

Incorporating Arterial Viscoelastic Modelling for the Assessment of Changes in Pulse Wave Velocity Within a Cardiac Cycle Using Bramwell-Hill Equation

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Abstract

Aims: This work presents a method & instrumentation to measure pressure-dependent intra-cardiac cycle variations in local blood pulse velocity $PWV_{(P)}$ using Bramwell-Hill (BH) equation by incorporating Kelvin-Voigt type viscoelastic modelling.

Methods: A pilot in-vivo study on 8 subjects was conducted to verify the technique's functionality. The carotid diameter D and pressure P waveforms (sampled at 1 kHz) were measured using our extensively validated image-free ultrasound technology ARTSENS and a calibrated tonometer respectively.

Results: Measurement system captured high fidelity P and D signals. Employing the viscoelastic modelling, elastic P - D curves were obtained and $PWV_{(P)}$ was calculated. The reliability of these curves was verified by comparing the stiffness index derived from the fit (β_{fit}) against the theoretically calculated value β_{ref} which strongly correlated ($r = 0.98$, $p < 0.05$). The systolic PWV (PWV_s) was approximately 20% higher than diastolic PWV (PWV_d). The group average PWV_s and PWV_d were higher for hypertensive subjects.

Conclusion: The proposed technique reliably measures the intra-cardiac cycle variations in $PWV_{(P)}$ and addresses various key considerations associated with non-invasive implementation BH equation for the same.

1. Introduction

Local pulse wave velocity (PWV) is a physiological parameter with paramount clinical importance, owing to its potential to characterize the local arterial stiffness providing early information on the risks associated with a host of cardiovascular events and hypertension [1]. The local PWV is not constant throughout a cardiac cycle but increases with the increase in distending pressure; termed as incremental local PWV. Only in recent years, this phenomenon has attracted the interest of the investigators, and its clinical importance has come to light. Studies have demonstrated its pathological significance in diagnosing Ehlers–Danlos syndrome [2], increased left ventricular

mass index [3], hypertension and cardiovascular risks [4]. Recently, we developed a calibration-free, cuffless blood pressure (BP) measurement method exploiting these intra-cardiac cycle variations in local PWV [5].

The phenomenon of incremental local PWV and its potential applications are still minimally explored, owing to its measurement challenges. The effect of arterial wave-reflections on the morphology of the forward propagating blood pulse waves, even in the early systolic region, limit pulse transit time-based methods to be employed for measurement of incremental local PWV without robust wave separation techniques. The Bramwell-Hill (BH) equation-based assessment of local PWV, that exploits the relationship between the arterial pressure (P) and diameter (D), is considered to be the reference standard non-invasive method [6,7]. Direct implementation of this method for the measurement of incremental local PWV is however challenging as the arteries are viscoelastic in nature, [8] but the method needs the elastic relationship between P and the D .

We present a method and the instrumentation for measuring incremental local PWV using BH equation. The method incorporates viscoelastic modelling of the artery to extract the effective viscous and elastic components of pressure. The obtained elastic component of pressure along with the measured luminal diameter is then used for evaluating the incremental local PWV. While discussing the important observations from the in-vivo study conducted, we present how the developed system addresses the methodological considerations of real-time non-invasive implementation of the BH method.

2. Methodology

2.1. Background

The arteries in the circulatory system are hyper-elastic and the circumferential stress on the arterial walls during the blood pulse propagation results in a non-linear circumferential strain [9]. Therefore, the elastic properties of the arterial walls are a function of the circumferential stress induced by the instantaneous blood pressure, $P(t)$.

The local PWV, being a direct function of the elastic modulus of the arterial walls [9], changes with the $P(t)$ within the cardiac cycle. The increase in the blood pulse propagation velocity with the increase in distending pressure during the systolic phase of the cardiac cycle is termed as incremental local pulse wave velocity $PWV_{(P)}$. BH equation [6], as in (1), relates this local PWV to the instantaneous pressure variations (dP) with corresponding diameter variations (dD), and blood density (ρ).

$$PWV = \sqrt{\frac{D(t) dP(t)}{2\rho dD(t)}} \quad (1)$$

In spite of the simplicity of this local PWV evaluation method, it may be remembered that obtaining an elastic P-D relationship curve for the calculation of $dP(t)/dD(t)$ is not trivial. The primary challenge is the intrinsic viscoelastic nature of the arteries. More clearly, if the arteries were only elastic in nature, the $P(t)$ and $D(t)$ would have exhibited an ideal exponential relationship [10], as given in (2). Here the P_d and D_d are diastolic pressure and diameter respectively and the exponential coefficient β referred to as stiffness index.

