

Systolic peak foot-to-apex time interval, a novel oscillometric technique for systolic blood pressure measurement

Amir M. Benmira^{a,b}, Antonia Perez-Martin^{a,c}, Sarah Coudray^a, Iris Schuster^{a,c}, Isabelle Aichoun^a, Jérémy Laurent^a, Fethi Bereski-Reguig^b, and Michel Dautat^{a,c}

Background: Noninvasive blood pressure (BP) measurement is essential for the study of human physiology but automatic oscillometric devices only estimate SBP and DBP using various, undisclosed algorithms, precluding standardization and interchangeability. We propose a novel approach by tracking, during pneumatic cuff deflation, the time interval from the foot to the apex of the systolic peak of the oscillometric signal, which reaches a maximum concomitant with the first Korotkoff sound.

Method: In 145 study participants and patients (group 1), we measured the systolic brachial artery blood pressure by Korotkoff sound recording, conventional oscillometry, and our fully automated systolic peak foot-to-apex time interval (SFATI) technique. In 35 other patients (group 2), we compared SFATI with intra-arterial measurement.

Results: In group 1, the concordance correlation coefficient was 0.989 and 0.984 between SFATI and Korotkoff sounds, 0.884 and 0.917 between oscillometry and Korotkoff sounds, and 0.882 and 0.919 between SFATI and oscillometry, respectively, on the left and right arm. In group 2, it was 0.72 between SFATI and intra-arterial measurement, 0.67 between oscillometry and intra-arterial measurement, and 0.92 between SFATI and Korotkoff sounds. In 40 study participants, the reproducibility study yielded a concordance coefficient of 0.95 for SFATI and 0.94 for Korotkoff sounds.

Conclusion: SFATI BP measurement shows an excellent concordance with the auscultatory technique, offering a major improvement over current oscillometric techniques and allowing standardization.

Keywords: auscultation, automation, Korotkoff sounds, noninvasive measurement, oscillometry, SBP

Abbreviations: CCC, Lin concordance correlation coefficient; CVRF0, group of subjects without cardiovascular risk factor or disease; CVRF1, group of subjects with one cardiovascular risk factor or disease; CVRF>1, group of subjects with several cardiovascular risk factor or disease; DBP, diastolic blood pressure; DBP_K, DBP measured by the auscultation technique; DBP_{osc}, DBP measured by conventional oscillometry; MBP, mean blood pressure; MBP_{osc}, mean blood pressure measured by conventional oscillometry; NIBP, noninvasive blood pressure measurement; OMWE, oscillometric waveform envelope;

Pad1, arm cuff pressure corresponding to the first maximum of the systolic peak foot-to-apex time interval; PAT, pulse arrival time; SBP_{IA}, SBP measured by radial artery catheter; SPB_K, SBP measured by the auscultation technique; SPB_{osc}, SBP measured by conventional oscillometry; SFATI, systolic peak foot-to-apex time interval measurement technique; t_{ad1} , time at which the systolic peak apex delay reaches its first maximum; t_{f-a} , time from the foot to the apex of the oscillometric waveform systolic peak

INTRODUCTION

Blood pressure (BP) is not only the most often measured variable in the clinical setting, but also an essential tool for human physiology research. Automatic oscillometric devices are now recommended by several scientific societies or leagues [1–3] for noninvasive BP measurement (NIBP). However, although they provide clinically acceptable values of mean arterial BP (MBP), they only estimate SBP and DBP. They are validated by comparison with the auscultation of Korotkoff sounds (International Organization for Standardization ISO 81060–2:2013) [4,5]. Oscillometric measurements are commonly based on the amplitude of the systolic oscillations recorded in the pneumatic arm cuff during its deflation, drawing the oscillometric waveform envelope (OMWE). The cuff pressure corresponding to the maximum OMWE amplitude is generally admitted as MBP [6]. SBP and DBP were initially read at fixed percentages (or ratios) of the OMWE

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^aVascular Medicine and Laboratory, Nimes University Hospital, Nimes, France, ^bBiomedical Engineering Laboratory, Faculty of Technology, Aboubekr Belkaid University, Tlemcen, Algeria and ^cResearch Unit (Female characteristics of dysfunctions of vascular interfaces), Montpellier University, Montpellier, France

Correspondence to Professor Michel Dautat, Vascular Medicine and Laboratory, Nimes University Hospital, Place du Professeur Robert-Debré, 30029 Nimes, France. Tel: +33 (0) 4 66 28 33 13; fax: +33 (0) 4 66 02 81 38; e-mail: michel.dautat@univ-montp1.fr

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maximum amplitude, with multiple causes of error [7,8]. The OMWE shape is highly variable, depending on cardiac rhythm, movement artifacts, respiration, cuff size [9,10], deflation rate [11], and so on, which contributes to over or underestimation of the actual SBP and DBP in proportions that largely depend on the NIBP device and its algorithms [12]. Many different approaches have been proposed to improve the oscillometric determining of SBP and DBP, and have been thoroughly reviewed by Forouzanfar *et al.* [13]. The diversity of techniques and ongoing research illustrate the limits and pitfalls of current oscillometric devices, especially for SBP and in patients with increased arterial wall stiffness [14–16].

As automatic oscillometric devices use undisclosed algorithms that change over time with technical improvements, they are not interchangeable [6], and the auscultation method remains the usual clinical reference, whereas direct intra-arterial measurement is the gold standard [6].

