This full text paper was peer-reviewed at the direction of IEEE Instrumentation and Measurement Society prior to the acceptance and publication.

A Bi-modal Probe Integrated with A-mode Ultrasound and Force Sensor for Single-site Assessment of Arterial Pressure-Diameter Loop

Rahul Manoj
Department of Electrical Engineering
Indian Institute of Technology Madras
Chennai, India
rahul_manoj@smail.iitm.ac.in

Raj Kiran V
Department of Electrical Engineering
Indian Institute of Technology Madras
Chennai, India
ee15d020@smail.iitm.ac.in

Nabeel PM
Healthcare Technology Innovation Centre (HTIC)
Indian Institute of Technology Madras
Chennai, India
nabeel@htic.iitm.ac.in

Jayaraj Joseph
Healthcare Technology Innovation Centre (HTIC)
Indian Institute of Technology Madras
Chennai, India
jayaraj@htic.iitm.ac.in

Mohanasankar Sivaprakasam
Department of Electrical Engineering
Healthcare Technology Innovation Centre (HTIC)
Indian Institute of Technology Madras
Chennai, India
mohan@ee.iitm.ac.in

***Abstract*— There is an ever-increasing interest in the research community towards the development of advanced in-vivo diagnostic and screening tools for cardiovascular diseases. Various methodologies often do not account for potential errors in arterial pressure and diameter measurements. This paper highlights these pitfalls through the design and instrumentation of a bi-modal probe integrated with A-scan ultrasound and force sensor. This probe is used for simultaneous and single-site assessment of pressure – diameter (PD) loop of superficial arteries. In-vivo measurement of PD loop is a gateway to study the mechanical properties of artery, design and development of vascular grafts and clinically significant for measurement of arterial stiffness, local pulse wave velocity, and central blood pressure. The novelty comes with the usage of an image free A-scan mode of ultrasound, which makes it possible to keep the force sensor and ultrasound transducers very close, solving one of the challenges faced by state-of-the-art techniques in single site measurement. In addition to this, in-house-developed acquisition hardware and software ensures matched frequency response and time synchronization for both pressure and diameter signals. Signals were reliably recorded with an SNR of 20 dB and constructed PD loop is in the clockwise direction with pressure signals leading diameter signals.**

Keywords—Pressure-diameter loop, tonometry, carotid artery, viscoelastic, diameter waveform, pressure waveform, bi-modal probe, hysteresis

I. INTRODUCTION

Hemodynamic loops such as pressure-diameter (PD) provides the stress-strain relation of the artery. The PD loop is the gateway to assess the mechanical properties of the artery due to age and pathological conditions. More specifically, evaluation of arterial stiffness [1], local pulse wave velocity (PWV) [2], elastic and viscous properties of the arteries [3], and development of vascular grafts [4] with matching stress-strain characteristics is made possible by the assessment of PD loops. Clinical significance of PD loops to assess the functional properties of artery, comes at a time when cardiovascular diseases continue to remain the primary cause of morbidity and mortality all over the world [5]. In this context, there is always a need to improve the existing methodologies that can improve the cardiovascular risk stratification of an individual [6]–[8].

The PD loop reveals the non-linear elasticity and viscoelastic nature of the artery. Arterial structure consists of (a) smooth muscle cells (SMC) – under neural activity contracts and expands the geometry altering elastic modulus and viscosity, (b) elastin – rubber-like protein synthesized by SMC and is linear elastic with low elastic modulus (< 10 MPa), can sustain considerable stress and strain and (c) collagen – nylon-like protein synthesized by SMC. Collagen fibres are thinner than elastin, providing the tissue with the strength and integrity to prevent excess dilation. It is inelastic, and modulus increases with the increasing strain (10MPa-100MPa) [9]. Collagen is responsible for the non-linear elastic behaviour of the tissue. At lower strains, collagens are in folded form and do not contribute to the elasticity, and as strain increases, the fibres straighten and bear the stress [10].

Ideally, a PD loop should be constructed from single-site measurement; only then it will be reflecting the actual physiology. State of the art in simultaneous pressure and diameter recordings combine B-mode imaging linear array probe and force sensor as discussed in [11]–[15]. The design of the force sensor and associated instrumentation is often driven by application, for instance, in [12], for measurement of regional mechanical properties of aorta, instantaneous aortic measurements were estimated from calibrated subclavian pulse tracing, generated by use of a small funnel positioned over the target artery at its point of maximal impulse, and connected via silastic tubing to the strain gauge transducer. In [13], to assess the viscoelastic properties of peripheral arteries, a 6 mm diameter strain gauge transducer is fit with a con-cylinder made of plexiglass to reduce the contact area to 1.5 mm to measure the palpating pressure of peripheral arteries. For the assessment of vascular reactivity, in [14], a custom pressure transducer and signal conditioning circuit were developed. To study the effect of hypertension on the viscoelasticity of large arteries [15], a probe with Miller micromanometer (later known as Miller tonometer), which has the same frequency response as miller catheters were used. In [11], for PD loops pressure signals were captured using Pulse Pen®, another commercial form of the tonometer. All these works reported the use of an imaging system coupled with variants in tonometry sensors. There are several shortcomings and measurement pitfalls while integrating force sensors with conventional B-mode imaging systems. A

