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

Cuffless Evaluation of Arterial Pressure Waveform using Flexible Force Sensor: A Proof of Principle

Rahul Manoj
Department of Electrical Engineering
Indian Institute of Technology Madras
Chennai, India – 600 036
e-mail: rahulmanojktym@gmail.com

Nabeel P M
Department of Electrical Engineering
Indian Institute of Technology Madras
Chennai, India – 600 036

Raj Kiran V
Department of Electrical Engineering
Indian Institute of Technology Madras
Chennai, India – 600 036

Jayaraj Joseph
Healthcare Technology Innovation Centre
Indian Institute of Technology Madras
Chennai, India – 600 113

Mohanasankar Sivaprakasam
Department of Electrical Engineering
Healthcare Technology Innovation Centre
Indian Institute of Technology Madras
Chennai, India – 600 036

***Abstract*— In recent years, thin, flexible force sensors have appeared and been widely used as pressure sensors. These sensing elements are now emerged into robotics, sport, and instrumentation applications due to their thin and flexible construction with the ability to operate at low pressures. However, their potential applications in medical instrumentation as a non-invasive force/pressure sensing element has not been explored widely. In this work, we investigated the performance of a commercial flexible force sensing resistor (FSR) to assess arterial pressure waveform (in units of mmHg) from the captured skin surface pressure, with a one-time calibration. Extensive in-vitro experimental work on this approach was conducted using a fully automated arterial flow phantom. The phantom was specially designed to resemble the anatomy of the human neck, comparing a carotid vessel encompassed with a tissue-like silicone material. The pulsatile flow of blood mimicking fluid with programmable flow rate and pulse rate provided an in-vitro system simulating blood circulation through the human carotid artery. A custom hand-held probe and signal acquisition hardware was developed to acquire the pulsatile force acting on the tissue surface due to the transmural pressure. A calibration model was developed to estimate the morphology of true transmural pressure, using a clinical-grade catheter inserted into the phantom as the reference standard. Following the one-time calibration, FSR sensor continuously captured arterial pressure waveform with a root-mean-square-error less than 8 mmHg. Studies were conducted under various simulated test conditions and evaluated the accuracy of pressure wave assessment. The effect of operator dependent hold-down pressure on the sensing performance of FSR was also investigated. Overall, the proposed approach provided a cost-effective system for continuous assessment of arterial pressure waveform with potential applications in unobtrusive, long-term monitors.**

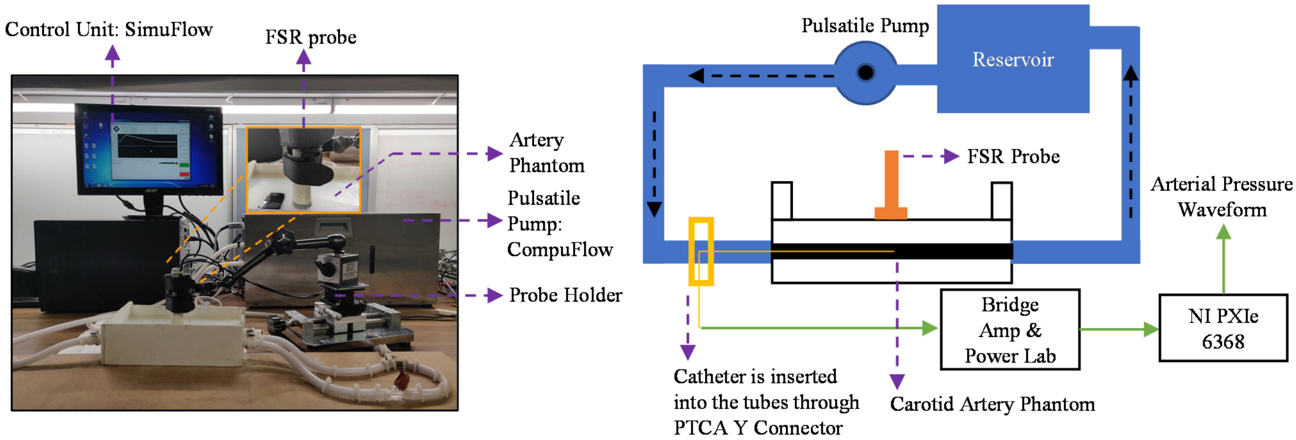
Keywords*— *Arterial pressure; calibration; carotid phantom; cuffless blood pressure; flexible force sensor; pressure waveform; ubiquitous blood pressure.

