Are cuffless devices challenged enough? Design of a validation protocol for ambulatory blood pressure monitors at the wrist: the case of the Aktiia Bracelet

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***Abstract* — The US and European guidelines for the diagnosis and management of hypertension recommend the introduction of systematic home and night Blood Pressure (BP) monitoring. Fully-automated wearable devices can address the needs of patients and clinicians by improving comfort while achieving measurement accuracy. Often located at the wrist and based on indirect BP measurements, these devices must address the challenges of ambulatory scenarios. New validation strategies are needed, but little guidance has been published so far.**

In this work, we propose an experimental protocol for the validation of cuffless wrist BP monitors that addresses ambulatory environment challenges in a controlled experimental setting. The protocol assesses the robustness of the measurement for different body postures, the ability of the device to track BP changes, and its ability to deal with hydrostatic pressure changes induced by different arm heights.

Performance testing using Aktiia Bracelet is provided as an illustration. The results of this pilot study indicate that the Aktiia Bracelet can generate accurate BP estimates for sitting and lying positions and is not affected by hydrostatic pressure perturbations.

***Clinical Relevance*— Automated cuffless BP monitoring is opening a new chapter in the way patients are being diagnosed and managed. This paper provides a guidance on how to assess the clinical utility of such devices when used in different body positions.**

I. Introduction

A. Hypertension and prediction of cardiovascular risk

Hypertension is a significant risk factor for cardiovascular morbidity and mortality. However, the definition of hypertension varies across countries and its interpretation depends on the BP measurement technique that is used [1,2]. Three methods co-exist today when it comes to estimating BP [3], *i.e.* Office Blood Pressure Monitoring, Home Blood Pressure Monitoring (HBPM) and Ambulatory Blood Pressure Monitoring (ABPM).

Professional (office) BP Monitoring relies on a single measurement that can be either performed by a health practitioner at the upper arm using auscultation or calculated as a mean of multiple measurements performed by an automated oscillometric device [4]. Even though the measurement conditions are controlled by the clinician, they can be affected by a general stress related to the medical visit, a white-coat effect [5].

Contrary to the office monitoring, self-measured HBPM is performed in an out-of-clinic scenario and usually spans over a period of several weeks, providing a better clinical solution. The measurement is generally taken twice per day with an oscillometric cuff at the upper arm or at the wrist. The patient is instructed to initiate the measurement when seated and relaxed, with the device at the heart level.

Compared to the HBPM, the ABPM increases the resolution of the BP patterns during a typical day. The patient is monitored out-of-clinic over 24 hours using an oscillometric device at the upper-arm. The device automatically triggers the measurements during the day (every 20 minutes) and during the night (every 1h). ABPM provides clinically relevant data, such as BP variability and nocturnal hypertension.

With more than two decades of available longitudinal data compiled on ambulatory patients, there is enough evidence to state that the best predictor of end-organ damage and cardiovascular events are the BP measurements at home, and in particular during sleep [6]. Based on this evidence, the EU and the US guidelines for the management of hypertension integrate now the systematic use of ABPM [1,2].

B. Fully Automated Cuffless BP Monitoring

Although ABPM has multiple advantages over other clinically used BP monitoring techniques, the measurement relies on the inflation of the cuff around the arm that causes patients discomfort and pain. This limitation leads to a reduced compliance and a lower number of measurements available per patient, in particular during the night [5,7-9]. There is thus a clear need for technologies to satisfy both patients and clinicians, capable of performing BP measurements accurately and seamlessly integrating into a patients' daily routine.

A new category of fully automated wrist-located cuffless devices is currently under development [3]. These devices give hope for widespread longitudinal day and night BP monitoring. Either based on semi-occlusive or non-occlusive sensing technologies, these devices will be the first of a kind, providing both day and night BP profiles without any lifestyle interference. However, when validating these devices, one should consider that the measurement may be taken at different body positions that will generate important hydrostatic pressure artifacts.