978-1-7281-5386-5/20/$31.00 ©2020 IEEE

detailed discussion on these can be found elsewhere [16]. It is essential, for any design of a new probe, to satisfy these methodological considerations, to assess actual physiology of PD loops.

In this work, we present the design and instrumentation of a bi-modal probe for simultaneous assessment of PD loop. The article starts with addressing the functional requirements for any bi-modal sensor system that needs to be satisfied for assessing actual physiology of the arterial walls using PD loops, followed by the design of bi-modal probe – hardware and software architecture. The results focus on the reliability of signals devoid of measurements induced errors, ambiguity regarding the direction of the hysteresis loop and variations in the shapes of PD loop due to possible phase shifts. The scope of this paper is limited to only in-vivo methods, and hence invasive methodologies are not discussed.

II. Materials and Methods

A. Functional Requirements for a Bi-modal System

In order to examine exact physiology of arterial walls, it is essential that phase shift between pressure and diameter signals contain no contributions from the measurement system. If the sensors used for acquiring pressure and diameters signals are from different manufacturers and comes with proprietary acquisition systems, it may not be possible to have matched frequency response from two different acquisition systems. Hence, it is necessary for a bi-modal sensor system to ensure matching frequency response for both the signals being recorded. It is also crucial to characterize the phase shift due to acquisition systems before further signal processing and make appropriate compensations. Most of the proprietary acquisition devices that comes with the sensor have limited control for setting the desired sampling rate. It will be required to up-sample or down-sample a set of recorded signals to match the sampling rate of the other. Therefore, time-synchronized and simultaneous signal acquisition ensuring the same sampling rate for both the acquisition device becomes essential. An inherent practical limitation of current multi-modal sensory system is that single-site in-vivo measurements are not feasible, owing to the form factors of the commercially available transducers. Any measurement device must follow all the functional requirements stated above to ensure true arterial physiology is getting recorded as PD loop.

B. Design of Ultrasound-Force Bi-modal Probe

The intended usage of the developed probe is to simultaneously acquire high frame rate A-mode ultrasound scan along with skin surface force at the target artery site. The sensor arrangement is optimized for the carotid artery. The carotid artery is superficial in nature, easily accessible as well as a direct branching from the aorta resembles central nature [17]. The probe consists of a of custom ultrasound transducer (diameter: 5 mm, centre frequency: 5MHz, spatial half-angle < 1.3°) and a tonometer (SPT-301, Miller Instruments) separated by a centre-to-centre distance of 2 mm. The ultrasound transducer is labelled as channel A in the Fig.1. The tonometer is used to acquire the skin surface force resulting from the transmural blood pressure at the carotid artery. Considering the form factor of the sensors, the centre-to-centre distance from tonometer to channel A ultrasound transducer is optimally kept at 2 mm. This positionally offset between sensors are compensated in software by shifting the resulting diameter waveform obtained from channel A transducer by local transit time equivalent to 2 mm, to ensure single site measurement. To achieve this, a second ultrasound transducer (identical to the first) labelled as channel B separated by a centre-to-centre distance of 35 mm from channel A transducer is used. Local PWV is calculated from local transit time between the two diameter waveforms [4]. The local PWV information is used to make corrections for the position offset of the bi-modal probe. All the sensors are enclosed in a 3D printed enclosure with a handgrip, for user-friendly operation and alignment.

In order to perform, bi-channel arterial diameter measurement, the A-mode ultrasound signals in pulse-echo mode needs to be captured for far and near walls of the artery. The sharpest echoes are received when the transducers are aligned perpendicular to the pulsating artery walls. The narrow half-angle beam width and poor off-axis sensitivity ensure measurements are performed along the true diameter of the artery.

C. Hardware Unit for Force Measurement

The transmural blood pressure from superficial arteries like radial, brachial, carotid and femoral can be acquired from skin surface using applanation tonometry principle [18]. A tonometer is a MEMS-based force sensor that can pick up skin surface pulses when the artery is applanated against bone or muscles structure beneath. The principle involves applying an optimal hold-down pressure with the probe on superficial arteries such that the circumferential stress on the arterial wall is balanced and pressure waveform can be recorded. The probe needs to be oriented with appropriate hold-down pressure to register waveforms with maximum amplitude in a repeatable manner.

