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Characterizing the Effect of Hold-Down Pressure for Local and Regional Stiffness Markers

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Abstract— **Vascular aging occurs due to pathologies and old age. Early detection of stiffness markers and arterial geometry parameters in the carotid artery serves as an essential indicator for the progression of vascular aging. The assessment of stiffness markers is typically conducted using ultrasound and tonometer-based devices. However, both types of devices present challenges, requiring skilled operators and exhibiting variability in results due to different hold-down pressures when different operators are involved. In this study, we aim to quantify the impact of hold-down pressure on diameter-based measurements and evaluate its effects on local and regional stiffness markers. To carry out this investigation, we utilized ARTSENS Plus device along with a multi-modal probe comprising an ultrasound transducer and a tonometer. A-mode ultrasound scanning was performed on the left common carotid artery of each participant, tonometer indicated the applied hold-down pressure on the participant's skin. Four trials were conducted at hold-down pressure levels of 50, 100, 150, and 200 mmHg, and RF echo frames were recorded. ARTSENS Plus signal processing algorithms were applied to obtain the recorded frames' carotid diameter and pressure, central pressure, and local and regional stiffness. The beat-to-beat repeatability of diameter values was examined, and the coefficient of variation was calculated to assess the consistency of the measurements. The system's signal-to-noise ratio exceeded 25 dB. The results section delves into the impact of hold-down pressure on diameter, carotid pressure, and stiffness markers, providing insights into the variables influencing the reliability of the measurements in this cardiovascular assessment. From all the results and observations optimal hold-down pressure can be slightly higher than diastolic pressure.**

Keywords—A-mode ultrasound, arterial stiffness, arterial geometry, pressure-strain elastic modulus, carotid to femoral pulse wave velocity, pulse transit time (PTT).

I. INTRODUCTION

Vascular aging can result from aging itself or various pathologies. Evaluating stiffness, particularly in the aortic or central arteries, serves as a metric to quantify vascular aging. The assessment of the common carotid artery is vital in gauging the overall condition of the cardiovascular system, emphasizing key parameters known as stiffness markers [1], [2], [11]. Vascular aging refers to increased arterial stiffness. As stiffness increases, the heart operates under elevated stress, leading to a rise in pulse pressure. In response to this, the artery undergoes structural wall adaptations. The quantification of these structural changes in the artery involves stiffness markers, derived from the artery's pressure and diameter[3]. Carotid to femoral pulse wave velocity, a regional stiffness marker is considered the gold standard for stiffness measurement [1]. Assessment of regional stiffness markers occurs along the arterial trajectory. Over the past two decades, there has been an increasing focus on measuring local stiffness by examining the relationship between pressure and diameter specific to a given artery segment. These markers offer stiffness measurements for a particular portion of the artery. The significance of stiffness is crucial in managing cardiovascular diseases as it influences both end-organ damage and cognitive decline. Moreover, risk factors such as diabetes and obesity directly impact stiffness.

ARTSENS Plus[4] was developed and validated, it evaluates local and regional markers in a single operation. This technology circumvents the challenges associated with the devices in the market. Commercially available devices in the market use tonometry for stiffness measurements [4]. However, hold-down pressure is one of the potential factors that introduce variability in the measurement performed by commercially available devices. Such kind of problems are addressed using an A-mode ultrasound probe where applanation is not required to capture the carotid wall dynamics. Ultrasound modality directly captures information from the artery and is minimally affected by the tissue between the artery and the surface. However, hold-down still may affect the readings from the A-mode ultrasound probe which can create variability in local and regional stiffness markers. Hence in this paper, we are trying to characterize our system to establish its usability in terms of reliable carotid measurement and determination of optimal hold-down pressure.

