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Preliminary validation system for cuffless blood pressure measurement

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Abstract: The development of a non-invasive, cuffless, continuous, wearable device for the measurement of blood pressure is a complex endeavour due to the high specificity at each measuring site and the need for high accuracy. Proof-of-concept and validation of a prototype should be performed at an early stage for functionality assessment. Additionally, the emergence of biological computer models allows for in-silico research, which results should be verified in a practical experiment. To grant an optimal preliminary assessment of a prototype, this work aimed to develop and validate accurate in-vitro and ex-vivo arterial models, with simple construction and easily available components. The comparison between a silicone tube and a porcine artery as a mimicked human radial artery was based on the stiffness parameter. Flow pressure is controlled by a centrifugal heart-like pump. Pressure values are extracted with ultrasound and a commercial piezoresistive pressure sensor is used for pressure validation. The porcine artery showed much more realistic stiffness values (β=15.360) than the silicon tube (β=543.420), which was very stiff in comparison to the typical in-vivo radial artery stiffness (β=9.5). The decrease in stiffness of 97.173 % (from the silicone tube to the porcine artery) led to an acute decrease in the derived pressure error. This work serves as guidelines for the development of a low-budget arm phantom, as the simple setup allowed for a primary validation of a proof-of-concept ultrasound-based sensor for the measurement of pressure.

Keywords: BP monitoring, cuffless, mimicked arm, stiffness, ex-vivo validation.

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1 Introduction

Along with body temperature, respiratory and pulse rate, blood pressure (BP) is a vital sign that helps detect and monitor health problems. Ambulatory BP monitoring (ABPM), which consists of measuring BP periodically for at least 24 hours, was introduced to shorten the diagnosis time and improve the measurement accuracy, avoiding the "white-coat" effect [1]. It has been proven that ABPM is superior to office BP diagnosis/management of hypertension, but it is not widely popular due to the patient discomfort of systemic inflation and deflation of the arm cuff [2]. To provide a more comfortable and practical alternative to the common oscillometric arm-cuff ABPM, BP research has been focused on wearable, cuffless BP measurement. Tonometry, photoplethysmography, and ultrasound (US) are modalities that indirectly measure BP by tracking hemodynamic phenomena [3]. Currently, there is no DIN ISO for the validation of cuffless BP monitoring devices. However, researchers usually adapt the directives in the DIN EN ISO for automated sphygmomanometers, published in 2018 [4], to their novel device validation. In 2014 (and amended in 2019) IEEE created a standard for cuffless, wearable BP measuring devices [5], but it is not widely used.

The rise of new and cutting-edge technology calls for validation of the prototype device at different stages (see Figure 1), where new validation systems are created and normalized in a lab environment. It would be unfeasible to undergo a human clinical trial still at a stage of proof-of-concept, as it needs approval, which takes time and costs that are unreasonable at the initial stages of the research. Additionally, the advance in biological computer models (e.g. cardiovascular tree [6]) catalyses the research in different fields. Such is the case of using an open-source pulse wave database of the cardiovascular system (which includes pressure, luminal diameter, and flow velocity waveforms) and comparing different mathematical models (e.g. linear, exponential, logarithmic model) that take as input hemodynamic changes of the artery (e.g. luminal diameter, blood flow velocity) and correlate it to a BP reading. All recent US-based BP monitoring studies use the exponential model to relate hemodynamic changes to BP. However, the authors revealed in the 25-year-old subjects in-silico study (with mean