$$P(t) = P_d e^{\beta \left(\frac{D(t)}{D_d} - 1 \right)} \quad (2)$$

However, the viscoelastic nature of the arterial wall yields a hysteresis loop between P and D , contrary to an exponential curve. Therefore, quantifying the viscous component is essential to obtain a relationship curve between the elastic component of $P(t)$ and $D(t)$. For this, we have incorporated Kelvin-Voigt type arterial viscoelastic modelling. In this approach, the recorded $P(t)$ could be expressed as the sum of elastic and viscous pressure components ($P_e(t)$ and $P_v(t)$ respectively) [8].

$$P(t) = P_e(t) + P_v(t) = P_e(t) + \eta \frac{dD(t)}{dt} \quad (3)$$

' η ' is the viscosity index. (3) can be re-written as (4).

$$P_e(t) = P(t) - \eta \frac{dD(t)}{dt} \quad (4)$$

The viscosity index η can be estimated by iteratively updating its value in (4), such that the area of the loop between $P_e(t)$ and $D(t)$ is reduced to minimum; indicating hysteresis elimination. Now an exponential curve fitted on this minimal area loop can be approximated as the purely elastic relationship between P and D . The $PWV_{(P)}$ now can be evaluated using the exponential curve constructed between the $P_e(t)$ and $D(t)$.

$$PWV_{(P)} = \sqrt{\frac{D(t) dP_e(t)}{2\rho dD(t)}} = \sqrt{\frac{D(t) d\left(P(t) - \eta \frac{dD(t)}{dt}\right)}{2\rho dD(t)}} \quad (5)$$

2.2. Multimodal probe design

A multimodal probe was developed to facilitate simultaneous measurement of P and D from the carotid artery. The probe consists of a broadband, focused single element ultrasound transducer (center-frequency = 5 MHz, spatial half angle < 1.3 degrees, diameter = 5 mm) to acquire A-scan ultrasound frames for continuous

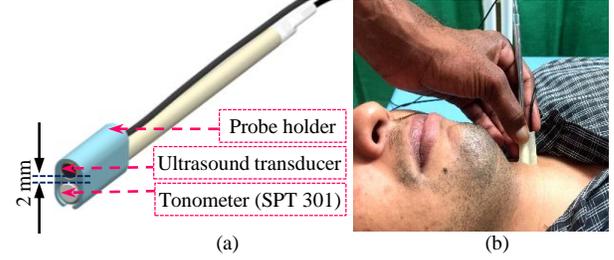


Figure 1. (a) Schematic of the measurement probe, (b) Probe placement

measurement of D and a calibrated tonometer (SPT-301, Millar Instrument) to measure the continuous P . The distance between the pressure transducer and the single element ultrasound transducer is kept minimal for single site measurement. The probe schematic and placement are shown in Fig. 1.

2.3. Hardware Architecture

The signal acquisition hardware consists of a dedicated analog front-end (AFE) to interface the ultrasound and the pressure transducer. The ultrasound AFE comprises of necessary pulser-receiver circuitry for operating the ultrasound transducer in pulse-echo mode and obtaining A-scans at high frame rates, using our ARTSENS[®] technology [11]. The pulser-receiver was implemented using a high-speed digital input-output card (NI PXIe 6556, National Instruments). To digitize the received ultrasound A-scan frames a high-speed digitizer (NI PXI 5154, National Instruments, sampling rate = 50 MHz) was used. Likewise, the AFE for the tonometer consists of ADInstruments' PowerLab and BrigidAmp. For digitization of the preprocessed pressure signals, a data acquisition card (DAQ; NI PXIe 6368, National Instruments) was employed with a sampling rate of 1 kHz. To have matched frequency response for both the modules, the scan rate of the ultrasound was also configured as 1 kHz. A trigger pulse by NI PXIe 6556 enabled simultaneous and synchronized acquisition.