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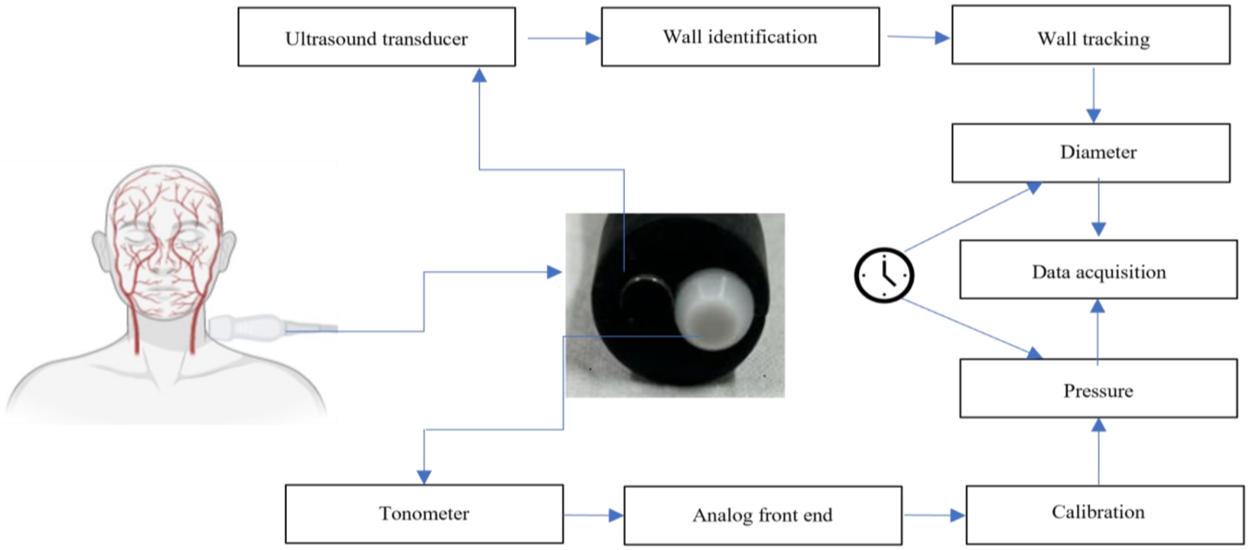

Fig. 1 experimental setup and data collection

This paper addresses the usability of the ARTSENS Plus device for diameter measurement and derived pressure measurements based on which the stiffness markers are evaluated. The objective of the study is to assess the impact of hold-down pressure on obtaining reliable diameter measurements of blood vessels and to evaluate its subsequent effects on local and regional stiffness markers. These markers are particularly sensitive to alterations in blood vessel geometry and pulse pressure. To accomplish these objectives, we have integrated a pressure sensor with the ultrasound probe of the ARTSENS Plus device to carry out this investigation. Section II delves into the instrumentation, study design, study protocols, data collection, and data processing, while Section III presents the analysis results. The paper lists its limitations in Section IV and concludes in Section V with a summary of all results.

II. MATERIALS AND METHODS

A. *Instrumentation*

The multi-modal arterial probe of i) a single channel focused ultrasound transducer (center frequency: 5 MHz, diameter: 5 mm, spatial angle < 1.3o), ii) a pressure sensor (SPT 301 Tonometer Cartridge, Millar Instruments, USA), iii) thigh cuff. The pressure sensor is integrated into the ergonomic probe, with a center-to-center distance of 5 mm as illustrated in figure-1. The thigh cuff is a bladder-based pressure cuff wound around the femoral artery, to capture pulsations from the femoral artery, under sub-diastolic pressure inflation.

Data from the tonometer and femoral sources are captured at a relatively low sampling rate of 250 Hz, utilizing the low-speed ADC pins within the acquisition system. The tonometer data undergoes signal conditioning through an analog front end (INA-125) [5], while the femoral data is subjected to signal conditioning using a quad operational amplifier analog front end (AFE). The tonometer is calibrated to show the applied pressure in mmHg. The hardware configuration includes a pulser-receiver system built around a high-speed ultrasonic pulser (STHV-748, STMicroelectronics Co. Ltd., Shanghai, China) that operates a single-element broad-band ultrasound transducer in pulse-echo mode. An Arm Cortex M4 microcontroller (LPC4370FET256, NXP Semiconductors B.V., Eindhoven, Netherlands) serves as the principal control unit, generating digital pulsing logic and RF frame acquisition. An inbuilt analog-to-digital converter, functioning at a sampling rate of 80 Mega samples per second, digitizes the RF signals received by the transducer.