The MEMS within the tonometer is a strain gauge resistive network in half-bridge. The bridge is excited with a precision voltage source unit that ensures 5V. The differential voltage output is expected from -0.5 mV to 7.5 mV, based on of sensitivity at 5μV/V/mmHg and range of operation from -50 mmHg to 300 mmHg at 5V excitation as per manufacture's manual. The differential signal may be subjected to any offset, which is corrected by an offset correction pre-amp circuit. The offset correction circuit involves pre-amplifying the offset with a small gain using an instrumentation amplifier (INA 125 – Texas Instruments) and subtracting the voltage at the inverting terminal of the second stage amplifier manually trimming it out using a 1 kΩ potentiometer, connected to a reference voltage as illustrated in the Fig.1. The gain of the second stage using the same instrumentation amplifier will amplify the signal to the required levels. The amplified voltage is then fed to a 14-bit ADC channel at 1kHz sampling rate of data acquisition device NI 6002 (National Instruments). The saving of the digitized force waveform is synchronized with that of the ultrasound echo signals, which will be discussed in subsequent sections.

D. Hardware Unit for Diameter Measurement

The ultrasound transducers are isonated by high voltage (±40 V) pulse train of width 100 ns using the pulser – receiver module (SHTV78 – STM Electronics). The required digital logic to control the pulser – receiver module to switch between transmit and receive A-scan signals in pulse-echo mode is programmed via a high-speed digital logic card (NI 6556 – National Instruments). The A-scan depth is set for 40 mm, and corresponding echoes for the entire depth would span 52 μs.

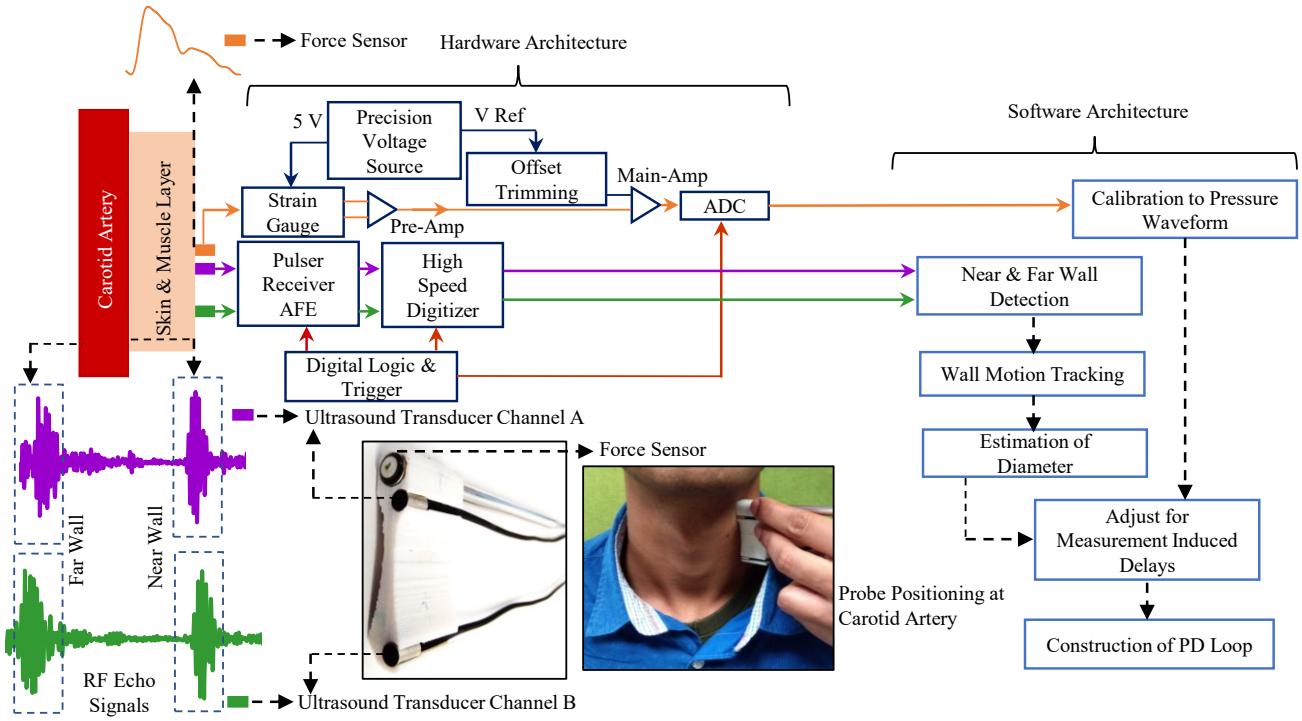

Fig. 1. Overall system architecture with hardware and software, probe design and positioning of probe at left carotid artery

