Advances in non-invasive blood pressure measurement techniques

Tuukka Panula, Jukka-Pekka Sirkiä, David Wong and Matti Kaisti

***Abstract*— Hypertension, or elevated blood pressure (BP), is a marker for many cardiovascular diseases and can lead to life threatening conditions such as heart failure, coronary artery disease and stroke. Several techniques have recently been proposed and investigated for non-invasive BP monitoring. The increasing desire for telemonitoring solutions that allow patients to manage their own conditions from home has accelerated the development of new BP monitoring techniques. In this review, we present the recent progress in non-invasive blood pressure monitoring solutions emphasizing clinical validation and trade-offs between available techniques. We introduce the current BP measurement techniques with their underlying operating principles. New promising proof-of-concept studies are presented and recent modeling and machine learning approaches for improved BP estimation are summarized. This aids discussions on how new BP monitors should evaluated in order to bring forth new home monitoring solutions in wearable form factor. Finally, we discuss on unresolved challenges in making convenient, reliable and validated BP monitoring solutions.**

keywords: blood pressure, non-invasive, continuous, hypertension, monitoring

I. Introduction

Hypertension is a health burden affecting more than a billion people globally [106]. It is a serious medical condition that significantly increases the risk of potentially life-threatening cardiovascular diseases, such as heart failure, coronary artery disease and stroke. Non-optimal blood pressure (BP) continues to be the leading global risk factor for the global burden of disease, leading to more than 10 million deaths and 212 million healthy life years lost each year. [37] At the same time, hypertension is the most common preventable risk factor for cardiovascular disease [76]. Fortunately, hypertension, when diagnosed, can be well controlled via medication and lifestyle alterations. However, the condition is mostly asymptomatic and fewer than 20% of people with hypertension have it under control [106]. Proper BP control has been shown to significantly reduce cardiovascular morbidity and all-cause mortality associated with hypertension [18]. Therefore, it is essential that BP is measured regularly and accurately to aid successful prevention and treatment of hypertension [70], [91]. The importance of hypertension management is highlighted by the stringency of thresholds for high BP in recent clinical guidelines. Recent hypertension guidelines define systolic BP (SBP) of $\geq$ 120 mmHg with diastolic BP (DBP) of $<$ 80 as elevated BP. Pressure readings higher than 130 mmHg or 80 mmHg for SBP and DBP, respectively, are categorized as Stage I hypertension. [35]

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In recent years, there has been growing interest in minimally invasive methods that can easily and accurately monitor BP, allowing one to track long-term changes and gain personalized actionable information. The technological advances mainly follow two paradigms. One aims to miniaturize existing cuff-based technologies, which are known to work to a reasonable accuracy, in a wearable form factor. The second concentrates on estimating BP from surrogate markers with the help of new data analysis tools. A notable difference is that most indirect methods involve passive measurement in the sense that no external stimulus is applied and can, therefore, theoretically provide continuous beat-to-beat measurements. In the traditional approach, BP information is extracted by auscultation or from a pressure sensor when external (cuff) pressure is applied. Furthermore, self-monitoring at home has become commonplace, but telemonitoring where measured BP readings are transmitted to the patient's physician is still uncommon, despite strong evidence of its potential benefits [12]. The technological advances in BP monitoring include the use of modern digital sensors and devices, machine learning techniques, wearable solutions, continuous monitoring of BP and the integration to digital health ecosystems.

Several review articles on blood pressure monitoring have previously been written. There are several reviews that focus on pulse propagation e.g. pulse transit time based blood pressure estimation [32], [68] as well as comprehensive surveys on the physical principles of blood pressure measurement [29], [75]. In contrast, this narrative review concentrates on recent evidence on technological maturity of all existing and emerging technologies and instruments while emphasizing the clinical validation. From recent studies we included those that proposed a new technique, algorithm or a new type of an instrument. We emphasised studies that included clinical validation, although proof-of-concept studies were included when new ideas were presented. Additionally, we summarize the main BP measurement principles, commercial activity and discuss the role of machine learning in BP monitoring.

II. Principles of Blood Pressure Measurement Techniques

BP is usually reported by both SBP and DBP readings. As the heart pumps blood into the circulation, it creates a pulsatile pressure gradient that travels along the blood vessels thereby creating a pulse wave. SBP is the maximum value the pressure waveform reaches during systole (the period of heart muscle contraction) and DBP is the minimum value during diastole (the period in between contractions). Pulse pressure (PP) is the difference of SBP and DBP during a single cardiac cycle. Cardiac pulse is defined as the pressure cycle between two subsequent minimums (diastolic feet) of the pulse. The mean arterial pressure (MAP) is the average pressure through one cardiac cycle and can be calculated from the arterial waveform by dividing the area under a single cardiac cycle with duration of the cycle [39]. Due to various physiological factors, such as the compliance of blood vessels (Windkessel effect), the prevalent BP varies in different parts

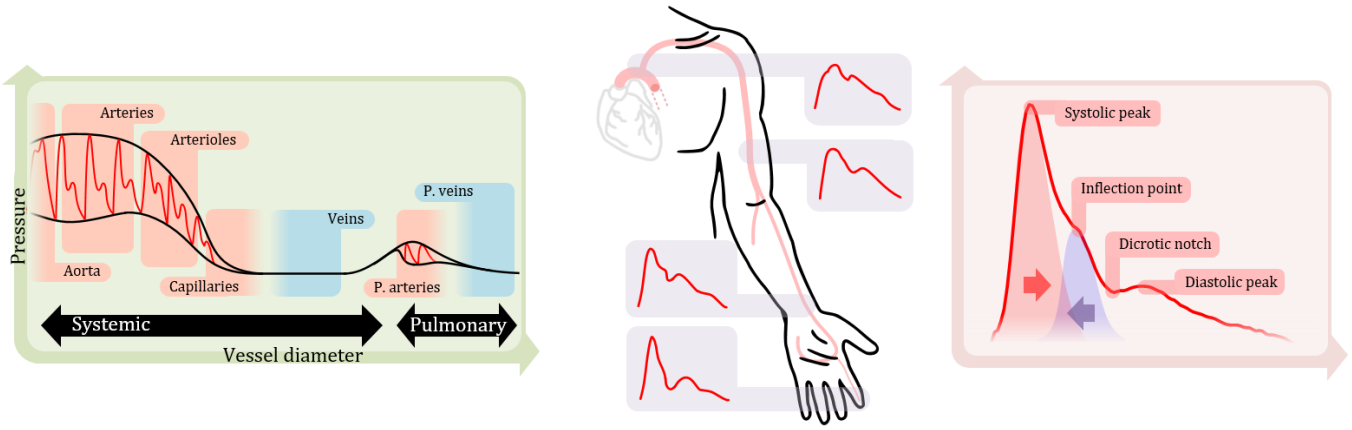

Fig. 1: Basics of BP. Left: BP in different points in the circulatory system. Pressure is at its highest when it leaves the left ventricle and travels through the major arteries. As the flow enters the arterioles, the pressure drops significantly and remains low in the capillaries and veins. Pressure rises again as the blood enters the right side of the heart and is pushed into the pulmonary circulation. Again, the pressure drops in the pulmonary capillaries and the blood enters the left atrium through pulmonary veins and is ejected into the systemic circulation. Middle: Due to wave reflection and the effect of arterial compliance, the pulse wave morphology changes as the blood travels along the arteries. Right: The arterial pulse is a result of superposition of distinct waves where the initial systolic wave is reflected from high resistance blood vessels. The location of the inflection point represents the velocity of the travelling wave and can be used to assess arterial compliance and elasticity.

of the cardiovascular system [39] as can be seen in Fig. 1. The pulse wave is actually a combination of the initial wave from the heart and its reflections as seen in Fig. 1. The traveling arterial pulse wave gets deformed due to wave reflection from high resistance vessels. The more elastic or compliant the arteries are, the more the PP is amplified in the peripheral arteries. Correspondingly, the PP remains the same (and usually high) in very stiff arteries throughout the vessel [64].

BP readings typically refer to the the pressure in large systemic arteries. It is most commonly measured in the brachial artery using an arm cuff [39]. However, the BP in other parts of the body differs significantly from the brachial pressure. The hydrostatic effect does not affect brachial artery readings as it is on the same level as the heart, but when BP is measured from other locations (e.g. wrist or fingers) large deviations may be seen [36]. In systemic circulation, where the heart has to deliver enough pressure to ensure sufficient tissue perfusion in the whole body, the BP is relatively high. In pulmonary circulation the pressure is significantly lower. Even in the systemic circulation, the BP varies from the high pressure arteries to lower pressure arterioles and microcirculation before reaching the very low pressure veins. The arterioles cause the greatest drop in pressure as they also have the greatest resistance in the vascular network. Although capillaries have clearly smaller diameter, indicating even higher resistance, their total cross-sectional area is much larger thus resulting in lower resistance.