Analyzing the oscillometric waveform changes during cuff deflation, we observed that the time interval from the onset (foot) to the apex of the SBP pulse peak [time from the foot to the apex of the oscillometric waveform systolic peak (t_{f-a})] increases and reaches a maximum concomitant with the first Korotkoff sound, as a result of constant although variable changes in the shape of the systolic peak in relation to reflected waves (Fig. 1). Moreover, in some study participants, t_{f-a} shows a second increase in the vicinity of MBP. Therefore, we built an algorithm using the systolic peak foot-to-apex time interval (SFATI) for the fully automated reading of SBP, and we performed a prospective observational clinical study for its comparison with the auscultation of Korotkoff sounds and conventional oscillometry in 145 study participants and patients (group 1), and with direct intra-arterial measurement in 35 patients (group 2) from the ICU.

MATERIAL AND METHODS

To test our SFATI technique in field conditions, we included study participants without and with cardiovascular diseases or risk factors (tobacco, systemic arterial hypertension, coronary disease, lower limb obstructive arterial disease, diabetes, chronic renal failure) in four age ranges: 18–30, 30–50, 50–70, and more than 70 years (Table 1). BP measurements were performed in the supine position after a 10-min rest. The only noninclusion criteria were: study participant unwilling or unable to provide an informed consent, or both upper limbs unavailable for measurement.

Additionally, we included 35 consecutive ICU patients with continuous direct intra-arterial BP monitoring via a radial artery catheter. Noninclusion criteria were unstable hemodynamic status, hypothermia less than 35.5°C, PaCO₂ more than 60 mmHg, severe bradycardia, or contralateral upper limb not available for the pneumatic cuff. Patients unwilling or unable to provide an informed consent (except for ICU patients) were not included.

The study protocol was approved by the Institutional Review Board (approval #15/05.04, 5 May 2015), which did not require consent for ICU patients.

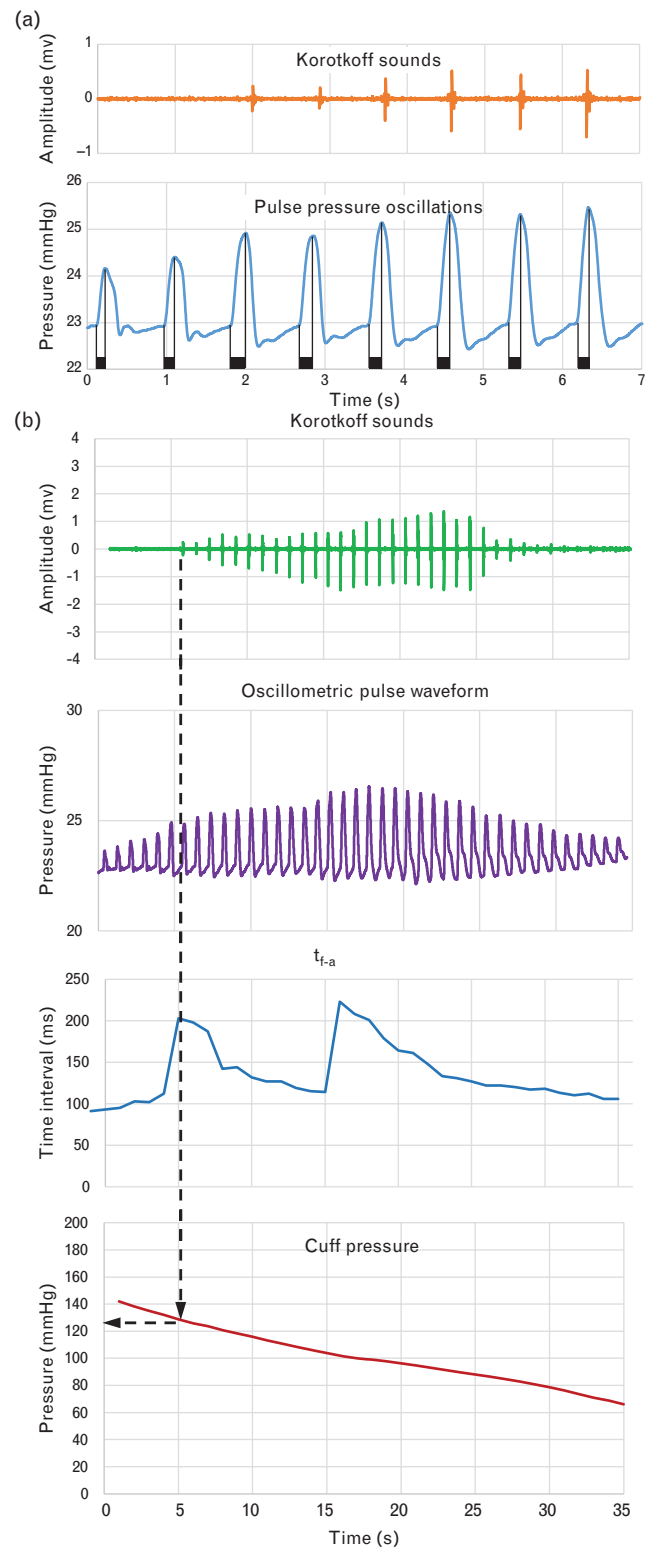


FIGURE 1 Korotkoff sounds, oscillometric pulse pressure waveform, and systolic peak foot-to-apex time interval (t_{f-a}) changes during cuff deflation (from study participant #46). (a) Changes in t_{f-a} at the appearance of Korotkoff sounds. (b): The Korotkoff sounds, the oscillometric pulse pressure waveform, the t_{f-a} curve, and the cuff pressure during deflation. SBP is measured at the time of the first t_{f-a} maximum. t_{f-a} , time from the foot to the apex of the oscillometric waveform systolic peak.