I. Introduction

Since the introduction of sphygmomanometers more than a century ago, blood pressure (BP) parameters have been measured with a pressure cuff from the brachial artery in various clinical diagnosis practices, and hypertension management. Ease of measurement and availability of myriads of auscultatory and oscillometric brachial BP monitors for routine clinical use, as well as self-evaluation of office/home BP, are the key virtues for continued use of this conventional technique. However, studies of cardiovascular physiology have shown that the absolute BP level varies throughout the arterial system due to the pulse pressure amplification effect [1]. This phenomenon is the combined effect of progressive changes in the elastic behaviour and geometry of the arterial vessels from the central to the peripheral sites, and multiple reflections of transit pressure waves over long arterial segments composed of vessels with different mechanical characteristics. Consequently, BP parameters assessed from the brachial artery using conventional devices are a poor surrogate for central aortic pressure (central BP) [2], [3], which is the pressure directly exerted on vital organs.

Application of central BP has broadened from the basic physiological research to a decisive tool for prediction of future

978-1-5386-8428-3/19/$31.00 ©2019 IEEE



(a) (b)

Figure 1. (a) Arterial flow phantom with FSR probe and holder, (b) schematic representation of the in-vitro experimental setup.

cardiovascular events and associated risk factors [4], [5], effective anti-hypertensive medication [6], and assessment of the prevalence of childhood hypertension [7]. Non-invasive, short- and/or long-term measurement of central BP using dedicated devices has become increasingly important in clinical domains. Therefore, it is imperative that a comprehensive discussion of various techniques and devices for central BP estimation and their limitations is consistent and meaningful.

There is a need for ubiquitous BP monitoring which is non-invasive, minimally obtrusive, non-expert operable for easily field-deployable or for wearable/smart phone or as a clinical standard [8]. Among the various techniques proposed for cuffless BP evaluation, arterial tonometry and pulse transit time-based methods are the two major principles used for cuffless evaluation of central BP parameters. The most direct non-invasive, cuffless technique for central BP measurement is based on the principle of applanation tonometry [9]. This approach requires the operator to suppress the arterial pulsations by externally applied pressure to capture the arterial pressure waveforms. Therefore, its measurement accuracy is influenced by the applied hold-down pressure and requires skilled operators to reliably capture arterial pressure waveforms. Continuously recorded signals from the common carotid artery using the tonometry sensor are used to estimate central BP parameters and aortic pressure waveform with best-case calibration. Devices such as SphygmoCor (AtCor Medicals) utilize tonometry on radial/carotid/femoral artery along with reference upper arm cuff-based BP measurements for the evaluation of central BP parameters and arterial stiffness by pre-calibrated transfer functions [10]. Non-invasive, cuffless evaluation of arterial pressure by characterizing the transit of pressure wave through the arterial tree has become popular over several years [8]. Techniques utilizing pulse arrival time (PAT; time taken by the blood pulse wave to propagate from heart to an arterial site) and pulse transit time (PTT; time taken by the blood pulse wave to travel between two distinct sites in the arterial tree) are the most widely researched in the area of cuffless BP. These approaches investigate the relationship of arterial pressure level with PAT/PTT by following the physiological principle that the pulse transit time estimates vary with the BP parameters, which depend on the arterial wall properties, mechanical characteristics and cardiovascular health conditions. The estimation of BP parameters is often performed by model or transfer function-based computation that requires calibration. In the early 2000s, Poon et al. introduced a logarithmic relationship between PAT/PTT and arterial pressure based on the Moens–Korteweg equation [17]. Almost all reliable PAT/PTT techniques reported in the literature directly followed this theoretical model or are implemented with suitable hypothetical optimizations [8]. In recent years, ultrasound-based techniques, a non-invasive method for direct evaluation of arterial dimensions, has also gained attention in cuffless BP research. Each usage scenario of central BP monitors poses unique functional requirements and challenges. However, there are underlying requirements such as ease of use, minimally obtrusive method etc. that are common to all cuffless, central BP monitors. Direct measurement of central BP parameters is the real challenge in non-invasive techniques due to the inaccessibility of the central arteries. Consequently, carotid artery pressure (carotid BP) assessed from the neck is often used as an indicator of central BP because of its close representation of the central aortic conditions [12-14].

