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ORIGINAL RESEARCH

Validation of a Suprasystolic Cuff System for Static and Dynamic Representation of the Central Pressure Waveform

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BACKGROUND: Noninvasive pulse waveform analysis is valuable for central cardiovascular assessment, yet controversies persist over its validity in peripheral measurements. Our objective was to compare waveform features from a cuff system with suprasystolic blood pressure hold with an invasive aortic measurement.

METHODS AND RESULTS: This study analyzed data from 88 subjects undergoing concurrent aortic catheterization and brachial pulse waveform acquisition using a suprasystolic blood pressure cuff system. Oscillometric blood pressure (BP) was compared with invasive aortic systolic BP and diastolic BP. Association between cuff and catheter waveform features was performed on a set of 15 parameters inclusive of magnitudes, time intervals, pressure–time integrals, and slopes of the pulsations. The evaluation covered both static (subject-averaged values) and dynamic (breathing-induced fluctuations) behaviors. Peripheral BP values from the cuff device were higher than catheter values (systolic BP–residual, 6.5 mm Hg; diastolic BP–residual, 12.4 mm Hg). Physiological correction for pressure amplification in the arterial system improved systolic BP prediction (r^2=0.83). Dynamic calibration generated noninvasive BP fluctuations that reflect those invasively measured (systolic BP Pearson R=0.73, P<0.001; diastolic BP Pearson R=0.53, P<0.001). Static and dynamic analyses revealed a set of parameters with strong associations between catheter and cuff (Pearson R>0.5, P<0.001), encompassing magnitudes, timings, and pressure–time integrals but not slope-based parameters.

CONCLUSIONS: This study demonstrated that the device and methods for peripheral waveform measurements presented here can be used for noninvasive estimation of central BP and a subset of aortic waveform features. These results serve as a benchmark for central cardiovascular assessment using suprasystolic BP cuff-based devices and contribute to preserving system dynamics in noninvasive measurements.

Key Words: cardiovascular dynamics ■ central pressure ■ cuff-based device ■ dynamic pulse waveform calibration ■ pulse waveform analysis

Elevated blood pressure (BP) is widely acknowledged as the predominant risk factor for cardiovascular disease.[1,2] Despite the considerable impacts on human health and the economic burdens of hypertension, a significant portion of individuals reporting elevated BP experience uncontrolled hypertension.[3,4] Recent understandings of cardiovascular disease are evolving and have shed light on the intricate interplay of hypertension and arterial hemodynamics in the development of BP elevation and cardiovascular risk.[4–6] Pulsatile hemodynamics have distinct contributions on the components of the pulse waveform and can serve as markers for risk assessment. To that end, pulse waveform analysis aims to decipher noninvasive pressure pulsations to interrogate central cardiovascular dynamics for clinical purposes.[7–9]

The gold standard for the central waveform measurement is aortic catheterization. As this procedure

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CLINICAL PERSPECTIVE

What Is New?

- Recent technological advancements have enhanced the fidelity of cuff-based pulse waveform acquisition devices, allowing for the capture of high-resolution waveforms that are comparable to those obtained using state-of-the-art invasive catheters.
- Using dynamic waveform calibration with subject-specific envelope functions generates blood pressure fluctuations linearly proportional to invasive measurements.
- The static and dynamic correlation between cuff and central pulse waveform features demonstrates strong concordance, particularly for parameters that do not directly measure waveform shape.

What Are the Clinical Implications?

- Enhanced noninvasive assessment: The strong correlations between cuff-based devices and invasive catheters highlight the clinical validity of noninvasive cardiac assessment. This advancement supports noninvasive cuff methods as a preliminary diagnostic aid before the need for invasive procedures, ultimately optimizing patient care.
- Dynamic cardiovascular monitoring: The dynamic cuff-based waveform calibration, employing a subject-specific envelope function, enables precise tracking of fluctuating cardiovascular behaviors. This approach performs an extensive characterization of the cardiovascular pressure waveform and provides physicians a comprehensive hemodynamic evaluation with the objective of augmenting diagnostic accuracy and patient monitoring.

Nonstandard Abbreviations and Acronyms

AdAm	ratio of diastolic blood pressure to mean arterial pressure pulsatile amplitudes
BTB	beat-to-beat
dPdt_dia	maximal diastolic fall rate
dPdt_fall	maximal systolic fall rate
dPdt_rise	maximal systolic rise rate
FF	form factor
RC	diastolic decay time constant
RMSE	root mean squared error
RT	rise time
SBP	systolic blood pressure
SPTI	systolic pressure–time integral
sSBP	suprasystolic blood pressure

is invasive and time consuming, several noninvasive methods have been proposed.[10] Applanation tonometry became the gold standard for noninvasive pulse waveform measurement after studies demonstrated the enhanced predictive capability of noninvasive central BP compared with brachial BP.[11,12] Subsequent research revealed that analyzing pulse waveforms from arterial tonometry is also proficient in capturing clinically significant cardiovascular hemodynamics.[13–16] Tonometry relies on flattening an artery between the tonometer and a rigid structure.[10,17] However, considering that arteries are predominantly surrounded by soft tissues, arterial applanation as described in principle is a clinical obstacle.[18] These challenges often lead to reduced measurement repeatability, even when administered by skilled clinicians.[10,19] As a result, the integration of applanation tonometry in clinical practice has faced obstacles, prompting exploration of alternative solutions that leverage cuff-based methods.

Occlusive cuff methods use a brachial cuff with inflate-and-hold capabilities to capture the pulse waveform.[20–29] The all-encompassing nature of the brachial cuff, encircling the entire arm, effectively confines the artery within its structure. Additionally, the automated functionality of cuff-based systems eliminates the need of a trained clinician during operation without undermining result variability. However, the main shortcoming of cuff-based pulse waveform acquisition devices is the low waveform resolution. Recent advances in medical technologies have addressed these issues by creating cuff-based systems with high-fidelity waveform acquisition.[30,31] Much discussion has been dedicated to selecting the cuff pressure for the most accurate representation of central pressure, yet no consensus has been reached.[20,24–26,31] The fluid dynamic principles behind the suprasystolic blood pressure (sSBP) hold pressure suggest that blocking flow in the subclavian artery would effectively create a pressure tap into the central cardiovascular system, giving the closest representation of a pressure-only central waveform.[31]

The present study performs a comparative evaluation between the noninvasive cuff-based pulse waveforms in the sSBP hold with those of a simultaneous recording from an invasive aortic catheter. The study uses a novel cuff-based device with proprietary pneumatic system to capture the dynamic pulse waveform on the subject's left arm with high fidelity. As depicted in Figure 1, the concurrency of the invasive and noninvasive measurements allows for a direct comparison between the peripheral and central waveform. The beat-to-beat (BTB) pulse waveforms are decomposed into a complete set of features that characterize the magnitudes, time intervals, pressure–time integrals, and slopes of the pulsations. This study analyzes the correlation of the feature's mean value and magnitude fluctuations to assess the static and dynamic