Vasodilation and vasoconstriction of the arterioles have a significant role in regulating the BPto ensure low pressure in the capillaries. [39], [44] In doing so, the velocity of blood flow is reduced to allow sufficient time for gas and nutrient exchange [44]. In veins, the flow is nearly non-pulsatile except in the large veins proximal to the heart [44]. These phenomena are described in Fig. 1.

A. Manual auscultation

Manual measurement is considered to be the most accurate non-invasive method for assessing BP and it is used as the gold standard reference in international protocols [97]. However, manual auscultation is an estimate of the true BP since it is not directly measured from inside the arterial lumen via cannulation. Even though it is an old technique, it is still used in clinical work as well as in international validation standards. It was initially conceived by the Italian physician Scipione Riva-Rocci in 1896 [16]. He used a mercury-filled sphygmomanometer connected to a brachial cuff to measure SBP. The pressure inside the cuff is manually pumped to a pressure that exceeds the SBP, so that the radial pulse cannot be felt. The cuff is then slowly deflated. Simultaneously, the radial pulse is palpated. When the pulse is felt again, SBP is read from the column of mercury in the sphygmomanometer. Due to the wide and long use of mercury sphygmomanometers, the unit mmHg (millimeters of mercury) is still used. One mmHg equals approximately 133 Pa. [82]

The Russian military physician Nikolai Korotkoff extended Riva-Rocci's method using auscultation [16]. Instead of radial artery palpation, a stethoscope is placed over the brachial artery as the cuff is deflated from supra-systolic pressure. When the listener starts to hear tapping sounds from the flowing blood, SBP is read from the sphygmomanometer. The sounds continue as the cuff is deflated, and disappear when the cuff pressure is equal to the DBP. The sounds are caused by the laminar flow of blood becoming turbulent under external compression and are known as Korotkoff sounds. The method is described in Fig. 2. An issue with manual auscultation and palpation techniques is that they require an experienced clinician and are prone to operator bias [75]. Another issue is the use of highly toxic mercury in sphygmomanometers, resulting in restricted use in many countries. Alternative instruments are nowadays recommended for clinical use by the World Health Organization [88]. Such devices include aneroid sphygmomanometers and digital sphygmomanometers emulating a mercury column with an LCD display. Such devices need to be properly calibrated and verified to ensure mercury-like performance.

B. Oscillometric method

The oscillometric method is the most common noninvasive BP measurement technique used by BP monitor manufacturers. The phenomenon was first noticed in the 19th century, but it only became widely used after the emergence of digital electronics [39]. Unlike the manual auscultation method, the oscillometric method measures only

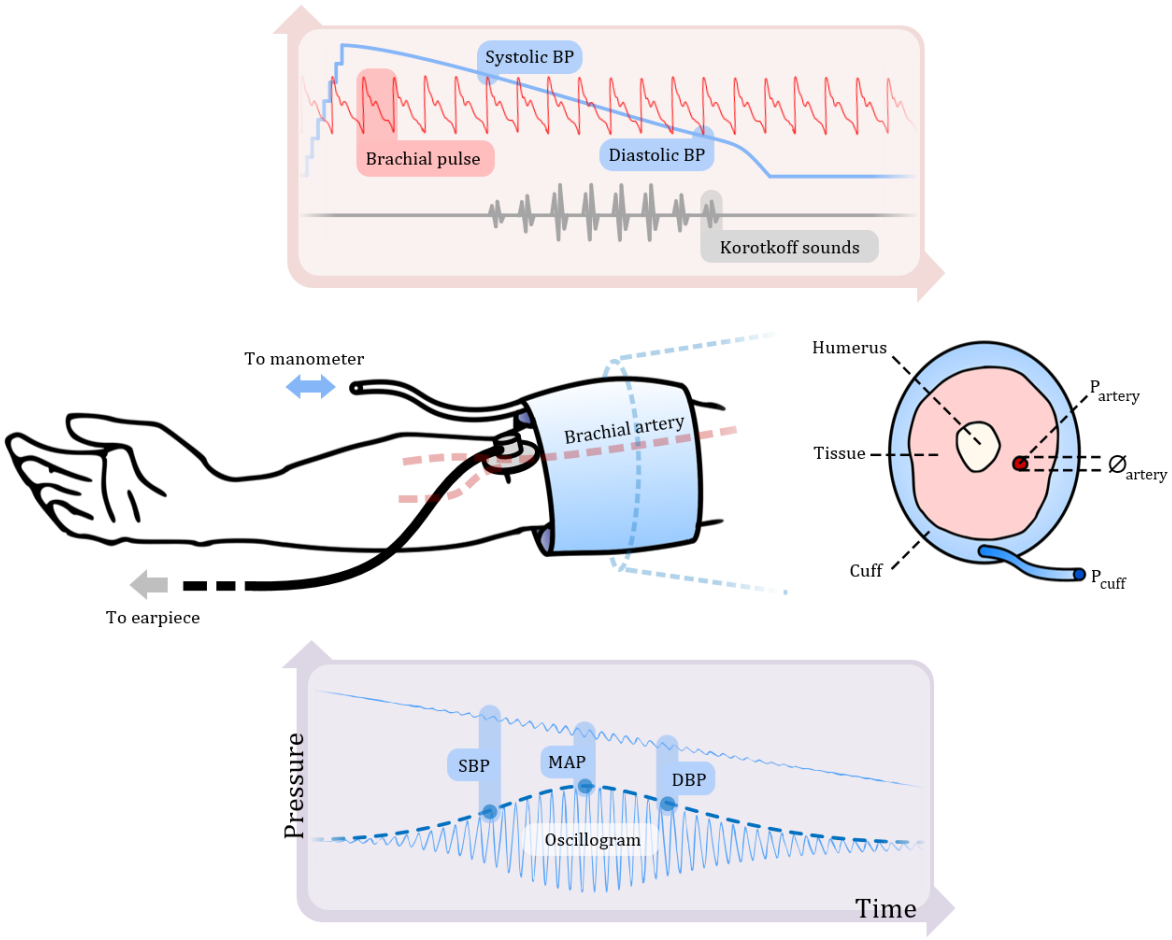

Fig. 2: BP measurement via brachial cuff using manual auscultation (top) and oscillometric method (bottom). An air-filled cuff is wrapped around the arm and inflated to supra-systolic pressure and then slowly deflated. The cuff is pneumatically connected to a mercury manometer or an automated BP instrument. In the manual auscultation technique, the clinician places a stethoscope on the brachial artery just below the cuff and listens to distinct Korotkoff sounds appear and disappear, marking SBP and DBP, respectively.

one value, MAP. SBP and DBP are approximated from the measured data. In this technique, a cuff is placed around the upper arm and the brachial artery. As pressure in the cuff is increased (over SBP), the flow of blood is completely occluded. When released, the amplitude of pulsations (or oscillations) measured in the cuff increase until the cuff pressure reaches the MAP. As the cuff pressure continues to decrease below the MAP, the pulsations start to decrease. Using signal processing a bell shaped curve (oscillometric envelope) is computed in the time domain along with the corresponding deflation curve. [6] In the traditional approach, SBP and DBP are then computed from the MAP using pre-fixed percentages derived from population studies (e.g., 50% and 80% of the MAP) and mapping these points to the cuff pressure curve. [36], [75]

Oscillometric devices suffer from some degree of uncertainty that is reflected in the recommendations of the US Association for the Advancement of Medical Instrumentation (AAMI) standard. The standard allows for $\pm$ 8 mmHg deviation compared to manual auscultation, which can often exceed the typical in-person BP variability [97]. The uncertainty is especially true for the common fixed ratio method [56], and differences are most prominent when arterial compliance and PP deviate significantly from typical levels. Several approaches have been proposed for improving the fixed ratio method. [36] A simple, yet effective, method is based on finding the pressure where the oscillogram envelope has the steepest slopes. However, in this method, accurate estimation of BP requires low-noise measurement. [25] Other solutions involve patient- specific modeling [8], [55], neural networks and pulse morphology analysis [36]. Fusing additional data to oscillometric BP estimates has also been proposed for improving the reliability [94]. BP fluctuations in the continuous arterial pulse waveform are used to estimate possible outlier readings [57]. A recent study (n = 20) explored optimal measuring sites (upper arm, middle forearm, wrist, finger proximal phalanx and finger distal phalanx) for cuff based oscillometry. It was concluded that the finger's distal phalanx was the second best site following the upper arm. The reported differences between the finger and upper arm measurements were ((mean $\pm$ standard deviation) mmHg) (-2.34 ± 6.82) mmHg, (-6.7 ± 12.9) mmHg and (1.7 ± 8.7) mmHg for MAP, SBP and DBP, respectively [57].

