PAT.

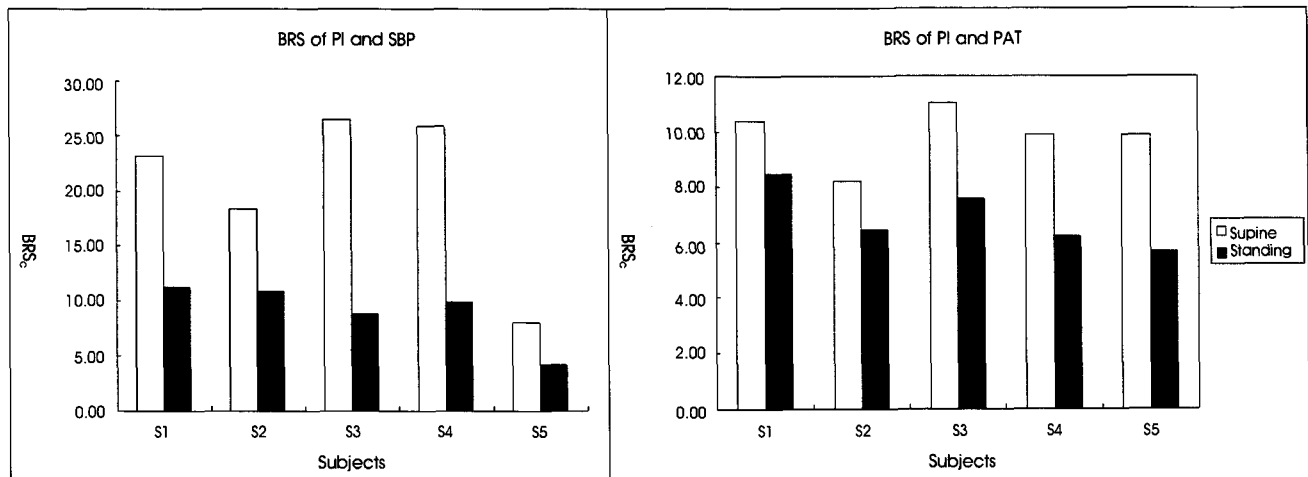**Fig. 5.** BRS values in two postures for both methods. Plot of Table 1. BRS$_C$ is the α value obtained using conventional spectral technique with PI and SBP. BRS$_N$ is calculated from PI and PAT without SBP.

the higher values of BRS$_C$ match the higher values of BRS$_N$. The BRS$_C$ values in supine and standing postures have a similar range to other reported values [9]. For example, BRS$_C$ decreases in standing posture, as does BRS$_N$, as shown in Table 1. BRS$_C$ can be defined as the slope of the relationship between pulse interval change and SBP change. In the new method, BRS$_N$ is the slope of the relationship between PI and PAT. Therefore, BRS$_C$ cannot be converted to BRS$_N$ directly. However, the graph in Fig. 5 shows that equivalent information can be extracted from BRS$_C$ and BRS$_N$.

IV. DISCUSSION

SBP measurement is complicated and the required instruments are expensive. For these reasons, we attempted to determine whether PAT can be substituted for SBP in calculating BRS. A number of estimates of SBP using the information from PAT have been made, but the correlation between SBP and PAT was not good enough for long-term measurements. The variance between subjects is very large because many parameters affect PAT other than SBP. However, previous reports and our results show that the correlation between PAT and SBP is high over short periods. By the definition formula of BRS, it considers only the amount of changes in PI and SBP over the short periods. Therefore, PAT may be used instead of SBP for the assessment of BRS if frequent calculations are made.

It is difficult to describe the relationship between BRS$_C$ and BRS$_N$ directly. As we can see in Fig. 5, data from all subjects showed that BRS$_C$ and BRS$_N$ decreased, but the decrement was not consistent. For example, subject 5 had a BRS$_N$ value

that was similar to other subjects but a BRS$_C$ value that was much lower. This suggests that there is not a fixed, generalized formula for converting BRS$_N$ to BRS$_C$. The HRV parameters, pulse wave velocity and blood pressure, are influenced by many kinds of physiological variables, just as is the case for BRS. The clinical assessment of BRS requires a strictly controlled measurement situation. Because the experiment in this study was done while conditioning breathing cycle, we believe that under controlled conditions, BRS$_N$ can be used to demonstrate short-term changes in SBP. With long-term monitoring, such as sleep or daily monitoring, BRS calculated from PAT has the advantages of a small measuring device, convenience and cost effectiveness. The measurements should be taken and calculations made every five minutes.

We used photoplethysmography to detect the pulsation point. Because only the precise timing is needed, rather than absolute physical values, other types of simple transducers such as cuffs or piezoelectric transducers could also be used also.

Further tests are required to fully assess our method. In our experiments, subjects were supine or standing with no other cardiovascular stimulation, and other conditions need to be examined. Respiration has the largest effect on blood pressure and heart rate in our experiments. In the conventional sequence technique used to calculate BRS, the slope is determined by respiration. In spectral analysis, respiration can be considered or excluded according to the aims of the experiment. BRS clinical measurements require that the protocol and stimulation are be strictly controlled. Among the parameters that must be controlled are the period, volume of inhalation and air resistance. Further studies should include a

strict stochastic study with pathological subjects.

V. CONCLUSION

BRS can be assessed in controlled breathing using PAT instead of SBP because of the close correlation between PAT and beat-to-beat SBP. There are benefits to this method because SBP requires expensive instruments and is inconvenient to measure.

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