C. Posture-related BP changes and hydrostatic BP bias

The measurement of BP at body positions other than "sitting and relax" can have a major impact on the measured values:

- Posture-related BP changes: BP is intrinsically different at different body positions, *e.g.* it is normally higher while

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standing than when lying supine. While HBPM is supposed to eliminate this effect by normalizing the measurement conditions, ABPM reports the BP values in different positions, without necessarily providing position data for each measurement.

- Hydrostatic BP bias: at a given moment BP is also different at each segment of the arterial tree. In particular, in sitting or standing position, BP is lower at the level of the head and higher in the feet, due to the hydrostatic pressure effect. ABPM and HBPM at the upper arm are minimally affected by this phenomenon (the measurement location is always close to the heart level), HBPM at the wrist deals with this effect by requesting the patient to place the wrist "at the heart level". Note that a difference of 10 cm in height below the heart level corresponds to a BP increase of 7.5 mmHg.

Hydrostatic BP bias is thus an effect that will play a major role in the usability of fully automated cuffless BP monitors. In particular, for BP monitors that are located at the wrist, different arm positions will generate different BP readings even in situations where the underlying BP at the heart level was unchanged. While these readings might be locally accurate, they do not depict actionable clinical information as the BP values required to diagnose or treat a hypertensive patient. Figure 1 illustrates some typical measurement conditions of daily life that can lead to hydrostatic BP bias larger than 20 mmHg.

In order to be successfully integrated into current clinical practices, fully automated cuffless BP monitors must find a way to deal with the hydrostatic BP bias and accurately track the BP changes in different body postures. Posture-related BP changes are especially critical in the context of indirect BP measurement, such as pulse wave analysis (PWA) or pulse transit time (PTT). Indeed, the posture change affects the state of a vascular bed and there is a risk that, depending on the algorithm being used, the device is unable to track these changes accurately.

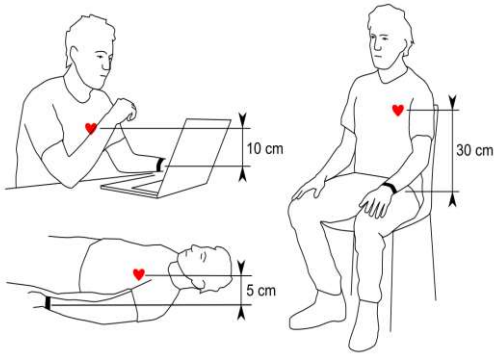

Figure 1: Three examples of the daily-life situations with the wrist below the heart level. The difference of height of 1 cm corresponds to a BP difference of 0.75mmHg, therefore the BP overestimation can be as high as 22 mmHg in the examples shown.

II. Design of an Experimental Protocol to Test Ambulatory BP Monitors at the Wrist

When it comes to validate the accuracy of BP monitors there are currently several standards and guidelines: the ISO81060-2 international standard [10], the IEEE1708 standard [11], and the ISO81060-3 draft international standard [12]. However, there are few, if any, details on how to practically assess cuffless devices' robustness in the ambulatory scenario, i.e. being able to accurately follow the BP changes due to posture change and being unaffected by hydrostatic bias. We suggest here a guidance on how to address the robustness to hydrostatic BP changes during a clinical validation.

A. Experimental protocol

During the clinical validation two devices should be used: a reference device (REF) that provides BP measurements at the heart level, and the device under test (DUT). It is important to note that the reference device should itself satisfy the requirements of being able to accurately track posture-related BP changes and be unaffected by hydrostatic bias. Then, during the data recording session(s), at least the following steps should be performed in addition to the ones described by the applicable standard:

0. Initialization: applicable only if the DUT is a calibrated device [3].
1. Baseline assessment: REF and DUT devices record BP in standard "sitting and relax" conditions [10].
2. BP change intervention: REF and DUT record BP while a physical or drug intervention is implemented in order to modify BP [12].
3. Body position intervention: REF and DUT record BP while subjects change their body position, including realistic scenarios foreseen by the intended use of the device, *e.g.* sitting, standing, lying, …
4. Hydrostatic bias intervention: while keeping the arm where REF is located in a standard measurement position, the arm where DUT is raised and/or lowered to different levels.

