Kaunas University of Technology

Faculty of Electrical and Electronics Engineering

Development and Investigation of Long-Term, Unobtrusive Blood Pressure Monitoring System

Master's Final Degree Project

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Kaunas, 2023

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Summary

Measurement of blood pressure (BP) plays a crucial role in healthcare by providing essential information about the cardiovascular well-being of a patient and aiding in the diagnosis and management of blood pressure related diseases. Traditional methods of monitoring blood pressure involve discrete measurements using cuff-based devices. These methods have some limitations, such as discomfort due to unnecessarily high pressure in the cuff and noise during cuff inflation. The latter can potentially disrupt sleep patterns during the night, subsequently impacting BP levels. Researchers have been actively exploring the development of long-term and unobtrusive blood pressure monitoring systems that offer continuous measurements without disrupting patients' sleep at night. These systems typically employ wearable sensors attached to the body, wrist, or finger, which then wirelessly transmit data to a monitoring device or cloud-based platform. However, one limitation of these systems is the calibration process, which is conducted only once in the evening and cannot guarantee long-term accuracy due to the possibility of drift. This report presents the findings and insights from the development and investigation of the ambulatory blood pressure measurement device (ABPMD). The aim of ABPMD was to provide an unobtrusive, completely noise-free measurement method, with pressure in the cuff not exceeding the systolic blood pressure (SBP) value. Furthermore, ensuring adjustable self-calibration and maintaining accuracy during continuous blood pressure measurements for extended durations was considered a primary focus. The report provides an overview of the system's design, implementation, and performance evaluation. During the evaluation stage, the ABPMD prototype was compared with the SOMNOTouch NIBP device as a reference. The assessment focused on the accuracy and precision of the measurements of systolic blood pressure, diastolic blood pressure, and mean blood pressure. The results show that none of the evaluated measurement methods met the criteria set by the British Hypertension Society (BHS) or the Association for the Advancement of Medical Instrumentation (AAMI). However, it is important to recognise that the accuracy of the cuffless reference device, the SOMNOTouch NIBP, may be potentially limited, as highlighted in the recent research literature. Therefore, it cannot be definitively concluded that the evaluated device does not meet international standards. There are potential avenues for further improving the accuracy and precision of ABPMD. These include the implementation of continuous control of signal quality, the integration of Korotkoff sounds recording to enhance intermittent calibration accuracy, and the improvement of the BP approximation algorithms by incorporating additional parameters such as age and body mass index (BMI). These improvements have the potential to enhance the performance of ABPMD and bring it closer to meeting the precision standards set by BHS and AAMI.

Andrej Slabov. Ilgalaikės, netrukdančios kraujo spaudimo stebėsenos sistemos sukūrimas ir tyrimas. Magistro baigiamasis projektas / vadovas prof. Vaidotas Marozas; Kauno technologijos universitetas, Elektros ir elektronikos fakultetas.

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Santrauka

Kraujospūdžio matavimas yra labai svarbus sveikatos priežiūroje, kadangi suteikia esminę informaciją apie paciento širdies ir kraujagyslių sistemos būklę ir padeda diagnozuoti bei gydyti su kraujospūdžiu susijusias ligas. Tradiciniai kraujospūdžio stebėjimo metodai apima pavienius matavimus naudojant manžetinius prietaisus. Šie metodai turi tam tikrų trūkumų, pavyzdžiui, nepatogumą dėl pripūtimo metu pernelyg didelio slėgio manžetėje ir triukšmo ją pripučiant. Pastarasis gali trikdyti miegą nakties metu, o tai gali daryti įtaką kraujospūdžio rodikliams. Mokslininkai aktyviai tyrinėja ilgalaikių ir netrukdančių kraujospūdžio stebėjimo sistemas, kurios leidžia atlikti nuolatinius matavimus netrikdant paciento miego. Šiose sistemose įprastai naudojami dėvimi jutikliai, tvirtinami prie kūno, riešo ar piršto, kurie vėliau belaidžiu ryšiu perduoda duomenis į stebėsenos prietaisą arba debesų sistemos platformą. Tačiau vienas iš šių sistemų apribojimų yra kalibravimo procesas, kuris atliekamas tik vieną kartą vakare ir negali užtikrinti ilgalaikio tikslumo dėl galimo pasirinktų parametrų nukrypimo. Šioje ataskaitoje pateikiamos ambulatorinio kraujospūdžio matavimo prietaiso (ABPMD - ambulatory blood pressure measurement device) kūrimo ir tyrimo išvados ir įžvalgos. ABPMD tikslas buvo užtikrinti netrukdantį, visiškai netriukšmingą matavimo metodą, kuomet slėgis manžetėje neviršija sistolinio kraujospūdžio (SBP) vertės. Taip pat buvo siekiama užtikrinti reguliuojamą automatinį kalibravimą ir išlaikyti tikslumą atliekant nuolatinius kraujospūdžio ilgalaikius matavimus. Ataskaitoje apžvelgiamas sistemos projektavimas, įgyvendinimas ir veiksmingumo įvertinimas. Įvertinimo metu ABPMD prototipas buvo lyginamas su SOMNOTouch NIBP prietaisu kaip standartu. Vertinant daugiausia dėmesio skirta sistolinio kraujospūdžio, diastolinio kraujospūdžio ir vidutinio kraujospūdžio matavimų tikslumui ir preciziškumui. Rezultatai rodo, kad nė vienas iš vertinamų matavimo metodų neatitiko Britų hipertenzijos draugijos (BHS) ar Medicinos prietaisų tobulinimo asociacijos (AAMI) nustatytų kriterijų. Tačiau, svarbu pabrėžti tai, kad, kaip nurodoma naujausioje mokslinėje literatūroje, naudojamo etaloninio prietaiso SOMNOTouch NIBP tikslumas gali būti ribotas. Todėl galutinės išvados, kad įvertintas prietaisas neatitinka tarptautinių standartų, daryti negalime. Vis dėlto, yra potencialių krypčių, kaip toliau galima tobulinti ABPMD tikslumą ir preciziškumą. Pavyzdžiui, įdiegti nuolatinį signalo kokybės kontrolę, integruoti Korotkovo garsų įrašymą, kad būtų padidintas periodinio kalibravimo tikslumas, ir patobulinti kraujospūdžio aproksimacijos algoritmus įtraukiant papildomus parametrus, tokius kaip amžius ir kūno masės indeksas (KMI). Šie patobulinimai gali pagerinti ABPMD tikslumą ir priartinti jį prie BHS ir AAMI nustatytų standartų.

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List of abbreviations and terms

Abbreviations:

ABPM – ambulatory blood pressure monitor;

ABPMD – ambulatory blood pressure measurement device;

ACC – accelerometer;

AAMI – advancement of medical instrumentation;

BP – blood pressure;

BPM – beats per minute;

CVD – cardiovascular diseases;

DPB – diastolic blood pressure;

ECG – electrocardiogram;

EMG – electromyogram;

ESH – European society of hypertension;

FDA – U.S. food and drug administration;

ISO – international organization for standardization;

HR – heart rate;

LOA – limits of agreement;

MAA – maximum amplitude algorithm;

MAP – mean arterial pressure;

mmHg – millimeters of mercury;

OPWE – oscillometric pulse waveform envelope;

PAT – pulse arrival time;

PEP - pre-ejection period;

PPG – photoplethysmography;

PWA – pulse wave analysis;

PWV – pulse wave velocity;

RMS – root mean square;

SBP – systolic blood pressure;

SDPPG - second derivative of photoplethysmography;

SQI – signal quality index;

WHO – world health organization;

Terms:

Diastolic blood pressure (DBP) – The lowest pressure level applied by the blood on the walls of the arteries during a cardiac cycle.

Hypertension – High blood pressure.

Mean arterial pressure (MAP) - Measure of the average pressure in a person's arteries over a single cardiac cycle.

Oscillatory – With regards to BP measurement, acquisition of oscillations of arterial pulse amplitudes by means of pressure sensor.

Photoplethysmography – An optical measurement technique for detecting blood volumetric changes in the microvascular bed of tissue per pulse.

Systolic blood pressure (SBP) – The highest pressure level applied by the blood on the walls of the arteries during a cardiac cycle.

Introduction

According to World Health Organization (WHO) statistics more people die annually around the globe from cardiovascular diseases (CVD) as compared to any other diseases. It was estimated that around 17.9 million people died from CVDs in 2016, representing 31% of all the global deaths. 85% of them were due to heart attack and stroke [3]. In the United Kingdom, cardiovascular disease is the second leading cause of death after cancer with 28% of deaths attributed to it. Despite a slight decrease in overall prevalence rates in the developed world, cardiovascular disease remains a considerable health and economic burden [4]. It is mainly due to the rising incidences of obesity and sedentary lifestyle.

One of the most common cardiovascular diseases is hypertension. Hypertension - or elevated blood pressure - is a serious medical condition that significantly increases the risks of heart, brain, kidney and other diseases. Hypertension is diagnosed, when it is measured on two different days, the systolic blood pressure readings on both days are ≥140 mmHg and/or the diastolic blood pressure readings on both days are ≥90 mmHg. One of the global targets for noncommunicable diseases is to reduce the prevalence of hypertension by 25% by 2025 [2]. Having that said, a continuous blood pressure monitoring could help to identify exact dose of the drug that a patient needs in order to keep the BP under control. Therefore, we need an inexpensive and accurate measurement equipment for monitoring BP available for ambulatory patients.

An accurate blood pressure measurement is vital in the prevention and treatment of blood-pressure–related diseases. Additionally, in serious cases monitoring cardiovascular homeostasis necessitates an accurate measurement of blood pressure. For years, the cuff-based sphygmomanometer and the arterial invasive line have been the golden standards for care professionals to assess BP. During the past few decades, the wide spread of the oscillometry-based BP arm or wrist cuffs have made home-based BP assessment more convenient and accessible. However, the discontinuous nature of the measurements, inability to interface with mobile applications, increased inaccuracy with movement, and the need for calibration have rendered those BP oscillometry devices inadequate for the next-generation healthcare infrastructure, where an integration, continuous data acquisition and communication are required. Recently, the indirect approach to obtain BP values has been intensively investigated, where BP is mathematically derived through the “time delay” in propagation of pressure waves in the vascular system. This creates a solid ground for the realization of cuffless and continuous BP monitoring systems, for both patients and healthy populations in both inpatient and outpatient settings [6]. The cuffless BP measurement method requires calibration to be done at a certain intervals. This is needed in order to prevent the estimated BP numbers from drifting from the actual BP values. Unfortunately, the calibration for cuffless devices in the long run is still poorly investigated due to various methods used for estimation of the BP.

Research methods: an automatic cuff-based ABPMD will be built for accurate BP monitoring during the night. It will combine few simultaneously operating BP measurement methods to increase the reading accuracy employing oscillometry and PPG signals. The device will be using noise free piezoelectric pump. Therefore, it will not disturb patients sleep. The maximum pressure in the cuff will be adjusted automatically according to PPG signal, removing excessive disturbance and increasing the battery life.

The aim of this project is to develop a long-term unobtrusive blood pressure monitoring system targeted for overnight measurements.

The objectives:

1. To conduct an analysis of the clinical significance and technologies involved in long-term ambulatory blood pressure monitoring.
2. To design and construct a prototype device suitable for unobtrusive nightly measurements of blood pressure.
3. To develop an operation algorithm for the measurement system.
4. To perform a quantitative comparison between the prototype device and a reference BP measurement device in long-term blood pressure monitoring scenarios.

1. Literature overview

1.1. Overview summary

Automated blood pressure measurement devices (ABPMDs) have become increasingly popular over the last decade, with a wide range of models available on the market. These devices can be divided into two main groups: cuff-based and cuffless.

Cuff-based ABPMDs use oscillometric techniques to estimate blood pressure. During cuff inflation or deflation, air pressure pulses are recorded and analyzed to extract systolic and diastolic blood pressure values using proprietary algorithms. However, it is important to note that this method only approximates blood pressure, as there is no universal way of extracting exact values of SBP and DBP from the oscillometric pulse data. Different approximation algorithms must be used for each case.

Cuffless ABPM devices use techniques such as photoplethysmography (PPG) and electrocardiography (ECG) to measure blood pressure without a cuff. PPG is the most commonly used technique in cuffless ABPMDs, which measures changes in light absorption caused by changes in blood volume in the skin. However, these methods are still being developed and may not be as accurate as cuff-based methods.

Recent research has focused on improving the accuracy of ABPM through machine learning techniques such as neural networks. One study found that adding 14 more PPG features improved BP estimation accuracy by 40% compared to conventional neural network methods. However, mean and standard deviation errors were still above the limits set by the Association for the Advancement of Medical Instrumentation (AAMI).

Overall, while automated blood pressure measurement devices offer convenience and ease of use, their accuracy may not be as reliable as traditional manual measurements using a sphygmomanometer. Further research is needed to improve their accuracy and reliability before they can fully replace manual measurements in clinical settings.

Over the last decade the market for automated non-invasive BP measurement devices has significantly expanded, offering a wide range of various models which come with their advantages and disadvantages. The automated ABPMs are generally divided into two main groups: cuff-based and cuffless. These two methods will be discussed in the following chapters in more detail.

1.2. Cuff-based ABPMDs

At the moment the majority of automatic ABPMDs are using oscillometric technique for estimating blood pressure. During the cuff inflation or deflation the air pressure pulses are recorded and then analysed to extract systolic and diastolic BP values using undisclosed proprietary algorithms. It is very important to note that this method of measurement only approximates BP, as there is no universal way of extracting exact values of SBP and DBP from the oscillometric pulse data. As the oscillometric pulse envelope is different during cuff inflation and deflation, diverse approximation algorithms have to be used in each case.

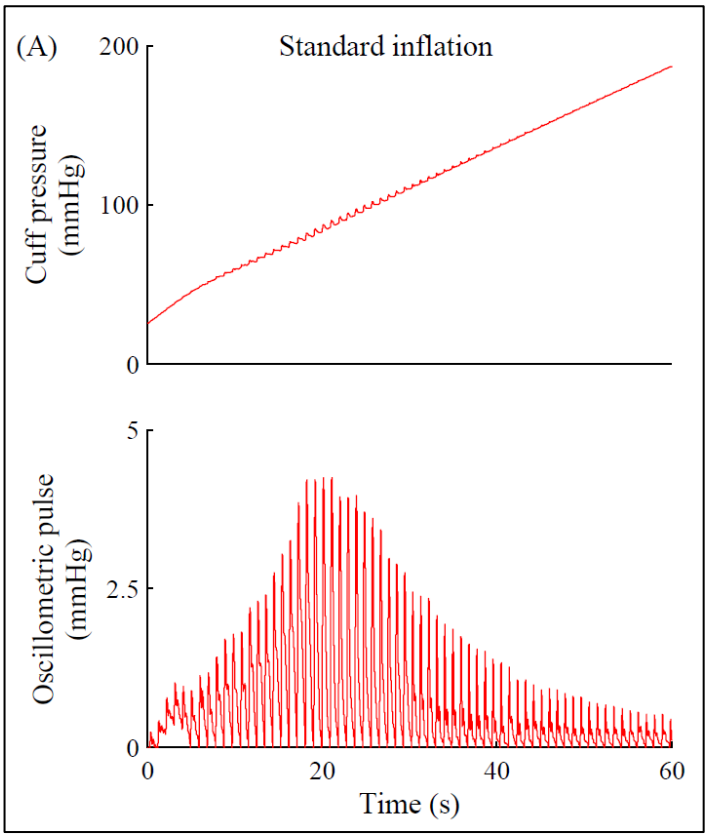

Fig. 1. Oscillometric BP measurement during inflation [5]

In Fig. 1 we can see the acquired air pressure oscillation data in the cuff during BP measurement which is plotted over time. To calculate BP values in the first place the reference amplitude is extracted (which is the maximum pressure pulse peak) for further processing. It divides the envelope into ascending and descending stages and is closely related to the mean arterial pressure (MAP). After that signal ratios with the peak amplitude are used for estimating the SBP and DBP values.

Even though it is very convenient way of measuring BP, it is error prone. The oscillometric waveform envelope shape is correlated to a number of physiological parameters which can vary:

- Soft tissue having non-linear biomechanical properties;
- Pulse pressure which is the difference between the SBP and DBP;
- Arterial compliance which changes with blood pressure;
- Heart rate (beats per minute).

Since these values cannot be kept fixed, variation in listed parameters will have a direct impact on BP results accuracy. Additionally, the measurement error can be further increased by noise or artefacts caused by movement of the patient.

Nevertheless, the market is flooded by hundreds of automatic oscillometric BP measurement devices with price ranging from €20 to over €1000. The market in 2020 valued at $1.4 billion for blood pressure monitoring devices. The cheaper BPMDs do not have validation certificates and, therefore, cannot be recommended for management of hypertension or diagnosis. However, the clearance of BP measurement device from AAMI/ESH/ISO (Association for the Advancement of Medical Instrumentation / European Society of Hypertension / International Organization for Standardization) or FDA (Food and Drug Administration) gives a certain degree of confidence that the measurement results will have comparatively small error.

If we take for instance “Withings” BPM Connect device (Fig. 2) which has passed the FDA clearance, we can see that it was validated under the following conditions:

- Clinical trial of 87 participants;
- Adults from the general population with an arm range of 22-42 cm;
- Participants had all grades of blood pressure;
- Three measurements were taken using BPMD and compared with three measurements obtained by two trained independent persons (by Korotkoff method).

The results were the following: the mean error calculated was -0.27 mmHg for SBP and -0.16 mmHg for DBP. The standard deviation error 7.46 mmHg and 5.85 mmHg respectively, which are within specification limits.