TABLE 1. Population sample description

	Whole population sample	No cardiovascular risk factor	One cardiovascular risk factor	> 1 cardiovascular risk factor
<i>n</i>	145	53	51	41
Sex ratio (M/F)	68/77	24/29	25/26	19/22
Age (years)	18–88; 45 (27–59)	21–62; 29 (25–47)	18–88; 49 (34.5–60.5)	18–83; 58 (41–71)
BMI (kg/m ²)	15.3–56.0; 24.2 (21.4–26.5)	16.8–36.7; 22.5 (20.1–25.0)	15.3–41.5; 25.7 (22.0–27.4)	17.1–56.0; 25.1 (22.1–28.1)
SBP _{osc} (mmHg)	62–223; 117 (110–133)	98–139; 113 (107–121)	90–223; 121 (111–143)	62–215; 125 (117–148)
DBP _{osc} (mmHg)	37–108; 73 (66–81)	53–86; 71 (66–77)	54–104; 74 (65–84)	37–108; 78 (69–87)
MBP _{osc} (mmHg)	42–139; 93 (77–93)	67–92; 82 (74–87)	61–139; 87 (79–98)	42–131; 93.5 (83–108)

SBP_{osc}, DBP_{osc}, MBP_{osc}, SBP, DBP, and mean systemic arterial blood pressure measurement by conventional oscillometry on the right arm. Results are provided as range and median (first to third quartile).

We used a MP35 data acquisition unit (Biopac, Aero Camino Goleta, California, USA) to record the Korotkoff sounds with a Biopac SS30L electronic stethoscope and the arm cuff pressure with a DPT-6000 pressure transducer (CODAN, Lensahn, Germany) calibrated with a Biomedical ProSim 8 vital signs simulator (Fluke, Everett, Washington, USA). The MP35 unit provided analog to digital (A/D) conversion with 24-bit resolution, at 1k samples/s for each channel, with a nominal signal/noise ratio greater than 89dB. The unfiltered direct current (DC) signal was recorded for cuff pressure measurement. The bandpass was set at 0.5–500 Hz for Korotkoff sounds and 0.5–30 Hz for cuff pressure oscillations. Depending on the study participant arm dimensions, we used either a 25.3–34.3 cm wide Adult-11 (Welch-Allyn, Skaneateles, New York, USA) or a 17–25, 23–33, or 31–40 cm wide Dura-Cuf (Critikon, Tampa, Florida, USA) pneumatic arm cuff. Signals were displayed and processed with Biopac Acqknowledge V4.2. Further signal analyses and calculations were performed using Matlab V7.1 (Mathworks, Natick, Massachusetts, USA). Korotkoff sounds were identified automatically on the recording after noise rejection using a threshold at 5% of the maximum amplitude. SBP (SBP_K) and DBP measured by the auscultation technique (DBP_K) were then read automatically on the recorded arm cuff pressure curve at the appearance and disappearance of the Korotkoff sounds.

With the pneumatic cuff wrapped around the arm and the electronic stethoscope installed immediately below the cuff along the brachial artery course, we proceeded to BP measurement during manual cuff deflation (at 2–3 mmHg/s) and recorded the whole procedure. In 20 study participants without and 20 study participants with cardiovascular risk factors or diseases, we repeated the measurement a few minutes later for reproducibility assessment. During the same session, we also measured oscillometric SBP (SBP_{osc}), DBP (DBP_{osc}), and MBP (MBP_{osc}) with a Dinamap ProCare 300 system (GE Healthcare, Chicago, Illinois, USA) on both arms.

In ICU patients, the DPT-6000 pressure transducer used to monitor intra-arterial BP was temporarily disconnected from the monitoring system and connected to the MP35 system for simultaneous recording with Korotkoff sounds and cuff pressure from the contralateral arm.

On the recorded signal, we first calculated the second derivative of the cuff pulse pressure (PP) waveform to identify and delineate each cardiac cycle whatever the pulse amplitude. We then removed, on this second derivative, all peaks the amplitude of which was under an empirically determined ratio of the mean amplitude of positive and negative peaks, respectively, to reject noise and identify, on the remaining peaks, the onset (foot) of the systolic peak and its apex, allowing measurement of the time from the foot to the apex of the oscillometric waveform systolic peak (t_{f-a}). The algorithm tracked t_{f-a} changes during cuff deflation and identified the time [time at which the systolic peak apex delay reaches its first maximum (t_{ad1})] and the corresponding pressure [arm cuff pressure corresponding to the first maximum of the systolic peak foot-to-apex time interval (P_{ad1})] of its first maximum value, then detected the occasional occurrence of a second maximum value (Fig. 1).

TABLE 2. SBP measured by conventional oscillometry, SBP measured by the auscultation technique, and arm cuff pressure corresponding to the first maximum of the systolic peak foot-to-apex time interval values of brachial artery SBP in the whole population sample

	Right arm			Left arm		
	P _{ad1}	SBP _K	SBP _{osc}	P _{ad1}	SBP _K	SBP _{osc}
Maximum	217.0	221.0	223.0	190.0	187.0	215.0
75% percentile	137.0	136.0	133.0	135.0	136	136.0
Median	119.0	119.0	117.5	118.0	118.0	116.0
25% percentile	107.0	109.0	109.8	105.0	105	107.0
Minimum	64.0	64.0	62.0	89.0	85.0	68.0
n	140	139	138	132	133	133

P_{ad1}, arm cuff pressure corresponding to the first maximum of the systolic peak foot-to-apex time interval; SBP_K, SBP measured by automatic reading of Korotkoff sounds; SBP_{osc}, SBP measured by conventional oscillometry.

