Determination of delay time in individual transfer function for central aortic pressure reconstruction

YU DanYang[1,2], XIANG HaiYan[3], LI DeYu[1], WANG YuQi[1] & YU MengSun[3*]

[1]*School of Biological Science and Medical Engineering, Beihang University, Beijing 100191, China;*
[2]*Department of Medical Engineering, the 201st Hospital of the Chinese Peoples's Liberation Army, Liaoyang 111000, China;*
[3]*Department of Aviation Medical Engineering, Institute of Aviation Medicine, Beijing 100142, China*

In previous research, time-delay (Δt) was a more important parameter than the reflection coefficient in the individual transfer function of central aortic pressure reconstruction. The Δt can be obtained by electrocardiography (ECG) or phonocardiography (PCG). Because the pre-ejection period remains an uncertain factor, the present study used ECG and PCG to define the delay time and analyzed the accuracy of the reconstruction results. The Δt_{pre} is the actual delay time derived from the aorta to the carotid pressure wave, Δt_{PCG} is the time delay between the aortic valve component of the second heart sound and the dicrotic incisura of the carotid pressure wave, and Δt_{ECG} represents the delay from the interval of the ECG R-peak to the foot of the carotid pressure wave. Compared with the measured aortic pressure, the reconstruction result obtained by $\Delta t = \Delta t_{PCG}$ slightly differed from the best result estimated by $\Delta t = \Delta t_{pre}$. However, the differences between the result obtained by $\Delta t = \Delta t_{ECG}$ and the best result were significant in terms of the diastolic blood pressure, and pulse pressure, and especially in terms of the augmentation index and root-mean-square-error. Thus, the Δt should be determined by PCG for central aortic pressure reconstruction in practice.

central aortic pressure, delay time, PCG, ECG

Compared with peripheral pressure, central aortic pressure provides more valuable physiological information and has a closer relationship with cardiovascular risk. However, direct measurement of central aortic pressure is invasive and uncomfortable. Therefore, alternative methods to assess central aortic pressure have been adopted and can be classified into two different categories.

One category is based on a population-based model that uses a generalized transfer function (GTF) between aortic and peripheral pressure, such as carotid artery, brachial artery, and radial artery pressure [1–7]. Studies that use this model provide acceptable estimates of aortic mean blood pressure and diastolic blood pressure (DBP). However, the pressure waveform and systolic blood pressure (SBP) are not ideal because the GTF is equivalent to a low-pass filter that cuts the high-frequency components of the pressure signal.

The other category derives that the individualized transfer function (ITF) is better than the GTF by establishing a pressure transmission model from the aorta to a peripheral artery [8–11]. Hahn demonstrated a new time domain system identification approach to the reconstruction of central aortic pressure [8]. Lowe also developed a model based on the theory of pressure wave reflections [9]. Stergiopulos and Westerhof constructed central aortic pressure by ITF based on the same widely recognized theory [10,11]. The ITF in-

volves two parameters and is optimized for a particular subject. One parameter is the delay time, which represents the travel time of the pressure wave between the measurement site and the central aorta, and the other parameter is the reflection coefficient. It has been validated that the accuracy of the reconstructed central aortic pressure is more sensitive to errors in delay time than to errors in the characteristic impedance at the measurement site.

These methods suggest that the delay time can be determined between the electrocardiography (ECG) R-peak and the corresponding upstroke in peripheral pressure. Given that the pre-ejection period (PEP) remains an uncertain factor and that the real pressure wave delay time cannot be easily obtained by synchronous measurement of the central and peripheral pressures in human experiments, the present study used ECG and phonocardiography (PCG) to define the delay time and analyzed the accuracy of the reconstruction results in an animal experiment.

1 Materials and methods

1.1 Measurements

Invasive cardiovascular data were obtained from two 20-kg anesthetized swine subjects. Two percutaneous sheath introducers were placed in the bilateral femoral arteries; the right catheter was fed over a wire to the root of the ascending aorta changelessly, and the left catheter was fed to the left carotid artery. The locations of the catheters were validated by cardiovascular angiography. Invasive blood pressure (BP) signals were recorded from the indwelling catheters in the peripheral artery and aorta; the catheters were coupled via stiff, fluid-filled tubing to external BP transducers (TruWave PX; Edwards Life sciences, Irvine, CA, USA), that interfaced to an analog-to-digital (A/D) conversion system via an interface cable, creating an amplification circuit.