Fig. 2. “Withings” BPM Connect (Withings company, France)

Therefore, the results might not be very accurate and the BPM will still pass the validation. Inaccurate BP values from oscillometric devices can be propagated as well from the same standards mentioned above: FDA or association for the AAMI/ESH/ISO. The validation procedure of all these organizations employs the comparison between the BPMD under test to the manual auscultatory technique using Korotkoff sounds. The devices under test can pass the validation with such high deviations as 10 mmHg in 18% of the measurements. Furthermore, the auscultatory technique has its own deviation relative to the true golden standard, invasive measurement. Hence, the actual error in oscillometry-based BPMD is likely to be even greater than expected [7].

Blood pressure can be measured on wrists as well using pressure with a cuff-based devices. Omron has presented the first FDA cleared watch called “HeartGuide” (Fig. 3). It can measure BP up to 100 times with a single charge. One of its disadvantages is that every time the measurement is done, the watch has to be kept at the level of the heart. The manufacturer recommends to place the arm wearing the watch on the chest while performing BP measurement.

Fig. 3. Omron cuff-based BP watch (Omron Healthcare Co., Ltd., UK)

In general WHO does not think that BP measurements on wrists or fingers are suitable for clinical use because of their lack of accuracy [2]. Nevertheless, "HeartGuide" device has passed FDA validation.

Another device using oscillometric method on wrist is from "Fitology" is shown in Fig. 4. Simple in use and well presented on official website. However, it does not have any type of certificate whatsoever. Even though it is very convenient to wear, BP measurement values obtained using this device cannot be trusted and used for diagnostic purposes.

Fig. 4. "Fitology" BP Wearable Blood Pressure Smartwatch (Fitologyhealth, China)

There are numerous researches done on automated BP devices using electronically recorded Korotkoff sounds. However, the devices employing this type of method cannot be found on the market. What is preventing developers from creating a robust BPMD which would use auscultatory technique (the golden standard)? The reason is straightforward, the sound recorded by microphone is prone to noise artefacts, which are naturally ignored by an expert examiner [1]. In order to accurately detect the SBP or DPB values we would need to pinpoint where exactly the Korotkoff sounds started and ended, and that is a very challenging task for an automated measurement unit.

Nevertheless, there are some attempts to use auscultatory method in semiautomatic BP measurement available on the market. The "Accutension Stetho" is using a smartphone application and specifically designed stethoscope that is connected to smartphone via 3.5 mm earphone plug. The phone camera captures the sphygmomanometer screen while recording the Korotkoff sounds. Application processes the data and then shows the result. This device has passed NSI/AAMI/ISO requirements and is mainly used for individual validation of BPMDs for each patient separately [8]. Fig. 5 below shows the patient performing measurement with "Accutension Stetho".

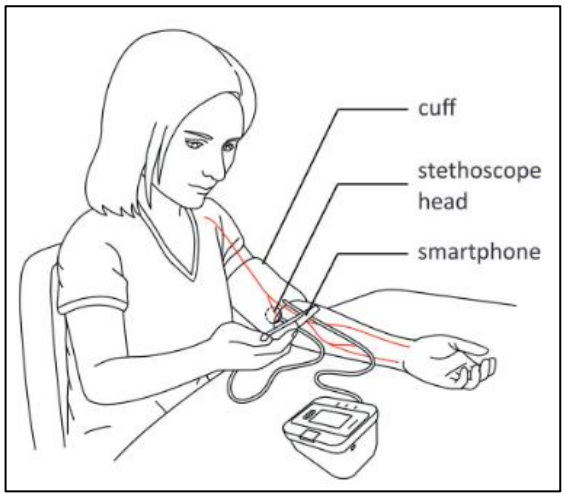

Fig. 5. Measuring BP with "Accutension Stetho" [8]

1.3. Cuff-based ABPMs

The 24-hour ambulatory blood pressure monitoring (ABPM) method is used as an additional method of examining patients, especially those struggling to manage hypertension. Currently, the method is increasingly recognized by doctors as ABPM can be used in many different clinical situations and provide a more accurate physiological description of systemic blood pressure throughout an entire 24-hour time period for patients either on or off antihypertensive drugs [25, 26].

However, a single measurement of a blood pressure provides information only for a particular moment in time and does not always reflect the real clinical picture. As well there might be a possible emotional and certainly physical discomfort during the monitoring (especially at night) as the cuff applies a substantial amount of pressure while measuring BP. Consequently, the interval between the measurements at night is increased making more room for ambiguity during the results analysis.

An example of ABPM profile is presented in Fig. 6. The graph shows BP and HR vs time, where we can see the boundaries of acceptable BP levels (during the day no more than 140/90 mmHg, and at night should not exceed 120/80 mmHg [25]). It can be seen that the measurements were done with 30 min intervals, except the night-time, where the intervals were set to 1 hour.

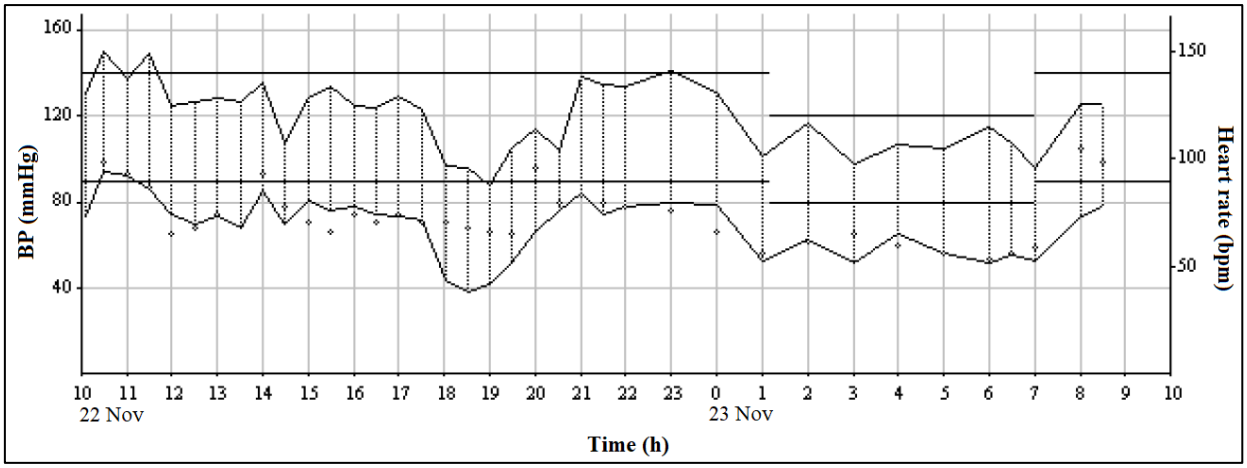

Fig. 6. 24-hours profile of the blood pressure levels [25]

The devices used for ABPM must be validated according to the established standards such as AAMI/ESH/ISO, FDA or British Hypertension Society (BHS). Only then they can be recommended for clinical use.
There are some devices available on the market which underwent reliable validation by numerous experts. One of them is Mobil-O-Graph a 24-hour ABPM. It has an intuitive and highly sophisticated interface compatible with leading clinical systems, and for the end user - standard USB port and Bluetooth. The software allows to easily generate a report in PDF format.
However, there are a few drawbacks associated with the Mobil-O-Graph device that should be taken into consideration. Firstly, it is able to perform measurements only at discrete time intervals, i.e. not capable to flexibility adjust the measurement frequency automatically. This limitation can be restrictive in certain situations where measurement intervals should be adjusted when BP rises or decreases. Secondly, the Mobil-O-Graph device employs a mechanical pressure pump, which generates noticeable noise during operation. This noise can be disruptive to patients, particularly during sleep, and may impact the quality of their rest and overall comfort during monitoring which in turn has a direct impact on BP value.
Other automated oscillometric blood pressure monitors which can be used for ABPM are from the company called Microlife. For example WatchBP AFIB ABPM have high accuracy and are clinically validated for use even in the following groups of risk: diabetes patients, children, elderly, during the pregnancy and pre-eclampsia. Nevertheless, this device suffers from the same drawbacks as the Mobil-O-Graph.

1.4. Cuffless BPMDs

Unobtrusive BP measurement devices are much more comfortable for patients to wear, as they are simply not causing any discomfort (cuff squeezing the arm) while performing the measurement. Unlike cuff-based they are capable of measuring beat-to-beat BP and do not disturb the night sleep. The disadvantage of such a comfortable device comes at a cost of greater complexity, lower accuracy and the need of a periodic adjustment, i.e. error correction with reference BP measurement device. It is important to note here, that the majority of bioengineering publications use the term ‘calibration’ instead of adjustment. According to International Vocabulary of Metrology the adjustment of a measuring system should not be confused with calibration. The latter allows to determine the deviation of the indication of the measuring device from a known value of the measurand provided by the measurement standard (such as ISO 17025), with associated measurement uncertainty. While the device adjustment means reduction of the system output error. Therefore, in this paper the term adjustment will be used onwards.

There are numerous of different of techniques out there for estimating a BP using non-invasive cuff-less devices with photoplethysmogram (PPG), which will be described in more detail below.

Biosignals: PPG. The photoplethysmogram helps to measure and keep a track of blood flow variations under the skin. A PPG sensor primarily consists of two devices: LED and photodiode. The former emits light at a specific wavelength penetrating the skin, and the latter detects reflected scattered light (Fig. 7). When the blood pulse passes under the LED the increased amount of red

blood cells absorbs more light. Hence, at that point of time less amount of light is measured by photodiode.

For PPG applications a green light emitting diode is preferred as it has a better signal-to-noise ratio, i.e. greater amplitude [17], and less motion artefacts compared with red, blue or near-infrared light signals [14]. The photoplethysmogram has DC and AC components. The AC portion is due to arterial blood flow which is in sync with the heartrate. The DC component is directly related to the skin, tissue, bone and non-pulsatile blood. Therefore, the signal must be filtered in order to extract the needed pulse waveform [13].

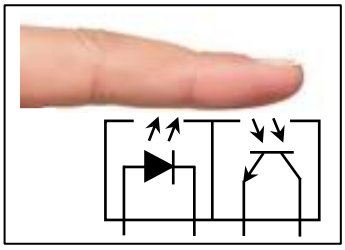

Fig. 7. PPG: light emitter and receiver

The biggest challenge during the PPG signal acquisition from a wearable device is movement artefacts, which renders the signal unusable. In one pilot study a volunteer was asked to wear a "SmartCare" PPG sensor on the wrist for a six consecutive days. The aim was to check the feasibility of continuously capturing PPG pulses in a daily life. The results have shown that only 30.5% of the acquired data had a reasonably high quality. It was the highest during the sleep and sedentary activities when the person is barely making any movements, and predominantly low quality signal while running or walking [12].

In addition to motion artefact the ambient light noise can have great impact the PPG waveform quality as well (Fig. 8). Therefore, it is of great importance to separate the high- and low-quality pulses for the next data processing stage in order to produce correct measurement results. M. Elgendi [15] proposed to use an optimal signal quality index (SQI) for classifying photoplethysmogram waveforms as opposed to complicated machine learning methods. The following eight SQI were suggested:

1. **Perfusion**: the difference between min and max amount of light absorbed during the pulse.
2. **Skewness**: the measure of symmetry of a probability distribution.
3. **Kurtosis**: statistically describes the distribution of the pulse around the mean.
4. **Entropy**: computes the difference between the probability density function of the pulse and a uniform distribution.
5. **Zero crossing rate**: the rate at which the waveform changes from – to + or vice versa.
6. **Signal-to-noise ratio**: the ratio of the signal to background noise.
7. **Matching of multiple systolic wave detection algorithms**: calculates the level of noise using different PPG algorithms.
8. **Relative power**: ratio of the power spectral density using different frequency bands.

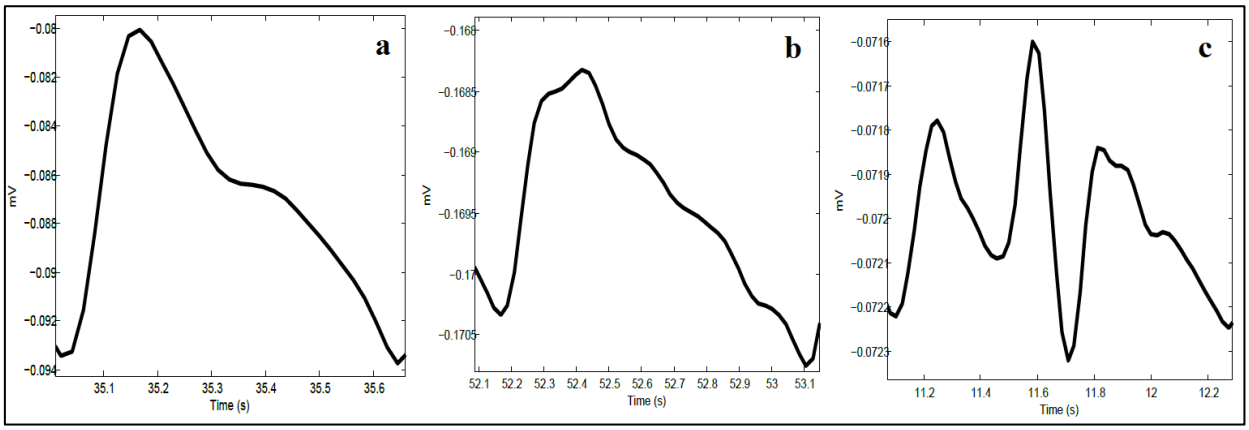

Fig. 8. PPG signal quality: a) excellent, b) acceptable and c) poor [15]

Another way of eliminating movement artefacts from PPG would be by the means of accelerometer, which could indicate an excessive movement of the patient during the signal acquisition. If the accelerometer output power exceeds a certain limit (which is set experimentally), the signal is marked as not compliant and is discarded [16]. After the clean waveforms are identified, they can be processed with different algorithms in order to extract the PGG pulse features of interest.

PPG sensor contact pressure against the skin most of the time is overlooked. It is understood that for precise measurements the sensor should be attached firmly to the skin to limits its shifting, and that impose the restrictions not only on patient's movements, but additionally in situations such as wound diagnostics (burn/ulcer/trauma) and skin healing evaluation. To date, no general standards have been established for clinical or fundamental PPG measurements of contact pressure. Recent studies have investigated the effect of contact force on the amplitude and timing of the PPG signal using spring-loaded conventional PPG probes and have shown that this force must be carefully controlled to obtain high-quality clinical data from the signals [28]. Incorrect contact measurement arrangement might cause the deformation of the arterial wall at the detecting site or simply block microcirculation in the capillaries. Therefore, it is of great importance to find the right sensor contact pressure when measuring PPG.

Pulse transit time. Pulse transit time (PTT) is the time that takes the blood pulse (pressure waveform) to travel between the two arterial locations where PPG signal is captured. To measure PTT two PPG sensors are required. As it was mentioned before PPG is susceptible to motion artefact and need pre-processing in order to filter out the drifting, smoothing and elimination of sudden changes in the signal due to patient movements, whilst keeping the recordings in sync [10]. Then the timing between the two pulses can be extracted by using various reference points: PPG waveform peak, foot, first derivative peak, etc. It was observed that PTT^{-1} is related to blood pressure (Fig. 9), which allows automatic, non-invasive, and cuff-less BP estimation [17, 20, 23]. The blood pulse travels through the artery faster if blood pressure is higher and slower if blood pressure is lower.

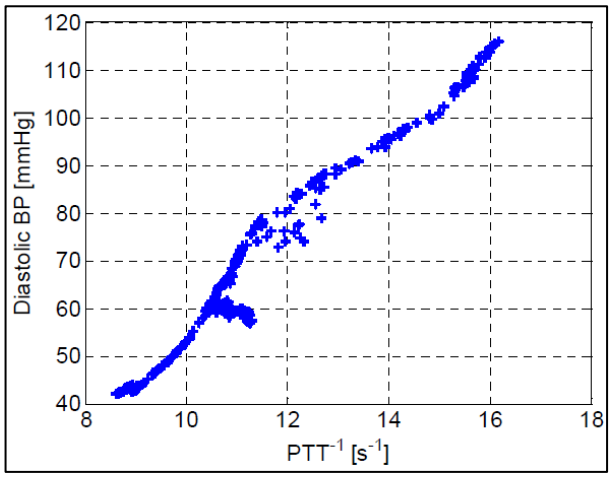

Fig. 9. BP is inversely related to PTT [17]

Pulse transit time is usually measured with two PPG sensors on the same artery. Farasha Labs has developed "CareUp" smartwatch (Fig. 10). It records two PPG signals simultaneously at two sites: left arm wrist and right hand index finger. The time delay between arrivals of two the peaks is the pulse transit time, and the heart rate value obtained from the same PPG signal. The disadvantage of such device is that the measurements cannot be done automatically, hence, the BP measurements during the night are not feasible.

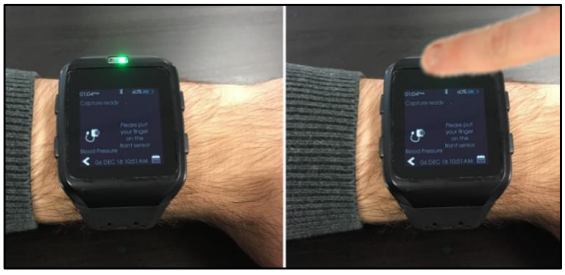

Fig. 10. "CareUp" smartwatch by Farasha Labs [13]

After that the linear model is used for estimation of SBP and DBP using (1) and (2):

$$SBP = A_S \cdot PPT + B_S \cdot HR + C_S; \quad (1)$$

$$DBP = A_D \cdot PPT + B_D \cdot HR + C_D; \quad (2)$$

Due to different physiological characteristics of the patients, the constants $A_{S(D)}$, $B_{S(D)}$ and $C_{S(D)}$ are experimentally tuned during the adjustment process. The adjustment involved measuring BP with a sphygmomanometer and entering SBP and DPB values into smartwatch. After that the validation was performed according AAMI standards, where the mean error was found to be within the limits, while the standard deviation error was less that 8mmHg only for DBP, and SBP was two points higher [13].

It should be taken into account that in many articles the pulse arrival time is referred to as PTT, which is incorrect. For consistency purposes PTT and PAT are separated into two distinct sections in this project.

