Acoustic Plethysmography for Aortic Pulse Wave Velocity Measurement: In-Vitro and In-Vivo Feasibility Study

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Abstract— **Large arterial stiffness is an indicator of vascular aging and is a prognostic marker of cardiovascular disease. Carotid-femoral pulse wave velocity (cf-PWV) is a gold standard technique for non-invasively assessing large artery stiffness. The state-of-the-art cf-PWV measuring devices necessitate expertise and are not pertinent for routine care in non-clinical settings. To address this gap, we have developed an acoustic plethysmography device for cf-PWV measurement. An in-vitro test on an arterial phantom was performed to ensure the device's reliability. Subsequently, an in-vivo study of 10 participants was conducted to assess the feasibility of the acquisition of the developed device. The in-vitro measurement accuracy was satisfactory, with a root mean square error of .4%. The in-vivo PWV results are consistent, with the normal ranges for the measured age group falling between 4 and 5.8 m/s. The beat-to-beat COV obtained from in-vitro and in-vivo studies were less than 4.2% and 4.86% respectively. The study's findings demonstrated that the proposed device has the potential to seamlessly provide cf-PWV. However, additional validation against the reference devices on a larger population is in progress and will be published in future publications.**

Keywords—Vascular aging, arterial stiffness, applanation tonometry.

I. INTRODUCTION

Aging is a key factor in the decline of heart function. The arteries degrade in structure and function as they age, a condition known as vascular aging [1]. Large arterial stiffness is a proxy of vascular aging and is a prognostic marker of cardiovascular disease, including atherosclerosis, coronary heart disease, and hypertension [2]. The onset of the disease often goes undiagnosed in its early stages until a severe cardiovascular event occurs. Thus, it becomes essential to devise methods for assessing arterial stiffness to identify accelerated or early vascular aging [3][4].

Various commercial devices have been developed for the assessment of carotid-femoral pulse wave velocity (cf-PWV) [5], [6]. Despite their availability, the utilization of cf-PWV measurements in primary care remains limited. This is largely attributed to the predominant use of tonometer sensors in these devices, which necessitates a skilled operator proficient in applanation tonometry. Applanation tonometry involves the use of a sensitive pressure sensor, the tonometer, which is applied against a rigid structure, typically the carotid artery in this context [7].

The challenge lies in the operator's need to consistently maintain optimal hold-on pressure and correct orientation, a task that can prove daunting for individuals lacking specialized skills [8]. The requirement for a dedicated operator with expertise in applanation tonometry poses a significant hurdle to the widespread adoption of cf-PWV measurement in primary care settings [9]. Not all healthcare facilities have personnel with the necessary training, and the lack of accessibility to such skilled personnel further hamper the integration of this technology into routine clinical practice [10]. Moreover, the cost associated with the equipment required for cf-PWV measurements adds another layer of hindrance to its widespread use. The tonometer sensors, being a critical component, contribute substantially to the overall expenses. There are other computerized recognition, segmentation and detection mechanisms but these are expensive [11-16]. Conversely, for a technology to gain traction in primary care or be embraced by general practitioners, it must exhibit characteristics such as full automation, user-friendly operation, and minimal demand for operator expertise [17]. Overcoming these challenges is crucial for making cf-PWV measurements more accessible, cost-effective, and feasible for routine use in diverse healthcare settings [18].

Addressing this gap, we developed a cf-PWV measuring device using a stethoscope-based acoustic plethysmography for measuring carotid signals and a cuff with a pressure sensor for femoral signals. Stethoscope-based acoustic plethysmography is used because it has a large surface area, is easy to use, and can stabilize the hold on pressure much better than the tonometer. Having a stable hold on pressure improves the reliability of the signal recorded. Furthermore, the stethoscope-type design of the plethysmography adds an advantage as it has always been the tool of choice for physicians [19]. Because it is frequently the first point of physical contact between patient and doctor, only minimal training is required. In this work, we have validated the acoustic plethysmography transducer for measuring cf-PWV