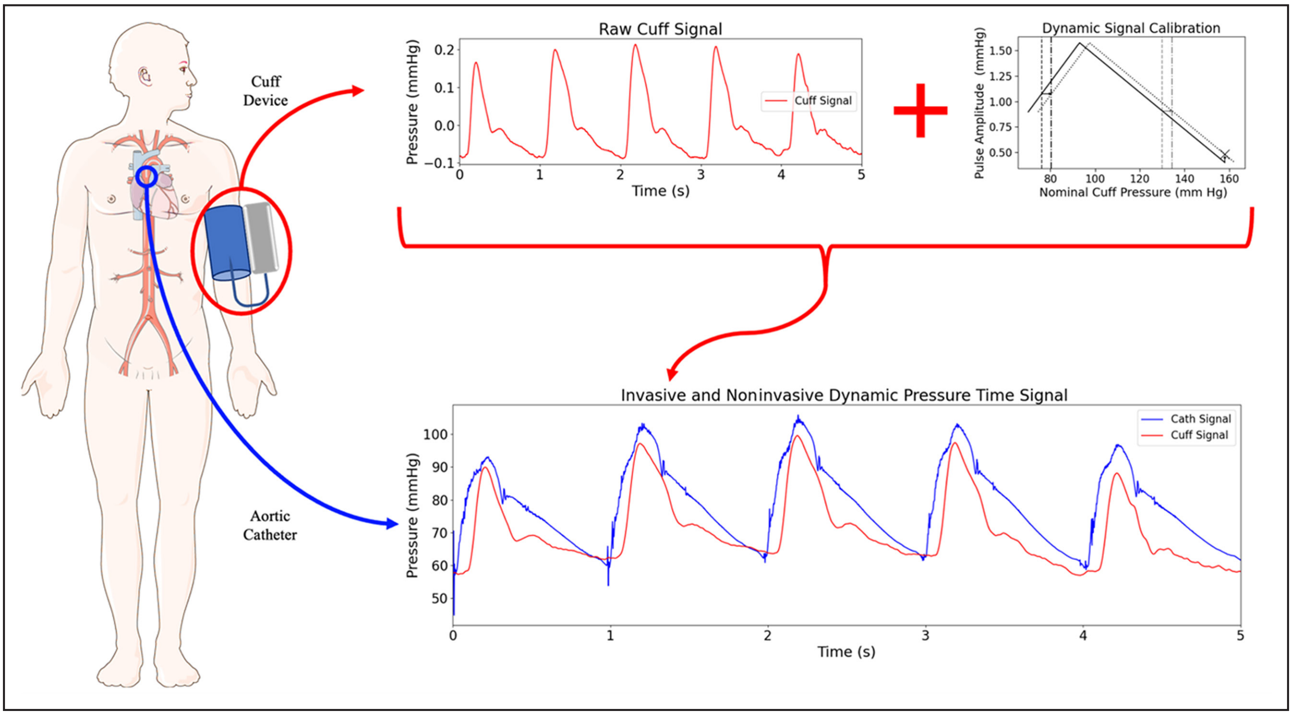

Figure 1. Overview of the study's invasive and noninvasive pulse waveform measurement methodologies.
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association between catheter and cuff. The aim of the current study is to determine the accuracy and reliability of the investigated cuff-based pulse waveform device with sSBP hold modality in measuring central cardiovascular waveform features.

METHODS

Data were obtained through a data transfer and use agreement between Caltech and Ventric Health. The authors do not own the data and do not have the permission or authority to share these data, per the agreement terms. The authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study Data

The study was approved by the institutional review boards of the testing centers, which included Western Institutional Review Board and Salus Institutional Review Board. All participants provided formal written informed consent. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Informed written consent was obtained from all study participants before any procedures were performed. The health centers that participated in the study included Princeton Baptist (Alabama), LSU Health Sciences Center (California), Long Beach Memorial Care Hospital System (California), Orange Coast Memorial Care Hospital (California), and Saddleback Memorial Care Hospital System (California).

Study Population

The study recruited subjects prescheduled for cardiac catheterization between September 2021 and September 2022. The main inclusion criteria were age≥21 years at the time of informed consent, referral for nonemergent left heart catheterization to be performed from either a femoral or radial access site, the ability to participate in all study evaluations, willingness to allow access to medical records, and ability to understand and sign informed medical consent. The main exclusion criteria included experiencing a severe cardiac event within a week of scheduled catheterization, inability to obtain a brachial BP measurement, and contraindication to cardiac catheterization by judgment of the interventional cardiologist.

Device Description

Noninvasive brachial pulse waveform acquisition was performed with the cuff device described by Tamborini et al.[30] The device consisted of a noninvasive BP module and a pneumatic system for high-fidelity pulse waveform acquisition. The noninvasive BP module is an original equipment manufacturer board (NIBP 2020 UP) with oscillometric BP capabilities and tourniquet mode. The pneumatic system integrates a pneumatic low-pass filter and a differential pressure sensor to function as a high-pass filter. This configuration enables the capture of the cuff-based pulse waveform at high signal resolution, independent of the cuff-inflation pressure. Optimal pressure sensing was configured with a ±3.73 mm Hg pressure sensor. The device was configured to perform a BP measurement followed by 3 instances of inflate-and-hold. For this study, the inflate-and-hold pressures were sequentially set to diastolic BP (DBP), mean arterial pressure (MAP), and sSBP (systolic [SBP] +35 mm Hg) for 30, 20 and 40 seconds, respectively. The total measurement lasted ≈140 seconds. An example measurement is shown in the bottom panel of Figure S1, where the oscillometric measurement occurs from seconds 0 to 20, the DBP hold occurs from seconds 35 to 65, the MAP hold occurs from seconds 70 to 90, and the sSBP hold occurs from seconds 100 to 140. The device's data rate is 1 kHz. The device employed in this study is limited to investigational use.

Data Structure

The data consist of simultaneous recording of invasive aortic catheterization, and noninvasive pulse waveform acquisition with a brachial cuff device (Figure 2). The study required cuff placement on the subject's left arm following standard cuff-placement guidelines. The cardiac catheter is a single-use solid-state catheter, the Mikro-Cath pressure catheter (Millar, Houston, TX). Cardiac catheterization was performed from either femoral or radial access site. However, for radial access, cuff placement on the left arm restricted catheter access to the right radial site exclusively. All data were captured using ADInstruments Powerlab hardware with the LabChart software (ADInstruments, Dunedin, New Zealand) at a sampling rate of 1 kHz. A full measurement with the brachial device was performed, resulting in simultaneous aortic and brachial waveform recordings.