2.4. Software Architecture

For the continuous evaluation of diameter using the A-scan acquired frames the automatic algorithms of our extensively validated ARTSENS[®] technology were employed [11]. The pressure signal was simultaneously acquired in a synchronized manner. The pressure signals were processed via low pass filter with cutoff frequency 15 Hz, in order to remove any high-frequency noise. For each pair of P and D cycles a P-D loop was constructed with P along the ordinate and D along the abscissa. A differential evolution optimization method was employed to estimate η for which the loop area is minimized and hysteresis is reduced. An exponential fit of the minimal area loop based on the method of least squares was

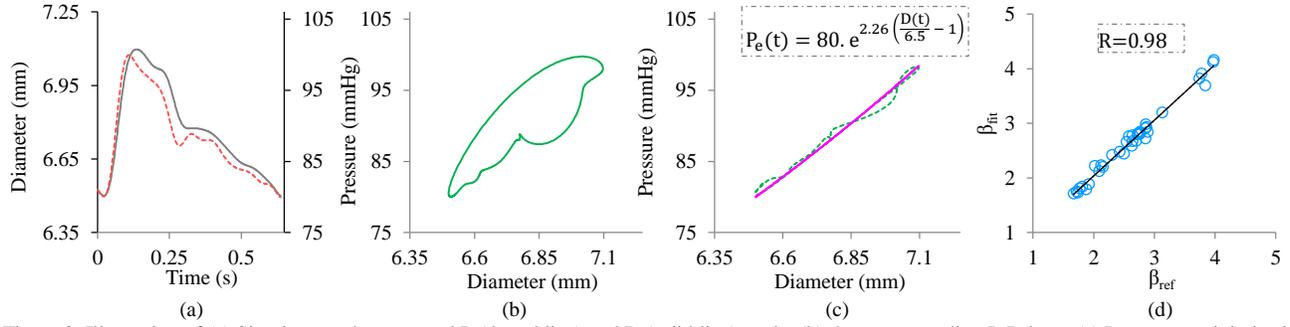


Figure 2. Illustration of (a) Simultaneously measured P (dotted line) and D (solid line) cycle, (b) the corresponding P-D loop, (c) Loop area minimized to obtain a P-D curve for elastic component of P; hysteresis-eliminated curve is shown in green and an exponential fit of the same is shown in pink along with its equation. (d) A regression plot of β_{fit} versus β_{ref} , demonstrating the reliability of P-D fit curves obtained for the recruited subjects.

obtained and was used for evaluation of the incremental local PWV using (5).

2.5. In-vivo experiment

The feasibility of the proposed incremental local PWV evaluation method was verified in-vivo on 8 subjects. Young subjects (group average age = 25.5 ± 2.7 years, normotensive = 4, hypertensive = 4) were recruited for the study. The study conformed to the Helsinki Declaration. All the subjects were detailed about the study and written informed consent was obtained. The subjects were allowed to rest for 5 minutes upon which the baseline BP and heart rate were recorded using an automatic BP monitor (SunTech® 247TM, SunTech Medical) and then the physiological measurements were performed. All the measurements during the course of study were performed by a single operator on the left common carotid artery while the subject was in the supine posture.

3. Results and Discussion

3.1. Reliability of acquired signals

The developed multi-modal probe and the measurement system have demonstrated the expected functionality, and performed simultaneous acquisition of high-fidelity pressure and diameter waveforms. A sample P and D cycle recorded from a particular subject are shown in Fig. 2(a). Inherent phase delays between the P and D waveforms are a major methodological consideration that compromises the accuracy of BH-based method. However, the P and D signals recorded by the developed system had negligible phase delays, due to the time synchronized acquisition, the matched frequency responses of the measurement modules, and closer proximity between the transducers. Another major methodological consideration that the proposed system addresses is the temporal resolution for the P and D signals. The proposed system provides high rate

ultrasound scanning capabilities that enabled high resolution P-D loops (Fig. 2(b)).