In ICU patients, we measured the intra-arterial SBP (SBP_{IA}) and DBP corresponding to the cardiac cycle at which the Korotkoff sounds, respectively, occurred and disappeared.

Statistical analysis

Data were tested for distribution normality with the d'Agostino and Pearson omnibus normality test. Results were expressed as mean \pm SD for continuous variables with normal distribution, median (first to third quartiles) for the others. Techniques were compared by linear regression with Pearson r^2 (for normally distributed variables) or Spearman r (for nonnormally distributed variables) calculation, Bland and Altman analysis with bias, and Lin concordance correlation coefficient (CCC) with two-sided confidence intervals. Strength of agreement was considered poor if CCC less than 0.90, moderate if CCC 0.90–0.95, substantial if CCC 0.95–0.99, and almost perfect if CCC at least 0.99. Intraobserver reproducibility was assessed by CCC. Comparisons between study participants without (group CVRF0), with one (CVRF1), or with more than one (CVRF>1) cardiovascular risk factors or disease were performed by analysis of variance (ANOVA) with the Kruskal–Wallis test. Comparisons between study participants with or without cardiovascular risk factors or disease for categorical variables were performed with the Fisher's exact test. Results were considered significant for P less than 0.05. Statistical analysis was performed with Prism V5.0 (GraphPad, La Jolla, California, USA), and CCC was calculated online at <http://www.niwa.co.nz/services/statistical>.

RESULTS

We included 145 study participants, of whom 53 had none, 51 had one, and 41 had more than one cardiovascular risk factors or disease: 31 were smokers, 49 had hypertension, 39 had diabetes, 12 had chronic kidney disease (of whom four required hemodialysis), seven had peripheral artery disease, and one had coronary disease (Table 1). In 19 study participants, one upper limb was not available for measurement (for instance, the arm with the arteriovenous fistula in hemodialysis patients). P_{ad1} measurement was feasible in all study participants. Oscillometry failed in one patient because of arrhythmia. In the whole population sample, none of the measured variable passed the normality test except right DBP_{osc}. In study participants without cardiovascular risk factor, all variables passed normality test

except age, BMI, right MBP, P_{ad1}, and t_{ad1}. In study participants with one single cardiovascular risk factor, only age, left and right SBP_K, and left and right P_{ad1} passed normality test. In study participants with more than one cardiovascular risk factor, BMI, right SBP_{osc}, and right and left t_{ad1} did not pass the normality test. Therefore, pressure values are presented here as median (first to third quartile) for consistency (Table 2).

Agreement between P_{ad1} and SBP_K (Fig. 2a) was close to 0.99 in the whole population sample and in study participants with one or more cardiovascular risk factors, and moderate (on the right side) to substantial (on the left side) in study participants without cardiovascular risk factor (Table 3). Agreement between P_{ad1} and SBP_{osc} (Fig. 2b) and between SBP_K and SBP_{osc} (Fig. 2c) was generally poor but reached moderate level on the right side in the whole population sample and in study participants with one or more cardiovascular risk factor and on the left side in study participants with one cardiovascular risk factor (Table 3).

The t_{f-a} value at its first maximum was greater in study participants with one or more than in study participants without cardiovascular risk factor ($P < 0.0001$; Table 4). Linear regression showed a significant correlation of t_{ad1} with SBP_K ($P < 0.0001$, $r^2 = 0.19$ and $P < 0.0001$, $r^2 = 0.12$), but not with DBP_K ($P = 0.11$, $r^2 = 0.07$ and $P = 0.79$, $r^2 = 0.002$), SBP_{osc} ($P < 0.055$, $r^2 = 0.10$ and $P < 0.099$, $r^2 = 0.003$), DBP_{osc} ($P < 0.06$, $r^2 = 0.098$ and $P = 0.53$, $r^2 = 0.012$), and MBP_{osc} ($P < 0.078$, $r^2 = 0.089$ and 0.89 , $r^2 = 0.0007$), respectively, on the right and the left side. ANOVA showed significant differences in right and left t_{ad1} between the CVRF0, CVRF1, and CVRF>1 groups ($P < 0.0001$ for all).

The second t_{f-a} maximum was present on one or both sides in 11 out of 53, 40 out of 51, and 34 out of 41 study participants, respectively, without, with one, and with more than one cardiovascular risk factors ($P < 0.0001$). It was present in six out of 84 study participants under 50 years old and in 47 out of 61 study participants 50 years old or older ($P < 0.0001$; Fig. 3). It was present in five out of 41 and 27 out of 43 study participants under 45 years old, and in six out of 12 and 47 out of 49 study participants 50 years old or older, respectively, without and with one or more cardiovascular risk ($P < 0.0001$).

The intraobserver reproducibility study yielded CCC of 0.95 (0.92–0.98) for P_{ad1} and 0.94 (0.89–0.96) for SBP_K.