B. Data analysis

In addition to the data analysis procedures described in the applicable standard, the retrospective analysis of the collected data should at least include the following steps:

1. Analysis of the performance of the DUT to track the BP changes induced by using drug or physical interventions. It is important to report the amount of REF BP change that was actually induced during the intervention.
2. Analysis of the performance of the DUT to track the induced BP changes from changing body position.
3. Analysis of the ability of the DUT readings to remain stable (similar to the REF) during hydrostatic bias intervention.
4. Analysis of the acceptance rate of the DUT across the different experimental conditions. For most of the devices performing indirect BP estimations (*i.e.* based on PWA or PTT) some measurements are automatically discarded by the algorithms because the data are too noisy or corrupted by motion artifacts. Thus, the acceptance rate describes the percentage of actual measurements that the DUT successfully performs (independently of their accuracy).

III. Example of automaticity testing using the Aktiia automated and cuffless bracelet

A. Context

Aktiia SA is developing a fully automated wrist cuffless BP monitor. The Aktiia Bracelet relies on off-the-shelf optical sensors that perform green reflective photoplethysmography (PPG) measurements on the skin vasculature of the wrist. Figure 2 illustrates the size and shape of the device. From the recorded optical signals, a library of Optical Blood Pressure Monitoring (OBPM) algorithms infers systolic BP (SBP) and diastolic BP (DBP). The technical characteristics of the device have already been described [13], and several pilot investigations and clinical trials have been published [14-16]. Because the device is fully automated (no button needs to be pressed to perform a measurement) and generates no discomfort to the patient (optical readings), then Aktiia Bracelet is particularly well-suited for long-term day and night monitoring of patients in daily-life conditions.

B. Materials and methods

In order to test the full automaticity performance of Aktiia Bracelet a first pilot study was performed following the guidance described in this paper.

Ten healthy volunteers (5 males and 5 females) participated in a pilot study. The anthropological data describing the study population are reported in Table 1. After giving informed consent, the reflective PPG signals were recorded at the participant's left wrist with the Aktiia Bracelet and the reference signals were recorded with a volume-clamp device finger cuff positioned on the central phalange of a middle finger on the contralateral hand (Nexfin, BMEYE BV, The Netherlands). The choice of volume-clamp for this pilot study was made because of its capability to track beat-to-beat BP changes, and for its previous published results of BP variation tracking during body position changes [17].

According to the procedures described in Section II, the following measurement conditions were studied:

- sitting with both arms positioned on the table, at the heart level
- standing up with both arms positioned on a stable support, at the heart level
- lying supine
- sitting with both arms positioned on the table, at the heart level, while performing an isometric leg extension
- sitting with the right arm positioned on the lap, ~20 cm below the heart level

The PPG data were retrospectively analyzed using the Aktiia OBPM Library of Algorithms. The assessment of automaticity performance was implemented by evaluating whether the Aktiia Algorithm was accurate across different body positions and during BP changes induced by the procedures. Accordingly, the acceptance rates from different scenarios were calculated, and the means and standard deviations of the error between the Aktiia Algorithm BP estimates and the reference at each scenario were computed.

Figure 2.: Illustration of the Aktiia Bracelet: an Automated Cuffless BP monitor at the wrist produced by Aktiia SA.

C. Results

The acceptance rates of Aktiia Algorithm across the different body position and maneuvers are depicted in Figure 3. During the supine position the maximum percentage of measurements was achieved (for 67% of the available epochs Aktiia Algorithm could generate BP estimates), and during sitting-related positions an acceptance rate of ~50% was achieved. However, during the standing position, the minimum percentage of measurements was achieved: for only 27% of the available measurements the Aktiia Algorithm generated BP estimates. The known amount of motion artifacts during the standing position forces the Aktiia Algorithm to reject the PPG signals because of low reliability. The means and standard deviations of the error for DBP and SBP across different body positions are also provided in Figure 3.

It is important to note that:

- Concerning the standard deviation of the error for both DBP and SBP, all body positions and maneuvers except standing achieved similar performances. In the standing position the standard deviation of the error for SBP exceeded 10 mmHg.
- Concerning the mean of the error for both SBP and DBP, all body positions and maneuvers achieved similar performances. Important to note here is the non-biasing results achieved in the arm on lap position. Because in this position the arm was placed ~30 cm below the heart level one would expect a systematic and significant bias of ~20 mmHg

Table 1: Statistics on study population and achieved BP changes during the different interventions.