C. Tonometry

In tonometry, the pulse is palpated using an instrument called a tonometer. A traditional tonometer is a handheld pen-like device with a pressure sensitive tip that is placed over an artery, described in Fig. 4 [30]. Like manual palpation, tonometry is based on applying external pressure perpendicular to the artery. Arterial tonometers have been available for a long time, and early devices using the same principle were in use in the 19th century [39]. However, the technology is prone to motion artefacts, incorrect placement and changes in counter

pressure. Correct applanation pressure is achieved when the external pressure from the tonometer equals the pressure (P_i) inside the artery, (i.e. the MAP). This enables maximum pressure coupling to the sensor. In the case of tonometry, the external pressure (P_e) is applied perpendicular to the tube surface and matched with the MAP. Thus, the transmural pressure (P_t) equals zero. Since the external pressure is kept constant, the transmural pressure is strictly zero only when the BP pulse is at the MAP. The tube, or the artery, is almost completely flattened and the radius r can be thought to approach infinity perpendicular to the external force vector. Then all pressure is directed both to the tonometer and the underlying stiff surface, usually bone. The operation can be summarized as:

$$P_t = P_i - P_e = \frac{\mu \cdot T}{r} \overset{r \to \infty}{\to} 0, \tag{1}$$

$$P_i = P_e, \tag{2}$$

where T is wall tension and μ is wall thickness. [64]

The pressure applied and thus measured by the tonometer is now equal to the internal pressure of the vessel. If too little pressure is applied, the pressure coupling is insufficient and with too much applied pressure, the artery is occluded, blocking blood flow. A common issue with tonometric instruments is that the technique is very sensitive to sensor misplacement and to the applied force, especially when operated by a human. The pressure values output by a tonometer are usually arbitrary and have to be calibrated to actual BP values using an arm cuff. [30]

D. Pulse wave propagation

Pulse wave propagation, either measured in time or velocity, can be used to estimate BP [29], [32], [68]. If the propagation time is used, then the generally used terms are pulse transit time (PTT) and pulse arrival time (PAT). PTT is the time it takes for the pressure wave to travel from one (proximal) arterial site to another (distal) [68]. Experimental studies have shown PTT to be linearly related to BP through the following model equation [68]:

$$BP = \frac{k_1}{PTT} + k_2, \tag{3}$$

where k_1 and k_2 are calibration parameters. Other models have also been proposed [68] and models including additional physiological parameters, e.g. heart rate [104], have been studied. A differential PTT (dPTT) is obtained when the delay is measured from two different sites of the body using the pulse arrival times [5]. For example, if the PTT is computed from two photoplethysmography (PPG) waveforms arriving at the finger and the toe, the value is determined between the delays from the aortic arch to the finger and from the aortic arch to the toe [14]. In either case, the time delay is computed between characteristic points in both waveforms. Typically, the foot is the preferred point because it is minimally impacted by wave reflections [68], [108]. PTT is typically measured using two PPG sensors, but alternative techniques and their combinations can be used as well, e.g., tonoarteriography, impedance cardiography, ballistocardiography and phonocardiography [28]. In contrast, PAT measures the time delay between the ECG waveform (R-wave) and the distal waveform [68], [108]. Since the reference point is the ECG waveform, PAT includes the pre-ejection period (PEP), and thus, PAT is the sum of PEP and PTT. PEP is determined by the ventricular electromechanical delay and isovolumic contraction period [68], [108] and it is a non-constant parameter. It can be a significant portion of the PAT, about 12–35% [80]. Therefore, it is not surprising that PEP can be a difficult factor in PAT-based BP prediction [108]. Figure 3 illustrates the difference between PTT and PAT.

A closely related concept is pulse wave velocity (PWV), which is computed by dividing the distance between the measuring sensors by the difference in the pulse arrival time at the sensor locations [61]. PWV is considered as the gold standard for measuring arterial stiffness [51], but it has also been used as an indirect estimate of BP [26], [41], [61] and has been shown to be an independent predictor of incident hypertension [47]. The commonly used physical model, the Moens-Korteweg equation [48], [66], relates the velocity of a pressure pulse to the elastic modulus of a thin-walled and distensible tube (artery) inside which the pressure pulse travels [19].

Pulse wave propagation based BP measurement, if clinically validated, would allow for continuous and convenient BP monitoring. Alternative methods, such as the ocillometric method used in ambulatory measurements only allow for automated intermittent measurements (e.g. every 20 minutes) and the volume clamp method (see II-F) is often inconvenient for the user. [82]. However, the popular PTT/PAT based techniques are limited by the need for calibration [68]. The calibration fits the model parameters, such as the ones in equation 3, using, e.g., pairs of measured PTT/PAT and BP values. Typically, a cuff-based oscillometric BP measurement is used during initial calibration and at regular intervals to adjust for sensor drift. Unsurprisingly, increasing the length of the calibration interval is associated with decreased BP estimation accuracy, although the decrease in accuracy might not always be so straightforward [27]. Consequently, the accuracy of long-term monitoring is a hindrance of this technique [85].

The link between pulse wave propagation and BP has been shown in numerous studies [14], [19], [40], [61], although experimental results about the strength of the relationship are varying. A study comparing different PATs (ear, toe and finger) and PTTs (ear-toe, ear-finger and finger-toe) found out that the best Pearson correlation coefficient of -0.63 was between the toe PAT and the SBP [14]. Significantly lower correlation coefficients of 0.44 and 0.37 have been obtained between the SBP and both the finger and the wrist PWV (calculated using PAT), respectively [84]. Then again, a strong correlation coefficient of 0.83 between a model computed SBP (based on PAT) and measured SBP has also been shown [41]. Somewhat contradicting conclusions have been presented about the relationship between PAT and SBP not being reliable enough (due to the included PEP) to use PAT as a surrogate marker for SBP where 95% limits of agreement between the measured and predicted SBP was $\pm$ 17.0 mmHg. In another study, PAT had a stronger correlation ($R^2 = 0.39$) with SBP than PTT ($R^2 = 0.33$) and PTT had a stronger correlation with DBP ($R^2 = 0.41$) and MAP ($R^2 = 0.45$) than PAT ($R^2 = 0.02$ and $R^2 = 0.08$, respectively). [80] Better performance of PTT over PAT has been presented where PTT was better than PAT at predicting DBP, MAP and SBP [108].

A less studied technique estimates PTT from mechanical motion signals and PPG [20], [62]. It has been found that such PTT correlates more strongly with BP compared to conventional PAT [62]. The improved performance was mostly credited to eliminating the variance in the delay caused by the PEP. Similar results on the performance of using mechanical motion signals and PPG for measuring the delay has been presented based on a system consisting of a watch with embedded accelerometer and PPG sensors used to record chest wall vibrations and wrist PPG signal simultaneously [20].