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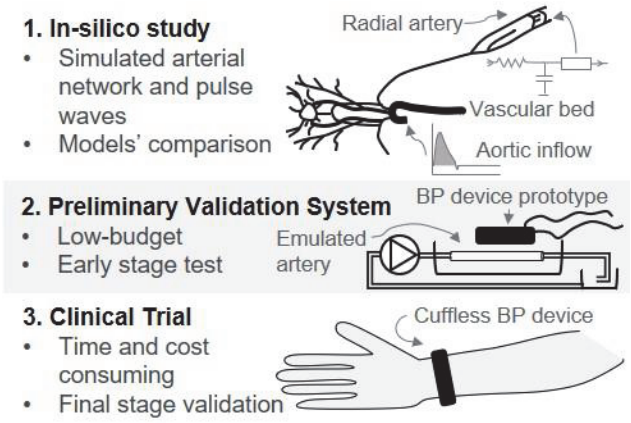

Figure 1: Development stages of a novel blood pressure device.

pulse pressure of (52.427±10.079) mmHg) that the linear model is the most accurate when compared to state-of-the-art models [7]. A computer simulation is not realistic enough to validate the linear model and proceed with the device development. Thus, the development of a simple cardiovascular setup is required as a preliminary validation of the working principle (Figure 1).

This paper proposes the use of an easily assembled cardiovascular phantom, with low-budget components, for accurate cardiovascular measurements. The development of the setup focuses on two parts and their corresponding functions: a pressure motor, which mimics the heart function, and a vessel, which mimics an artery. Concerning the behaviour of the vessel as a mimicking radial artery, evaluation of a commonly available silicone tube, as opposed to a porcine artery, is investigated in this work. Vessel comparison was based on the arterial stiffness index. Arterial stiffness has proved to be a predictor of cardiovascular events and is an important parameter of vascular health. Measuring an emulated vessel's stiffness may, therefore, ascertain whether it can mimic a human artery.

2 Materials and Methods

To validate the best performing mathematical determined by the in-silico study [7], the US-based device prototype and arm phantom were developed. An overview of the device prototype will be described, but notice that the US-based apparatus can be exchanged for another sensor. Thus, the presented arm phantom can be used for preliminary validation of other BP measuring device prototypes.

2.1 US-based device prototype

In a nutshell, the US-based device calculates the pressure in the vessel by determining the luminal diameter waveform. The probe functions in pulse-echo mode, in which it emits a US wave to each electrical triggered input, and an echo is created at each acoustic interface, which is received by the probe. By calculating the time of flight (TOF) between the maximum peaks of the echoes associated with the inner walls of the vessel, the luminal diameter of the vessel can be measured. After initial necessary calibration, the changing diameter can be converted to a pressure waveform through a linear mathematical model.

The US-based system consisted of three main parts: US sensor complex, signal acquisition block, and offline post-processing. The sensor complex is composed of a custom 5 MHz piezoelectric transducer (Fraunhofer IBMT, Germany), previously validated [8], and a pulser/receiver (DPR300, Imaginant Inc., NY) working at a pulse repetition frequency (PRF) of 2 kHz. The received echoes are amplified and filtered by a custom echo receiver board, previously validated [8], and acquired by a PC-oscilloscope (PicoScope 5243D, Pico Technology Ltd., UK) with 500 MHz of sampling frequency and a voltage resolution of 39.063 mV. Finally, post-processing of the data is performed in the MATLAB® environment (The Mathworks Inc, 2021) for the extraction of the maximum peaks of the inner walls, calculation of TOF, and conversion into a pressure reading at each trigger event.

2.2 Arm phantom

A similar physiological environment to the body was implemented for testing the system. Two mimicking arm setups were developed, differentiating the type of vessel used: a silicone tube or a porcine artery. A centrifugal pump was introduced to simulate the pumping of the heart. The heart-like pump, Zentrifugalpumpe MultiFlow (GAMPT mbH, Merseburg, Germany), regulates the flow to a negative sawtooth configuration which requires the configuration of flow velocity and pulse duration time. Every time the pump is turned on, the flow velocity must be slowly increased, starting at zero until the desired value.

The first experimental test was conducted with a fixed silicone tube immersed 4 mm deep in a tank filled with distilled (DI) water, which emulated the forearm. The soft and flexible silicone tube (hardness of 60 Shore A, ROTILABO® CarlRoth, Germany), with an inner diameter of 3 mm and thickness of 1 mm, mimics the radial artery. The DI-water was also used as the blood mimicking fluid.