Pulse arrival time. PAT is the time that it takes the pulse to arrive at PPG measurement site after R-peak of ECG (electrical depolarization of the heart left ventricle). Usually the time (PAT) between the PPG foot (on finger) and to the ECG R-wave at rest lies within the range from 180

ms to 260 ms [17] as shown in Fig. 11. Various locations on the body can be used for PPG acquisition, such as finger, wrist, toe, chest, forehead or ear. For consistency a specific point on PPG wave has to be used, such as peak, foot or maximums slope.

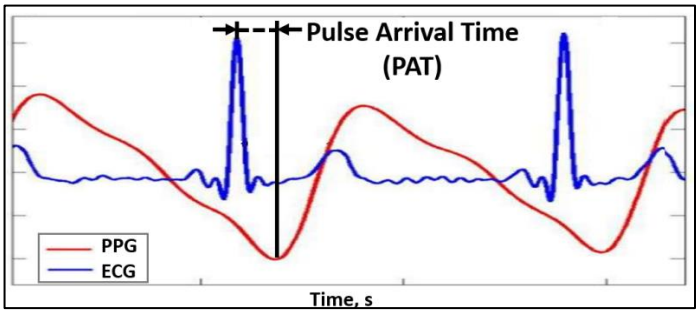

Fig. 11. PAT estimation from ECG-PPG

The PAT consists of the pre-ejection period and pulse transit time (3):

$$PAT = PEP + PTT; \quad (3)$$

PEP characterizes the isovolumetric contraction time of the heart, which is the time it takes for the myocardium to raise enough pressure to open the aortic valve and start pushing the blood out of the ventricle [9, 11, 18].

A number of researches have been done on PEP variation effect on PAT stability. It was shown that PEP accounts for quite considerable portion of PAT (12% to 30%), and since PEP cannot be assumed to remain constant it would be unsuitable to use PAT for BP estimation [19].

S.Cattivelli and H.Garudardi [9] in their work indicate that frequent adjustments are needed to keep the standard deviation error within the AAMI standards limits (< 8mmHg) for method implementing BP estimation using PAT. The maximum adjustment interval suggested was 1 hour and 20 minutes (Fig. 12).

The drawback of Cattivelli research is that the measurements data was gathered in one of the Boston hospitals and placed in Multiparameter Intelligent Monitoring in Intensive Care (MIMIC) database. Naturally, the data processing was performed without knowing all the measurement conditions, settings, instruments accuracy, latency introduced and synchronization between the signals. The authors of the MIMIC user guide [27] point out the following problems associated with their database:

- Probable missing data due to machine or patient disconnections, transmission and recording errors and human omissions.
- Important events may go unobserved.
- Possible errors in data matching and alignment where it came from different sources using different clocks.
- Previous statement leads to poor synchronization problem.

For that reason, we can trust the provided adjustment period of 1 hour and 20 min only to a certain degree.

PEP can be influenced by medications, stress, emotion or movement. Although it was found that PAT can lessen the diastolic pressure accuracy, however, others suggest that PAT improves systolic blood pressure and this method is still used in literature for its simplicity and ease of implementation [10].

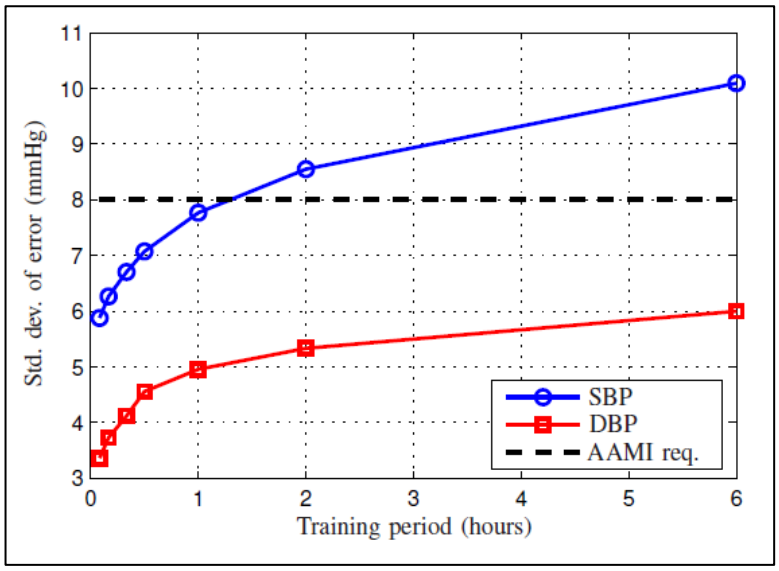

Fig. 12. Standard deviation and an indicator for adjustment period [9]

In his research D.Nachman at all [21] performed the study of the BPMD from "Biobeat Technologies" BB-613WP model (Fig. 13) using blood pressure measurement data from 1057 subjects. The device performs BP estimation using PAT (in the article they are calling it Pulse Wave Transit Time - PWTT). The device comes in the form of a smartwatch which is the first FDA cleared for non-invasive cuffless blood pressure monitor, measuring oxygen saturation (%SpO2), and HR. As it can be seen on the picture below it has two electrodes for measuring ECG, four red LEDs for %SpO2, and four green LEDs for PPG, and photodiode in the center for capturing reflected light from tissues. The patented photo sensor allows to detect even the smallest changes in tissue reflectance. Unfortunately, this device is intended only for professional use in clinics by trained medics.

Fig. 13. The "Biobeat" BB-613WP BPMD [21]

The results for this study are astonishing. The statistics from 1057 subject, after comparing the results with the reference cuff-based BPMD, show that the mean and standard deviation errors for SBP and DBP are 0.1/3.6 mmHg and 0/3.5 mmHg accordingly. There are outstanding results even when comparing to automatic cuff-based BPMDs [21].
BB-613WP has to undergo an adjustment as well with the cuff-based BP device that provides a reference BP values which are entered into a user's application.
Even though the article states that the adjustment is valid for three whole months, all the measurements were done right after the adjustment and currently a long-term adjustment research is ongoing.

Pulse wave velocity. Pulse wave velocity (PWV) determines the velocity of the blood pulse wave using two PPG sensors located on the same arterial branch with a known distance apart. PWV is another cuffless method for BP estimation. PWV is the speed of the pressure wave propagation in the blood vessels, which is based on the theory of wave propagation for fluids in elastic pipes [10].

PWV is not a practical replacement for the cuff-based BP devices as keeping PPG sensors fixed at the same distance would be unmanageable when patient is moving.

The main drawback of this method is that for continuous measurements of BP a constant adjustment is required - due to different physiological parameters for individuals or patient/probe movement [10].

Pulse wave analysis. Pulse Wave Analysis (PWA) refers to signal processing and extractions for certain characteristic features from the PPG waveform. This method requires the data only from a single PPG sensor.

Signal processing like filtering and feature extraction have been engaged in PPG waveform analysis. These features are typically used for creating models employing machine learning and deep neural networks for estimation of BP. The main disadvantages of this approach are: the process of capturing the PPG which is prone to motion artefacts due to movements, and that the relationship between the BP and the PPG waveform features is not fully understood yet [10]. Hence, more research is unquestionably needed for better understanding of this method.

The following Fig. 14 shows few out of many features of the photoplethysmogram waveform that are used for PWA:

- ST – systolic upstroke time;
- DT – diastolic time;
- Width 1 – width at 1/2 pulse amplitude;
- Width 2 - width at 2/3 pulse amplitude.

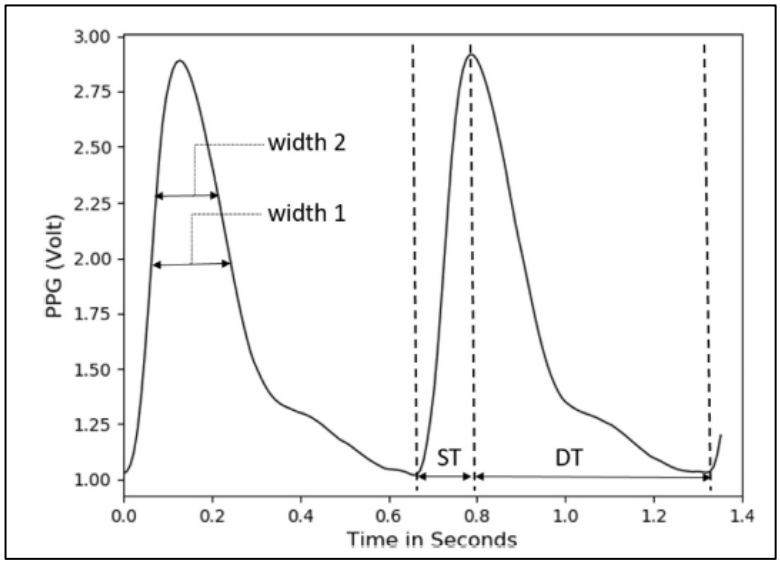

Fig. 14. PPG waveform features [10]

Many more features can extracted and used for accuracy improvement of the BP estimation. From the recent studies of vascular aging through the second derivative of PPG (SDPPG), PWV and SDPPG contain the information about aortic compliance and stiffness. These factors highly

correlated with blood pressure. Essentially, SDPPG is the acceleration of PPG and its waveform is in "W" shape with typically five sequential waves (Fig. 15).
The applicability of SDPPG for BP measurement was investigated through analysis of the relationship between blood pressure and SDPPG features. It was found that DBP has a good relationship with the amplitude ratios of peak "b" to peak "a" and peak "e" to peak "a". Though, not all the PPG pulse cycles can provide the second derivative waveform with clear "W" shape. This is related to PPG signal quality, movement artefacts and the fact that the waveform changes its form due to aging. The reflected wave due to faster propagation moves to the left as the artery walls are losing their elasticity as the patient gets older.
As blood is being ejected from the heart, a blood pressure wave is generated and travels along the walls of the arterial tree. This pressure wave is partly reflected at each arterial bifurcation or discontinuity due to the mismatch of hydraulic impedance. These reflected waves travel back to the heart. The resulting aortic pressure waveform is thus a superposition of the forward wave travelling from the heart towards the periphery and a global reflected wave travelling back to the heart [24].

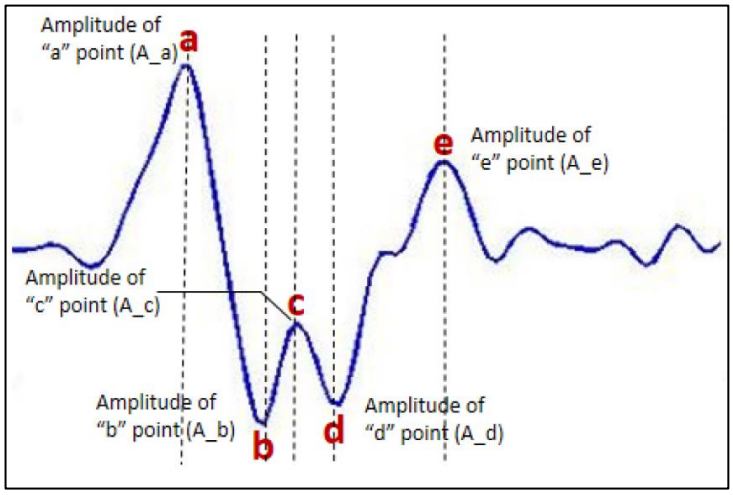

Fig. 15. "W" shaped SDPPG [22]

After adding 14 more PPG features the experimental results showed that the BP estimation accuracy can reach 40% improvement as compared with a conventional neural network method [22]. However, the mean and standard deviation errors were still above the limits set by the AAMI.
A study has been carried out that evaluated the accuracy of blood pressure measurements taken with smartwatches [32]. The study recruited subjects scheduled for 24-hour ambulatory blood pressure monitoring and provided them with a Samsung Galaxy Watch Active 2 smartwatch for simultaneous BP measurement on their opposite arm. Patients were asked to measure their BP as much as possible during a 24-hour period. The accuracy was assessed using sensitivity, specificity, and positive/negative predictive values. The study also used the Bland-Altman method to evaluate bias and precision, and BP variability was calculated using average variability, standard deviation, and coefficient of variation.
The results of the study indicate that the Samsung Galaxy Watch Active 2 displayed a systematic bias towards a calibration point, overestimating low BPs and underestimating high BPs in both normotensive and hypertensive patients. The device did not meet the standards for traditional non-

invasive sphygmomanometers, but this is not surprising since these standards are not fully applicable to cuffless devices. Thus, there is an urgent need for new standards for cuffless devices. The study concludes that smartwatch-based BP measurements are not ready for clinical use. However, when used in combination with a cuff-based BP monitor, smartwatches may provide valuable BP measurements. Further studies are necessary to validate wearable devices and to demonstrate new possibilities for non-invasive high-frequency BP monitoring. These findings have important implications for the use of smartwatches in healthcare settings.

A recently published a PPG-based PWA algorithm oBPM™ dedicated to the continuous monitoring of BP of very high accuracy in estimation of DBP**.** It was found that the calibration remains stable over the entire 3-month period, with estimation errors remaining stable over time and complying with the ISO 81060-2:2018 standard (mean error < 5 mmHg and SD error < 8 mmHg). Despite such a promising results, the study was performed with only 13 healthy volunteers participating in experiment and only one female. The same investigation regarding systolic and mean arterial pressure still remains to be performed [24].

The main limitation of PPG-based approaches is their indirect link with BP, thus they require a calibration procedure with an oscillometric cuff to be able to provide absolute measurements of BP (in mmHg). Minimizing the number of re-calibration procedures is a very critical aspect for the practical usability of PPG-based solutions. To this day, the long-term stability of calibration parameters remains largely untested in the literature.

2. Methodology

2.1. Design of unobtrusive device for long-term blood pressure monitoring

The proposed method uses an automatic cuff-based BP measurement device which records PPG and cuff pressure data. By recording two signals, it becomes possible to enhance the accuracy of measurement results during the processing of raw data. Furthermore, the PPG signal is employed to make adjustments accordingly to the maximum cuff pressure. The device is placed on the upper left arm. PPG is captured with Analog Devices MAX86916 IC, lightly pressed against the skin between the cuff and an elbow using a wide stretch band.

Fig. 16 shows block diagram of the ABPMD, where an accelerometer is used for detecting patient's arm movements. Three axis signals indicate that BP and PGP data might be contaminated with motion artifacts, i.e. noise. A certain threshold level is experimentally determined for all three directions: x, y and z. Their standard deviation values are compared against that limit which serves as a guidance for a possible motion artefacts in PPG signal and noise obtained in a cuff pressure data.

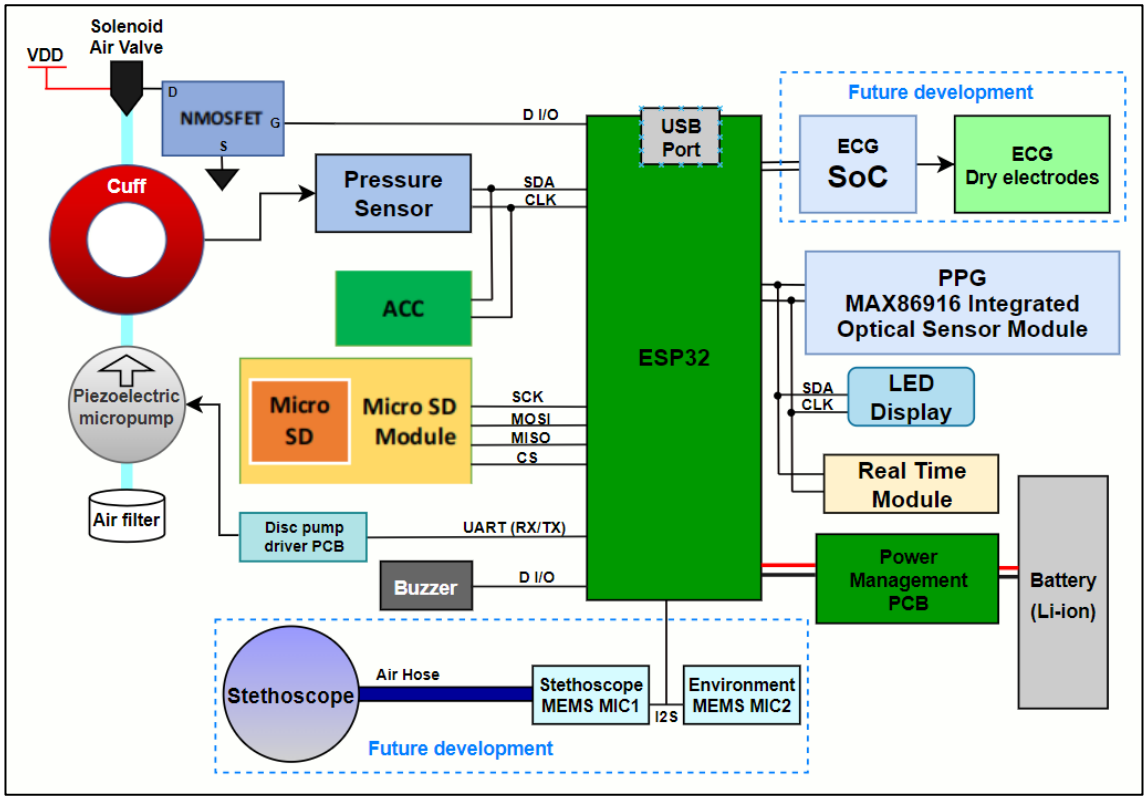

Fig. 16. Block diagram of the multisensory device

Real time clock (RTC) module allows the whole system to be synchronized after the power is reintroduced in case of power down or battery removal. RTC module is backed up with a battery cell to supply the minimum power required to keep the internal 32 kHz clock working, while all the rest of the device modules are powered off. It uses I2C interface and standard Arduino driver library that is readily available for use.

LED display provides information to user and is used for debugging purposes as well.