The piezoelectric PCG sensor has strong resistance to environmental noise. The sensor transforms mechanical vibration caused by opening and closing of the heart valve into electrical signals. In this study, these electrical signals and the two invasive BP signals were simultaneously measured with ECG at a sampling rate of 2000 Hz for each channel and digitized by a 16-bit A/D converter.

1.2 Calculations

The mathematical function used to describe the pressure reconstructed over a single uniform tube has two parameters [10,11]:

$$P_{rec}=P_{peri}\cdot\frac{1+\Gamma\cdot e^{-2j\omega\Delta t}}{(1+\Gamma)\cdot e^{-j\omega\Delta t}}, \tag{1}$$

where Γ represents the reflection coefficient at the peripheral site, taken to be real, and Δt represents the time delay between the peripheral artery and central aorta. According to eq. (1), the reconstructed ascending aortic pressure P_{rec} can be calculated by the peripheral pressure wave P_{peri}.

Some studies [12–15] used the ECG R-peak to compute the pulse transit time. However, R represents the ventricular electrical exciting time, not the true moment of ventricular ejection. The PEP includes the electro-mechanical interval of the latent period, preisovolumetric time, and isovolumetric contraction time, which can be altered by changing the human physiological and pathological conditions. Therefore, the exclusion of PEP could cause errors in the pulse transit time (i.e., delay time, Δt) [16]. The heart sound is an acoustic phenomenon caused by the mechanical events of the heart. Generally, only the first and second heart sounds (S1 and S2, respectively) can be perceived in a normal subject. S1 originates from closure of the mitral valve (M1) and tricuspid valve (T1). S2 originates from closure of the aortic valve (A2) and pulmonic valve (P2); A2 is prior to P2 in time [17,18]. The dicrotic incisura is the feature point of the reflection wave when the aortic valve shuts in a pressure waveform, and this study used the interval from the A2 of S2 to the notch to compute Δt.

For each subject, five cardiac cycle data were averaged. Method 1 is based on the Δt_{pre} between the foot of the ascending aortic and carotid pressure wave and eq. (1); by changing the value of Γ between 0.2 and 0.9 with steps of 0.05, the optimal Γ_{opt} was found, which can minimize the root-mean-square-error (RMSE) between the recovered and measured aortic pressure [11]. In Method 2, the Γ_{opt} and Δt_{PCG} derived from the A2 to the dicrotic incisura of the carotid pressure wave were used in eq. (1). Method 3 reconstructed the aorta pressure with the Γ_{opt} and Δt_{ECG}, which was the interval of the ECG R-peak to the foot of the carotid pressure wave. The reconstructed and aortic pressure waveforms were compared according to their RMSE, which was calculated as follows [10]:

$$RMSE=\sqrt{\frac{\Sigma(P_{aor}-P_{rec})^2}{N-1}}. \tag{2}$$

The augmentation index (AI) [19–22] quantifies the contribution of the reflected wave on the aortic pressure waves. The AI depends on ventricular ejection, the time of the reflected waves, and the amount of reflection. The aortic AI could indicate the stiffness of arteries and increases with age and blood pressure and is elevated in subjects with some risk factors for cardiovascular disease. The AI was calculated from the reconstructed results of the above three methods and compared with the AI of the ascending aortic pressure wave. Five measured cardiac cycle waves of Subject 1 are shown in Figure 1 to demonstrate the synchronous relations of each signal.
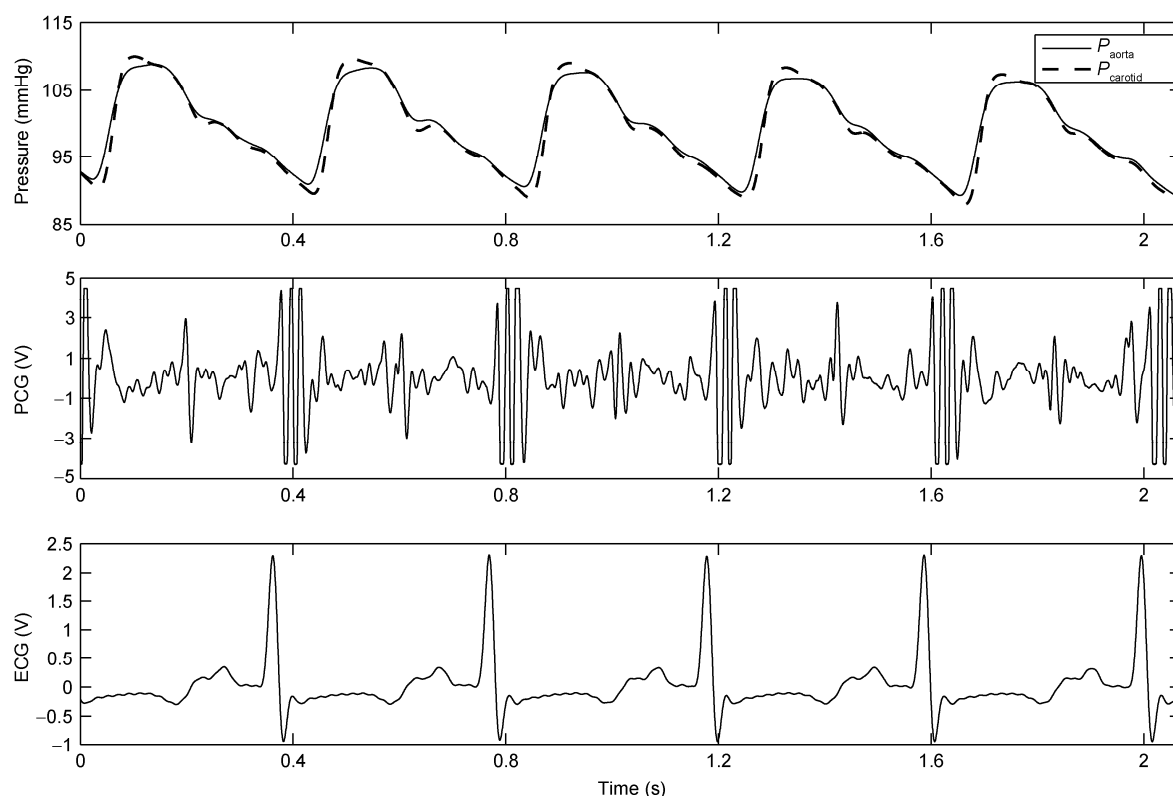
Figure 1 Five cardiac cycle signal waves. The first box shows the central and peripheral pressure; the solid line indicates the central aortic pressure, and the dashed line indicates the carotid aortic pressure. The second and third boxes are PCG and ECG, respectively.
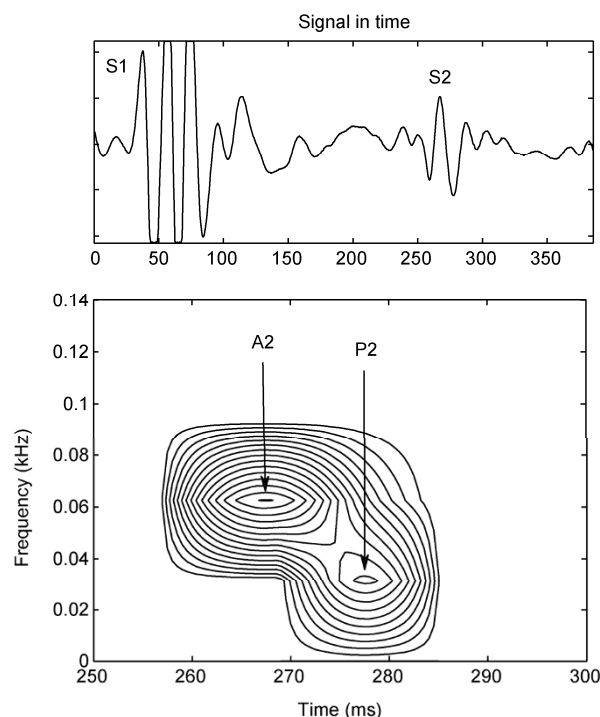
1.3 Identification of second heart sound

Identification of the A2 component is important to obtain the delay time Δt_{PCG} and the time-frequency analysis is a powerful tool for PCG signals. The fast Fourier transform can only provide a basic understanding of the frequency contents of the heart sounds [23]. Furthermore, the wavelet transform and short-time Fourier transform can provide more time-frequency characteristics of PCG [24–28]. We used a 1024 Hamming window to distinguish the two components, (A2 and P2) of S2 [18,23,24]. Figure 2 shows the time-frequency characteristics of S2.

