Mini-Symposia Title:

Recent Advances on Cuff-Less Blood Pressure Measurement I

Mini-Symposia Organizer Name & Affiliation:

Ramakrishna Mukkamala, Michigan State University

Mini-Symposia Speaker Name & Affiliation 1:

Ramakrishna Mukkamala, Michigan State University

Mini-Symposia Speaker Name & Affiliation 2:

Jay Pandit, Northwestern University and Bold Diagnostics

Mini-Symposia Speaker Name & Affiliation 3:

Roozbeh Jafari, Texas A&M University

Mini-Symposia Speaker Name & Affiliation 4:

Panayiotis Kyriacou, City, University of London

S Mini-Symposia Speaker Name & Affiliation 5:

Josep Sola, aktiia

Mini-Symposia Speaker Name & Affiliation 6:

Theme:

- ○ 01. Biomedical Signal Processing
- ○ 02. Biomedical Imaging and Image Processing
- ○ 03. Micro/Nano-bioengineering; Cellular/Tissue Engineering &
- ○ 04. Computational Systems & Synthetic Biology; Multiscale modeling
- ◉ 05. Cardiovascular and Respiratory Systems Engineering
- ○ 06. Neural and Rehabilitation Engineering
- ○ 07. Biomedical Sensors and Wearable Systems
- ○ 08. Biorobotics and Biomechanics
- ○ 09. Therapeutic & Diagnostic Systems and Technologies
- ○ 10. Biomedical & Health Informatics
- ○ 11. Biomedical Engineering Education and Society
- ○ 12. Translational Engineering for Healthcare Innovation and Commercialization

Mini-Symposia Synopsis— Max 2000 Characters

Cuff-less blood pressure (BP) monitoring is expected to improve hypertension awareness and control rates and may now be feasible due to recent technological advances in, e.g., wearable sensing. As a result, cuff-less BP monitoring devices are being widely pursued around the world. This two-part mini-symposia is about recent advances in cuff-less blood pressure measurement technology. The speakers are leaders in the field from academia and industry. This particular mini-symposium represents part one and covers pulse transit time and photo-plethysmography methods.

PPG-Based Pulse Transit Time for Cuff-Less Blood Pressure Measurement

Ramakrishna Mukkamala, Michigan State University

***Abstract*—Ramakrishna Mukkamala has focused on advancing blood pressure (BP) measurement in recent years. He will present results of two studies on photo-plethysmography (PPG)-based pulse transit time for cuff-less BP measurement. The studies indicate that PPG sensor contact pressure must be taken into account and that a PPG sensor on a toe rather than a finger affords reasonable BP tracking.**

Ramakrishna Mukkamala is a Professor in the Department of Electrical and Computer Engineering at Michigan State University. In recent years, the principal aim of his research program has been to innovate technologies to advance blood pressure (BP) measurement. His contributions include: (1) an oscillometric algorithm to estimate brachial BP more accurately with an automatic cuff device [1]; (2) an algorithm to indirectly measure central BP with an arm cuff device [2]; (3) an influential review paper on the pulse transit time (PTT) principle for cuff-less BP measurement [3]; (4) a nonlinear modeling method to calibrate PTT in units of msec to BP in units of mmHg [4]; (5) a PTT-based weighing scale system to track changes in BP [5]; and (6) smartphone devices for cuff-less and calibration-free BP monitoring [6, 7]. The review paper received a 2019 IEEE Engineering in Medicine and Biology Society Prize Paper Award (third place), while the smartphone BP work was published in Science Translational Medicine, received world-wide attention, and garnered the 2019 MSU All-University Innovation of the Year Award.

