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# Phantom Assessment of an Image-free Ultrasound Technology for Online Local Pulse Wave Velocity Measurement

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*Abstract*— **Cardiovascular community has started clinically adopting the assessment of local stiffness, contrary to the traditionally measured carotid-femoral pulse wave velocity (PWV). Though they offer higher reliability, ultrasound methods require advanced hardware and processing methods to perform real-time measurement of local PWV. This work presents a system and method to perform online PWV measurement in an automated manner. It is a fast image-free ultrasound technology that meets the methodological requirements necessary to measure small orders of local pulse transit, from which PWV is measured. The measurement accuracy and repeatability were assessed via phantom experiments, where the measured transit time-based PWV ($PWV_{TT}$) was compared against the theoretically calculated PWV from Bramwell-Hill equation ($PWV_{BH}$). The beat-to-beat variability in the measured $PWV_{TT}$ was within 3%. $PWV_{TT}$ values strongly correlated (r=0.98) with $PWV_{BH}$, yielding a negligible bias of -0.01 m/s, mean error of 3%, and RMSE of 0.27 m/s. These pilot study results demonstrated the presented system's reliability in yielding online local PWV measurements.**

*Clinical Relevance*— **The presented fast image-free system, contrary to the existing fast imaging systems, incurs simpler hardware, provides the potential to realize less-expensive modalities, and performs measurements in a fully automated fashion and online. This would accelerate clinical\field studies pertaining to local PWV and its clinical applications.**

## I. INTRODUCTION

Assessment of accelerated vascular aging has become critical for early preventive measures concerning cardiovascular events. Arterial stiffness is a reliable proxy of early vascular aging that, unlike the circulatory markers, increases consistently with age [1]. Clinically established gold standard measure of stiffness is carotid-to-femoral pulse wave velocity (cfPWV) [2]. This is measured across a long trajectory of the vasculature, all the way from the carotid to the femoral artery. This measure, therefore, inherently informs on the global stiffness of the vascular system and not the target-specific localized information. While clinically cfPWV's paramount importance is proven, local pulse wave velocity (PWV), in recent years, has gained attention as a parameter that provides information above and beyond this global measure of stiffness [3]. It is the measure of PWV from a single arterial site or across a small segment of target arteries. Various studies have demonstrated the potential and clinical relevance of local PWV, emphasizing the need for site specific stiffness information [3]. Functional properties of central arteries becoming a prime focus in the field of cardiovascular and hypertension risk management, local PWV (especially from easily accessible carotid site) proves to be an emerging measure. Advanced cuff-less blood pressure measuring technologies have been proposed in the recent decade that depend on local PWV estimates.

Ultrasound-based methods have emerged for measuring local PWV and have become popular, given their capability to access the blood pulses directly in the form of arterial distension, blood flow rate, or flow velocity. There are methods that perform indirect measurement of local PWV based on biomechanical relationships between any two parameters – blood pressure, flow rate, flow velocity, cross-sectional area, or diameter [4]–[6]. These methods require capturing a waveform pair from the enlisted hemodynamic signals, ideally from a single arterial site [3]. Synchronized and simultaneous acquisition of these waveform pairs is challenging with the current B-mode ultrasound modalities. Additionally, most of these methods are based on the assumption that the early systolic period is devoid of wave reflections, and therefore the effect of reflections may compromise their accuracies [7]. Though several studies have assessed the performance of these methods in a comparative manner, a univocal opinion still lacks in this regard. There is another category of methods that measure the local PWV by capturing the transition features of a blood pulse [7]. Since the local segments are inherently smaller, the capturing of transition features such as delay requires ultrasound systems that are way faster than the conventional ones [8]–[10].

Although such ultrasound systems could be currently built given the advanced technological support and availability of processors with super-speed and immense computing capabilities, they are inherently expensive, complex, and challenging to realize real-time systems. This makes them unsuitable for field-level studies and routine clinical usage. Therefore, given the ever-increasing recognition for local PWV's importance, there is a need for an easy-to-use, automated, fast ultrasound system for the measurement of local PWV in real-time. We have presented a fast image-free ultrasound technology to perform real-time, automated measurement of beat-to-beat local PWV. Its performance was assessed based on phantom experiments by comparing the measured PWV against the theoretically calculated PWV. The results on the measurement repeatability and accuracy are presented, and the advantages of the proposed system are discussed.