2 Results

In Figure 3, the delay times using the three methods are shown. The mean values of two subjects' Δt_{pre}, Δt_{PCG}, and Δt_{ECG} were 23, 46, and 81 ms, respectively. The Δt_{PCG} and Δt_{ECG} were longer than the actual delay time Δt_{pre}. The Δt_{ECG} was the longest for including PEP.

Table 1 lists the measured ascending aortic and carotid pressure values together with the reconstructed pressure values using the three methods. The errors in the reconstructed results of Method 1 compared with the measured aorta values were 1.23±0.60 mmHg for SBP and −0.95±0.51 mmHg for DBP. The best results were obtained

Figure 2 Short-time Fourier transformation of second heart sound.

by Method 1 (with $\Delta t = \Delta t_{pre}$) and the results of Method 2 (with $\Delta t = \Delta t_{PCG}$) differed slightly from those of Method 1.
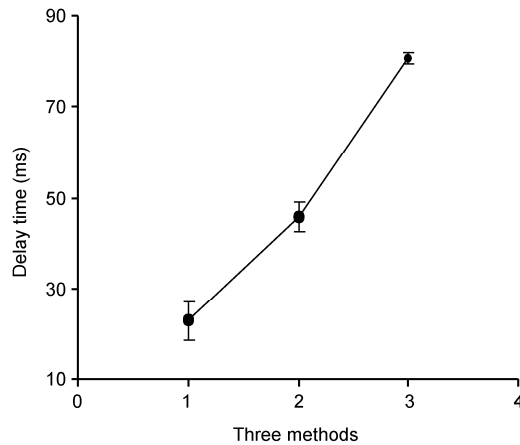
Figure 3   The delay time of two subjects. The 1, 2, and 3 represent the determination methods of the delay time by central aortic pressure, PCG, ECG and the carotid aortic pressure wave, respectively. The dots and error bars at 1, 2, and 3 represent the mean±standard error of Δt_{pre}, Δt_{PCG} and Δt_{ECG}, respectively.

However, the differences in the DBP, PP, AI, and RMSE of Method 3 (with $\Delta t=\Delta t_{ECG}$) were significant, especially for AI and RMSE.

The reconstructed results from the three methods are given in Figure 4. In both subjects, the results of Method 2 (with $\Delta t=\Delta t_{PCG}$) were similar to the results of Method 1 (with $\Delta t=\Delta t_{pre}$), which was the most accurate method with which to reconstruct the aorta. However, Method 3 (with $\Delta t=\Delta t_{ECG}$) gave the worst results; the waveforms of the reconstructed aortic pressure changed obviously and had no secondary rise.

3   Discussion

Previous research [10,11] only emphasized that the time-delay was the key parameter in pressure reconstruction and could be measured by ECG and PCG signals in practical application. The present study showed that the method using the measured Δt and averaged Γ was the simplest way to obtain results as accurate as those using the individualized Γ. Importantly, however, there is a considerable delay between the onset of electrical cardiac activity on ECG and the start of mechanical ventricular ejection [15]. This delay is the PEP, which comprises the electromechanical delay and the period of isovolumic contraction.

