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Robust, Beat-to-Beat Estimation of the True Pulse Transit Time from Central and Peripheral Blood Pressure or Flow Waveforms Using an Arterial Tube-Load Model

Guanqun Zhang, Mingwu Gao, Ramakrishna Mukkamala, *Member, IEEE*

***Abstract*—We proposed a technique for estimating beat-to-beat pulse transit time (PTT) from central and peripheral blood pressure or flow waveforms based on an arterial tube-load model of wave reflection. The technique effectively estimates PTT from the entire waveforms after mathematically eliminating the reflected wave. So, unlike the conventional foot-to-foot detection technique, this technique should be robust to artifact while revealing the true PTT (i.e., the PTT in absence of wave reflection). We compared the two techniques, as applied to blood pressure and flow waveforms, in terms of the ability of their PTT estimates to correlate with blood pressure (a) during baseline (for which the naturally occurring beat-to-beat changes were small), (b) during low heart rate (wherein wave reflection was profound), and (c) in the presence of actual measurement artifact. In all three cases, the PTT estimates of the arterial tube-load model technique yielded markedly superior correlation to blood pressure.**

I. Introduction

PULSE wave velocity (PWV) through the aorta is a useful marker of large artery stiffness that is relatively easy to measure [1]. Conventionally, PWV is measured as the ratio of the distance and pulse transit time (PTT) between central and peripheral arteries. PTT is, in turn, estimated by measuring blood pressure or flow waveforms at these two sites via non-invasive transducers and detecting the foot-to-foot time delay between the pair of waveforms.

The assumption underlying the foot-to-foot detection technique is that the foot of the central waveform represents a time before the return of the reflected wave to its measurement site. However, wave reflection may not always be negligible at the central waveform foot. For example, at low heart rate (HR), the reflected wave adds constructively to the forward wave. Thus, in this case, the technique can grossly underestimate PTT [2]. Further, this technique is not robust to the artifact typically present in the non-invasive waveforms. These two drawbacks of the foot-to-foot detection technique limit the utility of PWV.

In a previous study, we proposed a technique to estimate PTT using an arterial tube-load model of wave reflection [3]. First, the transfer function relating a measured central blood pressure waveform to a measured peripheral blood pressure waveform is defined in terms of the unknown parameters of the model. One of these parameters represents the PTT between the two measurement sites. Then, all of the parameters are estimated by optimal coupling of the two waveforms. So, PTT is effectively estimated from the entire waveforms, rather than just their feet, after mathematically eliminating the reflected wave. In this way, the technique should be more robust to artifact while revealing the true PTT (i.e., the PTT in absence of wave reflection). We applied the technique to high fidelity, invasive central aortic and femoral artery blood pressure waveforms measured during various interventions. Since there is no independent way to measure the true PTT, we evaluated the technique in terms of the ability of its PTT estimates to predict changes in blood pressure – the main, acute determinant of large artery stiffness. We found that the PTT estimates yielded cycle averaged blood pressure prediction errors that were ~15% smaller than those of the foot-to-foot detection technique.

In this study, we extended and further evaluated the arterial tube-load model technique for PTT estimation. Our new contributions here were specifically to demonstrate: (1) the ability of the technique to estimate cycle-to-cycle or beat-to-beat PTT; (2) the ability of the technique to provide useful estimates of PTT at low HR when the foot-to-foot detection technique totally fails; (3) the applicability of the technique to blood flow waveforms; and (4) the robustness of the technique to actual measurement artifact.

II. Methods

A. Arterial Tube-Load Model Technique

The arterial tree is modeled as a parallel arrangement of m uniform tubes with terminal loads as illustrated in Fig. 1a. The i^{th} tube represents the wave travel path between the central aorta and the i^{th} peripheral artery. Each tube has constant characteristic impedance (Z_{ci}) and allows waves to travel with constant time delay between the tube ends (T_{di}), both of which are determined by the large artery inertance and compliance. Note that T_{di} represents the true PTT between the central aorta and the i^{th} peripheral artery. The i^{th} load represents the arterial bed distal to the i^{th} peripheral artery. Each load has frequency-dependent impedance ($Z_i(\omega)$), which is determined by the small artery resistance (R_i) and compliance (C_i) while matching Z_{ci} at ∞ frequency.

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G. Zhang is with the Department of Electrical and Computer Engineering, Michigan State University, East Lansing, MI 48824 USA (e-mail: zhanggu2@msu.edu).

M. Gao is with the Department of Electrical and Computer Engineering, Michigan State University, East Lansing, MI 48824 USA (e-mail: gaomingw@msu.edu).