Pulse Waveform Calibration

Pulse waveforms captured with the brachial cuff device require a calibration process for scaling to physiological pressure units.[20,26,27,32] The envelope function was used to estimate the dynamic BP variation in response to the physiological breathing fluctuations. The envelope function is the relationship between nominal pressure and pulsation amplitude, typical of the oscillometric BP measurement in cuff-based systems.[33–35]

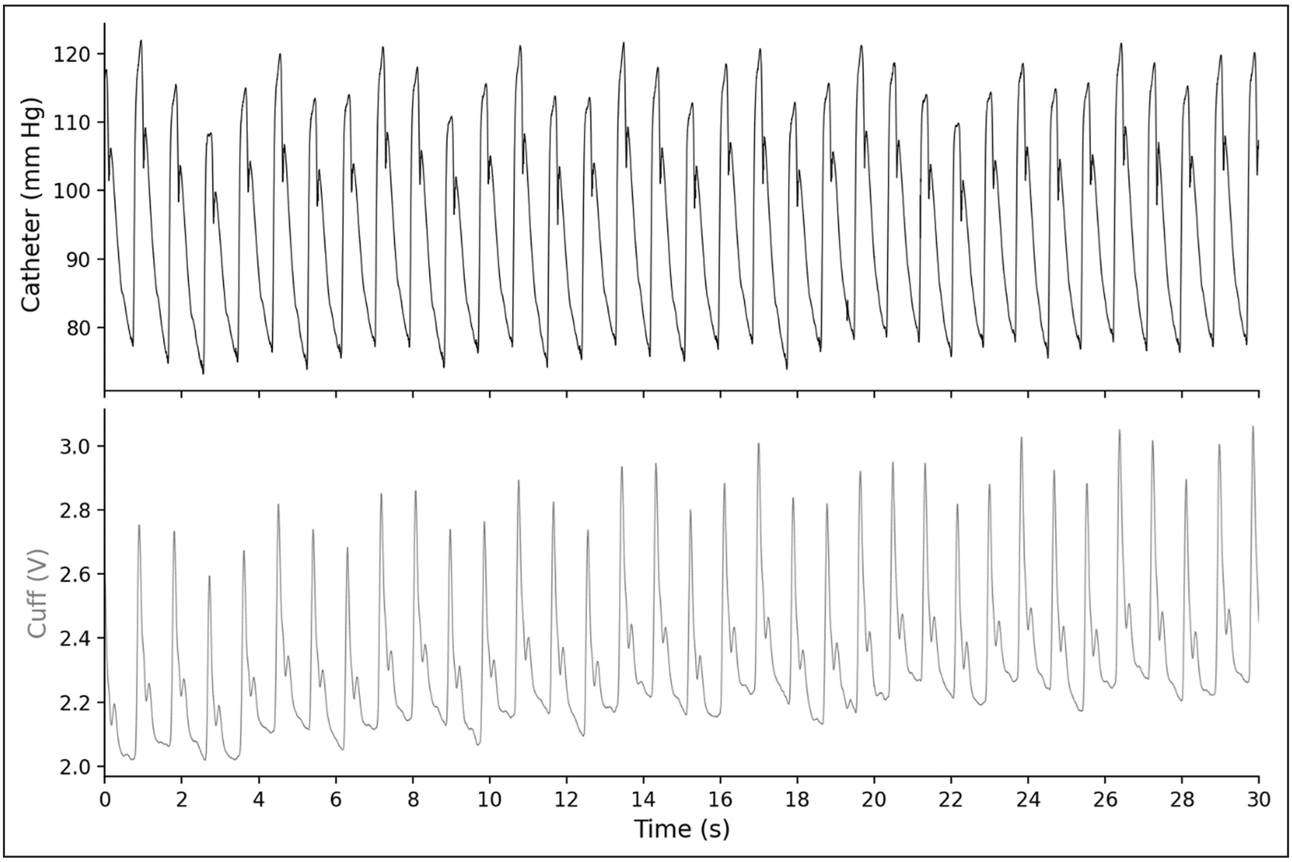

Figure 2. Example of the time series data from the study during the suprasystolic blood pressure hold.
Top panels show the pressure data from the catheter in units of mm Hg. Bottom panels show the cuff measurement data in units of volts (V). Time units are in s.

For each subject, an envelope function estimate was constructed using the pulse amplitude and nominal cuff pressure data pairs from the 3 pressure holds. At each pressure hold, the pulse amplitude and nominal cuff pressure data pairs are obtained by analyzing the BTB high-resolution signal and the gauge pressure signal, respectively. Assuming a linear interpolation between the sparse pressure holds and a stable average BP during the measurement, the envelope function can be estimated by averaging the data for each pressure hold (see Figure S2). Dynamic BP calibration was performed on a BTB basis by comparing the pulse amplitude and nominal cuff pressure data pair with the constructed envelope function. The difference in the expected pulse amplitude for a given nominal cuff pressure and the actual pulse amplitude was used to calculate the shift in BP (Figure 3A).

Statistical Analysis

Subjects were excluded if any of the following conditions were present in the measurement: severe irregular heartbeat, drifting pressure signal in catheter, any device malfunction, catheter calibration error, cuff sensor saturation, or incorrect measurement sequence. Figures S3 and S4 depict instances of distinct conditions observed in the waveforms that led to the exclusion of subjects from the analysis. The subject data were algorithmically processed to identify the longest segment of consecutive catheter and cuff high-quality pulsations in each pressure hold, herein referred to as sequential segments. Subjects were excluded when the sSBP hold sequential segment was shorter than 8 pulsations.

We compared SBP and DBP values between the brachial cuff and catheter measurements. Brachial BP values were reported by the device upon completion of the oscillometric cuff measurement. For reference, the oscillometric measurement is the straight-line segment from 0 to 20 seconds in the bottom panel of Figure S2. Catheter BP values were measured as the average SBP and DBP values in the segment corresponding to the oscillometric measurement; SBP is the systolic peak pressure and DBP is the minimum diastolic pressure. Models to account for BP value difference between peripheral (cuff) and central (catheter) were developed. At a physiological level, the difference in SBP peripheral and central values originates from forward and reflected pressure wave interactions. The SBP model for central pressure implemented a peripheral SBP value correction using the augmentation pressure from the sSBP hold waveform. The discrepancy between peripheral and central DBP measurements was attributed to the overestimation within the envelope function of the nominal cuff pressure at maximal pulse amplitude. This systematic error was corrected through the MAP values and the ratio of DBP to MAP pulsatile amplitudes (AdAm) from the cuff envelope function. Linear correction models for SBP and DBP are shown in Equations (1) and (2) below where a, b, c, d, and e are the correction coefficients. The coefficients for SBP and DBP cuff values are fixed to "1" in the equations, as their primary purpose is to address peripheral to central measurement discrepancies, whether physiological or systematic, rather than to perform scaling adjustments. Correlation strengths were measured with the Pearson's correlation coefficient (Pearson *R*), and the coefficient of determination (r^2); average error was assessed with the root mean squared error (RMSE).

$$\mathrm{SBP_{corr}} = \mathrm{SBP_{cuff}} + a \times \mathrm{AP} + b \tag{1}$$

$$\mathrm{DBP_{corr}} = \mathrm{DBP_{cuff}} + c \times \mathrm{AdAm} + d \times \mathrm{MAP_{cuff}} + e \tag{2}$$