B. *Study Design and Protocol*

A cross-sectional pilot study on 21 healthy volunteers was conducted at the Indian Institute of Technology, Madras, Chennai, India. Before the trials, a verbal inquiry was made regarding the consumption of substances known to affect arterial stiffness temporarily. The objectives of the study were (i) to conduct measurements at different hold-down pressure levels and understand the effect on stiffness measurement, (ii) based on the obtained results, to identify optimal hold-down pressure to enhance the established usability of the device.

The study proposal and protocol were reviewed by the institute ethics committee (IEC/2021-01/JJ/07). The study participants were informed of the study objectives and protocol in advance. Written consent on their voluntary participation was collected and the study adheres to the principles enlisted in the Helsinki Declaration for studies on human participants, as revised in 2013.

C. *Data Collection*

Anthropometric measurements were collected for each participant, followed by a 5-minute relaxation period. The brachial pressure cuff was positioned on the upper left arm, while the femoral cuff was tightened around the left thigh of the participant. Subsequently, blood pressure was measured using a clinical-grade oscillometric BP monitor (Sun Tech® 247 $^{\mathrm{TM}}$). Measurement of the distance from the carotid to the top of the femoral cuff was taken. All ultrasound and tonometric measurements were conducted on the left common carotid artery while participants were in a supine position. The artery's location was determined by palpation on the left side of the neck. Four trials of measurements were performed at hold-down pressure levels of 50-, 100-, 150-, and 200-mmHg for each participant. RF frames were recorded when the ultrasound probe was positioned perpendicular to the artery, and the tonometer indicated the pressure applied to the participants' skin. Due to the difficulty in maintaining a single pressure value, a tolerance of ±10 mm Hg was upheld throughout the study. Operators received animated visual feedback to assess signal quality. Continuous measurements of diameter and femoral pulses for 30 seconds were obtained, and for analysis, the top 10 cycles with the lowest coefficient of variation were selected.

D. Data Processing

ARTSENS algorithms [9],[10] were used to analyze the A-mode frames and obtain carotid diameter and pressure, central pressure, and local and regional stiffness. The obtained data were further analyzed to extract mean diastolic diameter and mean distension, with coefficients of variation computed for both parameters. Carotid artery stiffness markers were derived through the beat-to-beat diameter parameters and blood pressure data. Simultaneous acquisition of femoral and diameter pulses facilitated pulse transit time (PTT) calculation using an intersecting tangent algorithm. Using the carotid to the femoral cuff distance with a multiplication factor of 0.8 and the PTT, carotid to femoral pulse wave velocity was obtained.

E. Statistical Analysis

Measurements were documented in mean ± standard deviation (SD) format. Box-and-whisker plots were constructed using mean values and interquartile ranges to illustrate both similarities and differences. Beat-to-beat repeatability of diastolic diameter and distension measurements was calculated as the ratio of SD to mean, expressed as a percentage.