In a new test, the silicone tube was substituted by a porcine artery obtained from the local slaughterhouse. The inlet and outlet of the artery were attached by ligation with a suture thread to two metal male hose barb adapters acting as a connector between the artery and the flow circuit. The mimicked radial artery had a wall thickness of (0.68±0.10) mm, an inlet inner diameter of (5.13±0.11) mm, and an outlet inner diameter of (3.67±0.05) mm (measured with electronic callipers). The liquid used for forearm and blood mimicking was changed to a saline solution (%w/w=0.9 %) to prolong the artery's viability by maintaining a similar physiological osmotic pressure [9].

The stiffness parameter (β) was used to calculate the local stiffness [10]. The parameter is defined by a Log transformation of the pressure ratio divided by the ratio of distension; the relation results in a linear curve, whose slope represents the parameter. This relation can be written as eq 1, where DD (diastolic diameter) and DS (systolic diameter) are the artery's diameter at diastolic blood pressure (DBP) and systolic blood pressure (SBP), respectively.

$$\boldsymbol{\beta = DD \cdot ln(SBP/DBP) \cdot (DS - DD)^{-1}} \quad (1)$$

2.3 System design

A system was designed (Figure 2) with the previously described parts. A commercial piezoresistive silicon pressure sensor, ABPDANT005PGAA5 (Honeywell International Inc, 2020), was introduced in the setup (marked as (1), Figure 2) for calibration, comparison, and determination of the accuracy of the measurements. The US probe (marked as (2), Figure 2) receives the US echoes reflected from the vessel (marked as (3), Figure 2), which are filtered by the echo receiver peak detector circuit. The conditioned signal, in combination with the pressure signal, is acquired by a two-channel PC-oscilloscope and saved for offline post-processing.

The pump was configured with a pulse duration of 1 s and a flow velocity of 800 rpm. As the scope's buffer memory is limited (256 Msamples shared between active channels), 5,000 frames were collected, corresponding to 2.5 heartbeat cycles.

3 Results

The echo measurements in the silicone tube were compared with the porcine artery (Figure 3). At each vessel individually, two windows of echoes are distinguished through a temporal interval where no reflection is recorded.

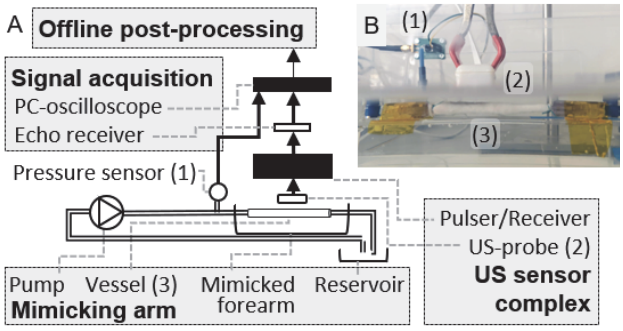

Figure 2: Cardiovascular pressure setup. (A) Schematic; double line: flow path, thick arrows: analogue signal path, and thin arrow: digital data path. (B) Figure highlighting a part of the experimental setup.

The two echoes in the first window correspond to the reflection of the vessel's anterior wall, that is, echo I is the reflection from the outer wall of the anterior wall and echo II is the echo produced by the inner wall of the anterior wall. The second window of reflections happens at the posterior wall, echo III corresponds to the inner wall and echo IV to the outer wall. Furthermore, a phase inversion in the echo signals at each wall reflection is noted.