Pulse waveform analysis was performed on the cuff and catheter sequential segment waveforms from the sSBP hold creating a set of 15 BTB parameters. Four main feature categories are extracted: magnitude, timing, pressure–time integral, and slope variables. Magnitude variables characterize the absolute values of waveform features in units of mm Hg; these include SBP, DBP, MAP, and pulse pressure. The timing variables characterize the waveform time interval in units of seconds, which include the systolic rise time (RT), systolic time, pulse time (PT), and diastolic time. The pressure–time integral variables characterize the area under the pulse waveform, including the systolic pressure–time integral (SPTI) in units of mm Hg×seconds; the diastolic pressure–time integral in units of mm Hg×seconds; and the mean of the unit scaled waveform, form factor (FF). The slope variables characterize the rate of change of pressure over time; these include the maximal systolic rise rate (dPdt_rise) in units of mm Hg/seconds, the maximal systolic fall rate (dPdt_fall) in units of mm Hg/seconds, the maximal diastolic fall rate (dPdt_dia) in units of mm Hg/seconds, and the diastolic decay time constant (RC) in units of seconds.

An analysis was conducted to investigate the association between cuff and catheter pulse waveform features in the sSBP hold sequential segment. The association was evaluated using 2 methods: static and dynamic. The static analysis evaluated the correlation on subject–mean pulse waveform feature values between cuff and catheter on the entire study population. The correlation was determined using the Pearson *R* and Spearman's rank correlation coefficient (Spearman *Rs*). The dynamic analysis evaluated the parameter BTB magnitude fluctuation association between cuff and catheter. At a subject level, the correlation was determined using the Pearson *R* and Spearman *Rs* method. The overall magnitude fluctuation behavior was assessed by analyzing the correlation coefficient

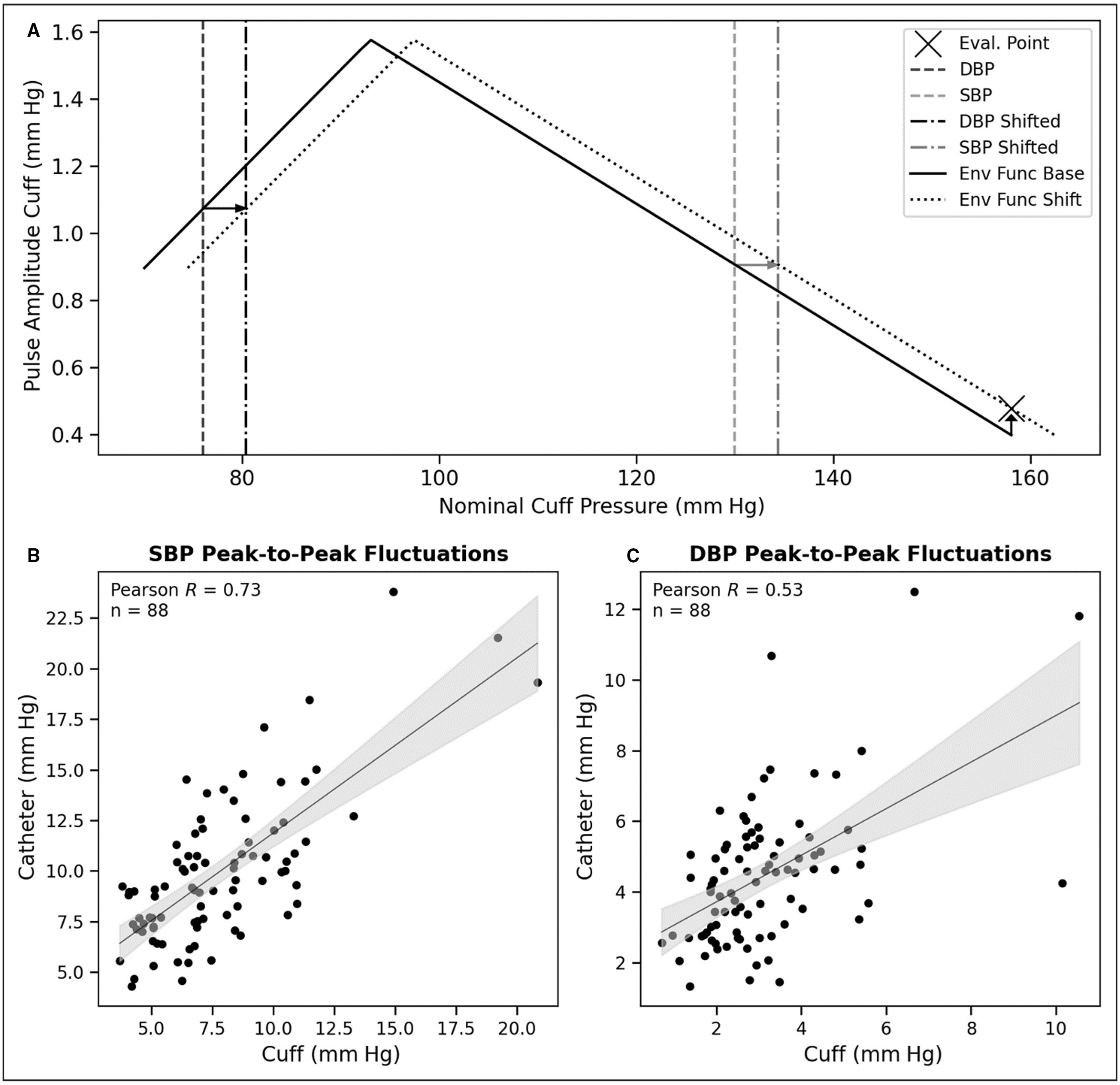

Figure 3. Overview of the dynamic calibration method using the envelope function.
A, Illustrative example of blood pressure shift calculated from the envelope function model specific to a subject. The legend delineates the following elements: "Eval. Point" represents the data point for the analyzed pulse waveform; "DBP" and "SBP" denote the diastolic and systolic blood pressure values from the oscillometric measurement; "DBP Shifted" and "SBP Shifted" indicate the diastolic and systolic blood pressure values corrected for breathing fluctuations; "Env Func Base" represents the envelope function calculate from the subject's average values; "Env Func Shift" represents the shifted envelope function to match the breathing blood pressure variation. **B**, Plots the breathing cycle peak-to-peak amplitude fluctuations of the SBP value in the cuff and catheter. **C**, Plots the breathing cycle peak-to-peak amplitude fluctuations of the DBP value in the cuff and catheter. Pearson *R* measures the strength of the linear correlation within the data; n represents the number of data points. Pressure is in units of mm Hg.

distributions of the entire study population. Linear mixed-effects models were created for each waveform parameter to evaluate the correlation between catheter and cuff, with patients treated as individual units. Linear mixed-effects models goodness of fit was evaluated using the conditional and marginal r^2 interclass correlation coefficient, and normalized RMSE.