In this talk, Dr. Mukkamala will present a pair of studies on PTT detected via popular photo-plethysmography (PPG) sensors. In the first study [8], the impact of PPG sensor contact pressure on PTT was investigated in 17 human subjects with a custom-made device. The results showed that PTT can change significantly with physiologic contact pressures (up to 22±2 msec, which translates to a BP error of ~11 mmHg). These findings were explained through a physiologic model accounting for nonlinear elasticity and viscoelasticity of arteries. Hence, PPG sensor contact pressure should be taken into account for cuff-less BP measurement. In the second study [9], PTTs detected with ECG and ear, finger, and toe PPG sensors were compared as markers of BP in 32 normotensive and hypertensive subjects undergoing a battery of BP-varying interventions. The results showed that toe pulse arrival time (time delay between ECG and toe PPG waveforms) tracked the BP changes significantly better than the other PTTs including the popular finger pulse arrival time (time delay between ECG and finger PPG waveforms). However, the correlation between toe pulse arrival time and BP was not high (-0.63±0.05). Hence, innovations in sensing proximal waveform timing in particular may be needed to realize cuff-less BP monitoring via PTT.

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[7] A. Chandrasekhar, K. Natarajan, M. Yavarimanesh, and R. Mukkamala, "An iphone application for blood pressure monitoring via the oscillometric finger pressing method," *Scientific Reports*, vol. 8, no. 1, pp. 18–23, 2018.

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Speaker 1 Synopsis

Jay Pandit MD, Assistant Professor, Northwestern University Feinberg School of Medicine

***Abstract*— Differential Pulse Arrival Time: A novel approach to continuous cuff-less blood pressure monitoring.**

I. INTRODUCTION

Blood pressure (BP) is a continuous and dynamic physiologic variable. The sphygmomanometer has been the mainstay of blood pressure detection for >100 years but provides only a snapshot of an important continuous physiologic variable.

Ambulatory cuff-based BP monitoring has demonstrated superiority over conventional, single-point office-based cuff measurements and has unveiled the important concept of nocturnal BP dipping, however it is plagued by poor compliance leading to limited use.

Current methods for continuous, non-invasive ambulatory BP monitoring include the use of pulse wave velocity and pulse transit time coupled to electrocardiographic timing of the QRS complex.

Pulse transit time algorithms typically neglect the post-ejection period and replace the travel distant with half the height as a surrogate. These assumptions have led to inaccurate and unreproducible conversions of PTT to BP.

We propose a novel method – differential pulse arrival time (DPAT) – to continuously estimate BP non-invasively. DPAT utilizes two identical anatomical sites for optical sensor data collection which circumvent the need to assume contributions from the pre-ejection period and the travel distance.

II. METHODS

12 normotensive subjects were fitted with a DPAT device and a Finapres Portapres ambulatory BP monitor. Each subject underwent a standardized protocol consisting of 2 minutes at rest, 2 minutes cold pressor at 40ºF, and 2 minutes at rest. The raw data from the DPAT devices were time-matched and compared with the Finapres BP trend.

Continuous DPAT-derived BP correlates well with cuff-based measurement of BP at rest and during cold-pressor in normotensive subjects.

A Bland-Altman analysis was conducted to assess data skew and bias.

*Research supported by NSF SBIR Phase I to Bold Diagnostics Inc.

Dr. Pandit does has disclosed cofounder status with Bold Diagnostics Inc.