III. RESULTS AND DISCUSSION

A. Reliability of Data

Table I summarizes the demography as well as the average BP and HR of the participants in the study. The RF echo signals from the ultrasound transducers had an SNR of 30 dB,

TABLE I: CHARACTERISTICS OF THE STUDY POPULATION (N=21)

Parameters	**Mean ± SD**	**Range**
Age (years)	25 ± 2.3	21-28
Height (cm)	174.23 ± 6.32	161-186
Weight (Kg)	68.96 ± 13.03	48-96
Brachial SBP (mm Hg)	111.86 ± 12.4	98-141
Brachial DBP (mm Hg)	68.62 ± 6.6	57-84
Brachial MAP (mm Hg)	82.3 ± 6.7	77-101
Heart rate (bpm)	69.04 ± 10.42	58-102

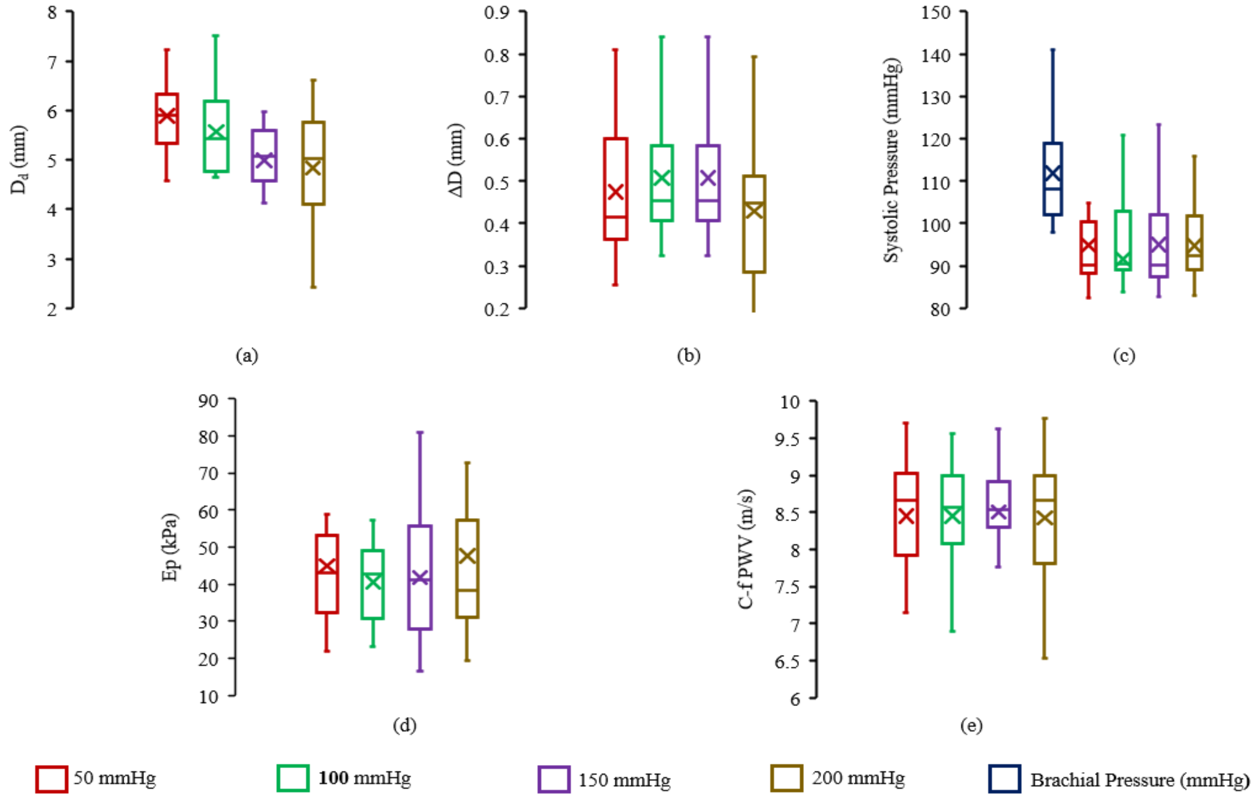

Fig. 2. Box and Whisker plot (a) End-diastolic diamter, (b) distension, (c) Spread of systolic pressure brachial vs carotid, (d) Pressure-strain elastic modulus, (e) Carotid to femoral pulse wave velocity