RESULTS

Participants

The study enrolled 202 subjects referred for nonemergent left heart cardiac catheterization. The subjects underwent simultaneous cardiac catheterization and cuff device measurements; the application of sSBP hold during cuff device measurement was well tolerated. This analysis required the latest device hardware, which was present in 159 recordings. Exclusion criteria discarded 41 individuals: 5 for severe atrial fibrillation, 13 for catheter malfunction, 7 for brachial cuff malfunction, 4 for incorrect procedure, and 12 for signal saturation. Algorithmic filtering excluded an additional 30 individuals.

The population analyzed in this study (n=88) was composed of 64% men, the average age was 65.8 years, and the mean body mass index was 28.7. In the study population, 82% reported hypertension, 72% reported hyperlipidemia, and 73% reported taking BP-lowering medications. High prevalence of cardiovascular disease is reported: 20% reported heart failure, 19% reported heart valve disease, and 16% reported left ventricular dysfunction. Table summarizes the main characteristics of the study population. Note that data are taken from case report forms, which have been filled using both patient self-reported information and medical records. The study population (n=88) underwent cardiac catheterization referral for various reasons, as summarized by Table S1 The primary indications encompassed abnormal testing (66%), angina (18%), and diagnostic purposes (11%). Each patient may have had ≥1 reasons for referral, and each reason was individually accounted for.

Table. Characteristics of study participants

Variable	Quantity (n=88)
Clinical characteristics	
Age, y	65.8±9.6
Sex, male, n (%)	56 (64)
Weight, kg	84.7±19.3
Body mass index, kg/m^2	28.7±5.4
Left arm circumference, cm	31.3±3.8
Race, White, n (%)	59 (67)
Comorbidities	
Hypertension, n (%)	72 (82)
Diabetes, n (%)	25 (28)
Thyroid, n (%)	12 (13)
Hyperlipidemia, n (%)	63 (72)
Kidney disease, n (%)	10 (11)
Smoker, n (%)	14 (16)
Blood pressure medications, n (%)	64 (73)
Cardiovascular disease	
Carotid artery disease, n (%)	20 (23)
Cardiomyopathy, n (%)	11 (13)
Heart failure, n (%)	18 (20)
Heart valve disease, n (%)	17 (19)
Heart surgery, n (%)	8 (9)
Left ventricular dysfunction, n (%)	14 (16)
Myocardial infarction, n (%)	15 (17)
Peripheral vascular disease, n (%)	12 (14)
Pacemaker, n (%)	3 (3)
Stroke, n (%)	1 (1)

Data in table are mean ± SD, unless otherwise stated.

Pulse Waveform Calibration

An envelope function estimate was constructed from the pressure hold data using the cuff nominal pressure and pulse amplitude. In 83 (94%) measurements, the largest average pulse amplitude was at the MAP hold; in the remaining 5 (6%) measurements, this occurred at the DBP hold. The envelope function and the sSBP pulse amplitudes were used to calculate the SBP and DBP fluctuations during the sSBP pressure hold. We evaluated the correlation between BP magnitude fluctuations in the catheter and cuff by comparing the subject average peak-to-peak BP fluctuation amplitudes within breathing cycles. A positive linear association between the catheter and cuff fluctuation magnitudes was found for both the SBP and DBP parameters (Figure 3B and 3C). The SBP values showed a strong linear association (Pearson R=0.73, P<0.001) and the DBP values showed a moderate linear association (Pearson R=0.53, P<0.001).

Evaluation of BP Values

SBP and DBP values were compared between the catheter and the cuff's oscillometric measurement, as shown in Figure 4A and 4C, respectively. The SBP values have a strong linear correlation (Pearson R=0.88, P<0.001) and a high coefficient of determination (r^2=0.65) between catheter and cuff. On average, SBP magnitudes are larger in the brachial cuff than the catheter (average SBP residual cuff–catheter=6.5 mm Hg). The SBP RMSE was 10.9 mm Hg. The DBP values were characterized by a linear offset between the catheter and cuff (average DBP residual cuff–catheter=12.4 mm Hg). The DBP results reported a strong linear association (Pearson R=0.79, P<0.001) but a negative coefficient of determination (r^2=−1.17). The RMSE for the DBP correlation was 14.2 mm Hg.

The SBP and DBP linear correction models were generated for the study population. Equation (1) was optimized to solve for the SBP correction coefficients giving a=−0.31 and b=−3.45. Equation (2) was optimized to solve for the DBP correction coefficients giving c=−29.92, d=−0.22, and e=33.86. The corrected SBP and DBP values from Equations (1) and (2) are plotted against the catheter SBP and DBP values in Figure 4B and 4D, respectively. The SBP relationship had an improved RMSE and coefficient of determination (RMSE=7.6 mm Hg and r^2=0.83). Marginal improvement in the linear correlation coefficient was also observed (Pearson R=0.92, P<0.001). The DBP

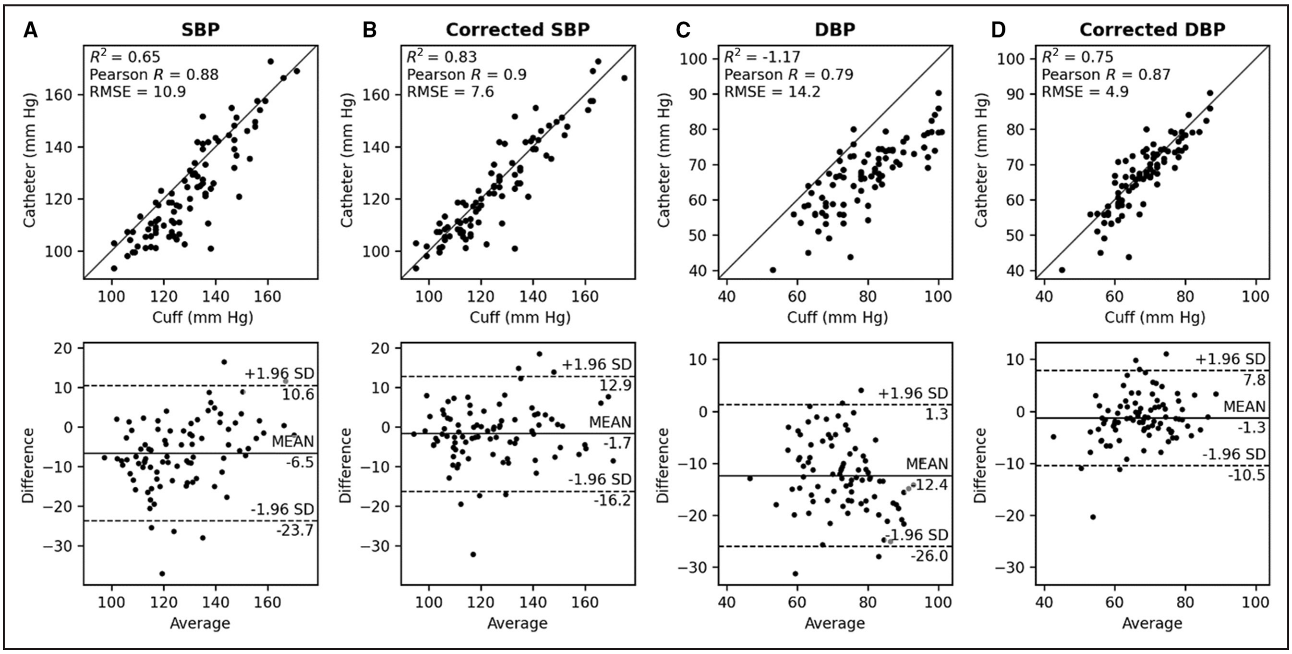

Figure 4. Overview of blood pressure values correlation between brachial cuff and aortic catheter for study population (n=88).