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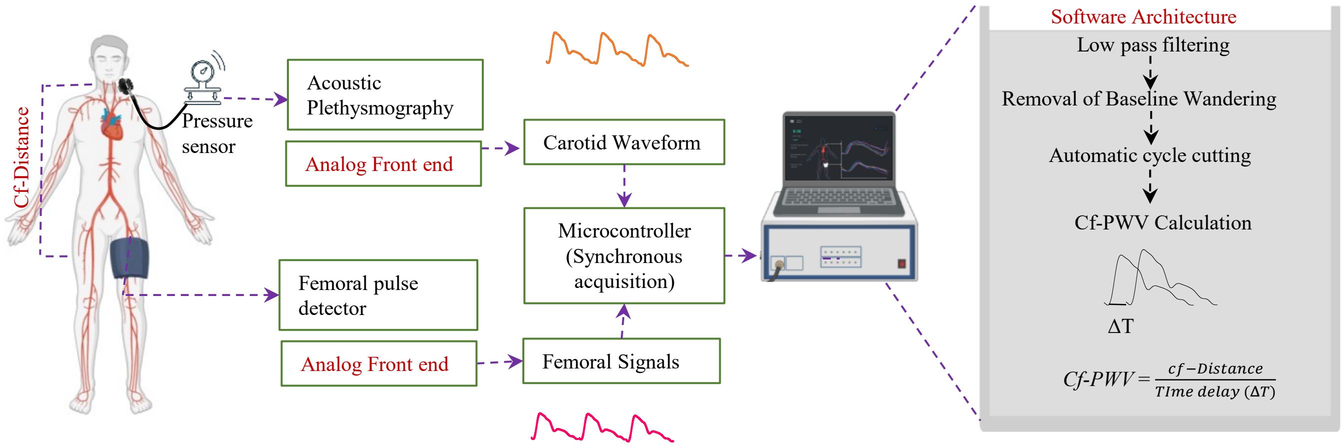


Fig 1. Cf-PWV measurement system block diagram comprising of the hardware and software architecture.

using dynamic arterial phantom configuration. On 10 participants, the feasibility of PWV measurement was assessed. Section II discusses the instrumentation, which includes hardware and software architecture, in-vitro assessment, and in-vivo protocol. The results from the observation is discussed mentioned in section IV, based on which research is outlined.

II. MATERIALS AND METHODS

A. *Instrumentation*

Hardware: The acquisition system comprises a) stethoscope-based acoustic plethysmography to acquire the pulse signals from the carotid artery, b) a cuff-based pulse detector to acquire pulse signals from the femoral artery, c) an acquisition system with a microcontroller that controls the simultaneous recording of pulse signals from the carotid and femoral artery. The acoustic plethysmography comprises a stethoscope head connected to the pressure sensor (MP3V5010GC6U, NXP semiconductors, United States) through tubing. The chosen pressure sensor offers a good sensitivity of 270mv/kPa and an acceptable operational range of – 0 to 6.9kPa. The pressure sensor is mounted on the custom PCB. The voltage signal from the pressure sensor is amplified at the analog front end to 0 to 3.3 V with an instrumentation amplifier of gain 50 dB.

The system's femoral pulse detector module comprises a bladder-type cuff and pressure sensor. The module inflates the thigh cuff to a sub-diastolic pressure level to pick up the femoral pulses without intervening with the blood flow. Both the carotid and femoral pulse waveforms are recorded simultaneously through a 12-bit analog-to-digital converter of the microcontroller. (LPC4370FET256E ARM$^{®}$ Cortex$^{®}$-M4 processor, NXP semiconductors).