Thus, this study confirmed the distinction of the reconstructed results computed by PCG and ECG and concluded that the optimal determination of the delay time is based on PCG. Further, the delay time was the interval from the A2

Table 1   Aortic, carotid, and reconstructed pressures[a]

	Measured		Reconstructed		
	Aorta	Carotid	Method 1 $\Delta t=\Delta t_{pre}$	Method 2 $\Delta t=\Delta t_{PCG}$	Method 3 $\Delta t=\Delta t_{ECG}$
SBP	109.6±2.3	110.3±1.7	108.4±2.6	108.1±1.3	105.9±3.9
DBP	92.4±2.7	91.8±3.3	93.3±2.2	93.1±2.8	97.9±2.2
PP	17.2±0.6	18.5±1.8	15.0±0.5	15.0±1.7	8.1±1.8
AI	−3.0±2.1	−10.9±4.2	−7.1±2.5	−7.8±3.9	−30.7±13.9
RMSE		1.61±0.57	1.36±0.35	1.62±0.32	5.22±1.21

a) Aorta, ascending aortic pressure; Carotid, carotid pressure; Δt_{pre}, time delay between ascending aorta and carotid; Δt_{PCG}, time delay from the A2 of S2 to the dicrotic incisura of the carotid pressure wave; Δt_{ECG}, interval of ECG R-peak to the foot of the carotid pressure wave; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; AI, augmentation index; RMSE, root-mean-square-error.
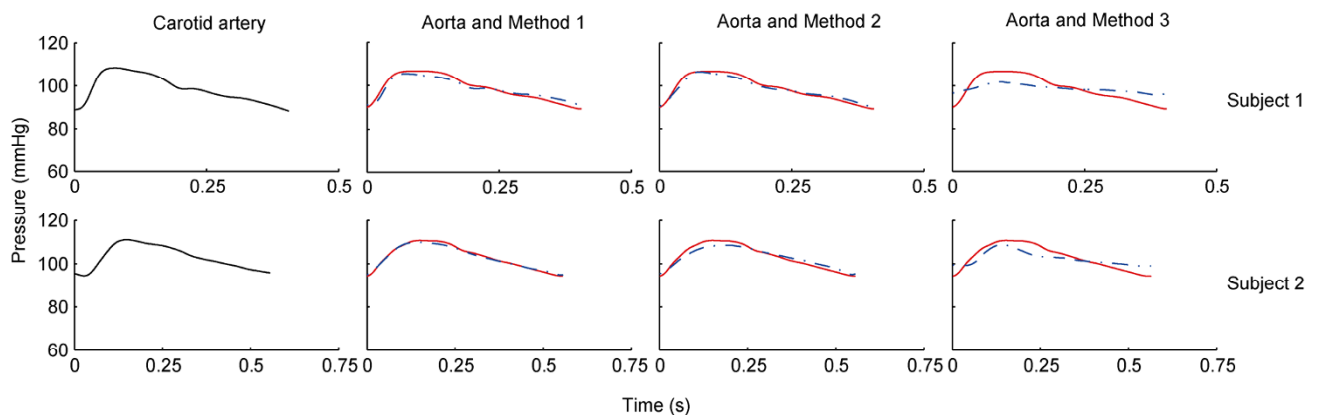
Figure 4   Reconstructed results from the three methods. The first column shows the carotid pressure; the others are the ascending aortic pressure (drawn) with the reconstructed pressure (dashed) using the three methods.

of the second heart sound to the notch of the peripheral pressure wave. We determined the moments of cardiac mechanical events by the heart sounds.

Figure 3 shows that both Δt_{PCG} and Δt_{ECG} are longer than the actual delay time Δt_{pre}, and that Δt_{ECG} is the longest interval. Given the Δt_{pre} must be obtained invasively, we used Method 1 only to explain the accuracy of Methods 2 and 3. Compared with Method 1, the reconstructed aortic pressure from Method 3 (with $\Delta t = \Delta t_{ECG}$) showed significant changes on the waveform and errors in DBP, PP, and AI. Nevertheless, the estimated result from Method 2 (with $\Delta t = \Delta t_{PCG}$) showed an ideal waveform and only slight errors in pressure values. The reconstructed result obtained by Method 2 (with $\Delta t = \Delta t_{PCG}$) was better than that obtained by Method 3 (with $\Delta t = \Delta t_{ECG}$).

Because patients who undergo cardiovascular angiography rarely receive two catheters, we conducted this animal experiment to simultaneously measure central and peripheral pressures. The use of animals is a limitation of this study, and the validity should be tested further in human experiments. The individual delay time obtained by PCG and the averaged Γ can then be used to reconstruct the central aortic pressure.

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