Blood pressure measurement begins by inflating the cuff by means of driving piezoelectric micropump (disc pump) which uses an air filter (syringe filter) with pore size < 120 μm. Since all the processing is done offline, the maximum allowed cuff pressure is set in configuration file on SD card. The pressure level is recorded by Honeywell pressure sensor (SSCSRNN1.6BA7A3) at a rate of 100 Hz.

To improve the accuracy of the SBP measurements photoplethysmogram is employed during the cuff inflation as well. Correlation or discrepancy between the oscillometric pulses and PPG data allows to set the level of confidence in the acquired blood pressure values. As a rule, pinpointing accurately systolic BP value is very challenging, therefore, adding a PPG measurement is beneficial. PPG sampling is performed at rate F_C = 100 Hz.

For PPG signal acquisition MAX86916 (Fig. 17) integrated optical sensor module is used. It includes four internal LEDs (green, blue, red and infrared), photodetectors, and low-noise electronics with ambient-light-rejection option. Communication to and from the module is accomplished entirely through a standard I2C interface. The I2C ESP32 driver was written exclusively for this project as it was not available from MAX86916 manufacturer.

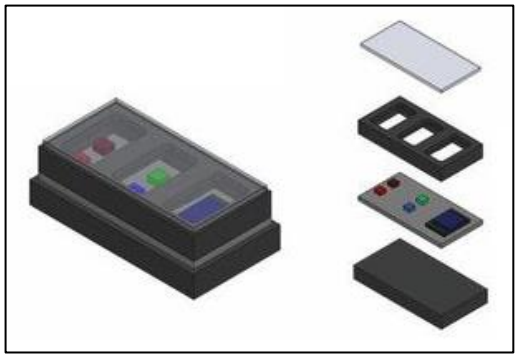

Fig. 17. MAX86916 module [Analog Devices, USA]

Currently all of the fully automatic blood pressure measurement devices based on oscillometry rely on DC motor pumps to inflate the cuff up to the required pressure level. Even though its size and power consumption have been optimized over the years, the noise level generated is still too significant and can wake up the patient when operating.

ABPMD device uses an innovative piezoelectric micropump, which has a small size, weights only ~5g and works at high frequencies, which lie outside the human frequency hearing range. That makes it practically noise-free and vibration-free. Additionally, it does not introduce pulsation into airflow, unlike conventional pumps. Along with a fast response (few milliseconds) that makes the disc pump perfect solution for BP measurements during the cuff inflation stage.

Fig. 18 below shows a piezoelectric pump with a small driver PCB on evaluation board from UK company “TTP Ventus”. It was used to evaluate suitability of the disk pump for the ABPMD application. To control the pump a custom UART driver was written for ESP32 microcontroller.

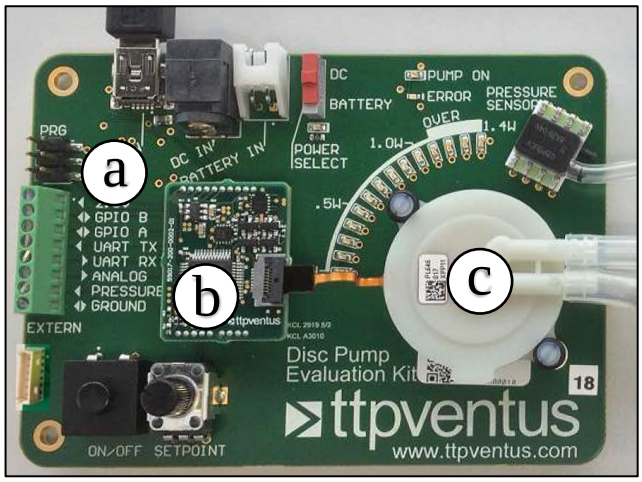

Fig. 18. TTP Ventus evaluation kit: a) evaluation board, b) driver board and c) disc pump

A unique 4-layer PCB was developed and manufactured for the ABPMD device (Fig. 19) on EasyEDA platform – online PCB design and circuit simulator. All of the components mentioned above were either soldered to this PCB or connected with wires.

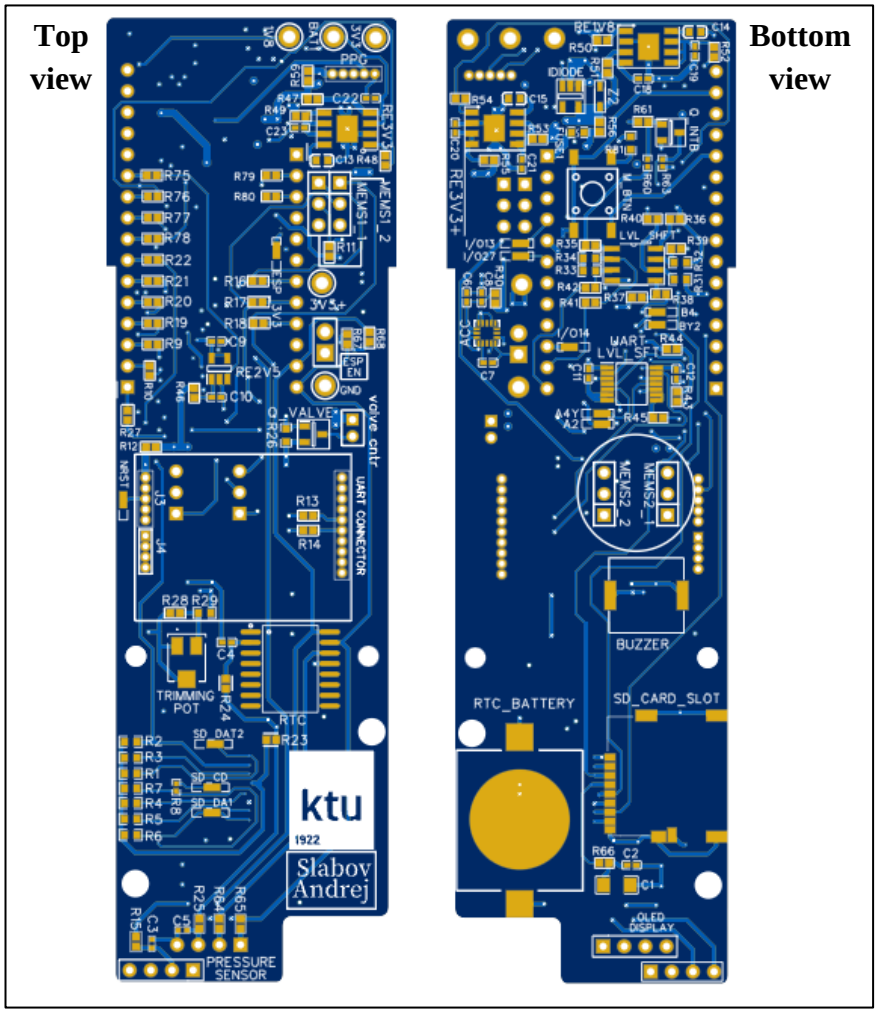

Fig. 19. ABPMD developed PCB

After the PCB was fully assembled and the functionality of each component verified, the next phase was programming ESP32 microcontroller. The programming of the ABPMD controller was carried out using the Visual Studio Code IDE with the aid of PlatformIO. This platform offers a

multitude of features and robust tools that are highly advantageous for handling large-scale projects like this. Additionally, multiple functions from FreeRTOS were employed to execute several tasks concurrently, thereby enhancing the efficiency of the system. All the measurement data is stored on micro SD card and the processing performed offline with Python.

To ensure the safety of patients during blood pressure measurements, specific safety checks have been incorporated into the process, particularly during pressure cuff inflation. The first safety check involves verifying that the pressure is increasing as expected. If the pressure fails to rise as anticipated, the pump is automatically switched off, and a warning message accompanied by an audio signal is displayed. To resume normal measurements, the user is required to restart the device.

Furthermore, a second safety feature has been implemented to prevent excessive pressure in the cuff. The maximum pressure limit can be adjusted through the configuration file stored on the SD card. Additionally, if the pressure fails to reach certain predefined levels within a specified timeframe, an audio signal is played, and an error message is displayed to alert the user. These measures aim to ensure the safety and well-being of the patient during the blood pressure measurement process.

As previously mentioned, a specific configuration file is utilized and stored on an SD card to facilitate user customization of device settings. The following settings can be adjusted through the configuration file:

- *Automatic_BPM_meas_start_(h)* - Atomatic BP measurement start time (hours).
- *Automatic_BPM_meas_start_(min)* - Atomatic BP measurement start time (minutes).
- *Automatic_BPM_meas_stop_(h)* - Atomatic BP measurement stop time (hours).
- Automatic_BPM_meas_stop_(min) - Atomatic BP measurement stop time (minutes).
- *Enable_automatic_BPM_24/7_meas_(1|0)_if(True)_0_to_3_settings_are_ignored* – Enable or disable BPM automatic measurement 24/7. If disabled the measurements are performed in auto mode only within the time frame indicated by the first four settings parameters at the top of this list.
- *Constant_BP_cal_interval_period_(min)* – This sets constant BP measurement interval
- *BP_calibration_minimum_allowed_interval_(min)* – By restricting the BP measurements interval to the specified duration, it ensures that consecutive measurements are not taken in the event of a restart or any unforeseen circumstances. This prevents back-to-back blood pressure measurements from occurring.
- *PPG_one_file_recording_length_(min)* - This setting determines the limit of PPG data size that can be written to a single file. To facilitate simple future processing, the data is split into multiple files based on a specified time interval. Every N minutes, a new file is created, which includes the month, day, and timestamps for easy data separation.
- *Max_BP_pressure_in_the_cuff_110_+_XX_(mmHg)* – This sets the limit of maximum pressure in the cuff. In the interest of safety, it is imperative that this limit is strictly adhered to and not exceeded.
- *Enable_BP_measurements_(1|0)* – If disabled, then only PPG and ACC measurements are performed and saved to SD card.

The device was integrated into a compact housing design (Fig. 20) that facilitates convenient access to the SD card and includes a USB 2.0 connector for effortless battery recharging.

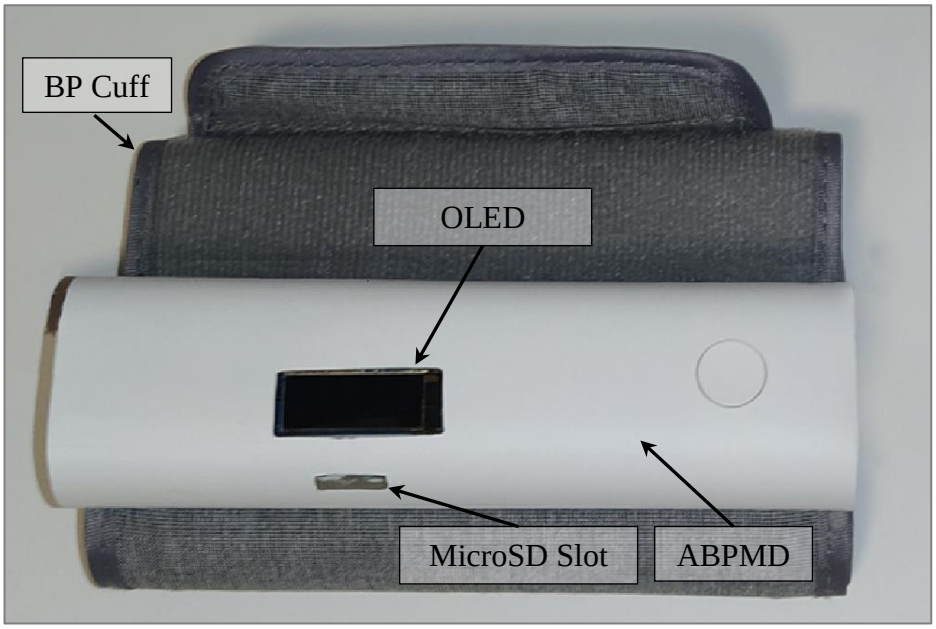

Fig. 20. Developed ABPMD measurement device

ABPMD acquired biosignals processing requires a complex data manipulation and specific signal filtering techniques. The following chapters will describe proposed processing algorithms.

2.2. Development of BP monitoring algorithm

This chapter describes ABPMD raw data processing and BP value estimation algorithms implemented in Python.

2.2.1. Initial oscillometric and PPG signal processing

Like any acquired raw signal, the PPG and oscillometric pressure data requires pre-processing before obtaining a meaningful BP values. The very first step is to use high-pass (HP) finite impulse response (FIR) filter for removing low frequency noise such as PPG DC, baseline drift and motion artefacts. The HP filter cut-off (f_c) frequency: 0.5 Hz [29]. After that low-pass (LP) FIR filter with f_c = 10 Hz used for removing high frequency noise: sudden motion artefacts, noise coupled from switching power supply, piezoelectric pump controller noise, etc.

Fig. 21 displays the unprocessed PPG and pressure data obtained from the ABPMD SD card. To conduct blood pressure estimations, it is necessary to extract oscillometric pulses from the gradually increasing pressure curve. Naturally, oscillometric pressure pulses carry useful information in the same frequency band as PPG (typically between 0.5 Hz and 5 Hz) as they have the same bio-hydraulic origin. Thus, the same low/high-pass filter coefficients can be applied to both signals.

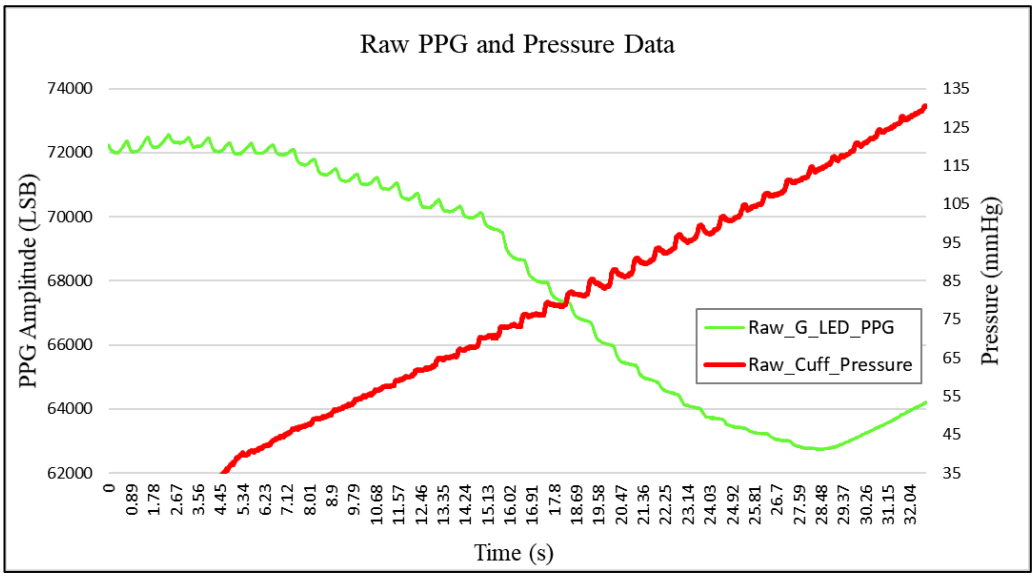

Fig. 21. Cuff pressure and PPG signal during inflation

After the initial processing stage, proposed algorithms are employed to facilitate subsequent processing and the estimation of blood pressure values.

2.2.2. Adaptive SBP measurement

ABPMD has the photoplethysmogram sensor located close to an elbow. When the cuff is inflated it occludes arterial blood flow which gradually reduces PPG amplitude as the amount of blood pushed under the constraint is decreasing. Once the cuff pressure reaches suprasystolic level arterial flow halts and PPG signal no longer carries pulsatile blood oscillations (Fig. 22). The last PPG pulse oscillation before fading out, can be used as to determine systolic blood pressure level simply by ready pressure level in the cuff.

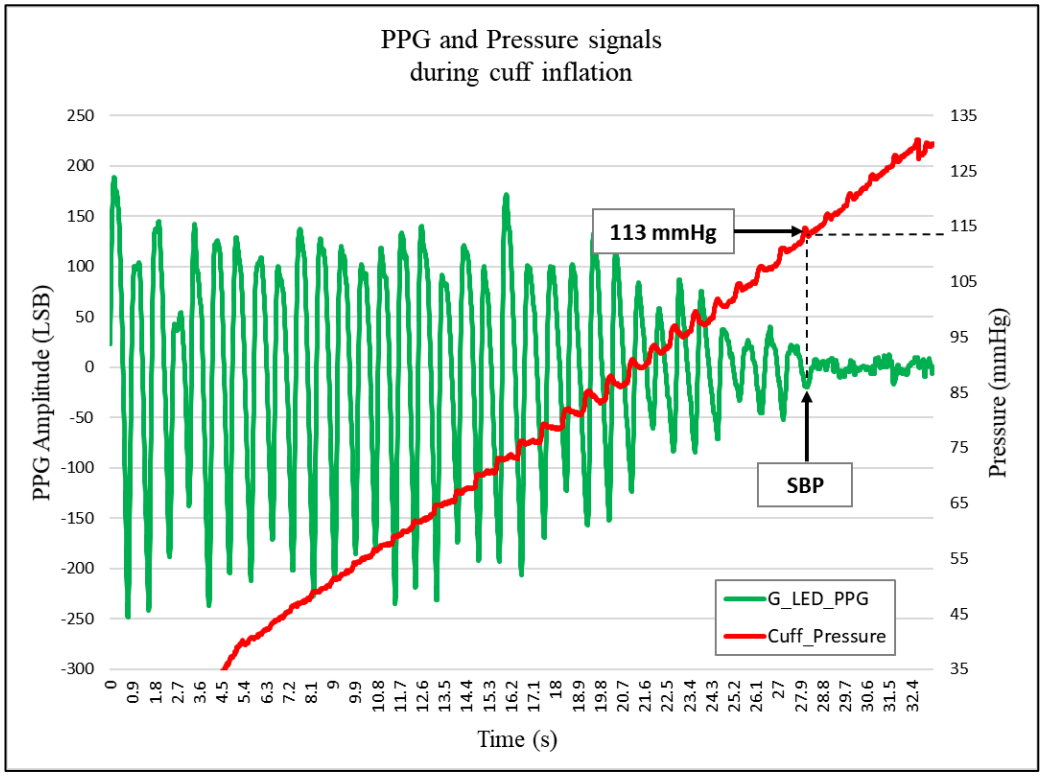

Fig. 22. Extracting SBP value from PPG signal

Furthermore, when the systolic blood pressure value is found, there is no more need to continue inflating the cuff. Hence, the measurement can be stopped without applying any additional unnecessary compression to patients arm. This method will contribute not only to device's longer battery life but as well to a better quality sleep by removing excessive disturbance.