R. Mukkamala is with the Department of Electrical and Computer Engineering, Michigan State University, East Lansing, MI 48824 USA (phone: 517-353-3120; fax: 517-353-1980; e-mail: rama@egr.msu.edu).

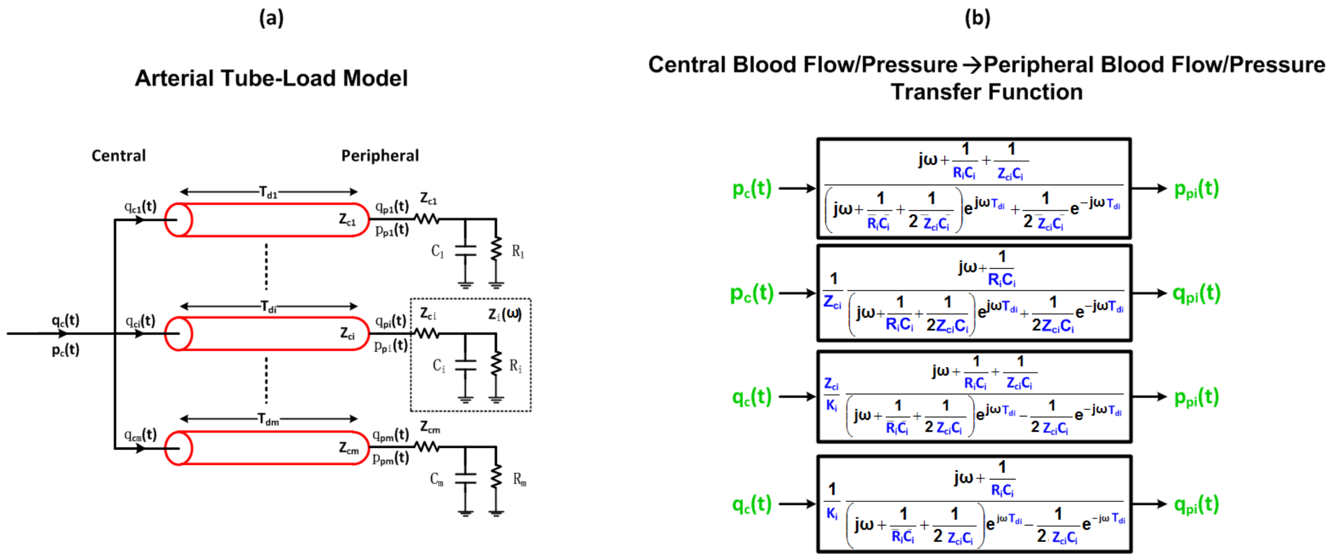

Fig. 1. Arterial tube-load model technique for estimating pulse transit time (PTT) from central and peripheral blood pressure or flow waveforms.

Waves traveling in the forward direction are reflected in the backward direction at the terminal load with relative magnitude and phase based on frequency per the wave reflection coefficient $((\Gamma_i(\omega)=(Z_i(\omega)-Z_{ci})/(Z_i(\omega)+Z_{ci}))$. Blood pressure or flow waveforms at the tube ends may therefore be expressed as the sum or difference of the forward and backward waves after time shifting by T_{di} when appropriate. From these expressions, transfer functions relating tube entrance (central) blood pressure or flow ($p_c(t)$ and $q_{ci}(t)$) to tube termination (peripheral) blood pressure or flow ($p_{pi}(t)$ and $q_{pi}(t)$) may be defined in terms of the unknown model parameters as shown in Fig. 1b. Note that total central blood flow ($q_c(t) = \sum_{i=1}^{m} q_{ci}(t)$) is utilized in place of $q_{ci}(t)$ here, as only the former is measurable. The assumption is that $q_{ci}(t)$ is proportional to $q_c(t)$. Importantly, however, the unknown proportionality constant (K_i) can vary from beat to beat.

To estimate beat-to-beat PTT, first, central and peripheral blood pressure or flow waveforms are measured. Then, all model parameters (T_{di}, R_iC_i, and $Z_{ci}C_i$ as well as Z_{ci}, Z_{ci}/K_i, or K_i when blood flow waveforms are measured) are estimated by finding the appropriate tube-load model transfer function in Fig. 1b, which when applied to one beat of the measured central waveform, optimally fits the corresponding segment of the measured peripheral waveform. This optimization is achieved by a least squares search over a physiologic range of the parameters. Finally, PTT for the beat is given as the T_{di} estimate.