The received echoes are amplified by analog front end (AFE) module, before digitization. The echoes are sampled at

The received echoes are amplified by analog front end (AFE) module, before digitization. The echoes are sampled at 50 MHz sampling rate using a high-speed digitizer card (NI 5154 – National Instruments), illustrated in Fig.1. The sampling and writing of the received echoes to a binary format file are performed in a timed manner using a trigger signal generated by NI 6556 at an interval of 1 ms. This trigger signal at 1kHz is used for synchronized acquisition and writing of force signals along with echoes at frames rates of 1 kHz to binary format file. The received echo signals undergo further processing to obtain diameter waveform. This ultrasound hardware circuit is the most evolved version of ARTSENS® technology developed by our group [19].

E. Synchronised Signal Processing

The program for acquisition and control of all the signals are written in National Instruments LabVIEW platform. A detailed illustration of the overall architecture is shown in Fig. 1. For ensuring a synchronized acquisition and writing of ultrasound echoes and force signals to a binary file for further signal processing, a software logic was implemented using NI 6556, by generating a trigger pulse of frequency 1 kHz. The trigger pulse is connected to both digitizer units of ultrasound echo (NI 5154) and that of force signal (NI 6002). The digitized waveforms are processed using an 8^{th} order bandpass filter with a lower cut-off frequency of 0.5 Hz and upper cut-off frequency of 14 Hz, to remove out of band noises. The filters used are zero-phase filters to ensure no additional shifts to the frequency components of the signals. The algorithm used for converting the A-scan echoes to diameter waveform is extensively validated by our ARTSENS® technology [19]. The automated algorithms of ARTSENS® continuously track the locations of echoes that corresponds to the far and near walls of the artery to compute the lumen diameter [20]. Once the diameter waveforms are obtained for both channels, along with corresponding force signal, an automated cycle cutting algorithm is employed to isolate individual cardiac cycle waveforms. The DC offset in force signal is then removed, normalized and calibrated to obtain pressure signals. This pressure cycle and corresponding diameter cycle is used to construct the PD loop.

F. Validation Study

An in-vivo validation study to test the feasibility of the developed device for reliable capturing of the signals and constructing the pressure-diameter loop is performed in a small cohort of 5 subjects with a mean age of 27±3 years. The cohort included only normotensive subjects. The study was carried out in compliance with the Helsinki declaration revised in 2013 by World Medical Association. Written informed consent was obtained prior to the data collection from the recruited subjects after explaining the study protocols. All subjects were comfortably seated for 10 min, for stabilizing blood pressure (BP) level and heart rate at the beginning of measurement protocol.

All physiological measurement was conducted in a supine position by a single operator in a temperature-controlled environment (23° C). The probe was placed at the left carotid artery. The carotid artery location was identified by palpation before the placement of the probe. By inspecting the signals recorded, appropriate hold-down pressure and correct orientation were adjusted to capture the signals reliably. Approximately, 20 – 30 continuous cycles were acquired for each subject. Brachial BP was measured with clinical-grade oscillometric BP monitor (SunTech® 247 – SunTech Medical) using a bladder-type pressure cuff, which was used to calibrate the force waveform.

III. Results and Discussions

A. Reliability of Signals

The developed bi-modal probe encompassing an A-scan ultrasound for arterial diameter measurement integrated with a force sensor has demonstrated the expected functionality.