On the graph above red line depicts pressure level in the cuff during the inflation stage. Piezoelectric pump power is being controlled by processor to keep the rising pressure curve straight. The rising pressure in the cuff slowly compresses the arm. Consequently, there is a reduction in blood volume within the peripheral blood vessels leading to a corresponding decrease in the PPG signal (green line).

Estimatiion of SBP from a PPG signal is a task that is a more complex than it may initially appear. Concequently, the two methods have been suggested to address this challenge. The first proposed method depicted in Fig. 23 is referred to as "PPG Envelope", which has the following algorithm:

1. Filter the raw PPG signal using Butterworth FIR band pass filter with cutoff frequencies of 0.5 Hz and 10 Hz.
2. Compute a PPG signal AC amplitude's bottom and top envelopes.
3. Subtract the bottom envelope array from the top envelope array. The subtraction operation generates PPG amplitude curve (Fig. 25 orange trace) that represents the change in PPG amplitude over time.
4. To remove high frequency components and leave only the gradual change in PPG amplitude, the signal is passed through LP FIR filter with F_C = 0.35 Hz.
5. In order to identify the location of the systolic blood pressure in time, a threshold is established using 3.5% of the maximum value in PPG amplitude curve array. When the curve fall below this threshold limit, it is considered that the pressure in the cuff corresponds to the patient's SBP.
6. A third-order polynomial fitting technique is used to determine the best-fit line of the pressure in the cuff during the cuff inflation phase.
7. The time obtained from step Nr4 is fitted into polynomial equation from step Nr6 to determine systolic BP value.

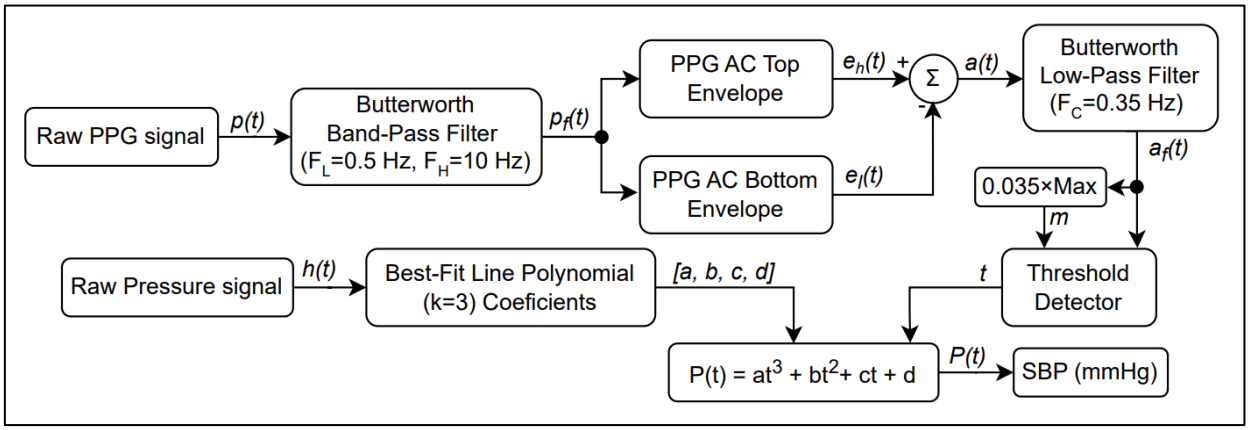

Fig. 23. "PPG Envelope" algorithm diagram

The second algorithm shown in Fig. 24 is called "PPG RMS". It is similar to "PPG Envelope" except for the steps 2, 3 and 4 which can be substituted with a single step:

1. Calculate a RMS value of the PPG signal for the initial three-second duration. Shift the three-second window by one sample forward and repeat RMS computation. Then continue shifting and calculating RMS for the remaining PPG samples. This produces a PPG RMS curve (Fig. 25 blue trace).

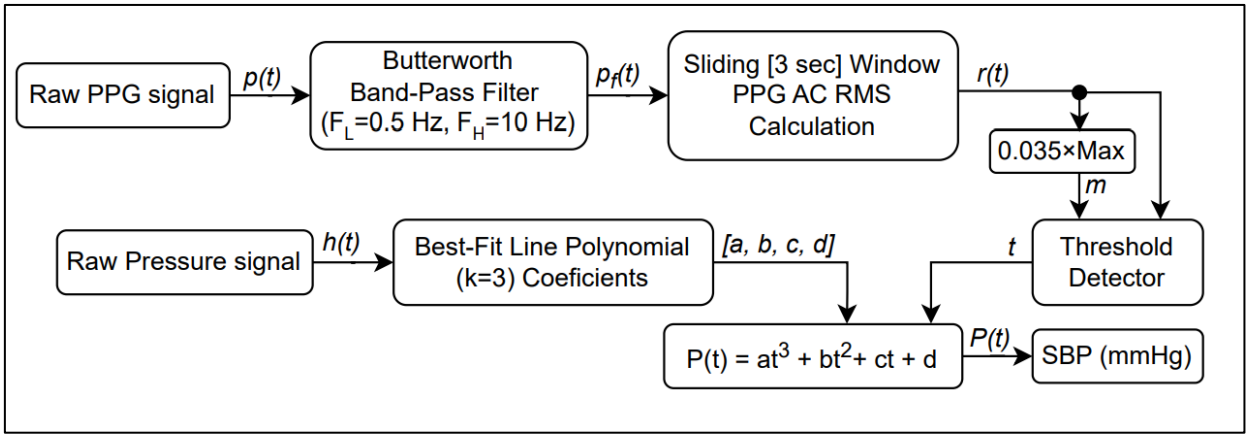

Fig. 24. "PPG RMS" algorithm diagram

The inclusion of the second algorithm was motivated by the presence of breathing modulations, as illustrated in Fig. 25 (orange line), which can cause an innaccurate identification of the systolic PB value.

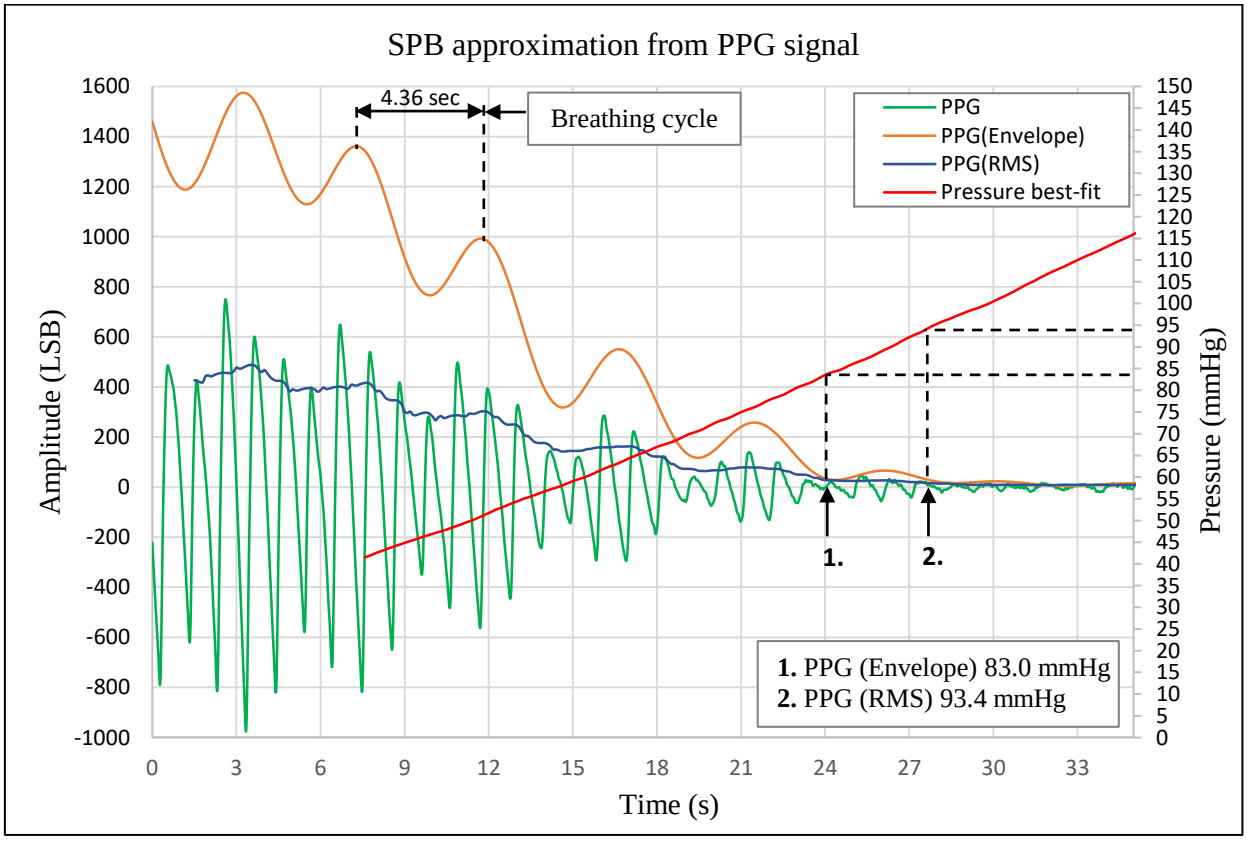

Fig. 25. SPB extraction using two proposed algorithms

In the graph above "Nr1" marker denotes the identification of SBP time by "PPG Envelope" algorithm, which corresponds to SBP value of 83 mmHg. However, due to an occurrence of

coincidence at that particular moment, the patient deeply inhales, as a result the blood pressure reduces. Consequently, the PPG envelope trace value falls below a chosen threshold, and the SBP is recorded erroneously too early. On the other hand, after ihaling the patient exhales which in turn rises his BP again. The marker "Nr2" represents the location where the "PPG RMS" curve identifies an SBP value of 93.4 mmHg. That makes the difference of 10.4 mmHg, which is quite significant, especially when comparing it to the AAIM standard sets, which have a maximum mean error of 5mmHg. Therefore, by computing the RMS value of at least of 3 PPG cycles in three-second window, the latter algorithm allows to filter out breathing modulations, thus, minimizing its effect on BP estimation.

Both algorithms, namely the "PPG Envelope" and "PPG RMS," are utilized during the measurement data processing phase for the purpose of comparison. By employing both algorithms in this study, it becomes possible to assess their performance.

2.2.3. MAP and DBP estimation

Mean Arterial Pressure (MAP) is calculated by averaging pressure in the arteries over one cardiac cycle, indicating the typical force propelling blood throughout the systemic circulation. Conventionally the mean arterial pressure (MAP) is calculated by (4):

$$MAP = DBP + \frac{SBP+DBP}{3}, \tag{4}$$

where DBP stands for diastolic blood pressure, i.e. the arterial pressure when the heart is between beats and relaxed. SBP represents systolic blood pressure - the arterial pressure when the heart contracts and blood is ejected into circulation. This formula considers the length of each phase of the cardiac cycle, as well as both systolic and diastolic pressures. Pulse pressure, which is an indicator of arterial wall strength and elasticity, is the difference between SBP and DBP. Adding one-third of the pulse pressure to the DBP produces an estimate of the average pressure throughout the entire cardiac cycle.

The disadvantage of 2.1 equation is that an assumption has been made that diastolic period as a fraction of cardiac cycle remains constant (i.e., 1/3) regardless of the heart rate. This has been proved incorrect by G. Rogers [30]. The fraction of diastole (F_D) reduces and gets closer to systole fraction (F_S) with the growing heart rate as shown in Fig. 26. F_S coefficient gradually increases and evens out when approaching heart rate of 200 BPM.

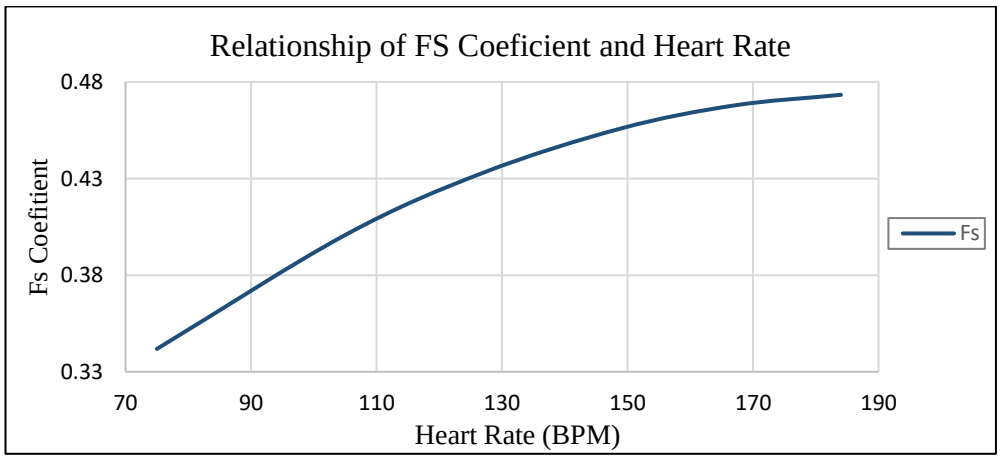

Fig. 26. Fraction of systole

Based on G. Rogers [30] experiment results the systolic fraction can be approximated using (5):

$$F_S = 0.1188758 + 0.0036927 \cdot BPM - 0.0000096 \cdot BPM^2, \quad (5)$$

SBP can be extracted from PPG signal as discussed previously as well as heart rate value. MAP - from OPWE (Fig. 27), leaving DBP the only unknown. Then DBP can be expressed using (4) and (5) as:

$$\mathrm{DBP} = \frac{(\mathrm{MAP} - F_S \cdot \mathrm{SBP})}{(1 - F_S)}, \quad (6)$$

where F_S is calculated by inserting heart rate into formula (5). BPM is obtained from PPG signal right before BP measurement begins.

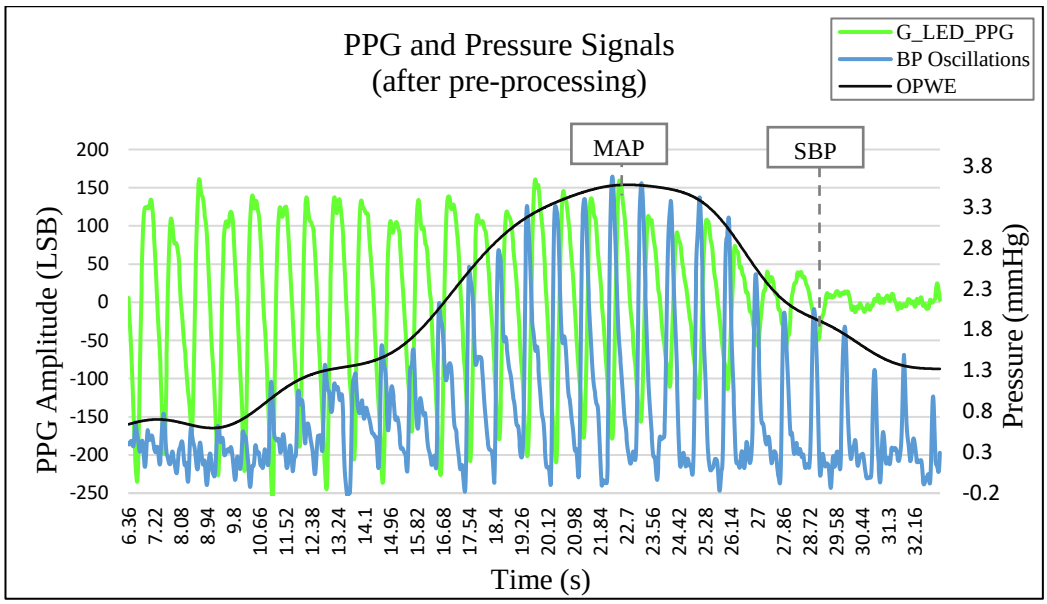

Fig. 27. MAP and SBP extraction from OPWE and PPG

With each cardiac cycle the pulse of blood flowing through the artery causes oscillations. As the pressure in the cuff increases, the amplitude of these oscillations rises until it reaches a maximum oscillation amplitude. This peak corresponds to the Mean Arterial Pressure and marks the envelope of the oscillations, which represents the BP Oscillometric Waveform Envelope (OPWE).

2.3. Reference oscillometric BP estimation algorithm

The Maximum Amplitude Algorithm is one of the most common in oscillometry measurements. It estimates MAP as a cuff pressure at the point of maximum OPWE and then uses two empirically derived ratios (α and β) to relate SBP and DBP to MAP (Fig. 28). Fixed ratios are predefined numerical values that are used to compute blood pressure values using information extracted from the pulse waveform envelope [33].