TABLE II: EFFECT OF HOLD-DOWN PRESSURE ON DIAMETER

Mean	50mmHg	100mm Hg	150mm Hg	200mm Hg
ΔD (mm)	0.47±0.14	0.5±0.14	0.47±0.12	0.43±0.17
D_D (mm)	5.9±0.7	5.6±0.83	5.0±0.75	4.8±1.13
ΔD - CoV (%)	7.4±4.30	5.1±3.08	7.3±6.33	8.3±7.01
D_D - CoV (%)	7.6±6.86	6.3±3.67	9.4±11.25	12.7±17.05

and the pressure signals from the femoral thigh cuff and carotid tonometry had an SNR of 25 dB each. All the signals had enough signal quality at all stages of the study protocol. The hold-down pressure-tagged diameter waveforms obtained from RF signal processing, and femoral pulse waves were continuous and quasi-periodic. Sufficient continuous cycles of diameter waveform and femoral pulse waveforms were extracted for analysis at each stage of the hold-down pressure.

B. *Effect on Carotid Diameter and Pressure*

Table II outlines the effect of operator hold-down pressure on carotid end-diastolic diameter (D_D) and distension (ΔD). The lowest CoV for ΔD and D_D was observed at the hold-down pressure of 100 mmHg, with a mean value of 5.6 ± 0.83 mm and 0.5 ± 0.14 mm respectively. Fig.2 (a)-(b) depicts an overall decrease in the mean values of ΔD and DD under the graded increase of hold-down pressure from 50 mmHg to 200 mmHg. Fig. 2(c) depicts the box-whisker plot of calibrated carotid pressure spread at the systolic level with a graded increase of hold-down pressure and against brachial SBP. The similarities in the spread of interquartile ranges between brachial SBP and carotid SBP at 100 and 150 mmHg were observed. Similar studies, on pressure-tagged diameters, have reported a decreasing trend of the D_D and ΔD [6], indicative of the significance of the hold-down pressure, enough to externally modify the arterial geometry measurements. In a phantom setting [7] as reported a maximum root-mean-square error of 7.12 mmHg on the effect of hold-down pressure on the calibrated pressure waveforms, using tonometry-like force sensors.

C. *Effect on Local and Regional Stiffness Markers*

Fig. 2 (d) depicts the variation of the local stiffness marker (Ep) at a graded increase of the operator hold-down pressure. Ep had the lowest CoV (7-9 %) at the hold-down pressure of 100 mmHg. The better reliability of Ep at 100 mmHg versus other hold-down pressures, may be attributed to the lower CoV in D_D, ΔD, and pressure measurements [8]. The mean values of Ep across the study population at 100 mmHg hold-down pressure was 40.55 ± 10.29. In comparison, the regional stiffness marker (C-f PWV) as depicted in Fig.2 (e) shows similar spreads in the interquartile ranges across the hold-down pressure and slightly lower CoV (8.77%) at 150 mmHg Hold-down pressure. From these observations, hold-down pressure plays a substantial role in the measurement of both local and regional stiffness markers. Similar studies, also report the challenges in the repeatability of measurements and the requirement of trained personnel to use ultrasound-based or tonometry devices, which may potentially arise from the variability induced in the measurements due to operator-dependent hold-down pressure.

D. *Limitations*

The primary limitation is the relatively small sample size and large step size in the increment of the hold-down pressure. Nonetheless, the arterial geometry parameters and the stiffness markers are sufficient for the initial feasibility study.

IV. CONCLUSION

The effect of hold-down pressure on arterial geometry and stiffness markers is presented here. In-vivo experiments to obtain the end-diastolic diameter, distension, and local and regional stiffness markers were demonstrated using the bi-modal probe and acquisition system. The device demonstrated an SNR of greater than 20dB and a beat-to-beat coefficient of variation of less than 15% for all levels of hold-down pressures. Our study results suggest that a hold-down pressure of 100 mmHg is the optimal choice for stiffness measurements. This pressure value is slightly higher than diastolic pressure, demonstrating optimal vascular stiffness measurements.

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