In this paper, we present a proof-of-concept evaluation of a non-invasive method for arterial pressure waveform using commercial flexible force sensing resistors (FSR). The method uses the recorded surface force acting upon the skin due to the transmural pressure of the target artery for the assessment of the pressure waveform. An extensive in-vitro experimental work on this approach was conducted using a fully automated dynamic arterial flow phantom, to demonstrate the proof-of-principle. Further, we have investigated the effect of the hold-down pressure on the accuracy of the pressure measurements obtained employing the developed calibration model.

II. MATERIALS AND METHODS

A. Arterial Flow Phantom

To evaluate the precision and accuracy of the proposed technique for the arterial waveform estimation, systematic in-vitro experiments were conducted in controlled laboratory settings. The experiments were performed on a dynamic arterial flow phantom setup. The arterial flow phantom arrangement developed for experimental validation has been illustrated in Fig.1. The model was developed using a carotid anthropomorphic vascular phantom with normal bifurcation (CNB-STXV – Shelly Medical Imaging Technologies). The carotid vessel was embedded in an acrylic box enclosure and filled with platinum cure silicone rubber (Ecoflex® 00-30). A dye-based ink (Kokuyo CamlinTM Royal Blue)-water slurry was driven through the phantom to simulate the blood flow. Arterial pulsations were created using a specialized fluid driving system, CompuFlow 1000 using the flow waveforms that were programmed and fed to SimuFlow III software (Shelly Medical Imaging Technologies). The experiments were conducted by configuring for different flow rates and pulse rates.

B. Reference Pressure Measurement System

A calibrated high-fidelity invasive pressure catheter (Millar SPR-882) was used for obtaining the reference intraluminal pressure waveform. The catheter was inserted into the artery phantom through a PTCA Y connector (hemostasis valve) in a way that its tip resided in the common carotid segment, 5 cm from the bifurcation. The catheter was interfaced to ADInstrurmnts Bridge Amp and PowerLab 4/35 that was controlled using the LabChart software. The processed pressure waveforms from Bridge Amp were further digitized using a data acquisition card (National Instruments-NI PXIe 6368) at a sampling rate of 1 kHz.

C. Surface Force Measurement System

The transmural blood pressure wave when traverses towards the skin surface through the tissues and muscles, tend to attenuate. Sensitive surface force sensors such as FSRs can be employed to acquire such surface pressures. In this work, we have explored on such sensor (Interlink Electronics - FSR 402, 13 mm diameter, full scale: 2 kg, minimum pressure: 11.3 mmHg) for the assessment of transmural pressure waveform. These FSRs are robust polymer thick film devices that exhibit a decrease in resistance with an increase in force applied to the surface of the sensor. For measuring the force exerted on the FSR, it was connected in a voltage divider circuit that yielded a voltage output proportional to the force. This output voltage of the divider circuit was connected to an op-amp based voltage buffer circuit to avoid any loading effect. The buffered output voltage was digitized using a data acquisition card (National Instruments-NI PXIe 6368) at a sampling rate of 1 kHz. In Fig. 2 the circuit for force measurement is illustrated.

D. Signal Acquisition and Processing

The digitized FSR and the calibrated catheter waveforms were simultaneously acquired and processed in real-time using the dedicated measurement software developed on LabVIEW. The developed software also controlled acquisition in-terms of configuration and synchronization. Since the catheter and the FSR systems were independent modules, a synchronized acquisition was necessary. For ensuring this a software logic was implemented, that controlled the digital card NI PXIe 6556 that generated a digital trigger pulse. The pulse generation rate was configured to 1 kHz which dictated the acquisition rate. The digitized signals were processed using a bandpass filter to remove the out of band noises. For this identical 8th order bandpass filters with the low cut off frequency of 0.5 Hz and the higher cutoff frequency of 10 Hz were used for both FSR signals

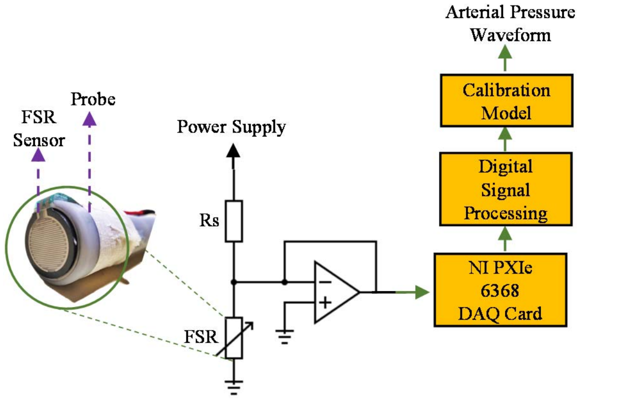


Figure 2. Hardware and software architecture of the surface force measurement system.

