# Invasive validation of a novel brachial cuff-based oscillometric device (SphygmoCorXCEL) for measuring central blood pressure
# （オシロメトリック法に基づく中心血圧測定法(SphygmoCor XCEL)の妥当性の検討）

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# Invasive validation of a novel brachial cuff-based oscillometric device (SphygmoCor XCEL) for measuring central blood pressure

Short title: Invasive validation of SphygmoCor XCEL

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**ABSTRACT**

**Background:** Studies have established the prognostic value of central systolic blood pressure and pulse pressure. The SphygmoCor XCEL device provides practical central blood pressure measurement for daily clinical use with its easy-to-use, operator-independent procedure. However, this device has not been validated against invasive measurement.

**Method:** Simultaneous oscillometric and high-fidelity invasive measurements of central systolic blood pressure and pulse pressure were compared for 36 patients who underwent coronary arteriography. Invasive measurement of brachial blood pressure was also performed. Oscillometrically measured brachial systolic and diastolic blood pressures were used for calibration.

**Results:** The difference between the invasive and the oscillometric measurements were -4.6±9.9 mmHg for central systolic blood pressure and -18.5±10.6 mmHg for central pulse pressure (mean ± standard deviation). We found strong correlation between the invasive and oscillometric measurements (central systolic blood pressure and central pulse pressure, respectively: $r = 0.91$ and 0.89; slope, 1.28 and 1.38; both $p < 0.001$). Although the large slopes of the regression lines indicated a systemic bias toward lower values when measuring in high pressure ranges, the bias was mainly due to calibration error rather than

device-specific error because errors of the central measurements correlated well with those of brachial measurements (systolic blood pressure and pulse pressure, respectively: $r = 0.80$ and 0.77; both $p < 0.001$).

**Conclusion:** The impaired accuracy of central blood pressure measurement was mainly due to calibration-derived, but not device-dependent, bias. Strong correlation between oscillometric and invasive measurements indicates that SphygmoCor XCEL warrants future investigations to determine the clinical validity of this device.

**Key words:** central systolic blood pressure, central pulse pressure, oscillometric method, invasive measurement, validation study

## INTRODUCTION

Central, rather than peripheral blood pressure (BP) can serve as a direct indicator of hemodynamic load to target organs including the heart and brain. Several reports support the rationale that central BP indicators, especially central systolic BP (SBP) and pulse pressure (PP), are superior to brachial BP indicators in terms of prediction of cardiovascular events.[1-3] Assessment of central BP may improve the identification and management patients with high risk for cardiovascular disease.

The noninvasive approach to measuring central BP is widely used in research. The SphygmoCor CP system (AtCor Medical, Sydney, Australia), which derives central BP based on radial applanation tonometry, is the most commonly used device for noninvasive estimation of central BP.[4] However, the use of this device requires a trained operator, and is not feasible in daily clinical practice. Recently developed brachial cuff-based oscillometric devices can estimate central BP in an operator-independent manner. Some of these devices have already been validated against established invasive aortic BP techniques, with acceptable results,[5,6] and have proven clinical effective.[7-9] As simple, effective, and noninvasive alternatives to central BP measurement are now available, it is expected that the use of central BP will become widespread in daily clinical practice in the near future.

The SphygmoCor XCEL (AtCor Medical), a novel brachial cuff-based device for estimating central BP, is designed for use in daily clinical practice and has already been applied in a recent international randomized controlled trial.[10] This device records brachial pressure waveforms using the brachial oscillometric cuff, and reconstructs the central aortic pressure waveforms based on a generalized transfer function (GTF) after calibration of cuff-derived brachial SBP and diastolic BP (DBP). There are two studies validating the SphygmoCor XCEL against the SphygmoCor CP, which is the most commonly used device.[11,12] However, both studies used the same cuff-derived brachial BP for calibration, and did not perform central BP assessment via an established invasive method for verification; thus, the presence of a similar bias of both SphygmoCor devices in relation to well-established invasive measurements cannot be ruled out. In particular, errors from calibration procedure (i.e., input errors; namely, errors in brachial BP based on the oscillometric method) have a crucial effect on the accuracy of central BP estimation (output errors).[13-16] Direct measurement of central and brachial BP by well-established invasive techniques is, therefore, necessary in order to assess the true magnitude of these errors. In this context, the purpose of the present study was to assess the validity of noninvasive central SBP and PP estimations derived from SphygmoCor XCEL measurements against reference values obtained from measurements with a high-fidelity

invasive catheter.