Overall, estimating BP from pulse wave propagation is not straightforward because factors such as PPG sensor contact force [24], [99] and BP independent smooth muscle contraction/relaxation [14] can affect the measurement. The accuracy of the technique varied between

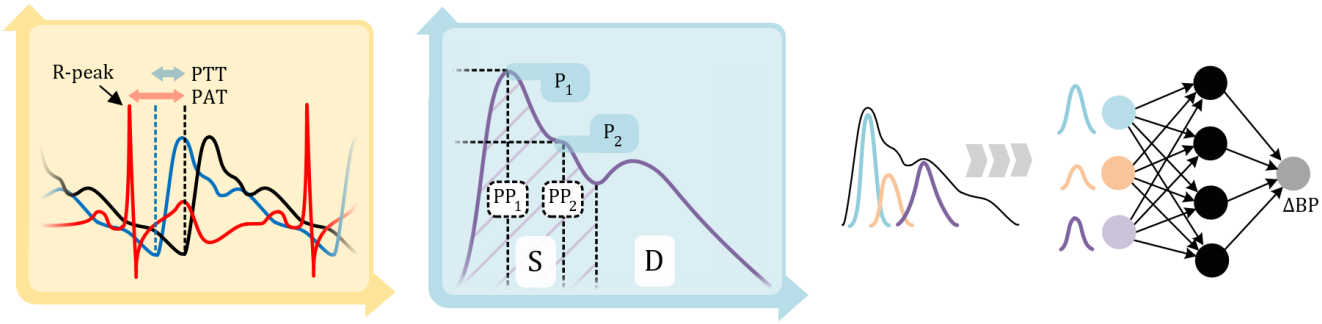

Fig. 3: Left: The difference between pulse transit time (PTT) and pulse arrival time (PAT). PTT represents the time between two pulses measured at two locations with, e.g., PPG. PAT is the time it takes for the pulse to travel from the heart to a peripheral artery (e.g. finger). It is calculated from the ECG tracing's R-peak to the peripheral systolic wave. Middle: Pulse wave analysis (PWA). Parameters extracted from the pulse are, e.g., pulse pressures PP_1 and PP_2 at points P_1 and P_2 as well as the systolic and diastolic areas S and D. Right: Pulse decomposition analysis (PDA). A single cardiac pulse is divided into wavelets which then can be passed to a machine learning algorithm in order to assess BP changes.

studies depending on whether PTT/PAT was used, the chosen model, and methods to perturb the BP, calibration frequency and time after which the measurements are taken after the calibration. However, the technique has attracted a fair amount of interest in the BP monitoring industry due the potential of continuous BP measurement and convenience for the user.

E. Pulse wave morphology

The arterial pulse waveform holds a plethora of BP information, which can be extracted using different pulse wave morphology analysis techniques. BP, and changes in it, affect the shape of the pulse via a multitude of hemodynamic phenomena [92]. Pulse wave analysis (PWA) utilizes the features extracted from the pulse contour, illustrated in Figure 3. These features include, e.g., PP, systolic and diastolic areas, augmented pressure, and augmentation index (AIx). AIx is computed as the ratio of the PP of the initial systolic peak (PP_1) to the PP at the inflection point caused by wave reflection (PP_2) [92]: $AIx = \frac{PP_2}{PP_1} \cdot 100(\%)$. In some devices, the peripheral pulse is transformed into aortic pulse via a generalized transfer function or a similar approach [64]. The extracted features can be entered into a mathematical model or a machine learning algorithm in order to derive actual pressure readings. Additional patient information, such as age, weight, height and sex may be integrated to improve accuracy. PWA methods usually require an initial brachial cuff calibration when used for BP tracking. As is the case with pulse propagation methods, PWA is best used for estimating relative BP changes instead of absolute BP values. [92]

A similar approach, pulse decomposition analysis (PDA), is based on assessing the cardiac pulse contour [13], [42], [92]. PDA relies on the analysis of the reflected waves seen in the arterial pulse waveform. In addition to the primary systolic pulse, the underlying theory suggests two pulses are reflected from two major reflection sites branching from the abdominal aorta: the renal arteries and the iliac arteries. The magnitude and place of these reflections are dependent on BP and flow velocity. By fitting this information to a model, BP changes can be estimated. [13] The technology is useful for detecting relative changes in BP, but needs initial calibration via, e.g., oscillometry. The theory of the major arterial reflection points requires further study. However, it remains unclear how much of the pulse morphology changes are induced by changes in the reflection waves and how much can be linked to transmural pressure changes and positioning in the pressure-compliance curve. The principles of PDA are illustrated in Figure3.

F. Vascular Unloading Technique

The Vascular Unloading Technique (VUT) or volume clamp method was invented by the Czech physiologist Jan Penaz in 1973 [15], [45]. This method enables continuous beat-by-beat BP monitoring [45], [75]. A typical VUT system consists of a main control unit and a finger cuff device connected via combined communication cable and pneumatic tubing. The main unit houses the pump and valves required for pressure management. The finger cuff unit consists of a wrist-mounted control unit and one or two miniature air cuffs that are placed around a finger(s). The cuff has both a light emitting diode (LED) and a photodiode, much like a pulse oximeter. This optical PPG system observes the pulsatile blood volume in the artery by measuring the light passing through it. A VUT device has a feedback control loop system that applies counter pressure to the cuff in order to keep the optical blood flow signal constant during each cardiac cycle. The feedback system requires a minimum of 30 Hz of bandwidth [45]. Different methods for finding an appropriate set point for the feedback system have been introduced, but there is no consensus on which is best [81]. When the optical blood volume increases, the feedback system decreases the cuff pressure and vice versa, thereby maintaining constant volume in the artery and thus a constant PPG reading. The actual BP can then be read from the cuff that is being continuously adjusted by the feedback system. VUT devices usually integrate a traditional oscillometric brachial cuff to the system for initial and periodic calibrations. The finger cuff pressure signal is converted to an equivalent brachial BP via a transfer function. The technology is illustrated in Fig. 4.

Volume Control Technique (VCT) is an experimental method introduced by CNSystems [38]. Similar to VUT, VCT relies on volume clamping. However, instead of "clamping" the full pulse contour, VCT uses beat-to-beat clamping. This is achieved by integrating over each cardiac pulse in the optical feedback signal and adjusting cuff pressure to keep the integral constant and the pulse contour stable. Compared to traditional VUT, VCT is easier to implement and miniaturize, since it does not require complex fast-switching pneumatics. The technology was implemented on an existing VUT device by customizing the firmware. It has been tested on 46 patients undergoing surgery resulting in MAP of (-1.0 ± 7.0) mmHg. These promising results are yet to be validated according to a standard protocol. [38]

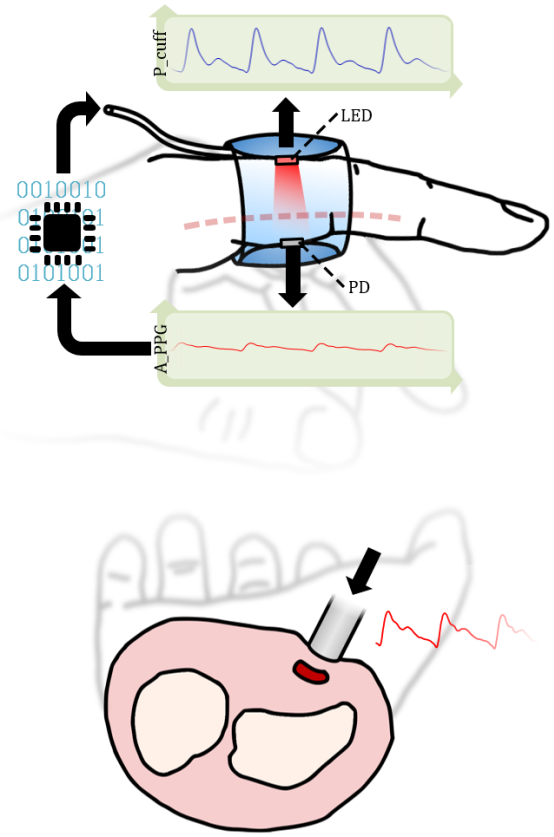

Fig. 4: Top: Vascular unloading technique (VUT). A miniature cuff equipped with a PPG unit is placed around a finger. A feedback system is used to apply pulsatile counter pressure to the cuff in order to keep the optical blood flow signal constant and thus the cuff pressure equals the intra-arterial pressure. Bottom: Conceptual image of arterial tonometry showing a cross section of the arm with radial and ulnar bones as well as the radial artery. A pen-shaped tonometer is pressed against the skin applying pressure to the artery. The volume changes in the artery are read via a pressure sensor.

G. Sources of inaccuracy

All of the methods described so far share two common factors: they are non-invasive and thus inherently inaccurate to a certain extent. Aside from intra-arterial cannulation, all BP measurement techniques experience a possibility of error. The degree of error considered clinically acceptable are defined by international standards [95]. The accuracy of the device has to be consideredat a population level, rather than for single measurements. Even a validated device can give highly incorrect readings on some individuals, in the worst case leading to a lack of treatment. Such individuals might belong to a so-called special population category in which blood pressure measuring devices validated with general population might not be accurate. For example, young children, pregnant women and people with atrial fibrillation can be considered as special populations [95], [96].

Manual auscultation can suffer from listener bias as well as from physiological factors, such as unclear fainting of Korotkoff sounds. Interestingly, due to the nature of the mercury column scale, readings are often marked as even numbers. However, the effect on accuracy is minor.