In ICU patients, SBP_{IA}, SBP_K, and P_{ad1} were normally distributed. Agreement was moderate between P_{ad1} and

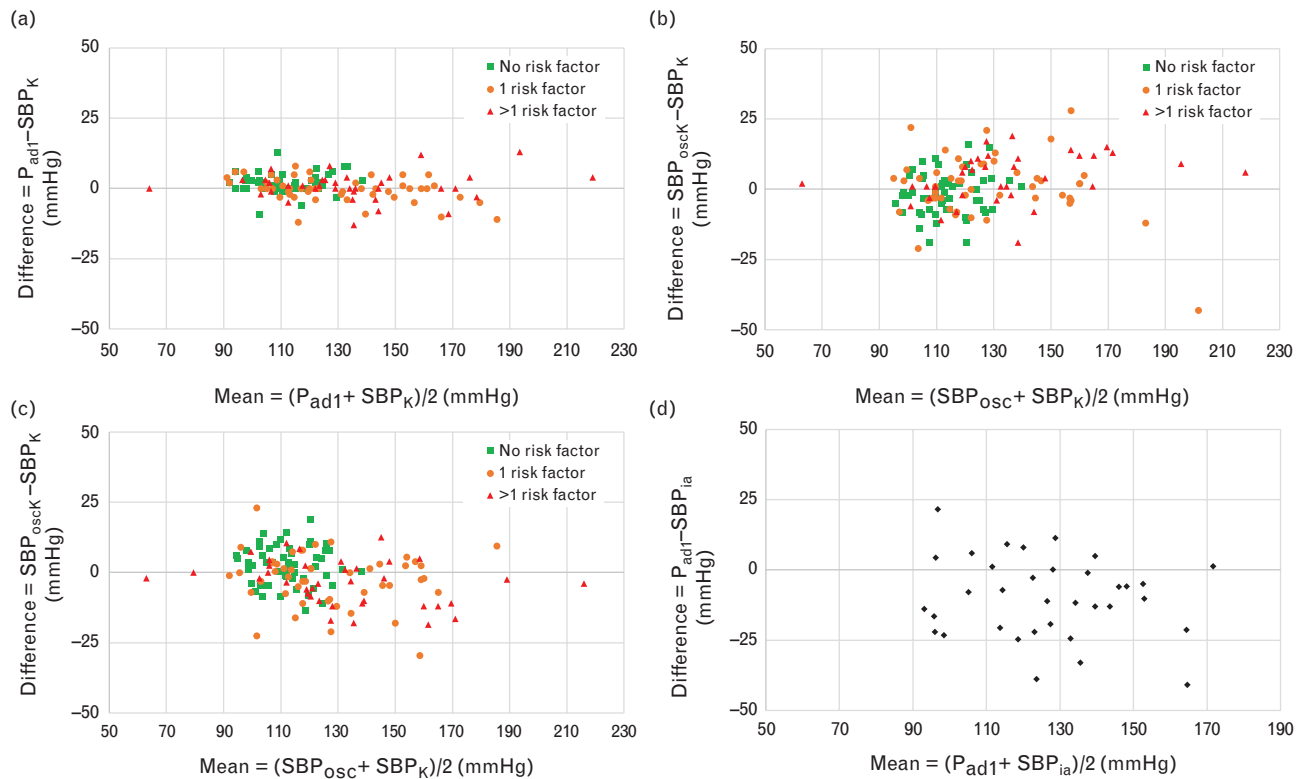


FIGURE 2 Bland and Altman plot of SBP measurement by the different techniques (right arm). (a) Systolic peak apex delay technique (P_{ad1}) vs. automatic reading of Korotkoff sounds (SBP_K). (b) Oscillometry (SBP_{osc}) vs. automatic reading of Korotkoff sounds (SBP_K). (c) P_{ad1} vs. oscillometry (SBP_{osc}). (d) P_{ad1} vs. direct intra-arterial measurement (SBP_{ia}). P_{ad1} , arm-cuff pressure corresponding to the first maximum of the systolic peak foot-to-apex time interval; SBP_K , SBP measured by the auscultation technique; SBP_{osc} , SBP measured by the oscillometry technique; SBP_{ia} , SBP measured by radial artery catheter.

SBP_K (Fig. 2d), but poor between P_{ad1} and SBP_{ia} as well as between SBP_{osc} and SBP_K (Table 5).

DISCUSSION

Systolic blood pressure measurement

In all study participants and patients, t_{f-a} showed a maximum whose occurrence during cuff deflation closely corresponded to the first Korotkoff sound, allowing fully automated SBP measurement with almost perfect correlation with the auscultatory technique. Moreover, study participants older and/or with cardiovascular risk factors showed not only a prominent first t_{f-a} increase, but also a second increase that was absent in most younger study participants and in study participants without cardiovascular risk factor. When compared with the auscultatory technique, P_{ad1} yielded much better results than oscillometry.

The arterial wall compliance depends on the transmural pressure, that is, in this setting, the difference between the intra-arterial BP and the pressure of surrounding tissues, which can be approximated to the cuff pressure. The transmural pressure is negative, keeping the artery closed, as long as the cuff pressure remains greater than the intra-arterial pressure. It decreases during cuff deflation and reaches a minimum when the intra-arterial pressure equates the cuff pressure, that is, at the exact time at which the first Korotkoff sounds occur, with the brachial artery compliance at its maximum. It then becomes positive, the PP overcoming the cuff pressure. The fact that t_{ad1} also reaches

its maximum at this exact time suggests that it is related to the same arterial wall mechanisms and characteristics as Korotkoff sounds.

Our SFATI technique must be compared with other techniques both from the technical and from the performance point of view.