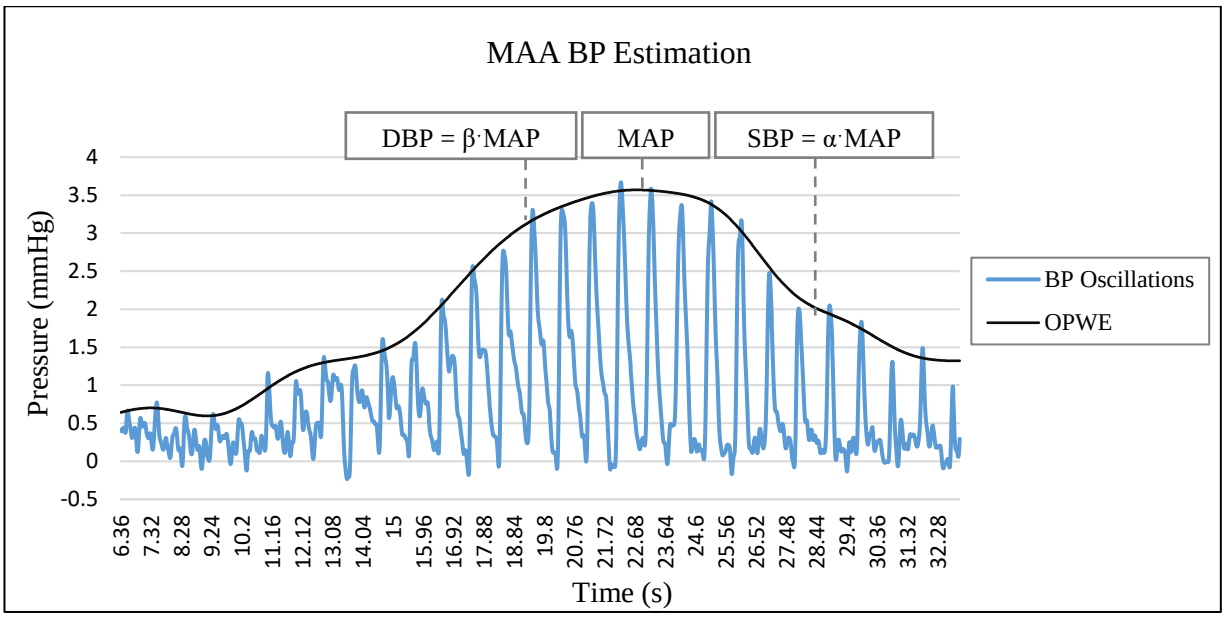

Fig. 28. BP estimation with MAA algorithm

These ratios determine the points at which cuff pressure coincides with SBP and DBP. Although MAA accurately estimates MAP, it is sensitive to variations in BP waveform, pulse pressure, and arterial compliance, making it difficult to precisely determine systolic and diastolic pressures. Moreover, the ratios used by MAA change based on variations in cardiovascular parameters across different health conditions, age groups, and populations. As a result, MAA is not a reliable method for accurate BP measurements, and it is recommended to use coefficient-free algorithms instead. However, it will be still used as a reference and orientation during the evaluation stage of this project.

2.4. Evaluation methods of the developed ABPMD device

Results over long period measurements of the ABPM will be compared against the reference device SOMNOmedics NIBP (SomnoMedics GmbH) measured data. NIBP stands for non-invasive blood pressure, i.e. unobtrusive. This device is a polysomnography system that measures many physiological signals during sleep, such as EMG, ECG, SBP, DBP, oxygen saturation, etc. SOMNOmedics measures blood pressure using the Pulse Arrival Time (PAT) by employing an innovative patented algorithm. SOMNOmedics measurement points are the left ventricle of the heart (determined by the 'R' peak of the ECG) and fingertip (detected by the plethysmograph).
The accuracy of a device requires a one-point calibration at the beginning of a sleep study. This calibration enables the software algorithm to estimate blood pressure parameters (SBP and DBP) from PAT measurements, allowing continuous blood pressure measurement throughout the day and night. The SOMNOtouch NIBP detects every single pulse wave, which makes it possible to continuously record and analyze "Beat-to-Beat" data (Fig. 29). This feature results in reduced artifacts and more reliable data points, providing valuable insights into a patient's blood pressure patterns. A study has been carried out and it was proved that this device fulfils European Society of Hypertension International Protocol revision 2010 requirements [31].

The continuous and non-invasive nature of the SOMNOtouch NIBP is highly beneficial for comparison measurements. As it does not require invasive procedures, it can be used repeatedly

without causing discomfort or disruption. Furthermore, it is non-reactive, meaning that it does not interfere with normal sleep patterns or other physiological measurements being taken at the same time, such as APBMD.

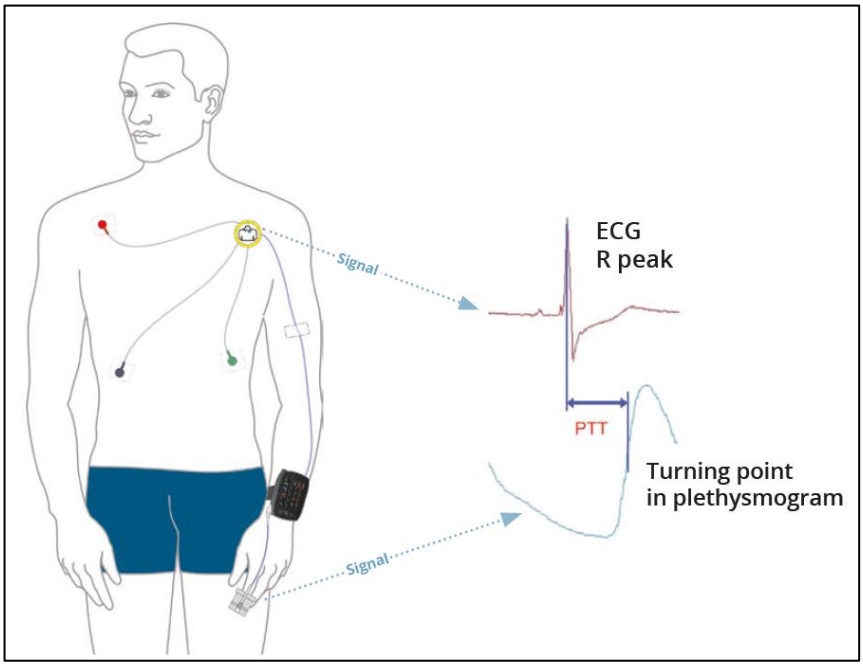

Fig. 29. SOMNOtouch NIBP device [somnomedics.de]

Overnight measurement were performed on volunteers to obtain PPG and BP oscillometric raw data using ABPM device simultaneously with SOMNOtouch NIBP. That allowed to evaluate results accuracy of the ABPMD device and real-life measurement challenges. The device continuously recorded multi-wave PPG data from four LEDs (red, infrared, green and blue) and BMA220 accelerometer. Oscillometric blood pressure measurement were triggered every 30 minutes using built-in real time clock. All the data were stored in micro SD card and later processed in Python script.

ABPMD performance evaluation

Accuracy of the device was evaluated against the reference device using Bland-Altman diagrams [34] with quantitative bias and limits of agreement (LOA). The Bland-Altman technique is a statistical approach for evaluating the consistency of two specific measuring instruments or methods. It includes plotting the deviations of the two measurement techniques against their average on a scatter plot, with each point corresponding to a set of measurements. The mean deviation (bias) is displayed as a flat line on the plot, while two parallel lines above and below the bias line indicate the limits of agreement.

The LOA indicate the variability in the differences between the two methods within which 95% of the data points lie. The Bland-Altman method can uncover any systematic deviations between the two measurements, such as one instrument frequently producing higher or lower measurements than the other. Additionally, it can detect outliers or extreme values that impact the agreement between the two techniques. Overall, the Bland-Altman technique is a valuable tool

for assessing the agreement between two measuring methods and detecting potential sources of error or bias.

A certain set of criteria must be met in order to validate a blood pressure measuring device. The validation process involves results comparison, specifically for systolic and diastolic blood pressure measurements, against two the international standard requirements: British Hypertension Society (BHS) and Association for the Advancement of Medical Instrumentation (AAMI).

The AAMI standard is used to evaluate ABPMD device and algorithms that measure systolic and diastolic blood pressure. According to this standard, the mean error (ME) and standard deviation (SD) should be equal to or less than 5 mmHg and 8 mmHg, respectively.

Additionally, BHS standard is employed to assess the performance of ABPMD. The standard evaluates the absolute error and divides it into three categories: A, B, and C. If the score falls below grade C, the study does not meet the minimum requirements of the BHS standard. In accordance with the standard, the absolute percentage error of prediction must be equal to or less than 5, 10, and 15 mmHg to attain grades A, B, and C, respectively. Table 1 shows cumulative percentage (CP) requirements for each grade.

Table 1. British Hypertension Standard validation requirements

Grade	CP (±5 mmHg)	CP (±10 mmHg)	CP (±15 mmHg)
A	60%	85%	95%
B	50%	75%	90%
C	40%	65%	85%
D	Failed		

Depending on the results of the validation, the device is either considered a pass or a fail, and specific recommendations for clinical use are provided accordingly.

Subjects

A total of 4 subjects aged 21 to 89 years (average 54) participated in the study. All participants were wearing ABPMD device and SOMNOtouch NIBP with a prior calibration using BPM Core (Withings, France). Measurements were performed throughout the night during the sleep. The average duration of each trial was 9 hours and 34 minutes, which resulted in 21 BP measurements per subject. No special instructions such as arm or body positions were required. The collected data forms a database that is subsequently utilized in the processing and analysis stages.

3. Results and Discussion

3.1. Results of ABPMD subsystems testing

Pressure sensor. Test BP pressure measurements were performed at night during patients sleep. The pressure in the cuff was slowly increased up to 120 mmHg while recording pressure values with sampling frequency 100 Hz. Since the data processing executed offline the max BP value was written in configuration text file on micro-SD card. Fig. 30 shows raw data from pressure sensor and a zoomed in curve of one of the measurements. The total recording time was 6.9 hours.

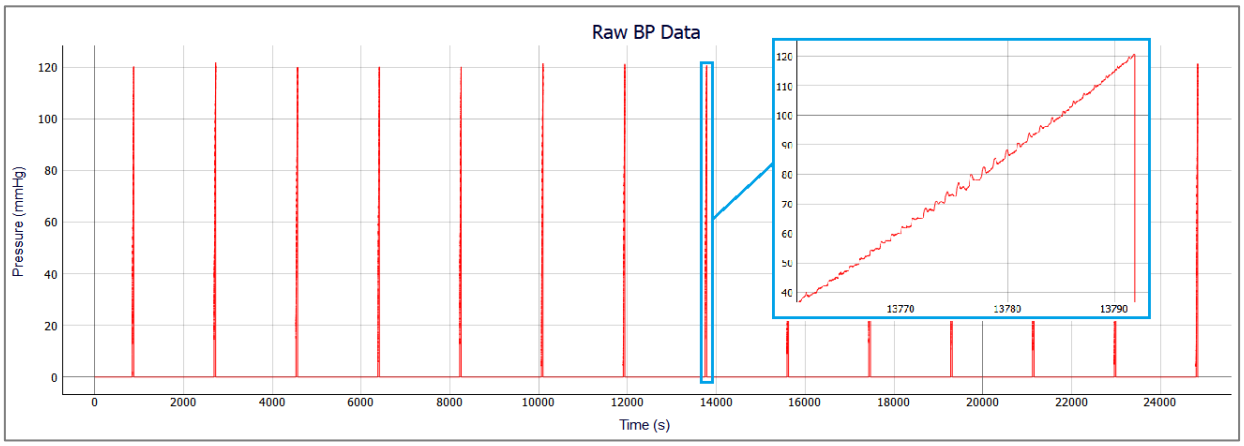

Fig. 30. Overnight BP measurement raw data with 30 min intervals

As predicted earlier, the measurement was completely free from sound, noise, and vibrations. This feature will be highly appreciated by users during their sleep, especially when compared to other ABPMDs that utilize electromechanical air pumps.

PPG sensor. To record PPG Analog Devices Max86916 IC was chosen as it has four separate multiwavelength diodes: blue, green, red and infrared. In most of the applications only the green diode is used for recording PPG as it is less susceptible to ambient light noise and movement artifacts. However, it is beneficial to analyze pulse waves at different depth of the skin using multiwave PPG sensor. So far red and infrared signal were very noisy when measuring in the elbow arm area. Therefore, only blue and green LEDs are processed in this project.
ABPMD was tested by performing 6.9 hours measurement during sleep. PPG signals are shown in Fig. 31. The sudden changes in values are due to motion artefact of the arm. These unwanted transitions were effortlessly removed on the basis of accelerometer data, which is discussed in the next chapter.

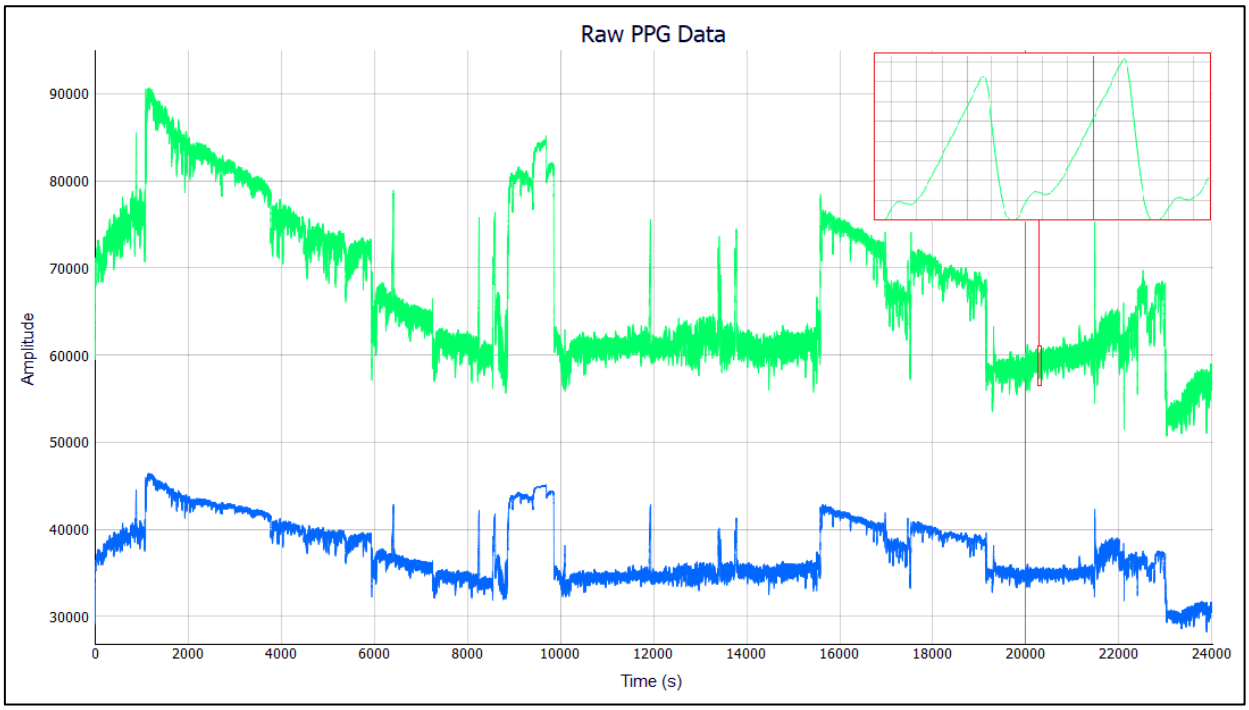

Fig. 31. 6.9 hours of raw PPG data

A small area is zoomed in the picture above which shows clean and stable PPG signal that requires minimum filtering. The following Fig. 32 shows PPG signal after applying a band pass FIR filter. Visually the data is of very high quality and suitable for further processing stages.

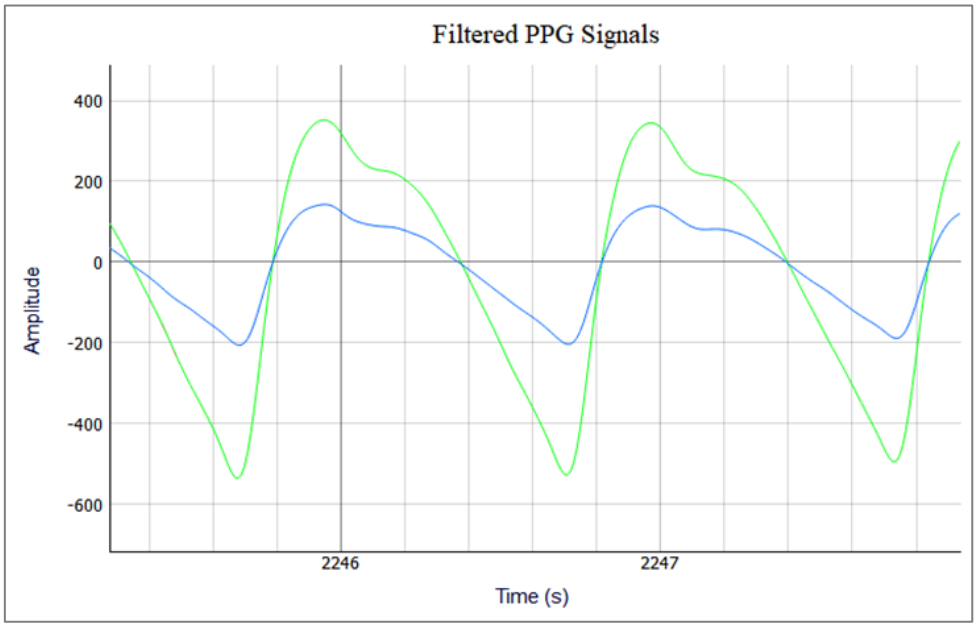

Fig. 32. Max86196 PPG Green and Blue LED signals

Acceleration sensor. A 3-axis digital accelerometer BMA220 (Bosch, Germany) has been integrated into ABPMD. The data is read via I2C interface at a rate of 100Hz with the highest sensitivity 2g. Fig. 33 shows data obtained during overnight measurements with a total duration of 6.9 hours. Blue trace denotes z-axis, green trace y-axis and red trace x-axis.