The oscillometric method has a clear source of inaccuracy. It does not directly measure SBP and DBP, instead estimating them based on the oscillogram and mean arterial pressure. Arterial compliance, e.g. the stiffness of the arteries, affects the shape of the oscillogram, which can distort the results. Wrong cuff size also has a major effect on accuracy. Large arm circumference is a factor too, and arm circumferences over 42 cm are considered to be a special population when deriving validation standards [95]. Common to all of the techniques relying on calibration (such as VUT, pulse morphology analysis and pulse propagation methods), the error introduced by the oscillometric calibration propagates throughout the measurement. [8], [39]

Pulse wave propagation methods suffer from the inherent inaccuracy of equating a variable to another one through a model. The amount of time the model is still valid after a calibration is another possible source of inaccuracies. Depending on the used sensor setup, PEP and sensor contact force on the skin can also be confounding factors, as noted earlier.

Tonometry is prone to sensor misplacement, motion artefacts and, if operated by a human, to incorrect applied pressure. Pulse wave morphology also suffers from inaccuracies caused by sensor misplacement and movement artifacts but even more so from the fact that blood pressure is estimated based on numerous features, and possibly also patient specific information, which work as an input to a complex model. Additionally, reduced blood perfusion in the extremities can make signal acquisition difficult. [39]

III. Recent advances and validation in blood pressure instruments

The technologies discussed above are used in various commercial devices and research prototypes. Most of the technologies discussed so far have been validated against an international standard protocol. The relevant standards used over the last decades are defined by the US Association for the Advancement of Medical Instrumentation (AAMI), the European Society of Hypertension Working Group on Blood Pressure Monitoring (ESH), British Hypertension Society (BHS) and the International Organization for Standardization (ISO) [17], [74], [105]. The differences between each standard include the study population size (AAMI, BHS: 85, ESH: 33) and the relative size of each BP population of interest, such as hypotensive and hypertensive subjects. As a result of collaboration between the standardization committees (AAMI/ESH/ISO), a new consensus document was released in 2018 (revised in 2019) in attempt to unificate the standards [95], [97]. In the AAMI/ESH/ISO standard, the study size is 85 including the minimum number of subjects within certain BP ranges ($\geq$5% of the reference SBP readings must be $\geq$160 mmHg, $\geq$20% must be $\geq$140 mmHg, and $\geq$5% must be $\leq$100 mmHg) [69]. In the case of continuous BP instruments, the validity of these protocols, which are designed for spot measurement BP devices, is questionable and warrants further investigation. These protocols are also specifically intended for validation of cuff-based instruments and should not be applied on cuffless devices, particularly those requiring calibration.

The Institute of Electrical and Electronics Engineers (IEEE) has published a standard protocol specifically for wearable cuffless devices, IEEE 1708-2014 [7]. An amendment was released in 2019 (IEEE 1708a-2019) [3]. However, the standard has not yet gained widespread use. The IEEE standard contains two major differences compared to standards for traditional cuff devices. The new protocol requires a noticeable change in BP to be induced and the calibration to hold for a period of time. The validation protocol is separated into two phases: phase I (n = 20) and phase II (n $\geq$ 65). If the results from the phase I do not meet the standard, the device is deemed inaccurate. If they do, the phase II is started. The only difference between these phases is the number of participants enrolled.

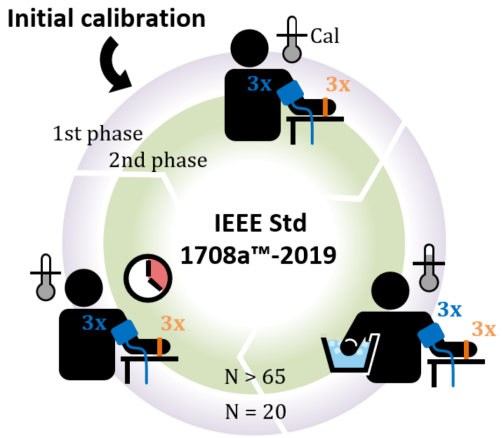

Fig. 5: IEEE Standard for Wearable, Cuffless Blood Pressure Measuring Devices first introduced in 2014. The protocol enables a more reliable way to assess the accuracy of continuous BP devices compared to traditional standards. As an example, cold pressor test is applied here for inducing BP change. However, other suitable methods may be used. [3]

There are three sets of measurements in each phase, which are described below. After the initial calibration specified by the manufacturer, the first measurement set is compared against manual auscultation. For the second set, a change in BP has to be induced. This can be done via a cold pressor test (CPT) [90], passive leg raising (PLR) [34] or exercise stress test [98], for example. The third set is made after a predefined period of time in order to make sure the calibration is still valid. Neither the method of inducing BP variation nor the length of time between the calibration and the final measurement set has been exclusively specified by the standard. The protocol is described in Fig. 5.

In some cases introduced below, a modified protocol (e.g., insufficient pressure range or sample size) has been used and, therefore, devices cannot be qualified as fully validated. One device has not met the criteria set by the standard and is deemed inaccurate. In many cases, multiple manufacturers have adopted the same technology due to expiration of patent rights or the technology can be implemented using different methods. Some modern instruments cannot exclusively be categorized into a single group, since they utilize multiple technologies. For example, the Caretaker 4 monitor uses oscillometry for initial calibration but relies on PDA for tracking BP [13], [42]. We will introduce one or more examples of each technique. A collection of the instruments is shown in Fig. 6.

A. Miniaturization of cuff oscillometry

The common digital BP devices used at the doctor's office and at home are based on cuff oscillometry. This technique has been miniaturized into various form factors and integrated into wearables. Omron Heartguide (OMRON Corporation, Japan) is a smartwatch that integrates a miniature cuff in the watch strap [50]. Similar to brachial cuff devices, the user has to sit still and initiate the spot measurement. The watch is placed at heart level in order to minimize errors introduced by the hydrostatic effect, and a basic oscillometric pressure response is measured. The device can be connected to a smartphone app for tracking 24-hour BP trends. Two different cuff sizes are available and both have to be validated separately. The standard size cuff is validated (n = 85) using the AAMI protocol for non-invasive BP measurement devices with SBP and DBP of (-0.9 ± 7.6) mmHg and (-1.1 ± 6.1) mmHg, respectively [50]. Even though multiple devices have previously used wrist cuff oscillometry, the Heartguide is the first one to miniaturize the cuff into a watch strap of reasonable size [21].

The Caretaker 4 (Caretaker Medical, US) is a wearable wrist-mounted monitor with a small inflatable finger cuff. It is used for continuous BP measurement, and relies on the oscillometric method for calibration. Oscillometric self-calibration has been validated (n = 126) according to the AAMI standard with SBP and DBP of (-1.4 ± 6.7) mmHg and (2.2 ± 6.4) mmHg, respectively. [13]

Finger-port (Elfi-Tech, Israel) is a small tabletop finger cuff device that uses dynamic light scattering (DLS) technology to measure blood flow alterations in the finger in combination with cuff deflation. The device can measure various vital signs in addition to BP. DLS technique is similar to PPG in that it measures the light scattered from blood cells to assess the pulsatile nature of blood flow. The device has not yet been validated according to any international standard protocol. [10]

B. Oscillometric finger pressing method

The oscillometric finger pressing method was introduced in 2018 [22]. In this technology, a smartphone is customized by adding a phone case with PPG and force sensors. This can also be achieved using the smartphone's internal sensors. [23] The user applies increasing force to the sensor, imitating cuff inflation. The app provides feedback on how much pressure should be applied, guiding the user. Blood volume oscillations in the finger are measured by the PPG sensor and an oscillogram can be filtered out of the optical signal. The force sensor registers the increasing pressure ramp. Standard oscillometric analysis can be performed using the combined optical and pressure signals. In the initial study (n = 32), the technique assessed SBP and DBP with an accuracy of (3.3 ± 8.8) mmHg and (-5.6 ± 7.7) mmHg, respectively. However, the device was compared against an oscillometric brachial cuff device (rather than gold-standard auscultation) and the study protocol did not strictly follow any international standard. Nevertheless, the study showed that, in principle, this type of technology could measure BP with a smartphone with minimal additional equipment.

Similar technology was introduced in a US patent application by Leman Micro Devices in 2014 [33]. The developed V-sensor houses a PPG sensor and a pressure sensor, along with other biosensors. Neither the operation principle nor the accuracy of the device have been fully disclosed as no peer-reviewed studies are available [4]. The company has announced in their press release that the sensor can be integrated into a smartphone or a wearable device. Like [22], the user applies pressure to the sensor while the app gives feedback to the user. The company claims that the technology is validated according to ISO standard with results of (-0.4 ± 7.2) mmHg and (-0.2 ± 6.0) mmHg for SBP and DBP, respectively [4].