Technical comparison

Conventional oscillometry relies on the OMWE amplitude and shape, considering that its maximum amplitude corresponds to MBP and using coefficients or algorithms (that can be quite different from one device to the other) to estimate SBP and DBP. Approximating the OMWE along line(s) of best fit, or using a probabilistic approach, has been proposed to improve this estimation [17]. Using the OMWE derivative allows avoiding empirical coefficients but is still prone to artifacts. Neural networks have also been used to learn from large datasets to separately estimate SBP and DBP, or to extract the characteristic features of the OMWE [17]. Mathematical models have been built as a basis for new algorithms tracking the effects of cuff pressure on transmural pressure, depending on arterial wall biomechanics and BP. These models allow developing better algorithms but still rely on a limited set of actually measured data [17].

The oscillometric waveform itself conveys hemodynamic information [18], whereas the OMWE is prone to artifacts and multiple influences [14–16,19]. Mafi *et al.* [20,21] looked at the PP waveform modulation and the

TABLE 3. Correlations between SBP measured by conventional oscillometry, SBP measured by the auscultation technique, and arm cuff pressure corresponding to the first maximum of the systolic peak foot-to-apex time interval values of SBP

Comparison	Lin CCC ρ_c	Two-sided 95% confidence interval	Pearson r^2	Bias (95% limits of agreement)
Whole population sample (n = 145)				
Right side				
P _{ad1} vs. SBP _K	0.984	0.977–0.988	0.969	0.83 (–7.60 to 9.26)
SBP _{osc} vs. SBP _K	0.917	0.886–0.940	0.844	0.90 (–17.62 to 19.41)
P _{ad1} vs. SBP _{osc}	0.919	0.888–0.941	0.847	–0.07 (–18.83 to 18.68)
Left side				
P _{ad1} vs. SBP _K	0.989	0.985–0.992	0.980	–0.30 (–6.24 to 6.85)
SBP _{osc} vs. SBP _K	0.884	0.841–0.916	0.784	–0.64 (–20.80 to 22.09)
P _{ad1} vs. SBP _{osc}	0.882	0.837–0.915	0.776	–0.37 (–22.45 to 21.72)
Study participants without cardiovascular risk factor (n = 53)				
Right side				
P _{ad1} vs. SBP _K	0.939	0.899–0.964	0.910	1.89 (–4.81 to 8.59)
SBP _{osc} vs. SBP _K	0.755	0.613–0.850	0.585	–1.53 (–16.34 to 13.28)
P _{ad1} vs. SBP _{osc}	0.750	0.611–0.844	0.622	3.42 (–10.26 to 17.09)
Left side				
P _{ad1} vs. SBP _K	0.953	0.921–0.972	0.916	0.85 (–6.57 to 8.27)
SBP _{osc} vs. SBP _K	0.654	0.467–0.785	0.438	–1.33 (–20.29 to 17.63)
P _{ad1} vs. SBP _{osc}	0.638	0.450–0.772	0.427	2.12 (–17.85 to 22.08)
Study participants with one cardiovascular risk factor (n = 51)				
Right side				
P _{ad1} vs. SBP _K	0.984	0.973–0.990	0.973	–0.24 (–8.75 to 8.27)
SBP _{osc} vs. SBP _K	0.892	0.819–0.936	0.806	–1.16 (–20.86 to 23.19)
P _{ad1} vs. SBP _{osc}	0.896	0.823–0.940	0.806	–1.43 (–23.76 to 20.90)
Left side				
P _{ad1} vs. SBP _K	0.991	0.984–0.995	0.984	–0.18 (–6.88 to 6.53)
SBP _{osc} vs. SBP _K	0.933	0.886–0.962	0.890	2.38 (–15.70 to 20.45)
P _{ad1} vs. SBP _{osc}	0.936	0.887–0.964	0.886	–2.56 (–20.78 to 15.67)
Study participants with more than one cardiovascular risk factor (n = 41)				
Right side				
P _{ad1} vs. SBP _K	0.985	0.972–0.992	0.972	–0.75 (–9.23 to 10.73)
SBP _{osc} vs. SBP _K	0.947	0.904–0.972	0.925	–4.11 (–12.47 to 20.69)
P _{ad1} vs. SBP _{osc}	0.947	0.901–0.972	0.915	–3.36 (–20.43 to 13.71)
Left side				
P _{ad1} vs. SBP _K	0.995	0.991–0.997	0.990	0.11 (–4.49 to 4.72)
SBP _{osc} vs. SBP _K	0.834	0.702–0.911	0.705	1.28 (–26.26 to 28.82)
P _{ad1} vs. SBP _{osc}	0.829	0.691–0.909	0.696	–1.17 (–29.21 to 26.87)

LinCCC, concordance correlation coefficient; P_{ad1}, SBP measured by the systolic peak foot-to-apex time interval technique; SBP_K, SBP measured by automatic reading of Korotkoff sounds; SBP_{osc}, SBP measured by conventional oscillometry.

maximum upslope of the systolic peak to improve NIBP. Some authors investigated the advantages of simultaneously recording ECG. Its first benefit is to get additional information, especially the pulse arrival time (PAT), which is inversely correlated with arterial wall stiffness. Ahmad *et al.* [22] showed that PAT follows the same pattern as OMWE during cuff deflation, and can be used conjointly to improve SBP and DBP estimation.

Our SFATI technique does not rely on the OMWE and MBP determination but on the time-domain analysis of the pulse waveform for immediate SBP assessment. It appears

intrinsically different of all previously published approaches, although it is in line with the works of Forouzanfar *et al.* [17] or Mafi *et al.* [20], and may be related to PAT and pulse transit time studies [22].