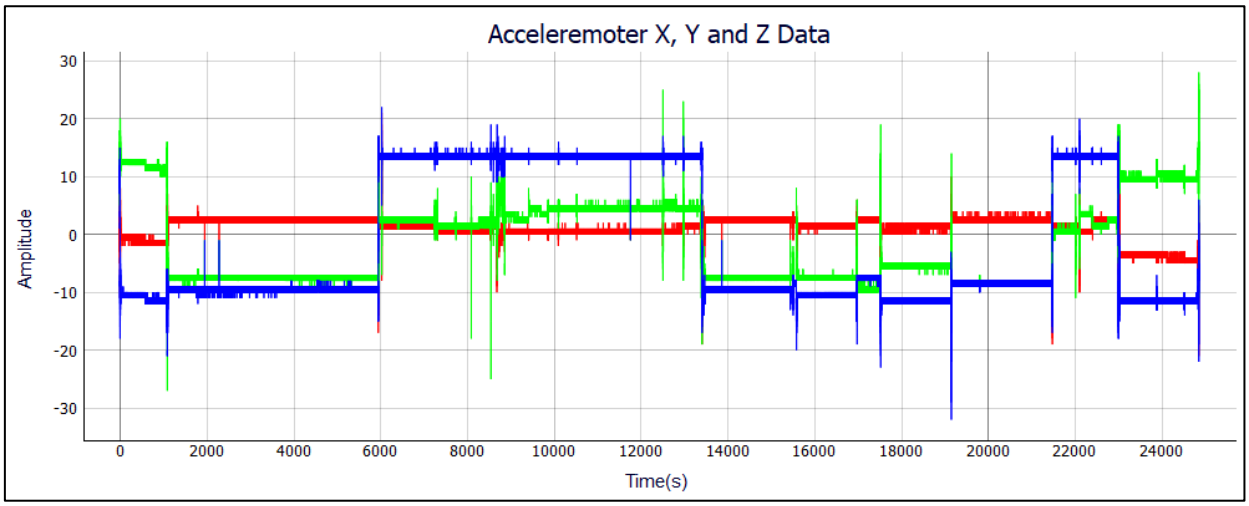

Fig. 33. Accelerometer data: blue – z-axis, green – y-axis and red – x-axis

The sudden changes in the graph lines indicate that patient has altered arm or body position. In those transitions PPG and BP signals were highly likely corrupted and were discarded. PPG signal should be processed only when accelerometer output is stable.

All three sensors delivered relatively stable and high-quality signal data during subsystem evaluation over a long period. No corrupted or missing data or unforeseen microcontroller resets were observed.

Additionally, device battery discharge testing was performed. Making BP measurements every 5 min and continuously recording PPG and ACC data, the battery endured more than 21 hours. With less frequent BP measurements, the device could work for about four days. Therefore, it can be concluded that ABPMD as a whole system can be used for a stable, long-term recording of biosignals.

3.2. Results of ABPMD evaluation

Evaluation of ABPMD is performed by comparing its measurements with the BP estimates obtained from reference algorithm MAA and the reference device SOMNOtouch NIBP. A separate assessment is conducted for SBP and DBP measurements.

The Bland-Altman plot (mean-difference plot) is a graphical tool used to evaluate the agreement between the two measurement devices. In this plot, the x-axis represents the average of two BP measurements being compared, providing a reference point for assessment. On the y-axis, the plot displays the difference between the two BP measurements (proposed method minus reference device), illustrating the magnitude and direction of the discrepancies. By visually examining the plot, one can identify systematic bias, proportional errors, or trends in the measurements, ultimately determining the level of agreement between the ABPMD and SOMNOtouch NIBP.

The Bland-Altman graphs provide a user-friendly and comprehensible visual representation of the data, allowing for easy interpretation and analysis. Additionally, in this study, the quantitative comparison of measurements is performed utilizing the established limits set by the British Hypertension Society and the Association for the Advancement of Medical Instrumentation standards. The tabulated presentation of measurement data demonstrates the adherence of the results to internationally recognized standards, providing a clear indication of their placement within these guidelines.

In this long-term study on blood pressure measurements, a total of 102 blood pressure values were obtained from various subjects at night during their sleep. Out of these measurements, 70 were selected as suitable for further analysis and processing. The remaining measurements were excluded due to the presence of excessive noise caused by motion artifacts in the pressure and PPG data.

3.2.1. SBP measurements

The Bland-Altman graph presented below illustrates the disparity in systolic blood pressure estimation between two methods: the Maximum Amplitude Algorithm (MAA) and the SOMNOtouch NIBP. Following the estimation of mean arterial pressure (MAP) by identifying the cuff pressure at which oscillation amplitude reaches its maximum, fixed ratios for were used for oscillometric pulse waveform envelope (OPWE) to estimate systolic pressure (SP) and diastolic pressure (DP). A fixed ratio coefficient of 0.55 was used to approximate systolic blood pressure (SPB) using the MAA method.
The Bland-Altman graph presented below (Fig. 34) illustrates the disparity in systolic blood pressure estimation between two methods: the MAA and the SomnoMedics device. Following the estimation of MAP by identifying the cuff pressure at which oscillation amplitude reaches its maximum, fixed ratios for systolic pressure and diastolic pressure were established. The results are presented for all the measurements from the database.

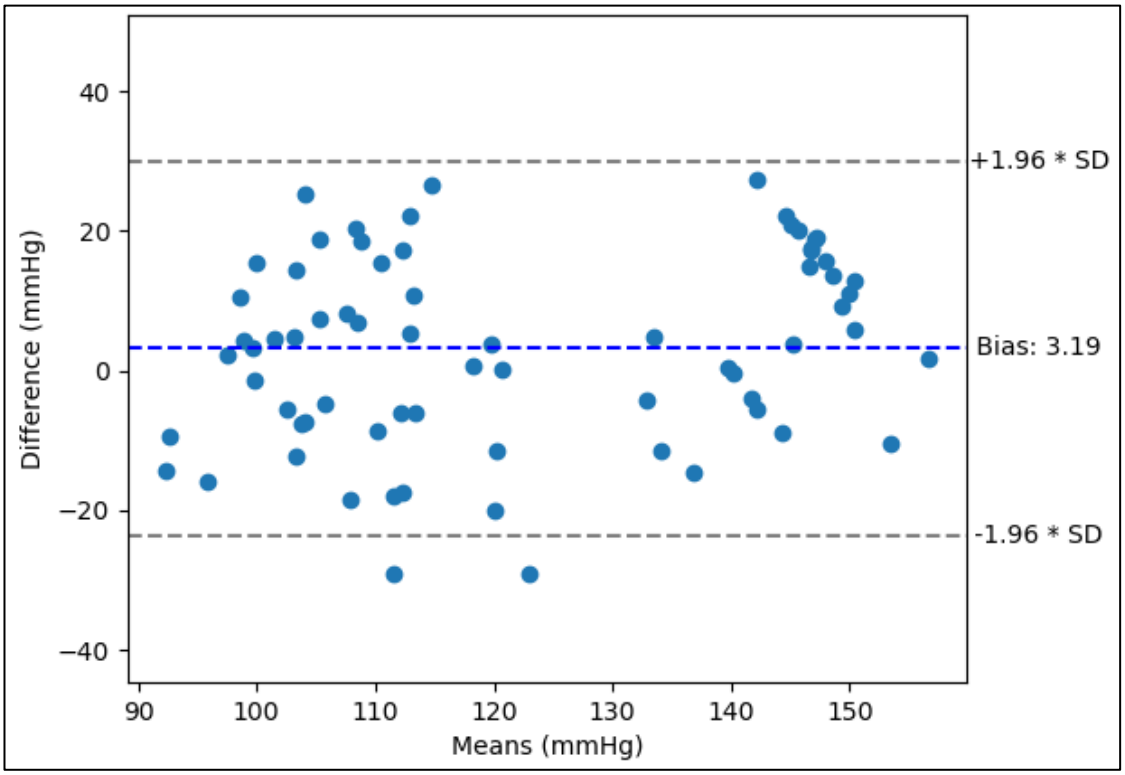

Fig. 34. Bland-Altman diagram for comparison of the reference algorithm MAA and reference device SOMNOtouch NIBP for SBP measurements

The bias which represents systematic difference between the two methods compared shows the error of 3.19 mmHg. It implies that, on average, reference device consistently measures 3.19

mmHg lower than ABPMD with MAA algorithm. Limits of agreement (LOA) of +30 and -23 mmHg represents the expected range of differences between the two measurement methods with 95% level of confidence. It means that, on average, one method tends to produce measurements that can be as high as +30 mmHg or as low as -23 mmHg compared to the other method. The wide range of the LOA indicates a significant degree of discrepancy or variability between the methods, suggesting a relatively low level of agreement.

Upon observation of the graph, it becomes apparent that the data points are clustered at two distinct locations on x-axis. This occurrence can be attributed to the fact that one particular subject in the study exhibits significantly higher BP levels compared to the other subjects.

The wide range of BP values helps in the proper evaluation of devices. The differences obtained between the devices, especially LOAs, are large; however, it is not yet clear which device is more accurate. The authors of the study [35] found poor agreement of the SOMNOtouch NIBP with another validated 24-h oscillometric ambulatory BP monitoring device.

Fig. 35 shows results of SBP value estimation using PPG signal AC components envelope as a reference for identifying the pressure point at which PPG oscillation ceased. This point was considered indicative of the systolic blood pressure value.

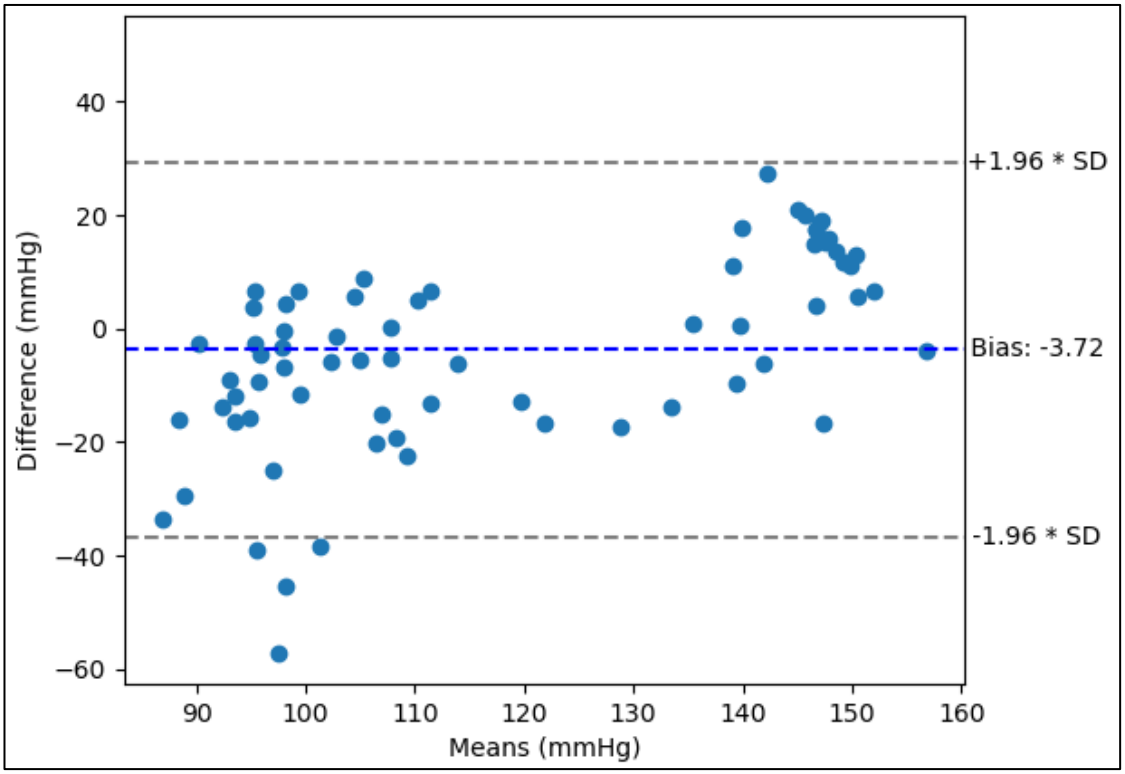

Fig. 35. Bland-Altman diagram for comparison of the proposed ABPMD (PPG Envelope) algorithm and reference device SOMNOtouch NIBP for SBP measurements

The bias of -3.72 mmHg suggests that, on average, the reference method recorded higher systolic blood pressure values compared to ABPMD measurement method being evaluated. This indicates a systematic tendency for the latter method to produce slightly lower readings.
Additionally, examining the distribution of values on the difference-axis (y-axis) reveals a relatively low level of precision. The data points seem to exhibit a considerable spread around the mean, indicating low precision measurement.

The results presented in Fig. 36 provide a visual representation of the SBP estimation using PPG AC signal RMS value in a three second sliding window. This method is similar to previous with PPG envelope. However, RMS SBP estimation method does not suffer from BP variation due to subject's breathing, which is seen as low frequency oscillation on PPG envelope curve. Ultimately, RMS can be considered as a method that quantifies the overall magnitude of the AC variations in the PPG waveform, which in turn simplifies detection at which point in time PPG signal disappears after the cuff pressure goes above SBP.

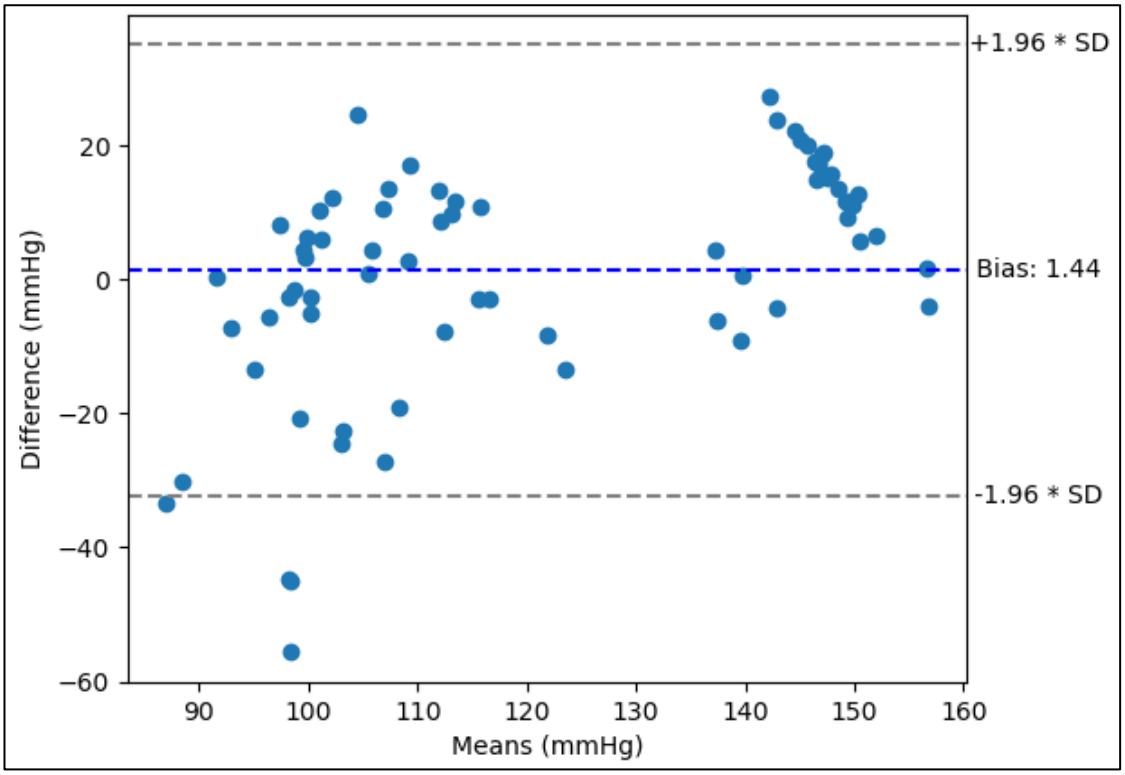

Fig. 36. Bland-Altman diagram for comparison of the proposed ABPMD (PPG RMS) algorithm and reference device SOMNOtouch NIBP for SBP measurements

The PPG-RMS estimation method exhibits the lowest bias error, with a value of 1.44 mmHg, when compared to the other two methods, MAA and PPG-Envelope. This indicates that, on average, the PPG-RMS method demonstrates a smaller systematic difference in systolic blood pressure (SBP) estimation. However, despite the lower bias error, the distribution of differences and wide Limits of Agreement in this graph suggest a relatively poor precision in the measurement. The data points show a considerable spread or variability around the mean, indicating a lack of precision in estimating SBP values using all three methods.

The following Table 2 provides a summary of SBP measurements comparison with two standards BHS and AAMI.

Table 2. ABPMD SBP results comparison with BHS and AAMI standards

British Hypertension Society Standard (Minimum requirement: 40%, 65%, 85%)				**Association for the Advancement of Medical Instrumentation Standard (ME < 5 mmHg, SD < 8 mmHg)**		
CP ±5 mmHg	**CP ±10 mmHg**	**CP ±15 mmHg**	**HBS Grade**	**Mean Error (<5 mmHg)**	**SD (<8 mmHg)**	**AAMI Pass/Fail**
SBP: MAA - SOMNOtouch **NIBP**						
24.3%	45.7%	62.9%	D	3.2 mmHg	13.6 mmHg	Fail
SBP: PPG (Envelope) - SOMNOtouch **NIBP**						
20.0%	42.3%	60.0%	D	-3.7 mmHg	16.8 mmHg	Fail
SBP: PPG (RMS) - SOMNOtouch **NIBP**						
22.9%	44.3%	64.3%	D	1.4 mmHg	17.1 mmHg	Fail

The findings presented in Table 2 indicate that none of the proposed methods, namely MAA, PPG envelope, or PPG RMS, have met the requirements set by the British Hypertension Society or the Association for the Advancement of Medical Instrumentation Standards. The primary factor contributing to this lack of compliance was the substantial disparity observed in the measurements, i.e., the high standard deviation of the measurement population. This discrepancy suggests insufficient precision in the measurement methods or processing algorithms chosen.
Nevertheless, it is essential to note that despite the failure to meet the standards mentioned, the bias error of the measurements remained within the acceptable limits defined by the Association for the Advancement of Medical Instrumentation. This implies that the systematic error of the measurement methods is relatively low.