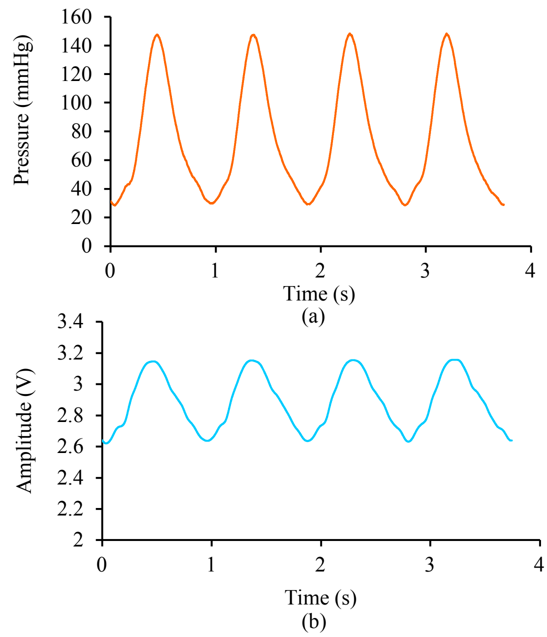


Figure 3. (a) Signals from catheter, (b) Uncalibrated signals from FSR

and catheter pressure signals. The filters used were zero phase filters that ensured no additional lags due to the frequency response of the band pass filter. These signals were recorded for continuous pulsation cycles.

E. Estimation of Arterial Pressure Waveform

Experiments were conducted for various test conditions (under various flowrates from 18 mL/s to 30mL/s) to investigate the correlation between invasive pressure and non-invasive FSR measurements. The FSR probe as shown in Fig. 2. was placed at 10 cm below the bifurcation of the carotid phantom. The probe was held stable at the measurement site using a stereotactic probe holder. The probe holder eliminates measurement errors due to variations in hold-down pressure (the external pressure applied by the operator to keep the force sensor above the artery in order to acquire reliable waveform). The total data sets were divided into parts. The first part for generating the calibration

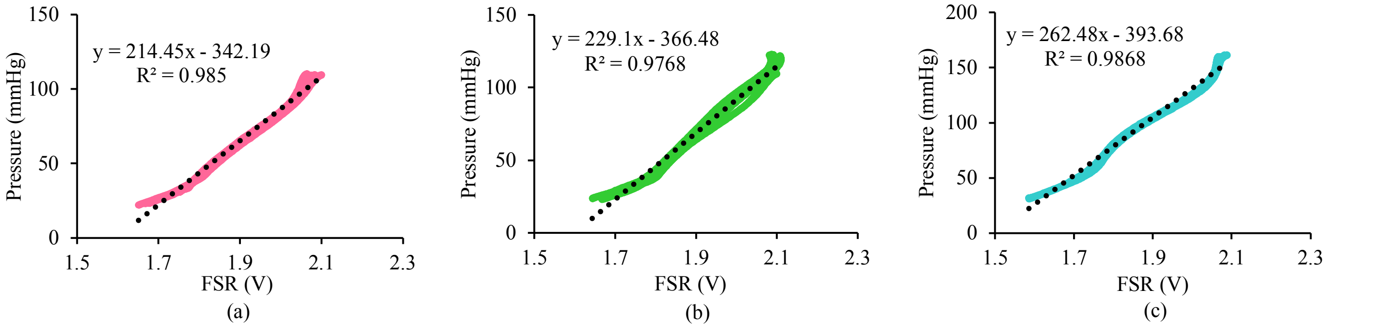


Figure 4. General linear trend for calibration of FSR signals and catheter pressure signals for different flowrate.

model, and the second for validating the FSR measurements against the reference catheter measurements. A linear calibration model was obtained for FSR signals against catheter pressure using the first set of the consecutive pulsation cycles. The accuracy of the calibration model was then tested against another set of cycles for the corresponding test condition (flow rates and pulsation rates). Since all force-based measurement systems are affected by the variations in hold-down pressure, its effect on the obtained calibration model and measurement accuracy were also further investigated.