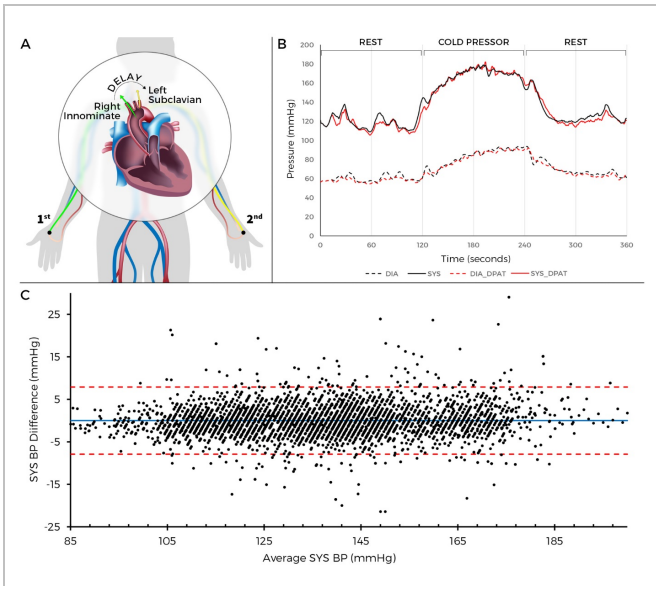

Figure 1. A)Trifurcation of aortic arch that leads to inherent delay in arrival of pulse between right hand and left hand giving rise to Differential Pulse Arrival Time (DPAT). B) Comparison of Finapres-derived BP (black) during a cold pressor test and DPAT-derived BP (red); correlation coefficient of 0.82. C) Bland-Altman analysis of systolic blood pressure data points.

III. RESULTS

Over 100 million DPAT data points were collected from 12 normotensive subjects (age range 20-50).
DPAT correlated with Finapres blood pressures with a correlation coefficient of 0.8 The root mean square error of the predicted blood pressure was ±4.76 mmHg for systolic BP and ±4.03 mmHg for diastolic BP. A Bland-Altman analysis of the systolic blood pressure difference did not reveal any significant bias within 95% limits of agreement.

IV. DISCUSSION & CONCLUSION

Differential pulse arrival time obtained by an optical sensor-based system is a viable approach to monitoring continuous BP in normotensive subjects. Future studies in elderly, hypertensive individuals are warranted.

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Cuffless Blood Pressure Monitoring using Bio-Impedance

Roozbeh Jafari, Texas A&M University

according to the World Health Organization. There is a significant value to measuring blood pressure continuously in the natural context of the user's environment. Our proposed technology, an unobtrusive, wrist-worn, cuff-less blood pressure monitor, can provide a wealth of information to physicians, help identify certain short-term dynamics/variations of blood pressure, and allow effective monitoring of response to medication, among other things. This study aims to develop a robust and reliable blood pressure monitor in the form of a wrist-worn device that uses bio-impedance sensors. These sensors measure pulse wave velocity (PWV) along with several other derivatives for cardiovascular parameters including heart rate and blood volume changes in arteries, which correlate with the blood pressure. The system will incorporate clever hardware design to localize underlying vasculature and focus on arterial sites for enhanced accuracy. Advanced machine learning techniques, leveraging both general and personalized models, are developed to convert bio-impedance measurements to blood pressure. After decades of relying on the inflatable cuff-based technique, this system could represent a significant change in how we measure blood pressure.

I. INTRODUCTION

Hypertension is a major risk factor for various diseases including coronary artery disease, heart failure, stroke and chronic kidney disease. A cornerstone of lowering cardiovascular risk is the management of hypertension, which affects one in four adults worldwide, causes an estimated 7.6 million deaths per year and results in the loss of 92 million disability-adjusted life-years. The diagnosis is usually made at a clinical visit, but evidence is abundant that measurement of blood pressure outside a clinical visit provides important prognostic information. A recent study comparing clinic blood pressure with 24-hour ambulatory blood pressure monitoring (ABPM) in 63,910 adults in Spain between 2004 and 2014 found that ABPM was more predictive of cardiovascular mortality than clinical visits, supporting the need for ambulatory measurements taken more frequently for each patient. There is an unmet need for a device that can unobtrusively and continually measure nocturnal blood pressure.

II. METHODS

Our proposed device is in the form of a wrist-watch and consists of an array of electrodes on the underside that make contact with the skin when worn. These electrodes sense bio-impedance at different points on the wrist, with the objective of detecting impedance changes in the tissue due to each pulse. Detecting the pulse using a pair of electrodes in different locations can be used to then infer the PWV/other derivatives for cardiovascular parameters as measured by bio-impedance and eventually BP.