C. Tonometry

BPro (Healthstats, Singapore) is a wristwatch radial artery tonometer that is used for ambulatory BP measurement. It requires initial calibration with a brachial cuff device. After calibration, the watch should provide accurate results for at least 24 hours. The device includes a watch head with a simple graphic user interface and a plunger that is to be pressed against the radial artery. The healthcare professional doing the calibration attaches the plunger to the wrist via double-sided tape to prevent it from moving while in use. The device is validated according to the AAMI and ESH standards with SBP and DBP of (-0.9 ± 7.6) mmHg and (-1.1 ± 6.1) mmHg, respectively. [72]

Our research group at the University of Turku proposed a table-top form factor BP instrument, finger artery non-invasive tono-oscillometric monitor (FANTOM), in 2020. A tonometric cuff-less mechatronic system is used to apply pressure on the fingertip and measure BP via oscillometric method. The device can record arterial waveform and assess central BP (CBP). An arbitrary validation protocol (n=33) comparing the device to an automated arm cuff monitor yielded results of (-0.9 ± 7.3) mmHg and (-3.3 ± 6.6) mmHg for SBP and DBP, respectively. [79]

D. Pulse propagation methods

BP estimation using PTT or PAT has been adopted by many companies and there have been efforts to measure absolute BP via PTT/PAT. However, it seems that it is best used for assessing relative changes in calibrated BP rather than used in spot BP measurements. Therefore, PTT/PAT might be highly suitable for ambulatory BP monitoring, but requires an additional instrument for calibration.

The Biobeat (Biobeat, Israel) and SOMNOtouch (SOMNOmedics GmbH, Germany) NIBP are smart wristband based devices that use PAT measured by ECG and wrist PPG to track BP [49], [71]. SOMNOtouch uses an ECG module with traditional ECG electrodes wired to the wrist device. Biobeat, on the other hand, uses a separate wireless and wearable ECG patch along with the wrist module. Both devices are calibrated with an oscillometric device. The devices measure the pulse arrival time from the ECG R-peak to the PPG pulse in the wrist or the finger. Biobeat conducted a study on 1,057 subjects comparing the system's accuracy to a sphygmomanometer resulting in SBP and DBP of (-0.1 ± 3.6) mmHg and (0.0 ± 3.5) mmHg, respectively [71]. The values fall in the range of the ISO 81060-2:2013 standard used in the study. However, the procedure was slightly modified since only one observer was used in the study rather than the two mandated in the standard. SOMNOtouch has been validated using the ESH protocol in a study consisting of 33 subjects resulting in SBP and DBP of (-0.4 ± 6.1) mmHg and (-0.1 ± 3.6) mmHg, respectively [49]. However, as the AAMI/ESH/ISO standards are designed for spot measurement devices that do not require initial calibration, the validity of such protocols for devices based on PAT is unclear. In both studies, the device was first calibrated to auscultatory BP values and the actual validation measurements were done immediately or a short time (15 min for SOMNOtouch) after the calibration. Therefore, the stability of the accuracy over longer periods of time and for large pressure variation remains uncertain. A recent study comparing SOMNOtouch to ambulatory oscillometric method during 24-hour measurement showed poor agreement between the two devices [73]. Since the underlying technology is similar, there is no reason to expect better results from Biobeat in the same study conditions.

Freescan monitor (Maisense Inc, Taiwan) is a handheld device that uses single-lead ECG and a form of applanation tonometry to measure BP using PAT. The user places the tonometer probe on the radial artery in order to measure radial pulse. The probe head also acts as an ECG electrode with the other electrode embedded in the device's grip handle. PTT is then calculated from the ECG R-peak to the foot of the radial pulse. The device is only suitable for spot measurements since it needs active user actuation. A measurement takes approximately 10 s. The device relies on initial calibration, which has to be performed only once for each subject. A validation study was carried out according to AAMI/ESH/ISO standard resulting in (3.2 ± 6.7) mmHg and (2.6 ± 4.6) mmHg for SBP and DBP respectively.

The Instant Blood Pressure app (AuraLife, US) was introduced in 2014 and sold via the Apple App Store and Google Play digital marketplaces. The app was finally discontinued the following year with around 150,000 units sold. The BP measurement of the app was based on calculating pulse transit time from SCG (seismocardiography) and PPG signals. The user would place the smartphone on their chest and hold their finger on both the camera and the flashlight. The subtle movement caused by the heart was registered using the phone's built-in accelerometer. The camera combined with the flashlight resulted in a PPG recording of the finger pulse wave. BP was then computed using the time between the aortic opening and systolic portion of the finger pulse. A 2016 study conducted using AAMI/ESH/ISO protocol showed that the app was highly inaccurate, yielding SBP and DBP results of (-1.2 ± 16.2) mmHg and (7.1 ± 10.8) mmHg, respectively. This suggests that the app categorized 80% of hypertensive patients as normotensive. A Federal Trade Commission complaint was filed against the company in 2016 after the study was released, but was later settled. [83]

Glabella is a smart glasses prototype developed by Microsoft for continuous BP monitoring. The device has three PPG sensors embedded into the frame of the glasses and uses them to measure PTT between angular, superficial temporal and occipital arteries. Similar to other PTT devices, Glabella relies on initial oscillometric calibration. In addition to the PPG sensor, the glasses feature an accelerometer unit for filtering out motion artefacts. A question arises regarding the research team's choice of the LED wavelength. The device uses green light which is known to penetrate only the most superficial layers of the skin, thus probing only dermal capillary and arteriolar blood flow. Red or infrared light is traditionally used for measuring arterial blood flow in the deep arteriovenous plexus. [65] However, the use of green LEDs enable easier placement of the sensors, since it provides acceptable signal quality anywhere on the skin. The accuracy of the device is not yet proven and only proof-of-concept measurements on a few people (n = 4) have been conducted. [43]

Recently, a method to estimate BP using multi-wavelength PPG signals was demonstrated [58]. Light at different wavelengths penetrate the skin at different depths and consequently probe different blood vessels. With shorter wavelengths (blue, green and yellow) the signal reflection comes mainly from the small vessels such as the arterioles and the capillaries, whereas longer wavelengths (red and infrared) penetrate deeper and the reflection originates from the arteries. It was demonstrated that the time delays between these signals correlate with BP. [59] Comparison between normotensive (n = 10) and hypertensive (n = 10) subjects yielded mean absolute differences against reference measurements of (2.2 ± 2.9) mmHg and (1.4 ± 1.8) mmHg for SBP and DBP, respectively [58].

E. Pulse wave morphology

Caretaker 4 uses PDA technology to track BP changes over time. After the initial BP values have been measured or alternatively entered manually, the device applies a constant pressure of 40 mmHg to the finger cuff. Pulsations in the cuff are recorded and analysed using PDA. Continuous BP monitoring accuracy has been validated (n = 24) separately to the oscillometric calibration yielding SBP and DBP of (-0.4 ± 7.7) mmHg and (-0.5 ± 7.0) mmHg, respectively [42].

The PWA approach is used by Valencell in their wireless earbud device. They have embedded a PPG sensor and the supporting electronics into an earbud, traditionally used for listening to music. Previous studies indicate that the ear is a suitable candidate for optical BP measurement offering high quality signal and robustness [101]. The device relies on optical pulse wave morphology analysis combined with machine learning. A white paper published by the company states that the device can achieve similar accuracy to an oscillometric cuff monitor with SBP and DBP of (1.7 ± 7.7) mmHg and (-1.1 ± 8.0) mmHg, respectively. [102]

Aktiia bracelet is another device relying on PWA of PPG signals. The Swiss company has developed a wearable wristband similar to the popular activity bracelets used for fitness monitoring. They use an off-the-shelf PPG sensor for measuring the optical signal. The device has to be calibrated with an oscillometric device. The company claims that with a single calibration, the device yields accurate results for up to two months [103]. They have published a study comparing the technology, which they call OBPM (optical BP monitoring), to an invasive BP catheter readings yielding interesting results [93]. They have also concluded a clinical trial fulfilling ISO standard requirements on 86 subjects. The study results have yet not been peer-reviewed but they claim the results fall in the range of the ISO standard with (5 ± 8) mmHg for both SBP and DBP [103].