	Age (years)	**BMI (kg/m^2)**	**ΔSBP (mmHg)**	**ΔDBP (mmHg)**
Mean	31,18	22,62	29,15	19,13
SD	7,40	2,47	11,38	6,73
Range	25	7,93	38,30	19,52

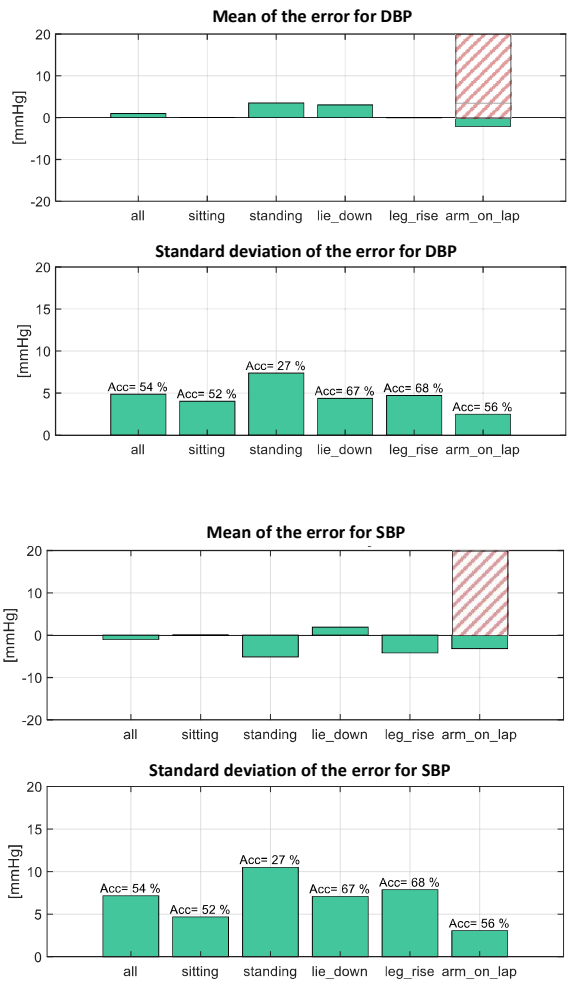

Figure 3: Upper panel, error distribution and acceptance rate (Acc) for different scenario for DBP. Lower panel, error distribution and acceptance rate on different scenario for SBP. The shaded red areas illustrate the hydrostatic bias that one would expect during the intervention "arm on the lap" in the case that Aktiia Algorithm was not robust to hydrostatic pressure changes (~ +20 mmHg).

D. Discussion

The results of this pilot study indicate that the Aktiia Algorithm is capable of generating accurate BP estimates, in particular during supine posture (67% of the time) and sitting-related positions (~50% of the time). As expected, the Aktiia Algorithm is only capable of generating BP estimates in the standing position a reduced percentage of time (~25%). The results also indicate that the Aktiia Algorithm is not affected by hydrostatic pressure perturbations induced by changes in arm position with respect to the heart level, with no significant bias observed when the measuring arm is lowered by ~20 cm below the heart level.

IV. Conclusion

In this work, we propose an experimental protocol for cuffless BP monitors at the wrist that addresses the challenges of the ambulatory environment in a controlled experimental setting. The protocol includes a BP change intervention, a body posture change intervention, and a hydrostatic bias intervention. In addition to reporting the accuracy metrics, it is important to report the acceptance rate of the device for each measuring condition. An example of the protocol implementation is provided by testing the performance of the Aktiia Bracelet device.

Cuffless wrist-based devices have a great potential to make ambulatory monitoring more appealing to the patients and provide the clinicians with a better BP profile on daily, weekly, and monthly scales. However, as a scientific community, we must be vigilant to validate these devices objectively. This protocol provides realistic testing of the performance of a cuffless wrist-based device and paves the way to improving the validation of similar devices in the future.

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