A and **B**, Results in the form of a true vs predicted plot (top) and Bland–Altman plot (bottom) for the systolic blood pressure (SBP) and the corrected SBP with Equation (1), respectively. **C** and **D**, Results in the form of a true vs predicted plot (top) and Bland–Altman plot (bottom) for the diastolic blood pressure (DBP) and the corrected DBP with Equation (2), respectively. R^2 quantifies the goodness of fit in the statistical analysis; Pearson *R* measures the strength of the linear correlation within the data; n represents the number of data points; MEAN denotes the average value of the data set.

relationship significantly improved RMSE and the coefficient of determination (RMSE=4.9 mm Hg and r^2=0.75). An improvement in the linear correlation coefficient was also measured (Pearson *R*=0.87, *P*<0.001).

Catheter to Cuff Association

The correlation between catheter and cuff pulse waveform features were analyzed with the static and dynamic method. Fifteen parameters were calculated for both the cuff and catheter waveforms during the sSBP hold.

The static analysis evaluated the association of pulse waveform feature mean values between cuff and catheter for the study population (Figure 5). A set of variables showed strong correlations for both linearity and rank (Pearson *R*>0.5, *P*<0.001; and Spearman *Rs*>0.5, *P*<0.001); these included the magnitude variables of SBP, DBP, MAP, and pulse pressure; the timing variables of RT, systolic time, pulse time, and diastolic time; and the pressure–time integral variables of SPTI and diastolic pressure–time integral. The moderately lower correlation coefficients for the RT parameter are likely associated with the feature's value dependence on wave shape. The strong correlations are indicative of a population-wide linear relationship between the cuff and catheter parameter feature. The other set of variables showed weak to moderate correlations in both linearity and rank (Pearson *R*<0.5 and Spearman *Rs*<0.5); these included the pressure–time integral variable of FF and the slope parameters of dPdt_rise, dPdt_fall, dPdt_dia, and RC. The weak correlation coefficient for both linearity and rank are indicative of lack of association between these variables in the catheter and cuff.

The dynamic analysis evaluated the association between the magnitude fluctuation behavior of pulse waveform features in the catheter and the cuff (Figure 6). For each subject, the BTB pulse waveform feature relationship of catheter and cuff was evaluated using Pearson *R* and Spearman *Rs*. For each feature, the population-wide associations were evaluated using a box plot (Figure 6C). A set of variables showed strong correlations for both linearity and rank (median Pearson *R*>0.5 and median Spearman *Rs*>0.5); these included the magnitude variables of SBP, MAP, and pulse pressure; the timing variables of systolic time, pulse time, and diastolic time; and the pressure–time integral variables of SPTI and diastolic pressure–time integral. A set of variables showed moderate correlations for both linearity and rank (median Pearson *R*>0.3 and median Spearman *Rs*>0.3), these included the magnitude variable of DBP, and the timing variable of RT. A set of variables showed weak correlations for both linearity and rank (Pearson *R*<0.3 and Spearman *Rs*<0.3)

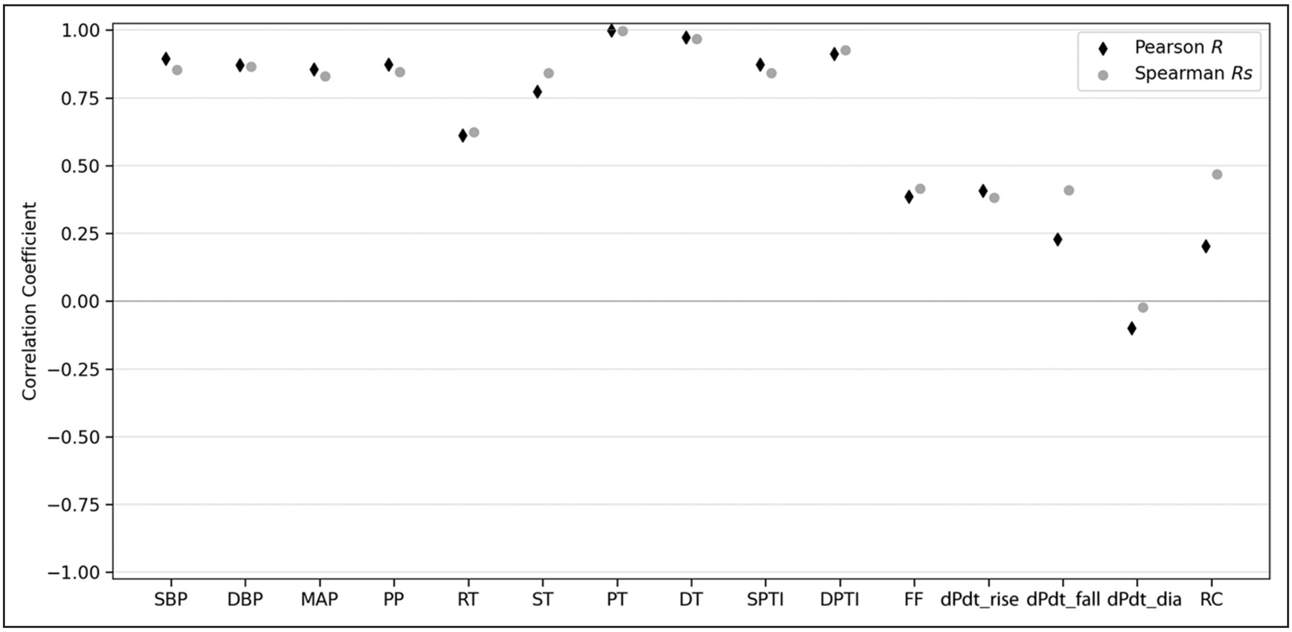

Figure 5. Plot shows the correlations for the static analysis (subject-averaged magnitude) of the catheter and cuff values for the pulse waveform feature set.

Correlation is measured using the Pearson correlation coefficient (Pearson *R*), a measure of the strength of the linear correlation, and Spearman's rank correlation coefficient (Spearman *Rs*), a measure of the strength of the monotonic correlation, tests. DBP indicates diastolic blood pressure; dPdt_dia, maximal diastolic fall rate; dPdt_fall, maximal systolic fall rate; dPdt_rise, maximal systolic rise rate; DPTI, diastolic pressure–time integral; DT, diastolic time; FF, form factor; MAP, mean arterial pressure; PP, pulse pressure; PT, pulse time; RC, diastolic decay time constant; RT, systolic rise time; SBP, systolic blood pressure; SPTI, systolic pressure–time integral; and ST, systolic time.

characterized by wide interquartile ranges; these included the pressure–time integral feature of FF and the slope parameters of dPdt_rise, dPdt_fall, dPdt_dia, and RC. The scattered correlation coefficients with mean and median close to zero indicated the lack of a consistent dynamic behavior across subjects.