Pulse morphology analysis has recently been put to use in smartphones as well. The OptiBP app (Biospectal, Switzerland) uses PPG combined with PWA to measure spot BP. Instead of a dedicated PPG unit, the app uses a smartphone camera and the LED flash to acquire the PPG waveform. The camera flash is used instead of a single LED with a specified wavelength and the CMOS (complementary metal oxide semiconductor) cell acts as an optical sensor. The CMOS cell registers red, green and blue light which are processed to represent the pulsatile blood flow signal. Morphological features are then extracted from the signal and passed to a mathematical model. The system was trained using gold-standard measurements from an invasive BP recording (n = 51) acquired in an operating room environment. In validation (n = 40) the device was assessed against manual auscultation yielding SBP and DBP results of (-0.7 ± 7.7) mmHg and (-0.4 ± 4.5) mmHg, respectively. An initial calibration to auscultation results and three consecutive measurements were made on both arms. This raises a question on the validity of the protocol. Subjects with variation of more than 12 mmHg of SBP and 8 mmHg of DBP between successive auscultation measurements were discarded. A protocol similar to the IEEE 1708-2014 standard should be used for this type of device that relies on individual calibration. [87]

F. Transdermal optical imaging

Transdermal optical imaging (TOI) for BP uses remote PPG to record facial skin blood flow alterations. [60], [67] A light source is directed to the skin and a camera is simultaneously used to measure the light reflected from the outer layer of skin (epidermis). The white light of the camera flash is a product of three LED's (red, green and blue). Since each wavelength penetrates through different layers of the skin, probing different blood vessels enable a more comprehensive picture of skin vasculature. Smartphone cameras are used to detect the small pulsations of the blood vessels in the skin and construct a map of 17 different sections of the face. The measurement data is entered to a machine learning model, which then outputs SBP and DBP. The model was trained using a data set of n = 1,328 measurements, of which 85% were used for training and 15% for validation. The study resulted in SBP and DBP of (-0.5 ± 8.9) mmHg and (-0.4 ± 6.2) mmHg, respectively. However, the accuracy and precision did not meet the requirements of the AAMI standard. In addition, the study was limited to normotensive subjects and may extrapolate to hypotensive or hypertensive cases, which are usually the most difficult to measure reliably. The statistical power of the collected dataset is not sufficient for drawing robust conclusions. The results suggest that there is indeed some BP information in TOI data, but the accuracy needs to be further verified.

IV. Modeling and Algorithms

The emergence of new computational techniques has opened new possibilities to improve BP monitoring and hypertension management. These techniques are typically based on models relating physiology with measured parameters or statistical models with recent emphasis on machine learning.

A. Physiological models

Inter-subject variability is one of the causes leading to inaccurate BP estimates. In the case of oscillometry, the arterial compliance is known to alter the shape of the pressure oscillation envelope and affect the estimated SBP and DBP when, for instance, the fixed ratio method is used. [25] Patient-specific algorithms for improved accuracy have been developed [54], [55] where a parametric arterial volume-pressure model is fitted to the measured envelope of the pressure oscillations. The best fit yields estimates for the SBP, DBP, and parameters describing the volume-pressure relationship. A similar idea was presented using a mathematical model for oscillometric measurements [8]. In the study, a simulated response was compared to BP dependent model output and the one providing the smallest least squares residuals revealed the most likely BP values. The model was accurate under different simulated arterial compliances. Another study included the Windkessel's model of the arterial system that includes total vascular resistance and compliance [11]. Combining it with the measured oscillometric envelope, it was found that the discrepancy between oscillometric and auscultatory measurements could be reduced.

B. Machine learning

A clear line of research benefiting from advancements in computational techniques, sensor development and data availability lies in continuous BP monitoring accompanied with machine learning models. [31] A continuous BP estimation study examined multivariate linear regression (MLR) and support vector regression (SVR) models with 14 features based on waveform morphology and time intervals (including PTT) from PPG and ECG. The model was tested on 73 subjects and performed reasonably well on the same subjects when tested 1, 3 days and 6 months after the model was created. [63] Another study using similar machine learning models was evaluated on several available databases containing roughly a thousand subjects. Using 10-fold cross-validation, average deviations of 5.7, 9.9 and 5.3 mmHg with negligible biases were obtained for DBP, SBP and MAP, respectively. Breaking away from the beat-to-beat continuous measurements, in an attempt to directly measure both SBP and DBP, a deep learning algorithm was tested on digital stethoscope measurements [78]. Digitized recordings were first converted into an image after which image classification techniques were used. This study involving 30 subjects showed promising proof-of-concept. Similar machine learning approach using features from PPG and ECG signals had success in separating normotensive vs. hypertensive, including pre-hypertensive, subjects. [53]

In a recent investigation, machine learning was used to estimate BP from pulse oximeter PPG signals. [86] Deep convolutional networks with 30 s PPG segments were used in the study of 329 subjects (60% training, 20% validation, 20% test) in a hospital environment. The BP was estimated and compared against a concurrent BP recording. For each subject, the first available BP reading was used for calibration. The reported mean absolute errors for SBP, DBP and MAP were (0.48 ± 9.81) mmHg, (0.44 ± 5.16) mmHg, (0.47 ± 5.63) mmHg, respectively. A stability investigation claimed that BP tracking precision was not weakened with signal durations up to 600 min. A related study considered indices derived from PPG morphology as a set of markers for BP [89]. A waveform simplifying model and subsequent analysis of the velocity and acceleration of blood flow was concluded to correlate with BP changes.