B. *Technique Evaluation*

To evaluate the technique, we studied invasive data previously collected from anesthetized animals. The data collection procedures are described in detail elsewhere [4, 5]. We specifically analyzed (a) high fidelity central aortic and femoral artery blood pressure waveforms simultaneously measured from a dog during a baseline period and low rate ventricular pacing achieved via AV node ablation and (b) central aortic blood flow and femoral artery blood pressure waveforms simultaneously measured from a swine before and after the infusion of several hemodynamic drugs. The blood flow waveform happened to be contaminated by enough real measurement artifact to obfuscate the detection of its feet.

We applied the technique to these waveforms to estimate PTT for each beat. We then evaluated the estimates through the correlation coefficient (r) between their reciprocals (1/PTT) and diastolic pressure (DP). For comparison, we applied various versions of the foot-to-foot detection technique and likewise evaluated them.

III. Results

Fig. 2 shows plots of DP versus the 1/PTT estimates for each beat from the high fidelity canine blood pressure waveforms during the baseline condition; Fig. 3 shows plots of DP and HR versus the 1/PTT estimates averaged over 15-sec intervals from the same canine waveforms but during the low HR condition; and Fig. 4 shows plots of DP versus the 1/PTT estimates averaged over 15 sec-intervals from the swine blood flow and pressure waveforms during the baseline and drug conditions. In all cases, the PTT estimates of the arterial tube-load model technique yielded visually and quantitatively superior correlation to DP than those of the best foot-to-foot detection technique. Most notably, during the low HR condition, the former technique revealed strong positive correlation, whereas the latter technique showed erroneous negative correlation indicative of increasing underestimation of PTT as HR decreased.

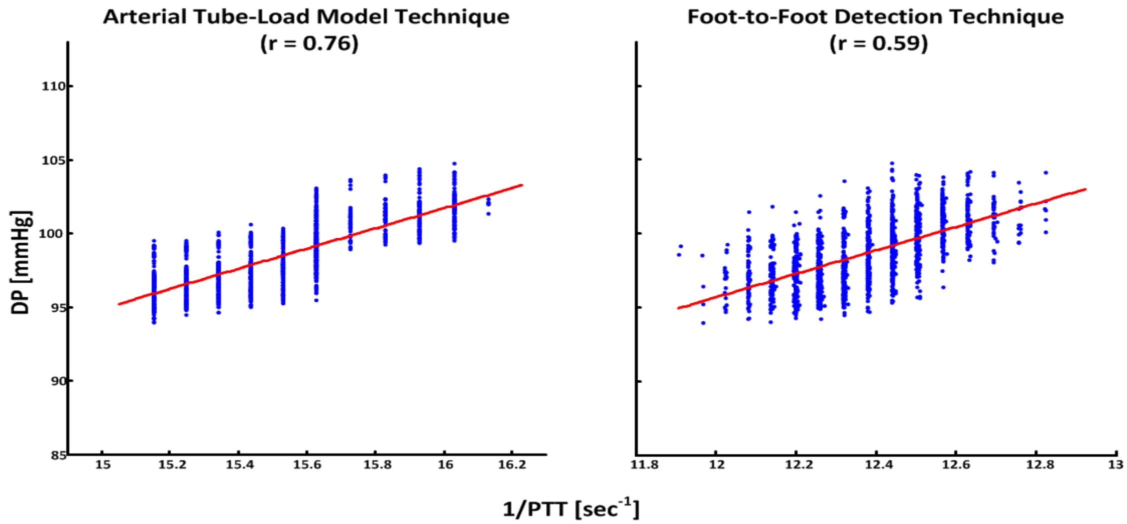

Fig. 2. Comparison of PTT estimates obtained from high fidelity blood pressure waveforms during the baseline condition in terms of correlating with beat-to-beat diastolic pressure (DP).