The linear mixed-effects model analysis demonstrated moderate to strong explanatory power across the set of parameters (see Table S2). Marginal r^2 values were consistently smaller than conditional r^2 values, indicating that incorporating random effects enhances variance explanation. Notably, for RT, FF, dPdt_rise, dPdt_fall, dPdt_dia, and RC random effects were the predominant factor. Furthermore, high intraclass correlation coefficient results indicated substantial clustering of data points around individual patients.

DISCUSSION

In this study, we evaluated the association between pulse waveform parameters from a brachial cuff device to those from an invasive aortic catheter. The key new findings of this study were that a large subset of pulse waveform features encompassing magnitude, timing, and pressure–time integral parameters showed strong correlations between cuff and catheter. Our observations were consistent between the static and dynamic analyses, affirming that cuff-based pulse waveform acquisition devices with sSBP hold pressure modalities offer accurate and reliable measurement of central cardiovascular features. These findings are pivotal for comprehending the relationship between central hemodynamics and peripheral pulse waveform components. Further validation in broader populations would establish the groundwork for using peripheral measurements in assessing cardiovascular risk.

Brachial SBP values measured using the oscillometric method are widely known to be higher than central aortic SBP values measured via an invasive catheter.[36–40] This study confirmed previously reported findings and proposed a simple correction model to adjust peripheral SBP values to central SBP (Figure 4). Larger-magnitude SBP in the cuff measurement compared with the catheter measurement was expected, as pulse pressure amplification is responsible for increased SBP toward the peripheral arteries.[32] The augmentation pressure parameter characterizes the contribution of the reflected pressure wave by quantifying the local pressure increase above the forward wave, directly targeting the source of the pressure difference. Therefore, brachial SBP correction with augmentation pressure is a simple and physiologically relevant method to address the pulse pressure amplification phenomenon. Figure 4A and 4B show that Equation (1)

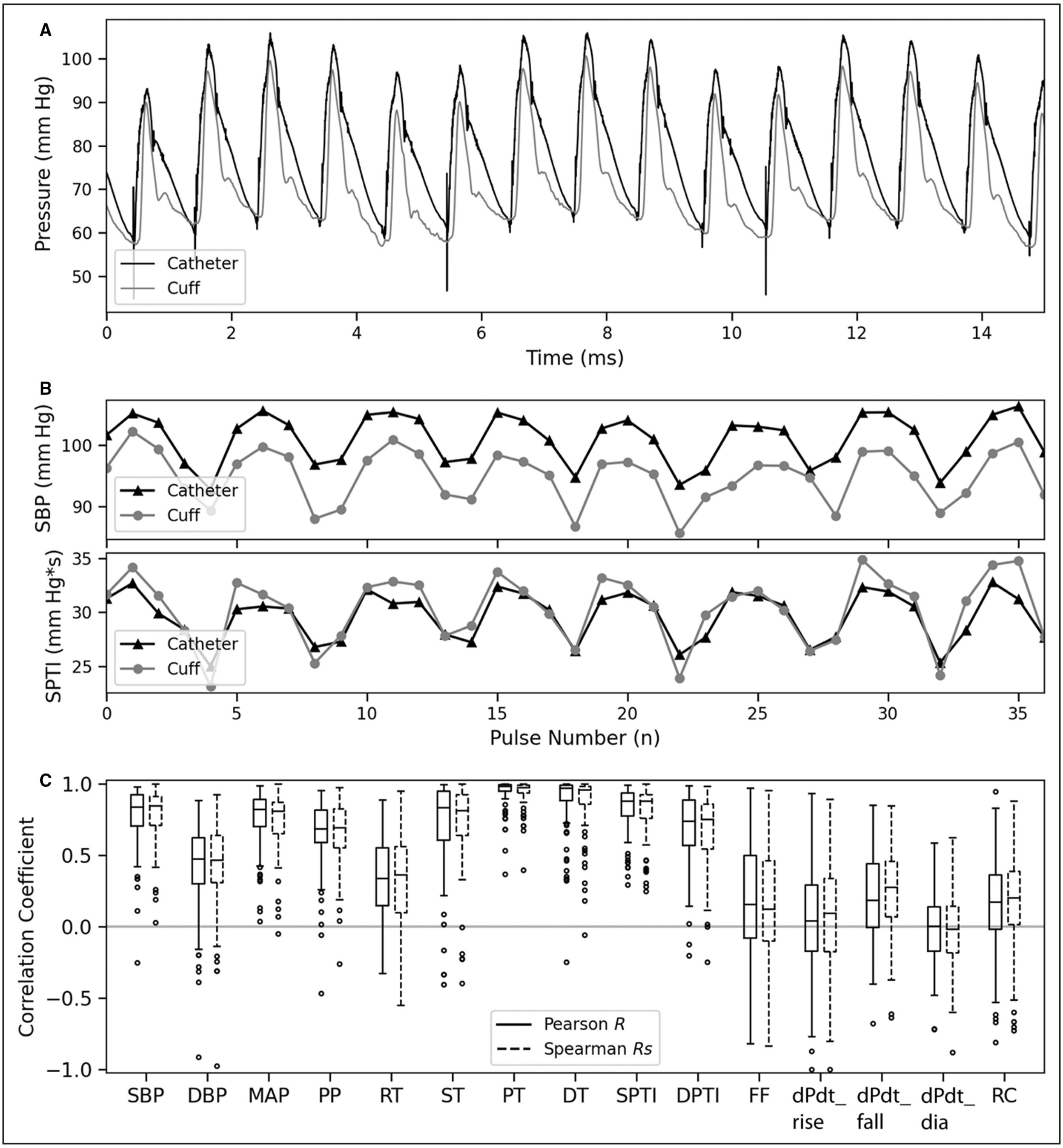

Figure 6. Overview of the dynamic pulse waveform behavior in response to physiological breathing patterns.
A, Shows the superimposed catheter (black) and dynamically calibrated cuff (gray) signals for a 15-s segment of the sSBP hold. **B**, Compare the SBP and SPTI parameters as a function of the pulse number for the catheter (black) and cuff (gray). **C**, Visualization of the correlation coefficients for the dynamic behavior of pulse waveform features between catheter and cuff. Outliers are shown with "o" markers. Pearson *R* measures the strength of the linear correlation, and Spearman *Rs* measures the strength of the monotonic correlation. DBP indicates diastolic blood pressure; dPdt_dia, maximal diastolic fall rate; dPdt_fall, maximal systolic fall rate; dPdt_rise, maximal systolic rise rate; DPTI, diastolic pressure–time integral; DT, diastolic time; FF, form factor; MAP, mean arterial pressure; PP, pulse pressure; PT, pulse time; RC, diastolic decay time constant; RT, systolic rise time; SBP, systolic blood pressure; SPTI, systolic pressure–time integral; and ST, systolic time.

improves the one-to-one correlation between catheter and cuff SBP. The decline in pulse pressure amplification with age is widely acknowledged, and this trend has been confirmed by the findings in Figure S5. However, our results reveal a smaller slope and weaker correlation strength compared with previously reported literature.[41,42] Given the high prevalence of comorbidities in our study population, a less pronounced effect of age on pulse pressure amplification was anticipated. Consequently, we can conclude that while our SBP correction addresses the physiology of the pulse pressure amplification, the inherent limitations in the diversity of the study population constrain the generalizability of our correction.