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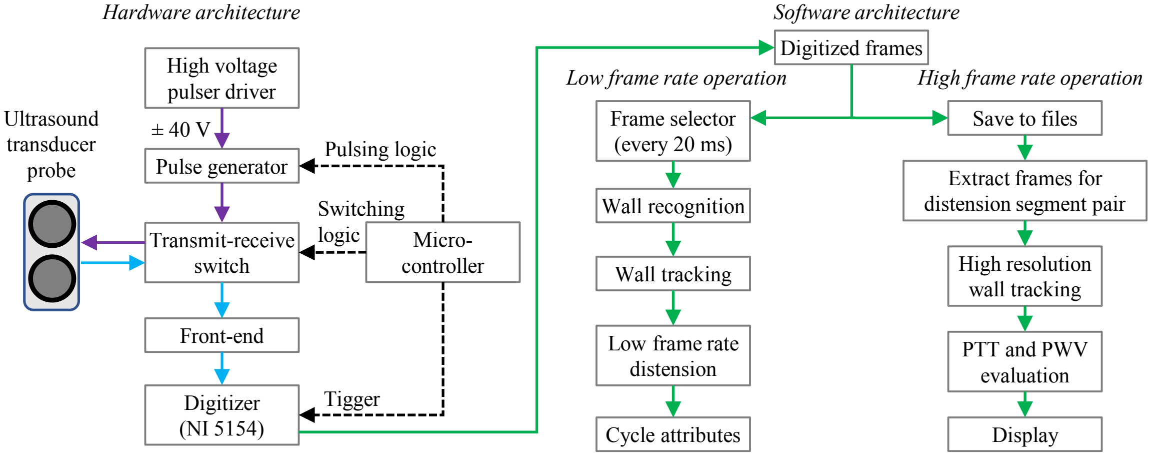


Figure 1. Schematic of the measurement system showing the hardware and software architecture.

## II. MATERIALS AND METHODS

### A. *Fast Image-free Ultrasound for Local PWV*

A schematic of the measurement system's acquisition hardware is shown in Fig. 1. The hardware unit operates a pair of identical ultrasound transducer elements (diameter = 5 mm, center frequency = 10 MHz) interfaced to it in transceiver mode. Such a mode of operation is implemented using a pulser and a receiver module. The pulser module insonates the ultrasound elements in transmit mode with high voltage (HV) pulses that are generated by a HV pulse driver. Upon transmission of radiofrequency (RF) pulse, the operating mode of the ultrasound elements is switched to receiving mode for a period that is sufficient to scan a configured depth. The received radiofrequency echo signals are digitized by a high-speed digitizer (PXI‑5154, National Instruments, US) at 200 MHz, resulting in a 1-dimensional A-mode frame. This digitization is triggered via an analog impulse, that is provided every time the transducer is switched to receiving mode. The frame repetition rate was configured to 500 Hz, the frequency at which pulsing of the transducers happens. The pulsing, mode-switching, and triggering impulse-signals are provided by a microcontroller (LPC4370, NXP Semiconductors, Netherlands).

The digitized A-mode frames are acquired to a computer, where the computing software processes them to evaluate a pair of distension waveforms. From this distension waveform pair for each cardiac cycle, the local pulse transit time and thereby the local PWV were calculated using,

$$\mathrm{PWV_{TT}} = \frac{\text{Propagation path length}}{\text{Pulse transit time}}. \qquad (1)$$

The propagation path length is given by the separation distance between the ultrasound element pair. The transit time is measured by locating a characteristic point, second-time derivative maximum (SDM), from the distension cycles pair and measuring the delay between them. Now, evaluation of distension waveforms requires identification of the arterial wall locations from the A-mode frames and tracking their motion continuously. Our group has earlier developed fully automated methods that can be applied to A-mode frames to identify arterial walls and track their motion continuously [11]. These methods are based on cross-correlation operation; therefore tracking the entire distension waveforms at a rate of 500 frames per second will restrict real-time measurement unless implemented on a graphics processing unit (GPU).