Software: Using LabVIEW, a custom-designed program for PWV measurement was made. The software developed was employed for real-time signal processing and computations. Simultaneously acquired carotid and femoral pulse signals were digitally filtered using a Butterworth low pass filter having a cutoff frequency of 10 Hz [20] and order 4. The cycles acquired are normalized and processed to remove baseline wandering. From the train of cycles, the individual cycles were extracted using a cycle-cutting technique, and their quality was assessed by checking the repeatability of the distinctive morphologies within the cycle, as well as the upward and downward slopes (ranging between 0 and 100). The characteristic point in the waveform was identified based on the intersection tangent method and pulse transit time (PTT) was calculated [21]. Further, the path length for the cf-PWV measurement was calculated using a subtraction method [22], where the distance between the carotid artery and the suprasternal notch is subtracted from the distance between the suprasternal notch and femoral artery. For each cardiac cycle PWV was calculated as a ratio of the path length measured to PTT. The recorded results were saved for further analysis.

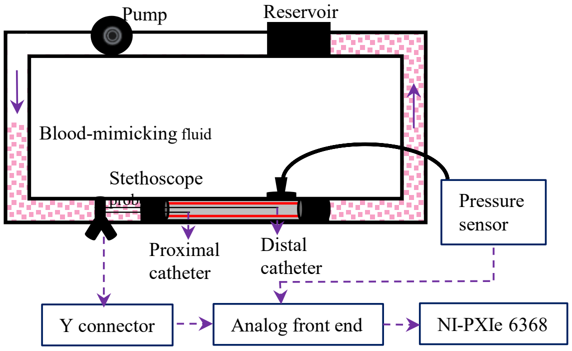


Fig 2. Illustration and schematic representation of the in-vitro experimental setup

B. *Validation of the system*

In-vitro Validation: In controlled laboratory conditions, a systematic in vitro experiment was carried out to assess the accuracy of the developed acoustic transducer probe for PWV estimation. The trials were carried out on a dynamic arterial phantom. A customized in-house built air pressure pump and a solenoid valve were used to generate arterial pulsations. The pulse amplitude and pulse rate were controlled based on the ON and OFF timings of the solenoid valve. Two high-fidelity catheters (distal and proximal) were inserted into the phantom, separated by a distance of 21cm. The stethoscope-type acoustic transducer probe was mounted exactly above the distal catheter on the silicone phantom using the probe holder. The pulse wave from the acoustic plethysmography and proximal catheter was recorded simultaneously to calculate PWVs. In order to validate, a reference PWV (PWVi) measurement is employed using the PTT obtained from simultaneously recorded pressure waveforms from two invasive pressure catheters separated by a distance of 21 cm. Fig 2 shows the illustration of the setup. The signals from both the catheters and the acoustic plethysmography probe are acquired using the data acquisition system NI PXIe 6368 at a sampling rate of 20 kHz [15]. The acquired signal is then filtered in the software with the Butterworth low pass filter having a cutoff frequency of 10 Hz [16] and order 4 and used for future analysis.

In-vivo feasibility assessment: The study was performed to assess the feasibility of the developed acoustic plethysmography transducer for measuring cf-PWV on human participants. The participants provided written informed consent. The study was conducted in compliance with the Helsinki Declaration of 2013 and was approved by the Institute review boards of the Indian Institute of Technology Madras (IEC/2021-01/JJ/07). The anthropometric measures were obtained, and the participants were asked to rest in a supine position for 10 minutes [23]. Blood pressure was taken from the brachial artery, and measurements were saved using the software. The thigh cuff was wrapped around the femoral artery.

The distance between the carotid and femoral artery was measured and recorded in the software for PWV calculation. The operator then palpated the left common carotid, and the acoustic transducer was positioned at the identified location [24]. The thigh cuff auto-inflates once reliable pulse signals start to appear from the carotid artery. Once the 10 cycles of carotid and femoral waveforms with the desired quality were captured, the results were displayed.