III. RESULTS

We have verified the feasibility of measuring BP using two bio-impedance sensors on the wrist with 3 cm distance between them. We managed to estimate systolic and diastolic BP accurately from wrist bio-impedance signals as shown in Fig. 1, in comparison to Finapres® NOVA. These experiments were done on 11 healthy subjects with sensors placed on the wrist along the radial and ulnar arteries to extract PTT and other features including peak to peak amplitude, HR, timing information between various peaks and valleys and areas under the curve for various segments of the signal from bio-impedance, which were converted to systolic and diastolic BP using regression models. BP was estimated accurately with correlation coefficient, mean absolute error (MAE) and standard deviation (STD) of 0.92, 1.71 and 2.46 mmHg for diastolic BP and 0.94, 2.57 and 4.35 mmHg for systolic BP [1].

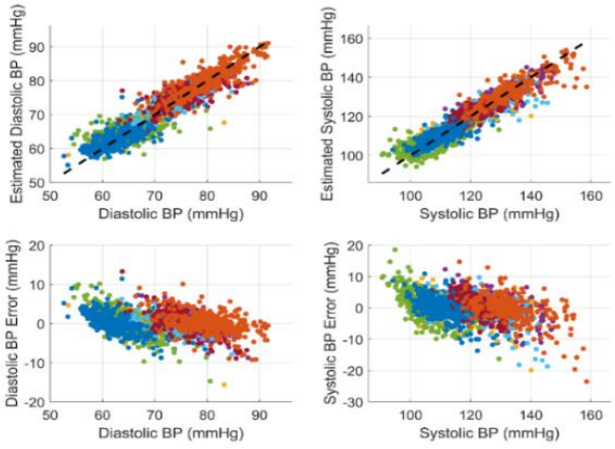

Figure 1. The estimated DBP and SBP for all subjects using features extracted from wrist bio-impedance signals

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In Vitro Investigation of the Relationship of Photoplethysmography with Blood Pressure Utilising Vessel - Tissue phantoms

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I. INTRODUCTION

Hypertension or high blood pressure is a leading cause of death throughout the world and a critical factor for increasing the risk of serious diseases, including cardiovascular diseases, such as stroke and heart failure. Hence, blood pressure is a vital sign that must be monitored regularly for early detection, prevention and treatment of cardiovascular diseases. Whilst current systems and techniques, such as the oscillometry BP monitoring technique, have seen wide clinical use and have been the focus of various studies, the fact remains that the need for a reliable, cuff-less and calibration free Non-Invasive Blood Pressure (NIBP) monitor is still on the top of many clinician's wish lists. To facilitate this work, a back-to-basics *in vitro* approach has been employed where various tissue-vessel phantoms have been developed so as to carefully control various parameters that affect the Photoplethysmograph (PPG) morphology and its relation with blood pressure.

II. METHODS

The *in vitro* setup consists of a custom made vascular tissue phantom, an arterial network and a pulsatile blood pump (BDC Laboratories) capable of altering stroke rate (heart rate), total volume flow, total peripheral resistance, fluid temperature, and compliance (through a Windkessel air-fluid reservoir). The arterial network is configurable to replicate any connecting arterial tree leading up to the phantom, where fluid pressure can be monitored at any point. Separate resistance elements can also be placed on this network to simulate the reflection of bifurcations in arterial branches, useful for the simulation of the Photoplethysmograph (PPG) waveform diachrotic notch. In this experimental setup a dual wavelength (red and infrared) reflectance PPG sensor was used. The first experiment carried out investigated the roles of blood flow and stroke rate against blood pressure in the phantom model. The second experiment was designed to assess PPG signals as they may appear in the oscillometry BP monitoring technique. This method is the most commonly used for either semi continuous monitoring in surgery/ICU setting or with General Practitioners (GPs).

III. RESULTS

In these experiments either heart rate (HR), or total fluid flow was continually altered whilst keeping the other parameter constant. The red and infrared waveforms from one of the experiments is shown in figure 1, below. Additional resistance elements were omitted from this setup, but the driving waveform was a sinusoid, and the resulting waveform is observed to show some of the characteristics of typical PPG morphology, namely the steeper systolic upstroke and the beginning of a diachrotic notch.