Hence, to perform real-time measurement of local PWV even by employing a general-purpose computer with basic configuration, a segment of high-resolution distension cycle (smaller than 1/4th of the entire cycle) was only evaluated beat-by-beat where the SDM would be likely situated. This was performed by implementing a two-tier evaluation scheme in the software. In the first tier, the arterial walls were recognized, and their motion was tracked continuously in the frames that were acquired at every 20th millisecond (=50 Hz). Along with that the continuous frames (acquired originally at 500 Hz, every 2 ms) were written to a file. For each individual distension cycle resulting from the low frame rate (LFR) tracking, two points (A and B) were annotated with their corresponding frame numbers, near and far wall locations. Point A corresponds to the end-diastolic minimum, and point B corresponds to the first derivative maximum.

In the second tier, the distension segment between these points is evaluated at a high frame rate (HFR) of 500 Hz by accessing the corresponding frames from the files employing the annotated frame numbers during the LFR operation. Since near and far wall locations for point A (start of the segment) are also annotated, these were used as the initially identified locations during the HFR tracking operation. The high-resolution distension segments pair are further resampled using cubic spline interpolation (sampling rate = 10 kHz), and local PWV is evaluated by measuring the local transit time as alluded earlier.

### B. *Phantom Experiment for Performance Assessment*

A phantom study was conducted to evaluate the performance of the proposed local PWV evaluation system. The phantom setup allowed controllable flow conditions for a systematic evaluation of (i) beat-to-beat repeatability and (ii) accuracy over a range of local PWVs. The schematic of the experimental setup is shown in Fig. 2. The phantom model consisted of an elastic vessel (with one end closed) filled with blood mimicking fluid, and it was sheathed with elastic silicon. The open end of the phantom was connected to an air-pump and solenoid valve arrangement that was controlled by a microcontroller for generation of a pneumatic pulse.

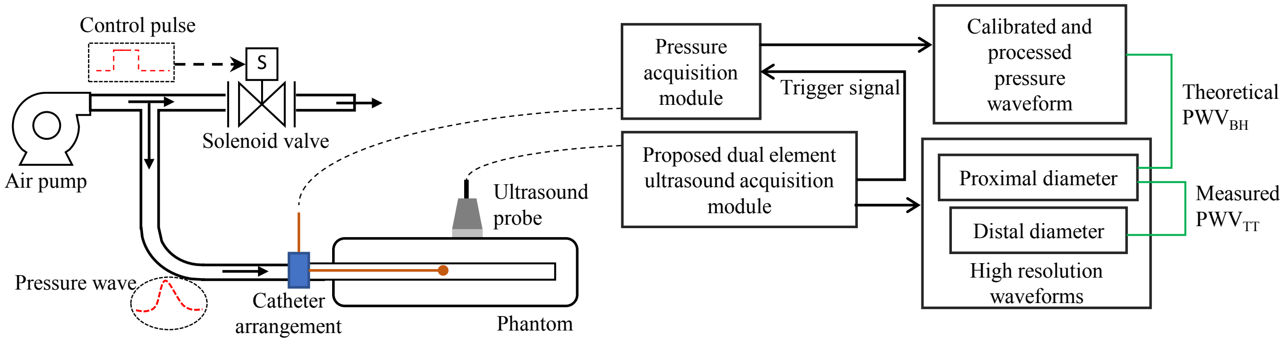


Figure 2. Schematic of the experimental setup and the hardware setup of simultaneous measurement of PWV by the proposed and the reference system.

While the air pump was operated continuously, the valve was opened and closed in a periodic manner to generate rectangular pneumatic pulses in the phantom vessel. This pressure-pulse pushed the fluid in the vessel towards the close end in a pulsatile fashion, which caused the vessel to distend and relax. Since for arterial pulses, the ascending slope is higher than the descending, the off-time of the solenoid valve was kept smaller than the on-time. The pulsatile fluid pressure in the vessel was varied by configuring the on- and off-timings. Therefore, these changes in pressure were reflected as changes in PWV.