C. Statistical Analysis

All the variables were presented as mean ± standard deviation. The coefficient of variation calculated as the ratio of mean to standard deviation was used to represent the beat-to-beat precision. Linear regression and the Bland-Altman analysis were performed to assess the agreement between the measurement between the developed system and the reference. Paired-t despaired to show the statistical significance of any difference between the groups, presented using the p-value. All analyses were performed using SAS®

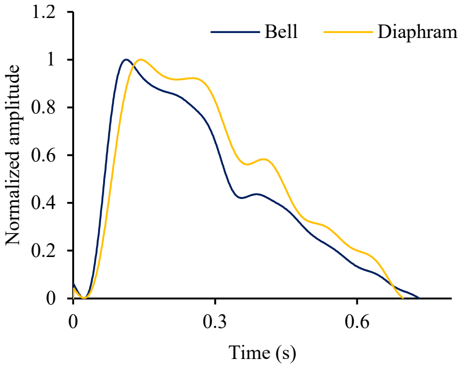
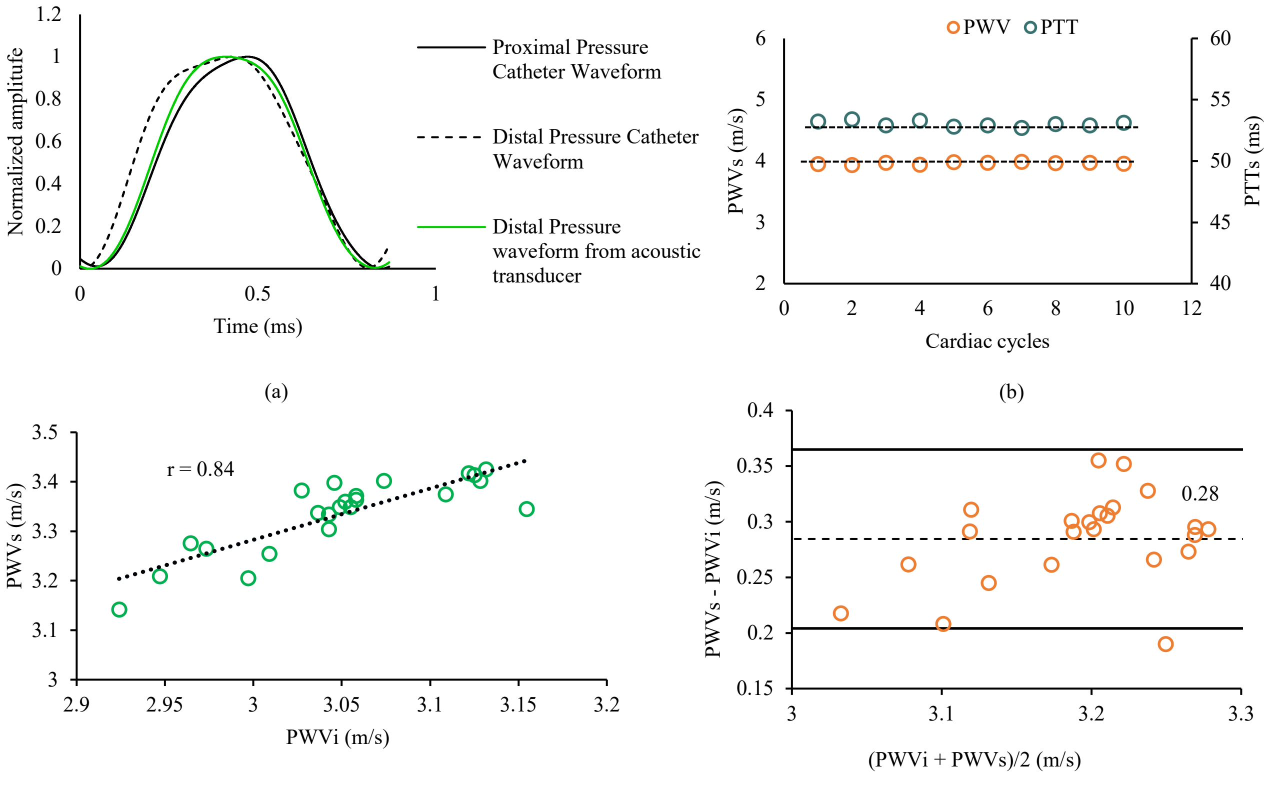