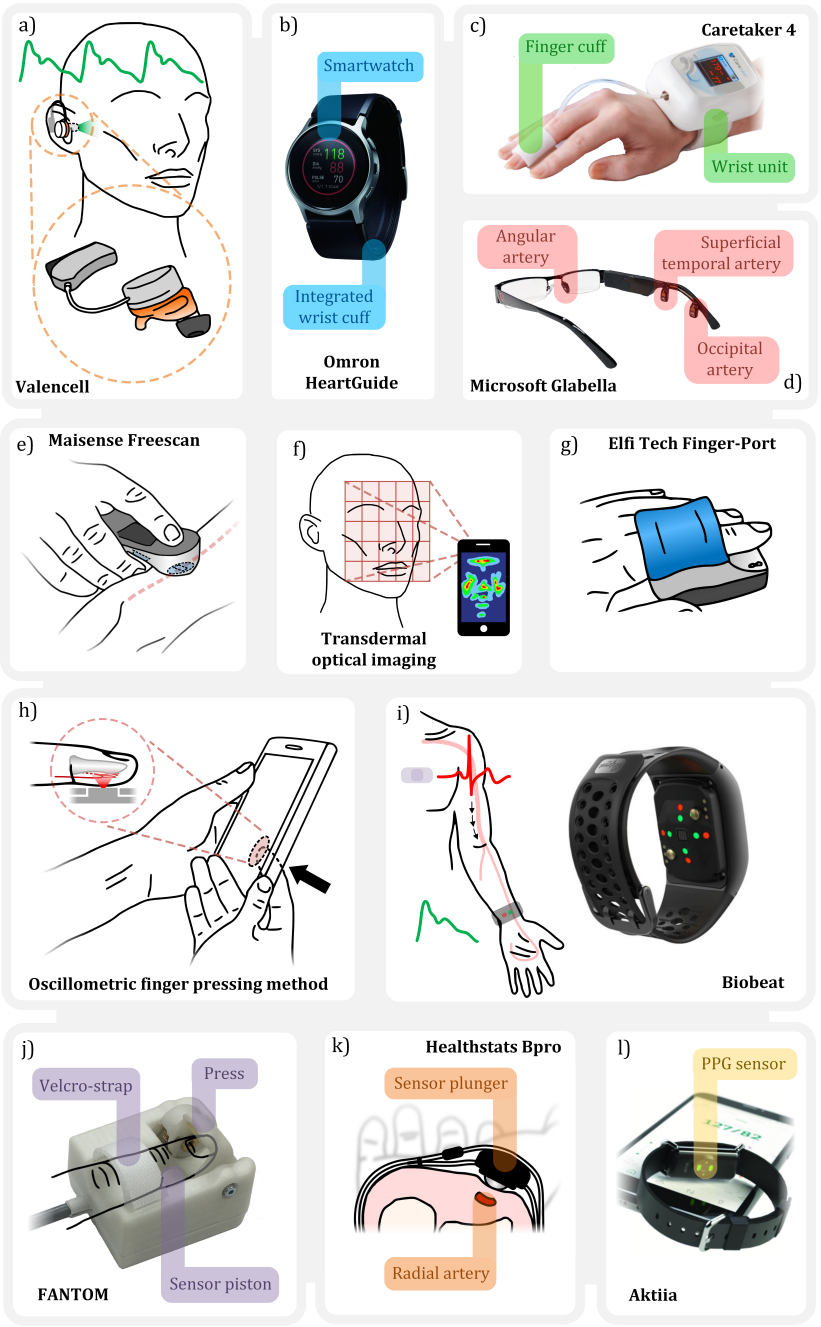

Fig. 6: Collection of recent instruments. a) Valencell ear-buds use optical pulse wave morphology analysis combined with machine learning [52]. b) Omron Hearguide is an oscillometric smartwatch with a miniaturized inflatable cuff. Figure adapted from [50] c) Caretaker 4 is used for measuring continuous BP via pulse decomposition analysis (PDA). Figure adapted from [42]. d) Microsoft has developed a smart glasses prototype relying on pulse transit time (PTT) acquired from three PPG locations. Figure adapted from [43]. e) Maisense Freescan is a handheld PAT device that utilizes ECG and tonometry [107]. f) Transdermal optical imaging (TOI) uses a smartphone camera to capture remote PPG and compute BP via AI techniques [60]. g) Elfi-Tech Fingerport uses an inflatable finger cuff along with micro dynamic light scattering (mDLS) technique to measure BP [10]. h) In oscillometric finger pressing method the user applies increasing pressure to the combined PPG and pressure sensor unit in order to measure BP [22]. Leman Micro Devices has developed the V-sensor which uses a similar approach [4]. i) Biobeat records simultaneous electrocardiogram (ECG) and wrist PPG in order to measure BP changes via PTT analysis. Figure adapted from [71]. SOMNOmedics' SOMNOtouch uses a similar approach [49]. j) Developed at University of Turku, FANTOM is a finger-worn device that uses tonometry combined with oscillometry for measuring BP and recording arterial waveform [79]. k) Healthstats BPro is a smartwatch-type device with a tonometric plunger that records radial artery waveform and in order to measure continuous BP [72]. l) Aktiia is a smart bracelet that uses PPG combined with pulse wave analysis (PWA) to track BP. Figure adapted from [93].

Device	Technology	Spot BP	Cuffless	Calibration	PWA	Beat-to-beat BP	Validation (n)	References
Omron Heartguide	Cuff oscillometry	Yes	No	No	No	No	AAMI (85)*	[50]
Healthstats BPro	Radial artery tonometry	No	Yes	Yes	Yes	Yes	AAMI, ESH (89)*	[72]
Elfi-Tech	Cuff oscillometry & mDLS	Yes	No	No	Yes	No	-	[10]
Caretaker 4	Cuff oscillometry & PDA	Yes	No	No	Yes	Yes	AAMI (126)*	[13], [42]
Smartphone (IBP app)	PAT	Yes	Yes	No	No	No	Failed (85)	[83]
SOMNOtouch NIBP	PAT	No	Yes	Yes	No	Yes	ESH (33)	[49]
Biobeat	PAT	No	Yes	Yes	No	Yes	ISO (1,057)*	[71]
Maisense Freescan	PAT	Yes	Yes	Yes	No	No	ISO (100)	[107]
Valencell	Ear PPG	Yes	Yes	No	No	Yes	ISO (147)	[52]
Smartphone (OptiBP app)	PPG PWA	Yes	Yes	Yes	No	No	(40)	[87]
Aktiia	PPG PWA	Yes	Yes	Yes	No	No	ISO (86)†	[103]
* FDA approval, † CE mark								
Microsoft Glabella	PTT	Yes	Yes	No	No	No	(4)	[43]
LMD V-sensor	Riva-Rocci & PPG	Yes	Yes	No	No	No	-	[4]
FANTOM	Tonometry & Oscillometry	Yes	Yes	No	Yes	Yes	(33)	[79]
Smartphone	Finger pressing method	Yes	Yes	No	No	No	(32)	[22]
Smartphone	TOI	Yes	Yes	No	No	No	(1,328)	[60]

TABLE I: A survey of the proposed devices and technologies. The devices have been divided into two categories: commercial (top) and research (bottom) devices. Spot BP indicates whether the device can be used to take single user activated BP measurements. The calibration column indicates whether the device has to be calibrated to external arm cuff readings. PWA column indicates whether the device outputs pulse wave morphology information to the user. Validation status is disclosed by naming the used standard (if one is used) and the number of subjects in the study. A superscript shows whether the device has gained US FDA approval or European CE mark.

Technological advancements have resulted in a significant effort in the use of wearables and smartphones for BP estimation. The benefits of such BP self-monitoring include average BP tracking over time, detection of concerning BP trends, and abnormal circadian BP patterns. [46] Communicating these measurements with a clinician using a telemonitoring system has the potential to improve hypertension management and reduce healthcare costs [46]. An example is the Cardiogram application where a long short-term memory network was used to predict hypertension using only heart rate and step count as inputs. Data were collected from 6,115 users with Apple watch for average period of nine weeks resulting in a reasonable prediction performance with area under the receiver operating characteristic curve $> 80\%$. [9], [100]. Currently there are over 180 apps for BP estimation designed for telemonitoring. Only a small fraction of these were developed in conjunction with medical experts, and evidence of rigorous validation is even rarer. [46] Currently, there are no mobile apps for BP measurement that have been approved by the US Food and Drug Administration or the European Commission. [46]

V. Discussion and conclusion

We surveyed the recent advances in BP monitoring and underlying principles behind them. Most efforts have been directed in developing continuous and cuff-less monitors, miniaturization of the cuff-based devices and finding new algorithms to improve the robustness and accuracy. BP monitoring devices are being developed towards a more wearable form factor that could be worn over long time periods and, hence, geared towards better continuous measurements. Cuffless BP monitoring solutions rely mostly on time delay between pulse waveforms measured at different locations and pulse morphology analysis combined with machine learning techniques.

Several studies have attempted to improve continuous BP monitoring accuracy with the use of models and machine learning techniques. Although good progress has been made, most studies have limited number of subjects and narrow BP distribution and do not use unified study protocols to allow direct comparison with obtained results. With the hope of new extensive public databases becoming available, more rapid progress could be made.

Some concerns have been raised on the rigor of the validation of cuffless devices [77], and although a standard has been proposed [7], it has not gained widespread use. It dictates that a validation of the calibration, requirement of this technology, and the ability to measure changes in the BP after varying time from the calibration. The BP monitoring industry is regulated and relies heavily on the established international standards.

This creates pressure for the manufacturers to do the validation according to a standard, even though it might not be suitable for a particular type of device. In fact, it might be easier for the device to pass the traditional standard requirements compared to a more suitable one designed for this exact type of device. With continuing development and more rigorous validation, continuous BP monitors have potential to become commonly used technology, although the benefits of truly continuous BP monitoring is yet to be established.

Solutions attempting to miniaturize cuffs are based on the well known oscillometric technique found in virtually all digital BP monitors. These devices have matured technology and validation standards. They can also be configured to automatically measure BP and thus are able e.g. to measure diurnal rhythm. However, they are unable to measure BP beat-by-beat unless complemented with pulse waveform measurement. It is evident that the trend is moving towards wrist devices and research is also conducted on finger BP.

The global BP monitoring market is projected to reach over USD

2 billion by 2025 with an annual growth rate of 9.1%. The global rise of prevalence of hypertension and cardiovacular diseases and governmental control being the key drivers. The digital BP monitors intended for home use accounts for 64.3% of the market with Omron Healthcare as the leading manufacturer. [1] Arm based digital BP monitors are the most common type, but wrist monitors are expected to gain popularity due to multi-parameter readings and smartphone integration [2]. BP monitoring has gained significant attention in the recent years and it is not expected to diminish given its global health burden. Although great progress has been made, no new monitoring principles have become commonplace in recent years. A continuous BP monitoring has had significant research and development interest in recent years. These continuous solutions are almost predominantly based on pulse propagation techniques such as the pulse transit time. A clear issue with these studies is that no rigorous validation is typically done although suitable validation protocol has been published. Additionally, confounding factors have not been thoroughly investigated and there is no solid understanding how continuous BP monitoring work in specialty groups and during daily activities. However, it is clear that multi-parameter, miniaturized solutions for home environments are currently being sought after with great interest and the use of machine learning becoming increasingly common.

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