### C. *Theoretical Local PWV Evaluation*

There is no non-invasive gold standard reference for local PWV measurement. However, Bramwell-Hill (BH) equation theoretically relates the PWV within a vessel segment to its distensibility (DC), and therefore, it has been used as a theoretical reference for local PWV in multiple studies reported in the literature [12], [13]. Pulse wave velocity using BH equation is expressed as,

$$\mathrm{PWV_{BH}} = \sqrt{\frac{\mathrm{A_D}\,\mathrm{dP}}{\rho\,\mathrm{dA}}}, \tag{2}$$

where dP is the instantaneous pulse pressure, dA is the instantaneous change in circumference area, and $\mathrm{A_D}$ is the minimum area (end-diastolic) for a vessel segment. Now, for the evaluation of $\mathrm{PWV_{BH}}$, pressure, and diameter recordings are needed from a single site of the vessel. For such a provision, a pressure catheter was placed inside the vessel near to the proximal ultrasound element, and the pressure signal acquisition was synchronized with the developed measurement system via an analog trigger signal. Such instrumentation allowed frequency-matched acquisition from the ultrasound and pressure modules at an equal rate of 500 Hz. The ratio dP/dA is evaluated at SDM characteristic point from the synchronously recorded pressure and diameter cycles and used for theoretical PWV calculation.

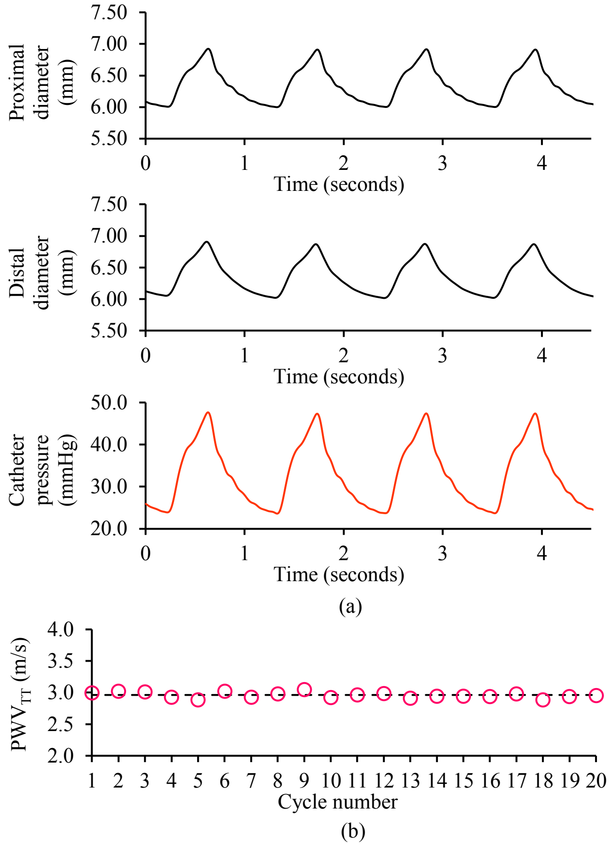
### D. *Statistical Analysis*

The comparison of measurements, $\mathrm{PWV_{TT}}$ versus $\mathrm{PWV_{BH}}$, was performed based on linear regression and Bland-Altman analysis. The correlation strength and its statistical significance were quantified by 'r' and 'p' values, respectively. The mean bias and limits of agreement (LOA) were computed to investigate the association between the measurements. The significance of the difference between the measurements was evaluated using a paired student's t-test. The beat-to-beat variability of PWV measurements for individual flow conditions is evaluated as the ratio of standard deviation-to-mean of measurements across 20 continuous cardiac cycles. The errors in measurement were reported as mean absolute percentage difference and RMSE.

## III. RESULTS AND DISCUSSION

### A. *Reliability of Signals for Local PWV Evaluation*

High quality A-mode frames with SNR > 30 dB could be recorded from the two channels of the ultrasound system, where the echoes of the near and far wall were well defined, sharp and strong. These frames ensured capturing of high-fidelity distension waveforms, a sample of which is shown in Fig. 3(a). Similarly, high-fidelity invasive pressure waveforms were captured in a synchronous manner. The waveforms together yielded the desired pulse wave velocity



(a)

(b)

Figure 3. (a) High fidelity proximal diameter, distal diameter and catheter waveforms representing the signal acquisition reliability. (b) Beat-to-beat PWV measured by the proposed system demonstrating repeatability.