Fig 3. Morphology of the waveform from the bell and the diaphragm of the acoustic transducer



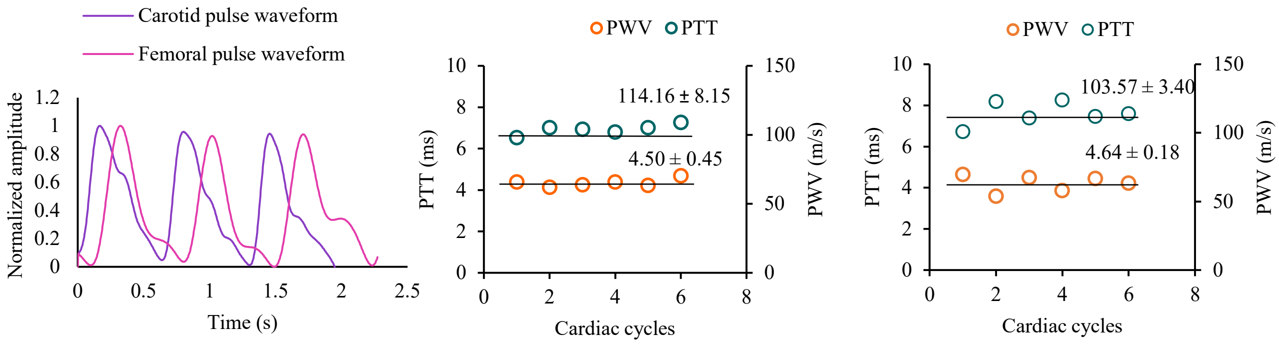
(a)

(b)

(c)

(d)

Fig 4. (a) Signals obtained from in-vitro experiment, (b) Beat to beat repeatability of the PWVs obtained at PP of 40 mmHg (c) The linear regression between PWVi and PWVs, (d) Bland-Altman plot between PWVi and PWVs.



(a)

(b)

(c)

Fig 5. (a) Carotid and femoral waveforms obtained simultaneously from a participant. (b) Participants with less beat-to-beat PWV variation. (c) Participants with more beat-to-beat PWV variation

TABLE I. PTT AND PWV MEASUREMENTS

S.No	PTT (ms)	Cov %	PWV (m/s)	Cov %
1	90 ± 3.82	4.4	5.1 ± 0.18	5
2	98 ± 2.87	1.2	5.4 ± 0.04	2.1
3	90 ± 5.44	4.9	5.3 ± 0.18	5.5
4	109 ± 6.07	3.6	4.9 ± 0.14	6.1
5	87 ± 8.33	6.6	4.8 ± 0.27	8.4
6	109.8 ± 2.4	2.3	5 ± 0.08	2.5
7	79 ± 3.34	3.3	4.5 ± 0.11	3.4
8	79 ± 3.34	5.3	4.1 ± 0.17	5.3
9	112 ± 5.20	5.8	5.8 ± 0.07	5.5
10	116.8 ± 3.20	4.7	4 ± 0.12	4.9

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III. RESULTS AND DISCUSSION

A. *Design Consideration*

An experiment comparing the two sides of the stethoscope's acoustic transducer (comprising a bell and a diaphragm) was conducted to determine which side is optimal for quantifying measurements. In Fig. 3, the pulse waveform obtained from both the bell and the diaphragm is illustrated.

Morphologically, when using the bell side of the transducer, the carotid pulse signal displayed a noticeable tidal wave and a distinct distensible dicrotic notch, with a signal-to-noise ratio (SNR) of 21 dB. In contrast, the diaphragm side provided more notches but lacked a clearly defined dicrotic notch, with an SNR of 4 dB lower than that of the bell, as depicted in Fig 3. Consequently, the bell side was selected for further investigation.