Performance comparison

Comparison with the auscultatory technique is required for validation of oscillometric devices, but results, when published, are generally reported as required to meet the international ISO standard (the mean value of the difference between oscillometric and auscultatory measurements repeated at least three times in each study participants must be within ± 5 mmHg with a SD < 8 mmHg; International Standard ISO 81060–2:2013) rather than as CCC. Auscultation is typically performed by two independent observers listening from the same stethoscope bell. Compared with Korotkoff sounds, oscillometry tends to overestimate SBP and underestimate DBP [23] or yield variable results [8,24,25], but has been reported to overestimate both SBP and DBP in study participants with increased arterial wall stiffness [16]. Landgraf *et al.* [26] observed that discrepancies between oscillometry and auscultation were greater in older study participants.

TABLE 4. Foot-to-apex time interval time at which the systolic peak apex delay reaches its first maximum depending on the number of cardiovascular risk factors

Number of cardiovascular risk factors	t _{f-a} (ms) right arm	t _{f-a} (ms) left arm
Any	124 (115–215)	126 (115–200)
None	118 (111–125)	121 (114–126)
One	154 (115–234)	149 (114–228)
More than one	175 (118–234)	167 (124–227)

Results are provided as median (lower–upper quartile). t_{f-a}, systolic peak foot-to-apex time interval.

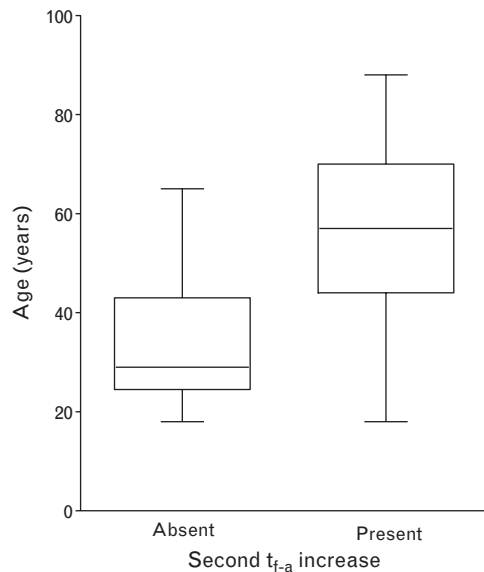


FIGURE 3 Age of study participants without or with a second increase of the t_{f-a} . Box and whiskers plots (the box limits are first to third percentile; the horizontal line is the median, the whiskers cover the range). t_{f-a} , time from the foot to the apex of the oscillometric waveform systolic peak.

Given the multitude of available oscillometric devices, their constant evolution, and the fact that they use undisclosed algorithm, generalization is impossible and a given study only allows conclusions about the sole devices it compares [27]. We used a widely used and validated oscillometric device, but our comparison results apply only to this specific device and cannot be extrapolated to oscillometry as a whole. Nevertheless, in a relatively large and diverse population sample, our SFATI technique yielded unparalleled correlation with Korotkoff sounds for SBP measurement, particularly in elderly study participants and/or study participants with cardiovascular risk factors or diseases. This is fortunate, as medical devices are expected to provide reliable results not only in healthy study participants but also and above all in patients.

In ICU patients, P_{ad1} showed poor (minimally better than Korotkoff sounds) correlation with direct intra-arterial measurement. Auscultation as well as oscillometry are known to be poorly correlated with direct intra-arterial BP measurement. Auscultation underestimated SBP and overestimated DBP [28], whereas oscillometry underestimated SBP and either over or underestimated DBP in lean and overweight critically ill patients [28–30]. In 301 patients, Mireles *et al.* [31] reported Pearson r values of 0.68, 0.67, and 0.62 when comparing oscillometric with intra-arterial measurement of SBP, DBP, and MBP, respectively.

Comparing auscultation and oscillometry with intra-arterial BP in 50 ICU patients, Ribezzo *et al.* [32] also reported poor agreement, especially for SBP, with a Pearson r ranging from 0.82 to 0.88.

Such differences between direct intra-arterial measurement and either auscultation or oscillometry should not be surprising, as the former measures BP itself, whereas the latter only indirectly assess its buckling effects on the arterial wall and the resulting flow disturbance. In other words, noninvasive measurements are mediated by the arterial wall, and, as such, depend on its biomechanics.

Our results in ICU patients did not yield better correlation between oscillometry and intra-arterial measurement than reported in the literature, but P_{ad1} was still closely correlated to SBP_K . This confirms that the first t_{f-a} increase during cuff deflation shares common mechanisms with the production of Korotkoff sounds and arterial wall motion. As such, it should be affected by changes in arterial wall stiffness, which our results indeed suggested.

Systolic peak foot-to-apex time interval and the arterial wall

In our study, older study participants and study participants with cardiovascular risk factors or disease not only showed a prominent first t_{f-a} increase, but also showed a second increase that was absent in most younger study participants and in study participants without cardiovascular risk factor or disease. This second t_{f-a} increase is probably related to distal pulse wave reflection, as it occurs when the brachial artery remains open during a larger part of the cardiac cycle, and is prominent in older study participants and study participants with cardiovascular risk factors in whom distal wave reflection is known to be increased. Cuff inflation reduces the brachial artery transmural pressures, which slows down and dampens the pulse wave. At lower cuff pressure, the pulse wave succeeds reaching the distal part of the cuff and propagates downstream, allowing distal reflection to occur and prolong the systolic peak.