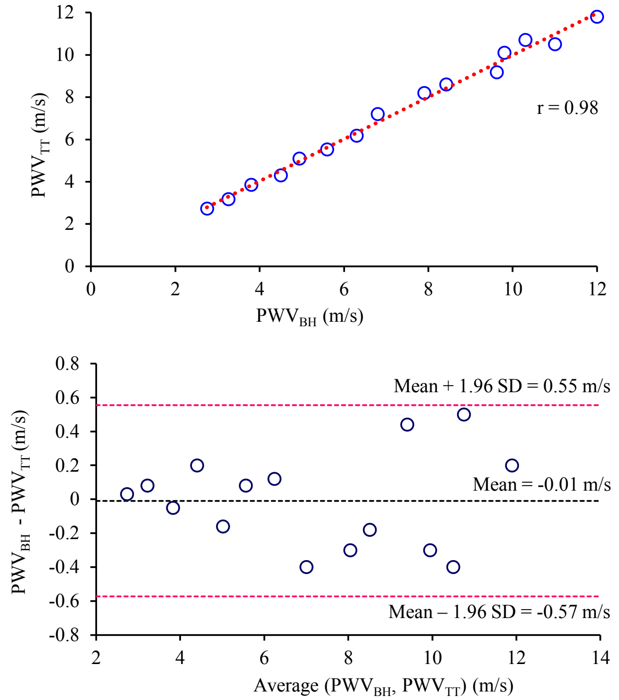


Figure 4. Comparison of measured versus theoretical PWV values employing linear regression and Bland Altman analysis.

measures in a beat-to-beat manner, as shown in Fig. 3(b). The resolution offered by the interpolated HFR distension segments for the PTT evaluation was 0.1 ms, which was adequate to measure transit times for a short vessel segment (such as 35 mm). The calibrated catheter measured pressure values with an error smaller than 1 mmHg. The resolution of vessel diameter measurements was ~150 µm, as experimentally evaluated by the measured 3 dB width of the transmitted ultrasound pulse. Since the pressure and ultrasound acquisition modules were synchronized with a hardware trigger signal, the lag between the pressure and area cycles was negligible. The system thereby captured reliable area and pressure information necessary for the theoretical $PWV_{BH}$ measurements.

### B. *Repeatability and Accuracy Performance*

The measured $PWV_{TT}$ was repeatable for continuous cardiac cycles with variability of 0.5% to 3% across different flow configurations. The PTT measured was 6.0 ± 6.1 ms, and likewise, the $PWV_{TT}$ measured was 7.2 ± 5.9 m/s. A linear regression plot comparing $PWV_{TT}$ versus $PWV_{BH}$ is shown in Fig. 4 (1st row). A strong correlation (r = 0.98) was observed between these measures, which was statistically significant ($p < 0.05$). The $PWV_{TT}$ measures are related to the $PWV_{BH}$ linearly, with the equation $PWV_{TT} = 0.99*PWV_{BH} + 0.06$ m/s. In Fig. 4 (2nd row) the BA plot comparing the $PWV_{TT}$ versus $PWV_{BH}$ is shown. As observed, the mean bias was -0.01 m/s, which was statistically insignificant ($p = 0.44$). The measurements agree with each other, within a 95% confidence interval of ± 0.55 m/s. The observed mean absolute percentage difference was 3.0%, and RMSE was 0.27 m/s. This demonstrated the method's ability to perform accurate and reliable PWV measurements.

## IV. CONCLUSION AND FUTURE WORK

We have presented a fast image-free ultrasound technology that is capable of performing online local PWV measurements. The system's accuracy and repeatability were demonstrated with the systematic and controlled phantom experiments over a wide range of PWV values. Such online systems facilitate a higher success rate of reliable measurements, large population studies, development of advanced cardiovascular screening tools and applications. For establishing the system's accuracy performance, multicentric in-vivo studies are underway. Developments are in progress to translate the system to a fully embedded form, thereby making it portable and amenable for field settings.

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