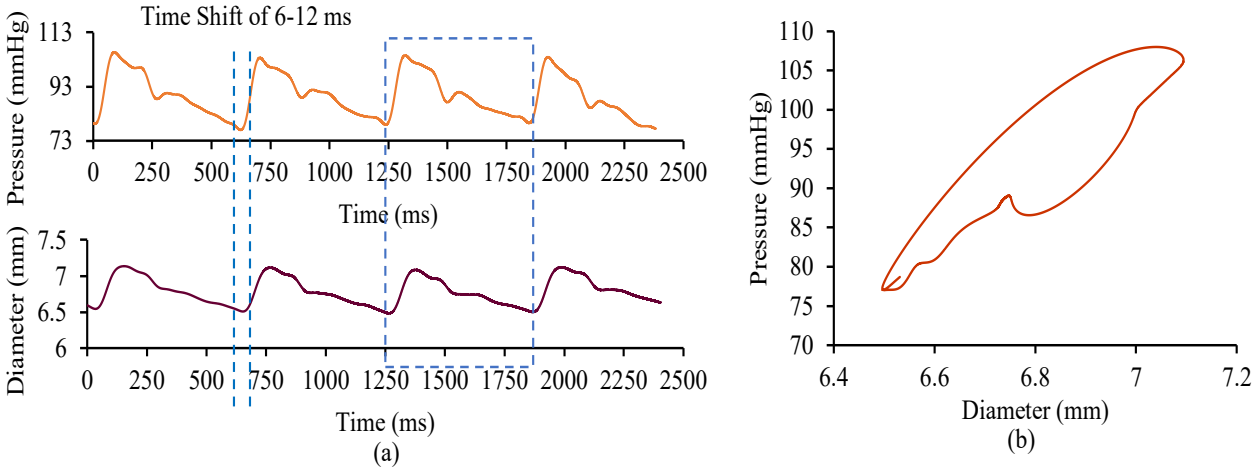

Fig. 2. (a). Continuous cycles of pressure and diameter waveforms, with pressure leading diameter, (b). PD loop constructed from one set of cycle

These waveforms are quasi-periodic and continuous, representing transmural blood pressure pulse morphology and resulting distension of the walls. Signals were reliably captured with an SNR of 20 dB. The diameter waveform from both the channels along with the force signal was up-sampled to 10 kHz, to reliably calculate local transit time and the phase shifts between diameter and force signal. The force signal consists of a DC level proportional to the hold-down pressure applied by the operator and an AC component which is the pressure pulse. It is found that in a majority of the works related to examining a PD loop [11]–[15], the sensors used for acquiring pressure and diameters signals were from different manufacturers and comes with proprietary acquisition systems; hence has a limitation to certain that the frequency response from two different acquisition systems to be the same. They would come with filtering and improved SNR circuitry that can produce a phase shift between simultaneously acquired pressure and diameter signals on different acquisition systems. It would be more of an instrumentation challenge to integrate sensors into a single acquisition device to ensure matching frequency response for both the signals recorded. Another solution would be crosswise filtering of the recorded signals with that of the other acquisition system [16]. Either way, it is vital to characterize the phase shift due to acquisition systems before further signal processing and make appropriate compensations. In this view, the circuity of the acquisition system for both the sensors was developed entirely in-house PCBs and integrated into a single system, to ensure the same frequency response for both sensors. The amplifier circuits were independently verified to have insignificant phase shifts between input and output over a wide range of frequencies.

Time synchronized signal acquisition and ensuring the same sampling rate for both the acquisition device is essential to investigate variations on a beat-to-beat scale. This ensures that the pressure and diameter signals correspond to the same cardiac cycle. The proprietary acquisition devices that comes with the sensor have fixed or limited control for setting the desired sampling rate. It is required to up-sample or down-sample a set of recorded signals to match the sampling rate of the other. Once the recorded signals are time-synchronized and sampled to the same frequency, it is subjected to further digital signal processing. Care must be taken to ensure both the signals are processed using the same signal processing algorithms to avoid phase lags between the recorded signals, being falsely attributed to functional properties of arterial walls.

An inherent practical limitation of the multi-modal sensory system is that single-site measurements are not feasible owing to the form factors of the commercially available transducers. A potential way to minimize this positional offset would be to keep sensors as close as possible without causing any cross talk or signal corruption and compensate with an appropriate time shift of the signals. In the present design, this offset can be corrected as a time shift in one of the signals, if the local PWV (m/s) on the same arterial segment and position offset (mm) is known beforehand. Local transit time from the two diameter waveforms was found to be 8.0-10.0 ms for 35 mm. Although insignificant, the channel A diameter waveform is shifted by 1.0-2.0 ms compensating for the position offset. To summarize, the developed bi-modal sensory system has position offset corrected and time-synchronized signal acquisition with identical frequency response, to ensure exact arterial physiology is getting recorded in PD loop.

B. Construction of Pressure-Diameter Loop

The force signal after removing the DC level and upon normalizing is calibrated to pressure based on linear calibration model as in (1)

$$P(t) = A \times f(t) + B, \tag{1}$$

where $P(t)$ is the transmural pressure, $f(t)$ is the force signal, after removing DC offset, which is highly operator sensitive term[21], A and B are constants.

As per literature, the calibration model used to transform any $f(t)$ to $P(t)$ is via known values of systolic (P_s) and diastolic (P_d) pressure values of brachial artery. Therefore, (1) becomes,