The length of the tubing in the acoustic-type stethoscope transducer introduces a potential delay between pulse signals from the carotid and femoral arteries. With a tubing length of 1m, we empirically determined the delay between the acoustic transducer and the sensor to be 3.03 ms. This delay was accounted for when assessing Pulse Transit Time (PTT) in both in-vitro validation and in-vivo feasibility studies.

B. *Validation Results*

In-vitro validation: In the in-vitro validation study, Fig. 4(a) displays a sample waveform obtained from the distal catheter, proximal catheter, and acoustic transducer. The beat-to-beat coefficient of variation (CoV) of the Pulse Transit Time (PTT) from the transducer was less than 4.2%. Fig. 4(b) presents sample beat-to-beat PTT and PWV recorded at a pulse pressure of 40 mmHg. The average PTT (over 15 consecutive cycles) between the distal and proximal catheter was 49.27 ± 1.0 ms, while between the proximal catheter and stethoscope, it was 45.02 ± 1.0 ms. Similarly, PWVi and PWVs calculated from the PTT with a known distance of 21 cm were 3.04 ± 0.06 m/s and 3.33 ± 0.07 m/s, respectively. No significant difference was found between the mean values of PWVi and PWVs ($p < 0.05$). The RMSE was 1.46%. Fig. 4(c) illustrates the regression between PWVi and PWVs, demonstrating a significant and strong correlation between both measurements ($r = 0.84$, $p < 0.001$). Bland-Altman analysis depicted in Fig. 4(d) confirms strong agreement between measurements. The mean bias was 0.28, statistically insignificant ($p = 0.12$), with confidence intervals of ± 0.08 m/s for bias. Validation experiments on the phantom showed that although the developed device was non-invasive, it provided comparable results with invasive PWV measurements, indicating the accuracy and repeatability of the acoustic plethysmography transducer and associated measurement system.

In-vivo measurement feasibility: A high-quality pulse waveform was acquired by the developed system from carotid and femoral arteries for cf-PWV calculation with the SNR of 21 dB and 30 dB, respectively. The sample of three sets of cycles obtained from a single participant is depicted in Fig 5(a). To assess the repeatability, beat-to-beat measurements were taken. Fig 5(b) and Fig 5(c) show the continuous beat-by-beat measurements from a participant with less CoV and higher CoV. The measures acquired from the ten recruited individuals are shown in Table. I, reported as the mean ± standard deviation (Mean ± SD). The maximum beat-to-beat COV of the measured PTT from multiple participants was less than 4.87%. The average PTT was 97.2 ± 13.85. From the PTT and the measured distance, the PWV calculated was 4.8 ± 0.53 which is in the range of 4 m/s – 5.8 m/s. The acquired results were within the expected range of cf-PWV for the measured age group [2], validating the capabilities of the proposed acoustic plethysmography and system to measure.

IV. CONCLUSION

The presented acoustic plethysmography method for measuring cf-PWV underwent thorough evaluation, including an in-vitro experiment to assess device reliability, yielding satisfactory results. These results showcased acceptable accuracy and beat-to-beat precision. The feasibility of the developed system was further examined through trials involving 10 human participants. The cf-PWV values obtained ranged from 4 m/s to 5.8 m/s, consistent with literature values for individuals of similar age groups. The coefficient of variation for beat-to-beat PTT (4.21%) and PWV (4.87%) measurements fell within an acceptable range, indicating the device's capability to consistently provide repeatable measurements across various cardiac cycles. Through experimental investigations, it was demonstrated that the measurement system could reliably conduct PWV measurements effortlessly using the acoustic plethysmography device.

One limitation of this study was that the in-vitro experiment was conducted empirically under limited conditions and couldn't cover varied PWV ranges due to flow constraints. However, ongoing validation with a gold standard device in a multicenter study is underway and will be detailed in our forthcoming publication.

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