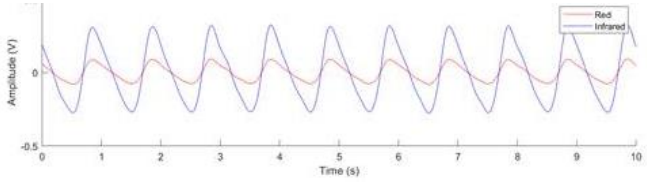

Figure 1. Red and Infrred PPGs from an artificial finger phantom with a stroke rate of 60 bpm and a total circuit fluid flow of 6 L/min. Signal to noise ratio (SNR) = 32.6 dB.

Correlation of flow rate or HR is shown in table 1 below. Both sets of results correlate well with changes in either parameter and demonstrate the high reliability of the model to quickly and accurately dial-in specific blood pressures using either or both HR or flow rate.

TABLE I. COMPARISON OF PHANTOM BLOOD PRESSURE WITH STROKE RATE AND FLOW RATE CHANGES

	MAP Blood Pressure (mmHg)		
	Minimum	***Maximum***	***R^2***
HR Range 60 – 160 BPM (+20 BPM Steps)	94	105	0.9705
Flow Range 6 – 9 L.min^{-1} (+0.5 L.min^{-1})	68	119	0.9960

The results of the oscillometry experiment were analysed, and the amplitude of the PPG's at each step produced the graph in figure 2. The infrared signal can be seen to exhibit a similar envelope to that of the desired oscillometric signal morphology. Relating the force applied to an equivalent pressure is a simple process of knowing the exact area over which the force is applied. However, there may complications in the model arising from the fact that the *in vitro* model cannot replicate complicated sympathetic and parasympathetic activity, therefore the effect of the materials themselves, specifically the elastic properties of the tissue and the vessels, may have a role to play. By varying this model for the exact same experiment, by only changing the elastic properties, may yield an insight into the effect of vessel compliance on real human PPG morphology and BP variations in those suffering from arterial diseases.

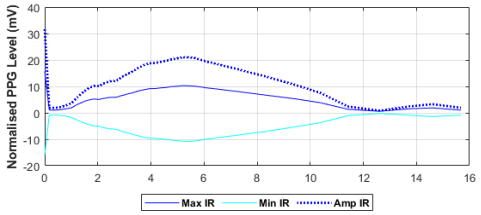

Figure 2. Infrared PPG amplitude response to increasing force on a vessel-tissue phantom, the x-axis represents the force applied in Newtons.

IV. CONCLUSION

So far the in vitro model presented here has been promising as it is in the unique position of being able to individually control nearly all parameters that are known or thought to contribute to blood pressure or arterial stiffness. Whilst it is currently difficult to replicate the vasodilator/contraction response in this setup, there is the promise of observing what happens to the PPG signal at the times when these biological responses fail. In this way we are confident that the *in vitro* setup and the experiments performed on it can evolve to yield insight into the complicated relationship between blood pressure, arterial stiffness and the photoplethysmograph waveform.

Aktiia Bracelet: Orthostatic-Robust Monitoring of Blood Pressure at the wrist

Josep Sola, Aktiia

How do you measure your blood pressure at wrist? For the accurate readings with a cuff-based device, the wrist should be positioned at the heart level. Indeed, due to hydrostatic pressure differences, lowering the arm results in higher blood pressure readings, while raising the arm results in lower readings. In out-of-clinic scenarios, when a physician does not control patient's arm and body position, this limitation generates usability constraints and is associated with inaccurate blood pressure readings. Aktiia addressed this limitation and developed a library of OBPM algorithms allowing to calculate blood pressure values from the optical signals acquired at wrist while remaining unaffected by hydrostatic pressure differences.

This talk will disclose the fundamental principle of the algorithms and will present the results of a pilot trial involving simultaneous monitoring by the Aktiia Bracelet and a gold-standard off-the-shelf volume clamp device while changing body positions. This approach provides an opportunity to obtain measurements agnostic to the wrist position in the out-of-clinic scenarios and thus improves the experience of blood pressure monitoring.