3.2.2. DBP and MAP measurements

The mean arterial pressure plays a critical role in the MAA algorithm, because it establishes the initial reference point to identify the Systolic and Diastolic Blood Pressure from Oscillometric Pulse Waveform Envelope. The accuracy of the MAP measurement is important, as any significant error in this value will propagate to the estimation of DBP for all ABPMD methods and SBP using MAA.
Fig. 37 presents a comparison between the MAP values estimated by MAA and the MAP values measured using the SOMNOtouch NIBP device. It helps to assess the agreement or discrepancy between the two measurement techniques and allows to identify the potential errors associated with MAP estimation in the MAA method.
The mean arterial pressure value is utilized in Equation (6) when estimating diastolic blood pressure for both PPG methods: Envelope and RMS. Therefore, it is essential to ensure that the MAP approximation obtained by the MAA method is as accurate as possible.
Fig. 37 illustrates a notable lack of accuracy in the measurement method, as indicated by a bias value exceeding 5 mmHg. A higher bias value observed indicates that the MAA method tends to measure MAP values higher than those obtained from the reference device. Additionally, the wide limits of agreement depicted in the graph suggest that the precision of the measurements is also poor.

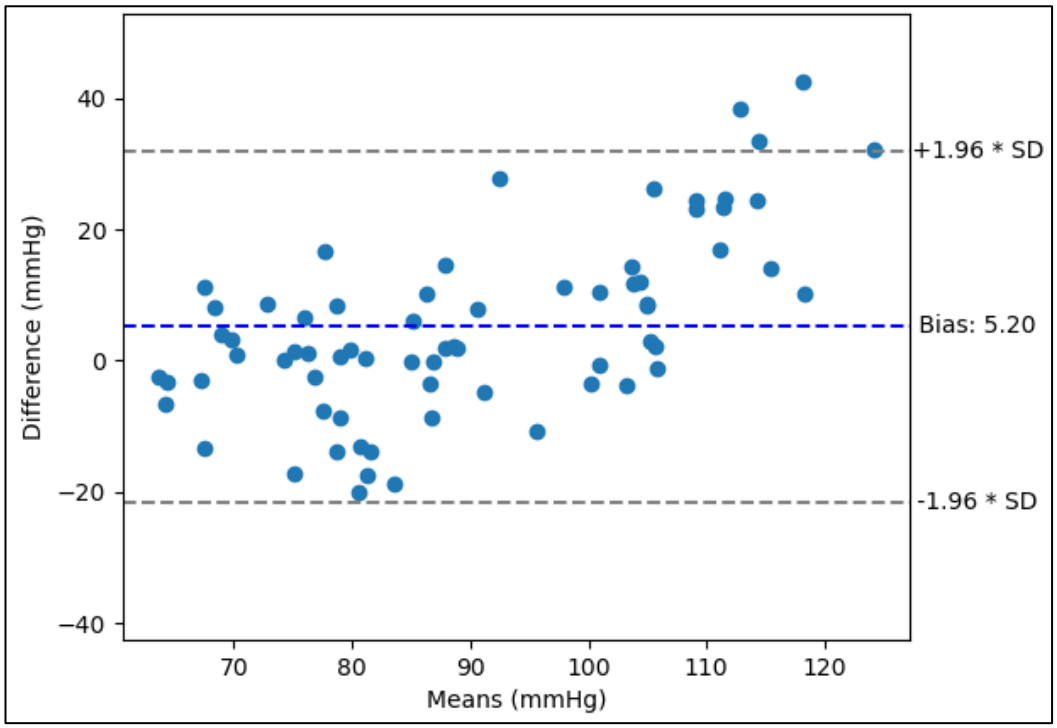

Fig. 37. Bland-Altman diagram for comparison of the reference algorithm MAA and reference device SOMNOtouch NIBP for MAP measurements

To estimate DBP with MAA method from OPWE a fixed coefficient of β=0.75 was used, which was found to be most accurate during the device testing stage. Fig. 38 shows comparison between MAA DBP estimation SOMNOtouch NIBP DBP results. The graph data exhibit a considerable proportional bias, i.e. underestimation of DBP values at lower range of BP measurements and overestimation at higher BP values.

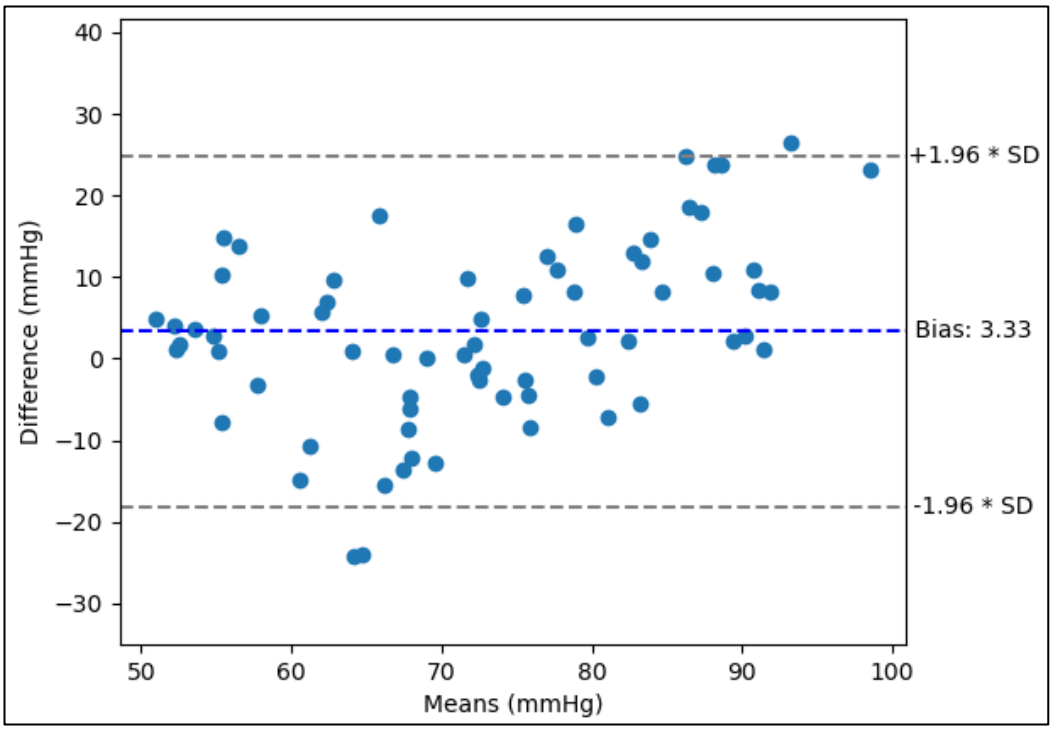

Fig. 38. Bland-Altman diagram for comparison of the reference algorithm MAA and reference device SOMNOtouch NIBP for DBP measurements

The bias value observed falls within the acceptable limits set by the AAMI (<5mmHg), indicating that the accuracy of the measurements is acceptable. However, the precision of the measurements is compromised by the wide LOA, suggesting a lack of consistency in the results.

The following two graphs show proposed PPG-Envelope and PPG-RMS-based DBP estimation methods comparison with reference device measured DBP. Both plots show a systematic error greater than 5mmHg, which could be due to the propagation of the error from MAP approximation as it is used for the calculation of DBP using equation (6). The similar data point's distribution can be observed as in SBP Bland-Altman graphs for the corresponding measurement methods.
The next two figures, Fig. 39 for PPG-Envelope and Fig. 40 for PPG-RMS, present a comparative analysis between the proposed methods and the reference device in estimating diastolic blood pressure based on pulse photoplethysmography. Both plots demonstrate a systematic error that exceeds 5 mmHg, which may be attributed to the propagation of errors from the mean arterial pressure approximation used in the DBP through Equation (6). Additionally, these graphs exhibit a similar distribution pattern of data points as observed in the Bland-Altman graphs for the corresponding SBP measurement methods. Unfortunately, the precision of the measurements is compromised too, evident by the wide LOA observed.

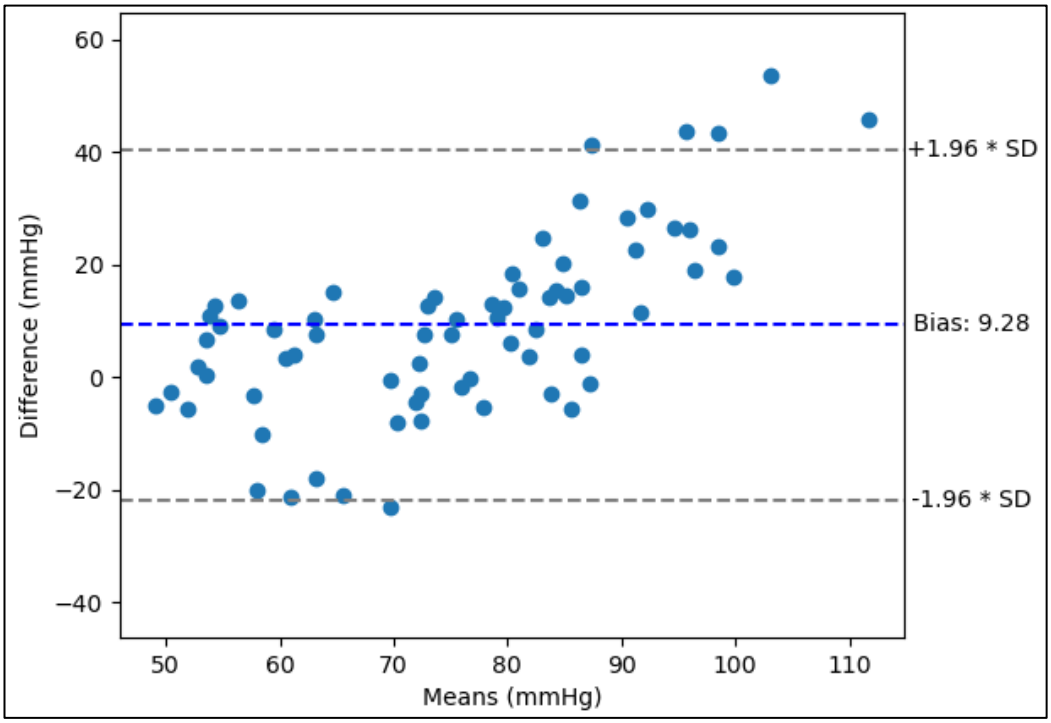

Fig. 39. Bland-Altman diagram for comparison of the proposed ABPMD (PPG Envelope) algorithm and reference device SOMNOtouch NIBP for DBP measurements

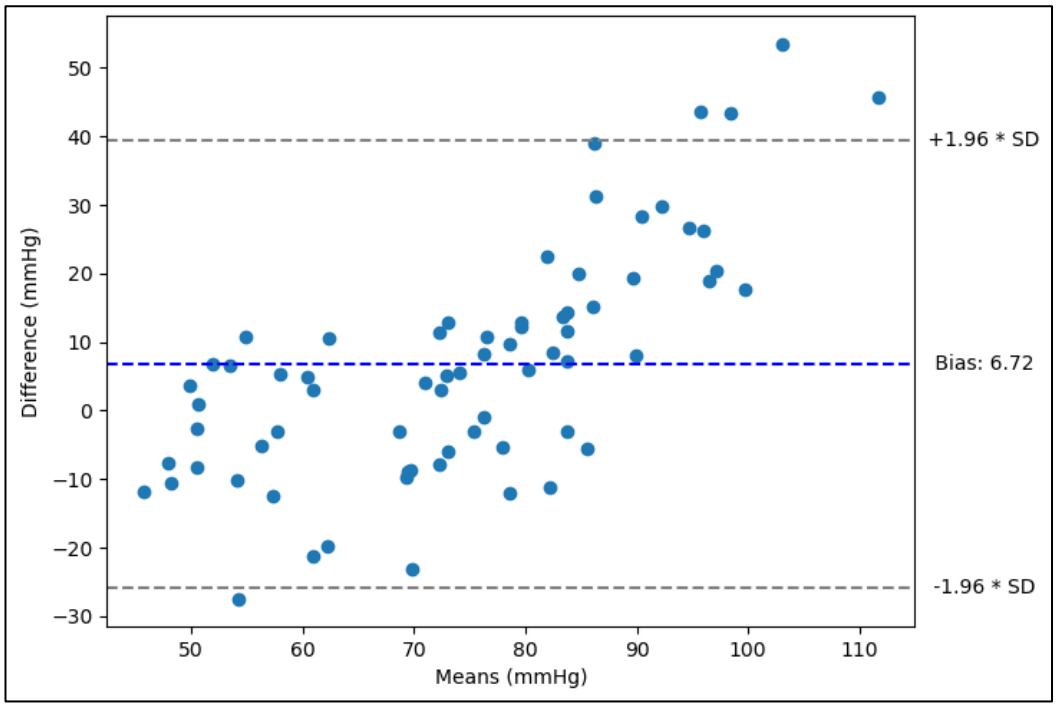

Fig. 40. Bland-Altman diagram for comparison of the proposed ABPMD (PPG RMS) algorithm and reference device SOMNOtouch NIBP for DBP measurements

Table 3 presents a comprehensive overview of the comparison analysis discussed above, comparing the results to the standards set by the British Hypertension Society and the Association for the Advancement of Medical Instrumentation. None of the methods evaluated met the requirements specified by BHS or AAMI. Although the mean error in the estimation of systolic blood pressure (SBP) fell within the AAMI standard mean error limit, only the MAA method showed a mean error in DBP estimation that satisfied this criterion.

Table 3. ABPMD DBP results comparison with BHS and AAMIS standards

British Hypertension Society Standard (Minimum requirement: 40%, 65%, 85%)				**Association for the Advancement of Medical Instrumentation Standard (ME < 5 mmHg, SD < 8 mmHg)**		
CP ±5 mmHg	**CP ±10 mmHg**	**CP ±15 mmHg**	**HBS Grade**	**Mean Error (<5 mmHg)**	**SD (<8 mmHg)**	**AAMI Pass/Fail**
DBP: MAA – SOMNOtouch **NIBP measurement**						
38.6%	61.4%	82.9%	D	3.3 mmHg	10.9 mmHg	Fail
DBP: PPG (Envelope) - SOMNOtouch **NIBP**						
24.3%	42.9%	62.6%	D	9.3 mmHg	15.9 mmHg	Fail
DBP: PPG (RMS) - SOMNOtouch **NIBP**						
17.1%	47.1%	70.0%	D	6.7 mmHg	16.6 mmHg	Fail

DBP and MAP exhibit similar accuracy and precision trends as seen in the case of SBP. Furthermore, the majority of the figures above demonstrate a proportional bias, meaning that the bias is dependent on the measured blood pressure value.

Conclusions

1. The analysis of the scientific literature shows an urgent need for the new methods of long-term, ambulatory, unobtrusive blood pressure monitoring. There are various methods to estimate blood pressure using cuffless wearable devices with known limitations in accuracy and precision. However, currently the golden standard for a long-term BP measurement is an oscillometric cuff sphygmomanometer, which is limited by rare, fixed in time measurements, and its obtrusiveness, especially during the night. This work is an attempt to develop Ambulatory Blood Pressure Monitoring Device (ABPMD) with an innovative, noiseless piezoelectric pneumatic pump and PPG signal-based monitoring to minimize maximum cuff pressure during the inflation phase, which could potentially reduce patient sleep disturbance to a minimum.

2. A functional prototype of the ABPMD device with innovative piezoelectric pump produces significantly less of audible noise than electromechanical pump, therefore, is less obtrusive to the user especially during sleep. The device exhibits robustness, allowing extended measurement experiments lasting up to 4 days, during which it is capable of recording multimodal data comprising PPG, ACC, and oscillometric pressure. Moreover, the device has passed a continuous 6.9 hours stress test, yielding positive results. The microcontroller firmware was effectively programmed in C++ utilizing Visual Studio Code and PlatformIO IDE with the integration of FreeRTOS functions.

3. Two algorithms, namely “PPG Envelope” and “PPG RMS”, were proposed and implemented in this study. Both are used to control the upper limit of the cuff inflation and subsequently estimation of systolic BP based on PPG signal. The primary objective of “PPG RMS” algorithm is to ensure invariant measurements in response to breathing modulations in PPG signal.

4. As a reference, the SOMNOTouch NIBP device was chosen for the performance evaluation of the newly developed ABPMD prototype. The performance was assessed in terms of accuracy and precision for SBP, DBP, and MBP. During the measurement the lowest bias error was obtained using “PPG RMS” SBP approximation method. Among the three methods used, the MAA DBP estimation method showed the highest level of precision. However, the performance results did not meet the standards established by AAMI and BHS.

5. Several factors could have contributed to the device's failure to meet international standards::
    - The potential limited accuracy of the cuffless reference device, SOMNOTouch NIBP as noted in the literature;
    - Prior to each night measurement, the calibration of SOMNOTouch NIBP using Withings device could introduce additional offset error;
    - Inaccurate MAP estimation from OPWE due to noise and breathing modulation in oscillometric signal.

Future directions

This report highlights the important findings and insights obtained in the field of long-term blood pressure and monitoring. However, it is crucial to recognize that there exists immense potential for further advancements and explorations in this area. A list of suggestions below can be considered for possible improvement of usability, accuracy and precision of the developed ABPMD:

- Integration of additional sensors either electrocardiogram (ECG) or additional PPG (more proximal to the heart) for pulse arrival (PAT) or pulse transit time (PTT) measurements accordingly and regression of blood pressure parameters;
- Continuous control of signal quality for discarding signals not adequate for analysis;
- Integration of a microphone for recording and automatic analysis of Korotkoff sounds to increase the accuracy of intermittent calibration;
- Enhance the proposed blood pressure approximation methods by incorporating additional parameters, such as age and body mass index.

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