Forouzanfar *et al.* [17] mathematically modeled the pulse transit time as a function of the arterial lumen changes under the cuff and showed that it can be used for a coefficient-free assessment of SBP, MBP, and DBP. Also using a mathematical model, Liu *et al.* [7] demonstrated that calculating SBP and DBP from the oscillometric envelope with fixed ratios measurement produces errors that increase when the arterial wall stiffens and/or the PP increases. Differences between oscillometric and auscultatory BP measurements are indeed greater in study participants with increased arterial wall stiffness [16], and have been proposed as an indicator of arterial stiffness, predictive of coronary lesions [33]. It is therefore all the more interesting

TABLE 5. Comparison between arm-cuff pressure corresponding to the first maximum of the systolic peak foot-to-apex time interval, SBP measured by radial artery catheter, and SBP measured by the auscultation technique in ICU patients ($n = 35$)

Comparison	ρ_c	Pearson r^2	95% CI	Bias (95% limits of agreement)	Difference (mmHg) Mean \pm SD
P_{ad1} vs. SBP_{IA}	0.72 (0.54–0.84)	0.80	0.64–0.89	–9.94 (–38.0 to 18.1)	–9.9 \pm 14.3
SBP_K vs. SBP_{IA}	0.67 (0.47–0.80)	0.77	0.58–0.87	–12.2 (–42.9 to 18.5)	12.2 \pm 15.7
P_{ad1} vs. SBP_K	0.92 (0.85–0.96)	0.93	0.86–0.96	–2.26 (–14.2 to 18.7)	2.3 \pm 8.4

CI, confidence interval; P_{ad1} , arm-cuff pressure corresponding to the first maximum of the systolic peak foot-to-apex time interval; SBP_{IA} , SBP measured by radial artery catheter; SBP_K , SBP measured by the auscultation technique; ρ_c , Lin CCC: Lin concordance correlation coefficient (lower and upper two-sided CI).

that our technique yielded its best correlation with Korotkoff sounds in older study participants and in study participants with cardiovascular risk factors.

The t_{f-a} changes we observed were significantly related to age and cardiovascular risk factors. This is another clue pointing at the arterial wall biomechanics as involved in both Korotkoff sounds and t_{f-a} changes. The relationship between t_{f-a} and arterial wall stiffness deserves further clinical investigation.

Limitations

Although we referred to the ISO validation procedure for oscillometric devices, we did not fulfill all of its requirements, especially regarding the distribution of limb circumference in the population sample. On the other hand, our sample was greater than the required number of study participants (180 vs. 85). Instead of asking two independent observers to listen to Korotkoff sounds, we used an electronic stethoscope, thus allowing automatic reading and providing objective records. Cuff deflation was manually controlled, at a 2–3 mmHg/s rate, and should be automatic and linear for greater convenience in routine clinical practice. We used a validated, widely available automatic oscillometric device for comparison, but the SFATI and oscillometric measurements, although performed during the same session, were not strictly simultaneous, which may partly explain the differences we observed, because of BP variability. Nevertheless, repeated P_{ad1} as well as SBP_K measurements during the same session showed substantial reproducibility. Anyhow, as current oscillometric devices often use undisclosed algorithms and are not standardized, we cannot generalize our findings [27].

In ICU patients, we performed NIBP measurement at the arm, whereas intra-arterial measurement was performed via a radial artery catheter on the contralateral side, which may also explain a difference. Nevertheless, this would have resulted in a systematic bias, which was not apparent in our study.

In conclusion, using time-domain analysis of the PP waveform instead of the amplitude of the oscillometric envelope, we designed SFATI, an innovative, straightforward, fully automated method for the measurement (rather than estimation) of SBP, obtaining almost perfect correlation with Korotkoff sounds. This easily implemented SFATI algorithm can be used as a complement of the algorithms currently used for MBP assessment and would overcome the main limitation of current oscillometric devices by providing accurate SBP results and allowing their long awaited standardization. We are now looking forward for the independent replication of our study and further investigation of its potential interest for the assessment of the arterial wall biomechanics.

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ORCID number: A.M.B., 0000 0002 8785 293X; A.P.-M.; 0000 0002 8527 7783; S.C., 0000 0002 6110 2583; I.S., 0000 0002 8735 4308; I.A., 0000 0002 1892 7256; J.L., 0000 0002

1853 2721; F.B.-R., 0000 0002 5788 6055; M.D., 0000 0002 9496 3857.

Conflicts of interest

There are no conflicts of interest.

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Reviewers' Summary Evaluation

Referee 1

Systolic blood pressure (SBP) was measured by means of a novel oscillometric technique and was found to have high correlation coefficient with SBP reading, measured with electronic stethoscope.

Because the presently available oscillometric devices have low accuracy, the development of an accurate automatic SBP measurement technique has great significance. However, high correlation coefficient does not assure a small measurement error. It is still necessary to validate the novel oscillometry using generally accepted practices: comparing it to the auscultatory sphygmomanometry, the common gold-reference, and applying a common criterion for

the mean and standard-deviation of the deviations between the two techniques.

Reviewer 2

The strength and novelty of the paper lie in the finding that the air pressure variation during cuff deflation, widely used for BP determination by the oscillometric method, contains identifiable “events” that mark the Korotkoff sounds used for detecting systolic BP. As a result, this fully automated method is free of assumptions associated with the oscillometric method. The weakness of the study lies in the lack of an attempt to add vascular measures, e.g., arterial stiffness, that might explain the reduced correlation between these two methods observed in some cohorts. A parallel search for “events” that mark the diastolic BP could be a great challenge.