Diastolic BP is typically considered constant from central to peripheral arteries.[40,43,44] Previous studies reported cuff measurements overestimating invasive DBP values.[45,46] This study also reported a higher DBP in the cuff compared with the catheter by 12.4 mm Hg with an SE of 0.7 mm Hg that can be attributed to systematic errors. Analyzing the constructed envelope function revealed inconsistencies in the cuff pressure for maximal pulse amplitude. In theory, the oscillometric envelope function has maximal pulse amplitude at MAP, and the DBP amplitude should be significantly smaller. In the data collected during the pressure holds at DBP and MAP, it was observed that a subset of 5 subjects (6%) had a pulse amplitude at DBP that was equivalent to or larger than that at MAP (AdAm>1). Furthermore, an additional 4 subjects (5%) had a DBP amplitude within 5% of the MAP amplitude (AdAm>0.95) (see Figure S6). These amplitude ratios contradict the intended shape and functionality of the envelope curve: maximal pulse amplitude at MAP cuff pressure with diminishing amplitude as pressure diverges. These findings would suggest that the reported DBP values are systematically overestimated by the oscillometric algorithm and the true peak of the oscillometric envelope is found between DBP and MAP. Potential explanations for such findings come from the combination of the BP variation within the breathing cycle and the intrinsically variable nature of the oscillometric BP measurement approach. The correction factor proposed in Equation (2) addresses the nature of this overestimation with the AdAm parameter and the MAP value. As shown in Figure 4C and 4D, Equation (2) improves the correlation between cuff-based DBP values and the true DBP measurement performed with the invasive catheter.

Cuff-based signal calibration involves scaling pulse waveforms derived from a brachial cuff to physiological BP values. Current methods statically scale all waveforms to SBP and DBP inevitably losing the dynamic fluctuations of BP, which originate from heart–lung interaction.[20,26,27,32] In this study, we evaluated a physiology-based approach to dynamically scale waveforms using calculated BP fluctuations. This method used the envelope function constructed for each patient and the pulse amplitude changes in the cuff on a beat-to-beat basis to estimate the BP variation for each pulse waveform (Figure 3A). The linear association between the BP fluctuations in the catheter signal versus cuff calibrated signal was strong for SBP and moderate for DBP (Figure 3B and 3C). The stronger association of SBP can be attributed to the inflation pressure of sSBP, which is positioned closer to SBP and thus more susceptible to SBP fluctuations. Indeed, the cuff pulse amplitude fluctuations showed stronger correlation with catheter SBP fluctuations than with DBP fluctuations (data not shown). The method presented here is a first step toward a calibration method for noninvasive pulse waveform measurements that conserves dynamic BP characteristics. BP fluctuations originate from the mechanical forces generated in the heart–lung interactions and serve as a diagnostic marker for conditions such as pulsus paradoxus.[47] Dynamic fluctuations are a fundamental component of cardiovascular function, and this approach closes the gap between noninvasive measurement modalities and their invasive counterparts.

Pulse waveform analysis performed in this study evaluated a set of 15 conventional parameters that characterize all major components of the waveform.[48–53] Two methods, the static and dynamic analyses, were used to interrogate the association of pulse waveform features, magnitudes and fluctuation behaviors, respectively. Interestingly, both methods identified the same subset of pulse waveform features to have a strong linear association between cuff and catheter. This parameter subset included SBP, DBP, MAP, pulse pressure, RT, systolic time, pulse time, diastolic time, SPTI, and diastolic pressure–time integral. These features represent cardiovascular properties that are consistent throughout the entire system, as they do not measure parameters that depend on the forward and reflect waves superposition. On the other hand, parameters inclusive of FF, dPdt_rise, dPdt_fall, dPdt_dia, and RC showed overall weaker cuff-to-catheter correlations. This second subset of parameters measures waveform morphology. The pressure waveform is formed by superposition of forward and reflected waves. Wave superposition is affected by speed, distance, and damping, effectively making this a multivariate problem. Thus, parameters describing the waveform shape cannot be linearly correlated between catheter and cuff. The results on this parameter subset reinforces the notion that a transfer function is a useful tool to address wave superposition for a full evaluation of the central waveform.

With the advancement of noninvasive cardiovascular technologies, we are observing an increasing interest in pulse waveform features that measure dynamic characteristics of the cardiovascular system, for example, heart rate variability and stroke volume variation.[54–56] The rising interest in studying the dynamic properties of the pressure–time signal will become of great importance to understand how our cardiovascular system responds to stimuli. Overall, this study highlighted a set of parameters that have a direct static and dynamic association with the invasive measurement. Ultimately, the intent is to further motivate and facilitate the diagnostic association of noninvasive parameters to central cardiovascular health.

Limitations and Future Work

Although this study contributes to a better understanding of the association between catheter and cuff waveforms, several limitations must be discussed. First, the subjects recruited for this study were prescheduled for left heart cardiac catheterization and exhibited high prevalence of comorbidities and concomitant medications. The study population is not reflective of a diverse and generalized cohort. While the correlations observed in the study have been physiologically justified, the magnitudes of these correlations might have been affected by this intrinsic limitation. These results must be further validated on a wider population. Another limitation was the subset of parameters analyzed. Pulse waveform analysis extracts quantitative parameters from a pressure–time signal. Multiple methods can be used to extract this information. The selected parameters influence the extracted information and consequently the results. Furthermore, some commonly used features were not calculated, since the information was not consistently present in both signals, for example, augmentation index and pulse wave velocity. Additionally, the envelope function calibration method was constructed with sparse data from the pressure holds. Several assumptions were necessary to implement this method. Further studies are necessary to study the full envelope function shape and its intraperson variation. Finally, the study exclusively compared our cuff-based device with the invasive catheter, the gold-standard measurement, to set a robust benchmark. Future work will compare commercially available noninvasive pulse waveform algorithms and devices for a comprehensive assessment of our system's advantages.

ARTICLE INFORMATION

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Disclosures

The authors have a pending patent with the US Patent and Trademark Office and Patent Cooperation Treaty for the cuff-based device and method. Caltech is in negotiation for potentially licensing the patent to a biomedical company.

Supplemental Material

Tables S1–S2
Figures S1–S6

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