III. Result and Discussions

A. Relibality of Surface Force Measurement

The developed FSR based hand-held probe and the associated measurement system has demonstrated expected functionality. Continuous FSR voltage waveforms proportional to the surface force exerted by the transmural pressure were reliably captured (SNR of 20 dB). In order to calibrate these force waveforms, the reference catheter was used to measure the transmural pressure in a synchronized manner. These waveforms were continuous and quasi-periodic, representing the pressure pulsations in the carotid phantom. The foot and peaks of these waveforms were observed to be aligned with negligible time-lag. Fig. 3, depicts a sample of catheter (calibrated)-FSR (raw) waveforms for continuous pulse cycle. The acquired FSR signals constituted a DC level proportional to the operator dependent hold-down pressure, and an AC component proportional to the pulsating transmural pressure. The increase in flowrate resulted in an increment in the peak-to-peak amplitude of the FSR waveform. This is attributed to the proportional changes in the transmural pressure due to the increased flow rate, as also seen in the catheter pressure waveform. This demonstrated the potential of FSR to non-invasively capture the transmural pressure waveforms. Having small form factor and being cost effective, FSR has the potential to be used as a patch sensor for multi-site continuous arterial pressure monitoring. However, it should be stressed that adequate hold-down pressure is essential to capture a stable and reliable waveform. The fidelity of the waveform is largely dependent on the sensitivity and operational range of the FSR. Additionally, the choice of sensitivity selecting resistor (Rs) dictates the resolution and range of FSR output.

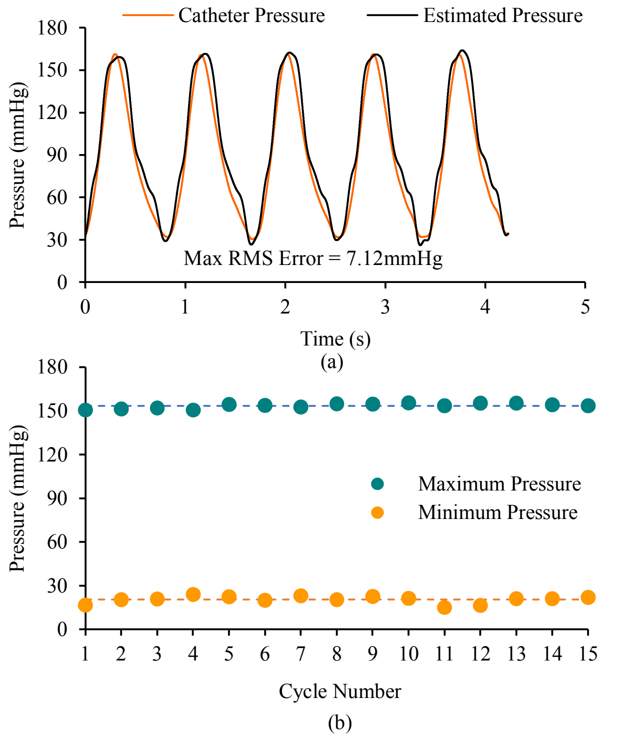


Figure 5. (a) Validation of calibration model, (b) beat-to-beat plot showing repeatability of measurement

B. Calibration Procedure and Measurement Accuracy

Individual cycles of these waveforms were directly used for constructing the calibration trends for different flow rates. Samples of scatter plots illustrating a linear trend between FSR raw cycles and the calibrated catheter pressure cycles are shown in Fig. 4. The correlation for these linear trends was significant with $r > 0.97$ and $p < 0.0001$. The implemented linear calibration model was of the general form as shown in (1) is obtained for the FSR signal against catheter pressure.