$$P(t) = \frac{\Delta P}{\Delta f} \times f(t) + P_d \tag{2}$$

where ΔP is the pulse pressure and Δf is the pulse force, defined as follows,

$$\Delta P = P_s - P_d \; and \; \Delta f = f_{mx} \tag{3}$$

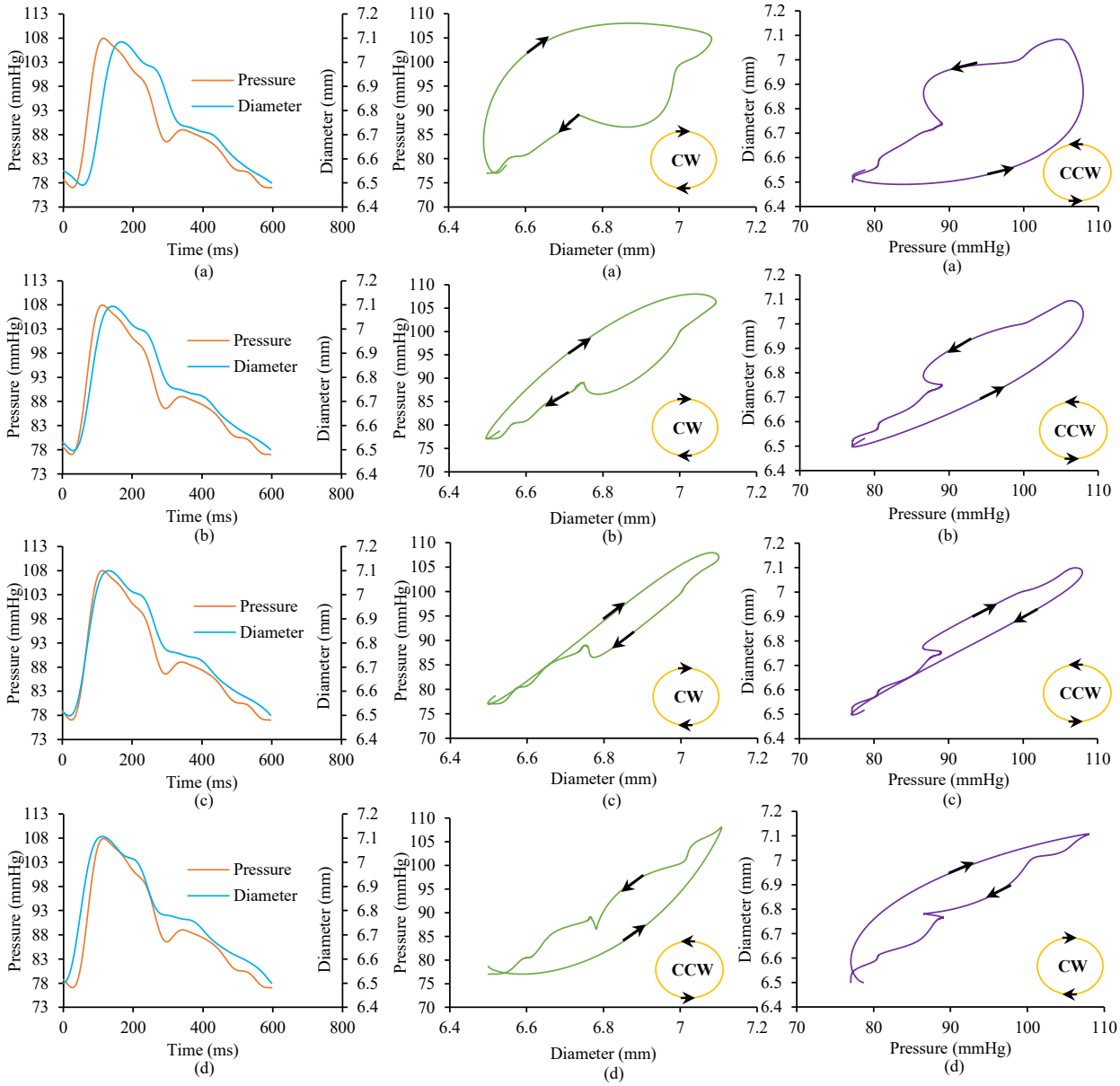

Fig. 3. Pressure and diameter waveforms for various measurement errors in phase shift, (a) pressure leading diameter by significant shift, (b) after eliminating measurement delays, (c) when diameter waveform gets shifted more, corrupting true PD loop, (d) pressure lagging diameter due to measurement errors

where f_{mx} is the maxima of $f(t)$ for the selected cardiac cycle (after DC offset removal).