3.2. In-vivo pressure-diameter relationship

Employing the arterial viscoelastic modelling, the η was estimated and the elastic component of pressure $P_e(t)$ was evaluated. The group average η for the hypertensive subjects was (3.66 ± 0.70) mmHg.s/mm and for the normotensive subjects was (1.62 ± 0.50) mmHg.s/mm. This trend of higher η for hypertensive subjects concurs with earlier reported similar studies in the literature [8]. A P-D plot constructed by using obtained $P_e(t)$ and measured $D(t)$ for a particular subject is illustrated in Fig. 2(c), indicating a hysteresis minimized curve. A curve fit based on least square minimization indicating the exponential P-D relationship is also illustrated in the same (Fig. 2(c)). For verifying the reliability of the obtained P-D fit curves the stiffness index derived from the exponential coefficient (β_{fit}) of the fit was compared against the theoretically calculated β (β_{ref}) using P_s , P_d , D_s and D_d obtained from the measured $P(t)$ and $D(t)$.

$$\beta = \frac{\ln(P_s/P_d)}{(D_s - D_d)/D_d} \quad (6)$$

Fig. 2(d) shows the regression plot for the β_{fit} versus β_{ref} measures obtained from all the recruited subjects (measured for 5 cycles per subject). The β_{fit} values were strongly correlated ($r = 0.98$, $p < 0.05$) to the β_{ref} values for all the subjects with an insignificant bias (bias = -0.04 , $p = 0.12$), indicating that the reliability of P-D fit curves for the measurement of $PWV_{(P)}$.

3.2. Incremental local PWV evaluation

The cycle-to-cycle exponential P-D fit curves were used to evaluate $PWV_{(P)}$ from individual cycles. Fig. 3(a), shows the $PWV_{(P)}$ for a particular subject (age = 28 years, BMI = 18.5 kg/m^2 , carotid $P_s = 85$ mmHg, $P_d = 60$ mmHg $\beta = 3.84 \pm 0.18$) obtained for 10 consecutive cycles, demonstrating the measurement repeatability. The $PWV_{(P)}$ plots obtained for all the recruited subjects are shown in Fig. 3(b). The systolic PWV (PWV_s) was on an

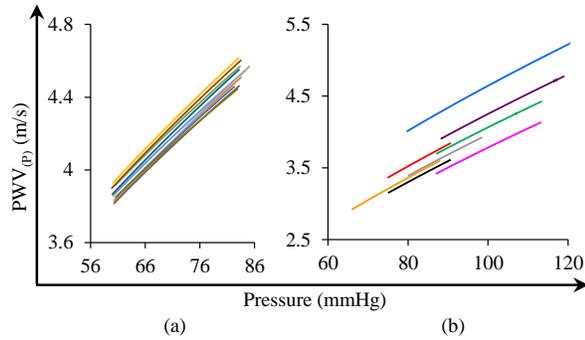


Figure 3. (a) Cycle-to-cycle $PWV_{(P)}$ for a particular subject, (b) $PWV_{(P)}$ measured for all the recruited subjects.

average 20% higher than diastolic PWV (PWV_d). The group average $PWV_s = (4.20 \pm 0.59)$ m/s and $PWV_d = (3.48 \pm 0.36)$ m/s. The mean change in diastolic to systolic PWV (ΔPWV) was (0.71 ± 0.26) m/s. It was observed that the PWV was higher for hypertensive subjects with $PWV_s = (4.65 \pm 0.49)$ m/s and $PWV_d = (3.76 \pm 0.26)$ m/s as compared to normotensives which were (3.74 ± 0.16) m/s and (3.20 ± 0.21) m/s respectively. These results concur with recently reported study on $PWV_{(P)}$ [4].

The literature on BH-equation based PWV velocity methods indicate use of linear fit models on the P-D hysteresis loop assuming a linear relationship between P and D [12]. Such an assumption would result in a constant PWV, that is independent of the systolic to diastolic changes variations in pressure. While attempts have also been made to fit non-linear models relating P and D on the obtained P-D loop, the key limitation was that the nonlinear model curves were fitted directly onto the hysteresis loop [13]. Further the study [13], did not report the variations in local PWV, but only the value at the minimum diastolic pressure. Our work, on the contrary, describes incorporation of Voigt type viscoelastic model for removal of the hysteresis to achieve a more reliable fit for measurement of $PWV_{(P)}$.

Conclusion

The proposed technique reliably measures the intra-cardiac cycle variations in $PWV_{(P)}$ and addresses various considerations associated with real-time non-invasive implementation of BH-equation for the same. The limitation of the present pilot study was that it was performed on a small cohort of young subjects. Therefore, multi-centric extensive studies on large population are in progress to validate the method, establish its measurement accuracy against an invasive reference standard and also investigate the phenomenon of incremental PWV in different arteries. Efforts on developing a compact portable prototype of the presented technology is underway to facilitate large scale studies.

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