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

Here, P(t) is the transmural pressure of the carotid phantom in units of mmHg, F(t) is the FSR signal in units of volts. A and B are the calibration constants that depend on the flow rate. Note that the proposed measurement system needs a one-time

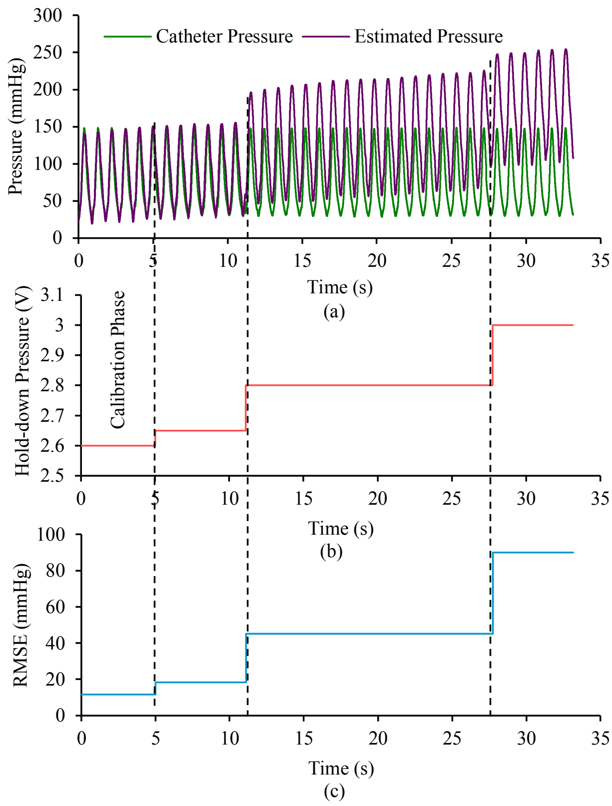


Figure 6. (a) Effect of hold-down pressure on the estimated arterial pressure waveform, (b) error analysis of the hold-down pressure influence

calibration to continuously capture P(t) using FSR alone. As stated earlier, the calibration constants were obtained for different flow rates varying from 18 mL/s to 28 mL/s, at a steady hold-down pressure, for a fixed pulse rate (time period = 920 ms). Using these constants, the one-time calibration was performed using enough pulse cycles (five consecutive cycles were used in the present model) for a given flow rate and hold-down pressure. Post the calibration procedure, the system was used for continuous capturing of transmural pressure waveform.

Fig.5(a) illustrate a sample of simultaneously captured catheter pressure waveform and transmural pressure waveform assessed using FSR by employing the calibration model. It is evident that the FSR-derived pressure pulse waveform preserved the morphology of the transmural pressure, as measured by the catheter. Similar performance was also obtained for other flowrates as well. A maximum root-mean-square-error of 7.12 mmHg was observed while comparing corresponding locus points of the estimated and reference pressure waveforms. Further to illustrate the beat-to-beat repeatability of the estimated pressure waveforms, the maxima, and the minima pressure levels were compared for consecutive pulse cycles (Fig. 5(b)). A maximum intra-beat variation of 6 % was observed for the measured values at different flow rates, demonstrating the measurement repeatability. These results validated the efficiency of the one- time calibration procedure.

C. Effect of Hold-Down Pressure on Measurement Accuracy

All the applanation based pressure measurement systems are prone to errors associated with the operator-dependent hold-down pressure. To investigate the effect of the hold-down pressure on the accuracy of the pressure measurements obtained by the developed calibration model further experiments were performed. In order to systematically perform this experiment, the FSR probe was held at a minimum hold-down pressure. Initially, the calibration model was derived for the test condition with a fixed flow rate of 26 mL/s. Employing this calibration model, the measurements were then performed by discretely incrementing the hold-down pressure for the same flow rate. The study results obtained for a particular test condition is illustrated in Fig. 6. In the figure, the reference catheter pressure waveforms are along with the calibrated pressure waveform for different increased hold-down pressure levels. The respective average root-mean-square-errors for these hold-down pressure levels are also depicted. It is evident that the hold-down pressure significantly affects the measurement accuracy applanation-based pressure measurement system. Eliminating the influence of hold-down pressure is practically challenging, especially while performing measurements on the human subjects by non-skilled operators. Employing an adaptive calibration technique to compensate for the influence of the hold-down pressure would greatly reduce the dependence of accuracy on operator expertise. Such approached will potentially provide cost-effective non-invasive solutions for continuous arterial pressure assessment.