Now, the pressure and corresponding diameter are free from any measurement induced phase shits, and plot between them should reveal the true PD loop for carotid artery, as shown in Fig. 2. The phase shift between pressure and diameter can be accounted as shown in (4)

$$T_{TOTAL} = T_{Freq} + T_{Syn} + T_{Off} + T_{TTT} + T_{Vis} \quad (4)$$

where T_{TOTAL} is the overall phase shift, T_{Freq} is due to frequency mismatch, T_{Syn} is due to any synchronization error between the sensors, T_{TTT} is the tissue transit time (time taken by the transmural pressure pulse to reach skin surface) and T_{Vis} is due to the viscoelastic nature of artery and interleaving tissue. The first three factors are due to measurement system, and the last two are physiology factors. At-most care went into design to eliminate or minimize the errors due to measurement system. To illustrate the feasibility of this probe, a validation study was conducted within a small cohort as mentioned earlier in the validation study sub-section. The mean value of f_{mx} is calculated from five consecutive cardiac cycles for each subject, and further to illustrate an application of PD loop, β index, which quantifies arterial stiffness is calculated from its standard formula as shown in (5)

$$\beta = \ln\left(\frac{P_{sc}}{P_{dc}}\right) \Big/ \left(\frac{D_s}{D_d} - 1\right) \quad (5)$$

where P_{sc} and P_{dc} are systolic and diastolic blood pressure at carotid artery, obtained from (2), and adjusted for the hydrostatic pressure, as measurements are taken at siting posture. D_s and D_d are systolic and diastolic diameter of carotid artery. The results of the study is shown in Table I.

In literature, many authors have interchangeably used PD and DP loops, ignored the phase shits and corresponding CCW and CW direction of loop, to clarify on this, a detailed

TABLE I. STUDY RESULTS

Subject ID (SBP/DBP) (mmHg)	Fmx (mV)	CoV in Fmx (%)	Beta	CoV in Beta (%)
A (114/75)	0.56±0.02	4.67	5.45±0.32	6.01
B (100/60)	0.76±0.04	6.08	5.15±0.35	6.91
C (115/77)	0.65±0.01	2.35	3.14±0.15	4.82
D (118/75)	0.92±0.04	5.11	4.01±0.08	2.14
E (121/79)	0.60±0.02	4.41	5.20±0.32	6.19

illustration is shown in Fig. 3, explaining various combinations of PD loops. If all the measurement induced phase shifts are corrected, it is observed that pressure waveform leads to diameter waveform by 6 ms – 12 ms between the fiducial point closer to the waveform foot.

The PD loop helps to understand the non-linear elastic nature, observed as the increasing slope of the PD curve (after eliminating viscosity) and viscoelastic nature as hysteresis loop. The former is contributed mainly by the elastin – collagen ratio, and later by smooth muscle tone of the artery [10]. We infer from the PD loop that the path taken for the distension cycle of an artery during the systolic phase and diastolic phase are different. This buffer plays a vital role by exchanging the kinetic energy of the flow to potential energy during the systolic phase and back into kinetic energy during the diastolic phase resulting in smooth and continuous blood flow. Physiologically the viscous nature is attributed to the reaction of vascular smooth cells against stretch (due to the transmural pressure), known as "Bayliss myogenic response" [22] and results in the observed hysteresis loop.

IV. Conclusion

In this work, we have presented the design and usability of a bi-modal probe for assessing the PD loop of the carotid artery. In this regard, we have outlined the functional requirements required to be satisfied while designing any PD loop assessment device. This includes matching frequency response or crosswire filtering of recorded signals, time-synchronized and matching sampling rate while acquiring and keeping the sensors as close as possible followed by time-shift one of the signals to correct the physical offset distance between the sensors used. Any of the measurement error as mentioned above would cause a false interpretation of the actual physiology of the arterial walls. The constructed PD loop is in the clockwise direction with pressure signals leading diameter signals, also validated by various works in literature [11]-[15]. The true hysteresis loop accounts for viscoelastic delay and tissue transit time delays only. Once true PD loop is obtained, further modelling, and processing can be performed to separate viscous and elastic components. By exploring this, works are progressing in our group towards using the uncalibrated force waveform and corresponding diameter waveform to obtain models for cuffless measurement of central blood pressure.

References

[1] P. Segers, E. R. Rietzschel, J. A. Chirinos, S. Editors, J. Powell, and G. Mitchell, "Brief Review on How to Measure Arterial Stiffness in Humans," *Arterioscler. Thromb. Vasc. Biol. ATVB*, no. March, pp. 1–10, 2020.

[2] P. M. Nabeel, V. K. Raj, J. Joseph, V. V. Abhidev, and M. Sivaprakasam, "Local Pulse Wave Velocity: Theory, Methods, Advancements, and Clinical Applications," *IEEE Rev. Biomed. Eng.*, vol. PP, no. c, pp. 1–1, 2019.

[3] R. D. Bauer, R. Busse, A. Schabert, Y. Summa, and E. Wetterer, "Separate determination of the pulsatile elastic and viscous forces developed in the arterial wall in vivo," *Eur. J. Physiol.*, vol. 380, no. 3, pp. 221–226, 1979.

[4] F. Montini-Ballarin *et al.*, "Elasticity response of electrospun bioresorbable small-diameter vascular grafts: Towards a biomimetic mechanical response," *Mater. Lett.*, vol. 209, pp. 175–177, 2017.