The amplitude of the echoes in the porcine artery (0.43 V for the inner anterior wall and 0.19 V for the inner posterior wall) is reduced if compared to the silicone tube (0.44 V and 1.55 V, respectively). Furthermore, it is noticeable that the phases at each interface are inverted between the silicone tube and the porcine artery (e.g., the phase of the echo I is inverted when comparing both vessels). When looking at the anterior wall window of the silicone tube (see Figure 3A), echo I had the highest amplitude, whilst in the porcine artery (see Figure 3B), it was echo II. The time between inner and outer wall echoes also decreased considerably in the porcine artery but both echoes remain distinguishable. In the test with the silicone tube, maximum distension of 28 µm was obtained and a stiffness parameter of 543.420 (from eq 1). In comparison, the maximum distension with the porcine artery was 1.413 mm and a stiffness parameter of 15.360.

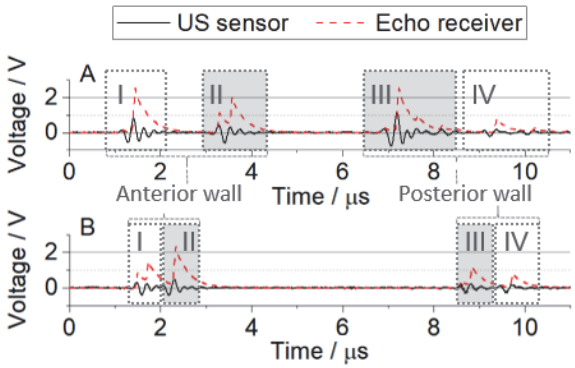

Figure 3: Echo profile of (A) the silicone tube and (B) the porcine artery.

4 Discussion

The echoes from the wall in the silicone tube were larger than from the porcine artery, which is due to a higher acoustic impedance mismatch and corresponding reflection coefficient. For normal incidence, the reflection coefficient is given by $Rr = (Za2 - Za1)^2/(Za2 + Za1)^2$, where $Za1$ is the acoustic impedance of the propagating material and $Za2$ is the reflecting material. In silicone/DI-water, Rr is $42.81 \cdot 10^{-5}$; whilst in soft tissue/saline solution, Rr is $3.585 \cdot 10^{-5}$. Therefore, a decrease in the received echoes' amplitude when using the porcine artery instead of the silicone tube, is significantly due to a higher acoustic impedance mismatch (more than one order of magnitude). However, these differences in acoustic impedances are not the only influencing factor, the decrease in echo amplitude in the porcine artery is probably in part due to probe positioning.

Although declared by the manufacturer as a soft and flexible vessel, the silicone tube revealed to be too stiff, with a much higher stiffness parameter if compared to the radial artery (β=9.500, data from an open-source database [6]). A softer silicone rubber tube could be an alternative concerning lab-to-lab transfer and repeatability.

The porcine artery pressure curves were much smoother when compared to those extracted from the silicone tube, which was due to a much smaller stiffness parameter and highly more compliant vessel, which more closely predicts the assessment of the measurement principle at the radial artery for a wrist wearable sensor. When using the compliant porcine artery, a completely different error profile is seen when compared to the silicone tube. The decrease in stiffness of 97.173 % (from the silicone tube to the porcine artery) led to an acute decrease in systolic error from 80 mmHg to 2.131 mmHg, respectively.

One could argue that the acoustic impedance profile of the human arm is much more complicated than the setups shown here, and the US waves would be much more attenuated by the tissue. Nevertheless, this study aimed to develop a system for early-stage validation of a cuffless BP measuring device. The next validation phase could be made in an arm phantom composed of polyvinyl alcohol or gel wax, which better emulates the forearm's acoustic characteristics [11].

5 Conclusion

Two experimental setups (in-vitro and ex-vivo) were created, differentiating between a silicone tube and a porcine artery to mimic the radial artery. The porcine artery had a stiffness of 15.360, very close to the radial artery, indicating the viability of the system as a mimicked arm. The simple low-budget mimicking arm, with flow pressure controlled by a heart-like pump, allowed preliminary BP monitoring device validation without the drawback of time consumption and clinical trial costs. Such a cardiovascular system is of high importance for the early-stage development of a novel ultrasonic device.

Author Statement

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