IV. Conclusion

In this work we have presented the feasibility of using a commercially flexible force sensor, FSR, to assess arterial pressure waveform. The method is based on a one-time calibration procedure that allows the raw output of the FSR that is proportional to the surface force, to be used for assessment of transmural pressure. An extensive in-vitro experimental work on this approach was conducted using a fully automated dynamic arterial flow phantom, to demonstrate the proof-of-principle. A catheter was used as a reference to validate the transmural pressure waveform assessed employing the FSR. A linear calibration model was derived between the catheter and the FSR waveforms, owing to the observation that they are linearly correlated to each other with a $r > 0.97$, and $p < 0.0001$. The calibration coefficients of the developed models were preserved for the fixed test conditions allowing the feasibility of one-time calibration. Employing the developed calibration models, the transmural pressure waveforms were continuously captured using the FSR. In comparison with the reference transmural pressure waveform, the morphology of the estimated pressure waveforms was preserved for all the test condition. A maximum root-mean-square-error for the measurements was 7.12 mmHg, validating the reliability of the proposed technique. Despite the reliability of the calibration procedure, it was demonstrated that the hold-down pressure compromises measurement accuracy. In conjunction with an adaptive calibration technique, these FSR based systems have the potential to provide a cost-effective easy-to-use tool for noninvasive assessment of continuous arterial pressure from the central arterial system.

References

[1] A. P. Avolio , L. M. Van Bortel, P. Boutouyrie, J. R. Cockcroft, C. M. McEniery et al., “Role of pulse pressure amplification in arterial hypertension: experts’ opinion and review of the data,” Hypertension, vol.

54, no. 2, pp. 375–383, 2009.

[2] 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, pp. 1719–1725, 2014.

[3] M. Kostapanos, C. M. McEniery, and I. B. Wilkinson, "Clinical relevance of central blood pressure - a critical review," Vasa., vol. 45, no. 6, pp. 451–460, 2016.

[4] R. Pini, M. C. Cavallini, V. Palmieri, N. Marchionni, M. D. Bari et al., "Central but not brachial blood pressure predicts cardiovascular events in an unselected geriatric population," J. Am. Coll. Cardiol., vol. 51, no. 25, pp. 2432–2439, 2008.

[5] A. Kollias, S. Lagou, M. E. Zeniod, N. Boubouchairopoulou, and G.S.Stergiou, "Association of central versus brachial blood pressure with target-organ damage," Hypertension, vol. 67, no. 1, pp. 183–190, 2016.

[6] B. Williams, P.S. Lacy, S. M. Thom, K. Cruickshank, A. Stanton et al., "Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes: principal results of the Conduit Artery Function Evaluation (CAFE) study," Circulation, vol. 113, pp. 1213–1225, 2006.

[7] N. Patel and N. Walker, "Clinical assessment of hypertension in children," Clinical Hypertension, vol. 22, no. 15, pp. 1–4, 2016.

[8] R. Mukkamala, J. -O. Hahn, O. T. Inan, L. K. Mestha, C. S. Kim et al., "Toward ubiquitous blood pressure monitoring via pulse transit time: theory and practice," IEEE Trans. Biomed. Eng., vol. 62, no.8, pp. 1879–1901, 2015.

[9] H. Miyashita, "Clinical assessment of central blood pressure," Curr. Hypertens. Rev., vol. 8, no. 2, pp. 80–90, 2012.

[10] L. Garcia-Ortiz, et al.,"Comparison of two measuring instruments, B-pro and SphygmoCor system as reference, to evaluate central systolic blood pressure and radial augmentation index," Hypertens. Res., vol. 35, no. 6, pp. 617–623, Feb. 2012.

[11] C. C. Y. Poon and Y.-T. Zhang, "Cuff-less and noninvasive measurements of arterial blood pressure by pulse transit time," in Proc. 27th Annu. Int. Conf. IEEE Eng.in Med. Biol. Soc. (EMBC), Shanghai, China, 2005, pp. 5877–5880.

[12] R. Kelly, M. Karamanoglu, H. Gibbs, A. Avolio, and M. O'Rourke, "Noninvasive carotid pressure wave registration as an indicator of ascending aortic pressure," J. Vasc. Med. Biol. vol. 1, pp. 241-247, 1989.

[13] P. M. Nabeel, J. Joseph, S. Karthik, M. Sivaprakasam, and M. Chenniappan, "Bi-modal arterial compliance probe for calibration-free cuffless blood pressure estimation," IEEE Transactions on Biomedical Engineering, vol. 65, no. 11, pp. 2392–2404, 2018.

[14] J. Joseph, P. M. Nabeel, M. I. Shah, and M. Sivaprakasam, "Arterial compliance probe for cuffless evaluation of carotid pulse pressure," PLoS One, vol. 13, no. 8, p. e0202480, 2018.