[5] "Cardiovascular Diseases." [Online]. Available: https://www.who.int/health-topics/cardiovascular-diseases. [Accessed: 12-Jan-2020].

[6] M. Forouzanfar, H. R. Dajani, V. Z. Groza, M. Bolic, S. Rajan, and I. Batkin, "Ratio-independent blood pressure estimation by modeling the oscillometric waveform envelope," *IEEE Trans. Instrum. Meas.*, vol. 63, no. 10, pp. 2501–2503, 2014.

[7] M. P. D. Pont and J. L. B. Marques, "Reflective photoplethysmography acquisition platform with monitoring modules and non-invasive blood pressure calculation," *IEEE Trans. Instrum. Meas.*, vol. PP, no. c, pp. 1–1, 2020.

[8] P. M. Nabeel, S. Karthik, J. Joseph, and M. Sivaprakasam, "Arterial blood pressure estimation from local pulse wave velocity using dual-element photoplethysmograph probe," *IEEE Trans. Instrum. Meas.*, vol. 67, no. 6, pp. 1399–1408, 2018.

[9] R. W. Holzapfel, Gerhard A. Ogden, *Biomechanics of Soft Tissue in Cardiovascular Systems*. Springer-Verlag Wein GmgH, 2003.

[10] P. Kalita and R. Schaefer, "Mechanical models of artery walls," *Arch. Comput. Methods Eng.*, vol. 15, no. 1, pp. 1–36, 2008.

[11] C. Giannattasio *et al.*, "Simultaneous measurement of beat-to-beat carotid diameter and pressure changes to assess arterial mechanical properties," *Hypertension*, vol. 52, no. 5, pp. 896–902, 2008.

[12] R. M. Lang, B. P. Cholley, C. Korcarz, R. H. Marcus, and S. G. Shroff, "Measurement of regional elastic properties of the human aorta: A new application of transesophageal echocardiography with automated border detection and calibrated subclavian pulse tracings," *Circulation*, vol. 90, no. 4 I, pp. 1875–1882, 1994.

[13] Y.-W. Shau, C.-L. Wang, J.-Y. Shieh, and T.-C. Hsu, "Noninvasive assesment of the viscoelasticity of peripheral arteries," *Medicine (Baltimore).*, vol. 25, no. 9, pp. 1377–1388, 1999.

[14] N. Pérez López, M. A. De Luca, G. Sivori, L. J. Cymberknop, and R. L. Armentano, "Real-time vascular response assessment by means of a dual pressure-diameter device: a preliminary study," *12th Int. Symp. Med. Inf. Process. Anal.*, vol. 10160, p. 1016014, 2017.

[15] A. Simon and J. Levenson, "Effect of hypertension on viscoelasticity of large arteries in humans," *Curr. Hypertens. Rep.*, vol. 3, no. 1, pp. 74–78, 2001.

[16] A. P. G. Hoeks, J. M. Willigers, and R. S. Reneman, "Effects of assessment and processing techniques on the shape of arterial pressure-distension loops," *J. Vasc. Res.*, vol. 37, no. 6, pp. 494–500, 2000.

[17] C. M. McEniery, J. R. Cockcroft, M. J. Roman, S. S. Franklin, and I. B. Wilkinson, "Central blood pressure: Current evidence and clinical importance," *Eur. Heart J.*, vol. 35, no. 26, 2014.

[18] G. L. Pressman and P. M. Newgard, "a Transducer for the Continuous External Measurement of Arterial Blood," *IEEE Trans. Biomed. Eng.*, vol. 10, pp. 73–81, 1963.

[19] J. Joseph, R. Radhakrishnan, S. Kusmakar, A. S. Thrivikraman, and M. Sivaprakasam, "Technical Validation of ARTSENS-An Image Free Device for Evaluation of Vascular Stiffness," *IEEE J. Transl. Eng. Heal. Med.*, vol. 3, no. April, p. 1900213, 2015.

[20] A. K. Sahani, M. I. Shah, R. Radhakrishnan, J. Joseph, and M. Sivaprakasam, "An Imageless Ultrasound Device to Measure Local and Regional Arterial Stiffness," *IEEE Trans Biomed Circuits Syst*, vol. 10, no. 1, pp. 200–208, 2015.

[21] R. Manoj and J. Joseph, "Cuffless Evaluation of Arterial Pressure Waveform using Flexible Force Sensor : A Proof of Principle," in *IEEE International Symposium on Medical Measurements and Applications (MeMeA)*, 2019.

[22] W. . Bayliss, "On the local reactions of the arterial wall to changes of internal pressure," *J. Physiol.*, vol. 28, no. 3, pp. 220–231, 1902.