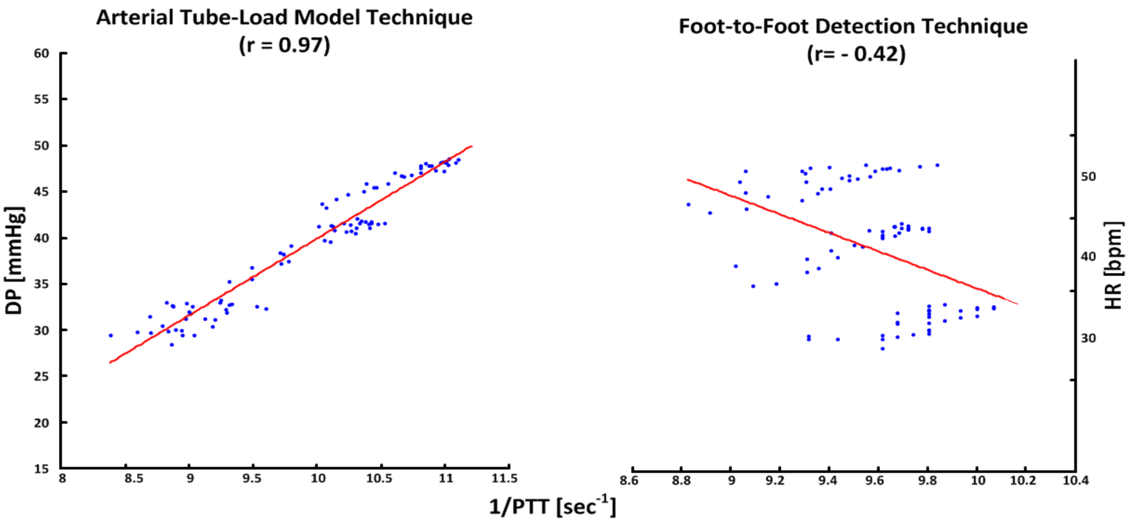

Fig. 3. Comparison of the PTT estimates obtained from high fidelity blood pressure waveforms during the low heart rate (HR) condition in terms of correlating with average DP.

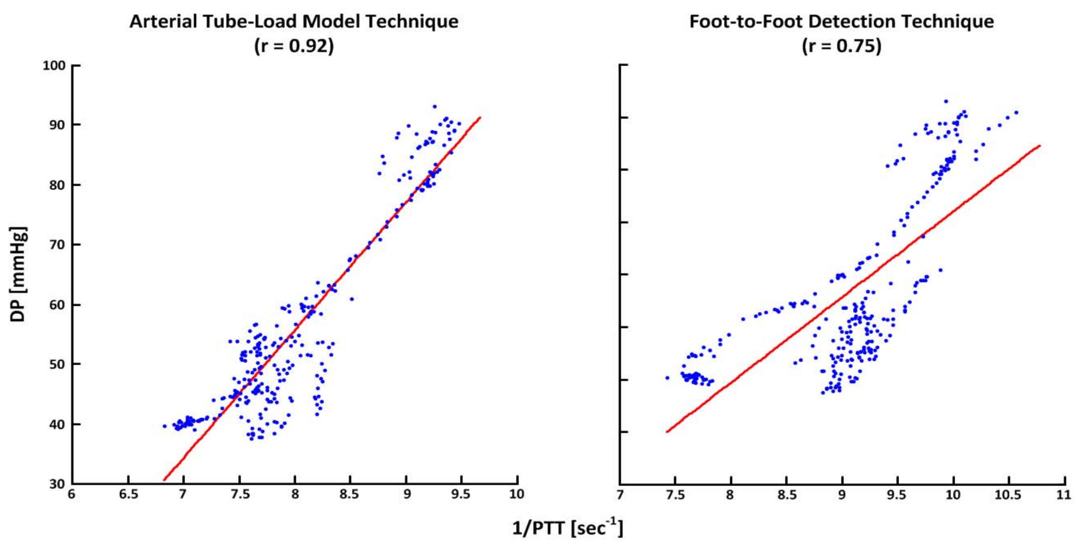

Fig. 4. Comparison of the PTT estimates obtained from lower fidelity blood flow and pressure waveform during the baseline and several drug conditions in terms of correlating with average DP.

IV. Discussion

In summary, we proposed a technique for estimating beat-to-beat PTT from central and peripheral blood pressure or flow waveforms using an arterial tube-load model. The technique effectively estimates PTT from the entire waveforms after mathematically eliminating the reflected wave. So, unlike the conventional foot-to-foot detection technique, this technique should be robust to artifact while revealing the true PTT. We demonstrated that the arterial tube-load model technique, as applied to blood pressure and flow waveforms, can indeed provide markedly better PTT estimation than the conventional technique when wave reflection is profound (low HR condition) and the effective signal-to-noise ratio is not high (presence of actual non-trivial waveform artifact and baseline condition in which the naturally occurring beat-to-beat changes were small).

We described the arterial tube-load model technique in the context of simultaneously measured waveforms. However, PTT is also often obtained from sequential measurements of the waveforms using the foot-to-foot detection technique in conjunction with ECG gating. As we noted previously [3], the arterial tube-load model technique can likewise be adapted to accommodate this practice. That is, first, the impulse responses relating a simultaneously measured ECG waveform to each of the central and peripheral waveforms are identified. Then, the technique is applied to the impulse responses instead of the waveforms to estimate PTT.

In conclusion, when central and peripheral blood pressure or flow waveforms are obtained for PTT estimation, the arterial tube-load model technique may offer the same capabilities as the foot-to-foot detection technique while significantly improving the estimation accuracy.

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