## METHODS

### Patients

Patients undergoing elective coronary angiography for assessment of coronary artery disease (CAD) at our institution were included. Exclusion criteria were unstable clinical conditions, arrhythmias during pulse recordings, moderate or severe valvular heart diseases, or exhibiting a difference of more than 5 mmHg between the left and right brachial SBP. The difference in brachial SBP between the two arms was assessed on the day before the study. Thirty-six eligible patients (13 female) were enrolled in accordance with the European Society of Hypertension International Protocol for the validation of blood pressure-measuring devices in adults.[17] This study was approved by our regional ethics committee, and all participants gave written informed consent. Patients were considered hypertensive if they exhibited brachial SBP ≥140 mmHg or brachial DBP ≥90 mmHg, or made use of antihypertensive drugs. Patients were considered as having diabetes mellitus if they exhibited fasting blood glucose levels of ≥126 mg/dL, HbA1c ≥ 6.5 %, or made use of hypoglycemic agents or insulin. Patients were considered as having CAD if they exhibited a stenosis of >50% in a major epicardial coronary artery, or if they underwent prior percutaneous coronary intervention.

**Measurement of central and brachial BP**

All measurements were performed in the supine position on the catheterization table. Usual medications were not withheld for this study, but no vasoactive drug was administered during the measurement.

For the invasive measurement, a homeostatic sheath (Radifocus, Terumo Medical, Tokyo, Japan) was placed via radial approach. The arm through which to cannulate the artery was chosen based on the Allen's test (right arm, 61.1%; left arm, 38.9%). A high-fidelity pressure wire (diameter 0.014", Certus® or Aeris®, St Jude Medical) was set at 0 mmHg, calibrated, and introduced through the guiding catheter into the proximal aortic root under radiographic guidance. Central aortic pressure waveform was digitally recorded at 100 Hz, for 30 to 60 seconds. The pressure guide wire was subsequently pulled to the brachium and the brachial pressure waveform was recorded in a similar manner. Invasively recorded pressure waveforms were analyzed for obtaining the BP parameters during the 30- to 60-second recording period. Finally, the values of the invasively-measured SBP, DBP and PP were calculated from the waveform.

The central pressure waveform was also recorded noninvasively with the SphygmoCor XCEL, simultaneously to the invasive measurement. The SphygmoCor XCEL consists of

a brachial cuff-based central BP estimating device validated against a tonometric device, the SphygmoCor CP. The brachial pressure waveforms were calibrated with cuff-measured brachial SBP and DBP, and then transformed to central aortic waveforms by the device's software using a GTF. A properly sized cuff, according to the manufacturer's instruction, was fitted on the contralateral brachium (the arm not used for the sheath insertion), and three repeated measurements were performed by trained investigators. Finally, the three recordings were averaged in order to calculate the noninvasively-measured SBP, DBP and PP values.

**Statistical analysis**

All data were analyzed using STATA 14.1 software. All continuous values were expressed as mean ± standard deviation (SD), and categorical variables were reported as percentages. Agreement between the measurements made with the SphygmoCor XCEL and with the invasive catheter was assessed using the paired samples t-test and the Bland-Altman analysis. Pearson's linear correlation test was used to analyze the correlations between BP values of the paired invasive and noninvasive measurements, and the correlations between the errors of brachial SBP/PP (input error) and central SBP/PP (output error). All P-values were two-tailed. P-values $<0.05$ were considered statistically significant.

## RESULTS

### Patient Characteristics

The 36 enrolled patients included 13 female patients (36.1%), 28 hypertensive patients (77.8%), 9 diabetic patients (25.0%), and 29 patients with CAD (80.6%, Table 1). Mean age of the patients was 69.1±13.5 years (range, 23-88 years). Twenty-eight patients (77.8%) were prescribed vasoactive drugs including renin-angiotensin system inhibitors, beta blockers, calcium-channel blockers, and nitrates.

### Comparison between SphygmoCor XCEL derived and invasive catheter derived BP

The SphygmoCor XCEL underestimated central SBP by 4.6 mmHg, and the SD of the difference was large (9.9 mmHg) (Table 2). The average of brachial SBP values noninvasively-measured was comparable to that of the invasive measurement, but the SD of the difference was also large (8.0 mmHg). The SBP scatter plots of noninvasive versus invasive measurements are shown in Figure 1A. Although the slopes and intercepts were distant from 1.0 and zero, respectively, for both central and brachial SBPs (central SBP: $y = 1.15 \cdot x - 28.8$; brachial SBP: $y = 1.15 \cdot x - 20.0$), the correlation coefficients ($r$) were very high (central SBP: $r = 0.93$; brachial SBP: $r = 0.91$). Bland-Altman plots of these data showed significant upward slopes for both central and brachial SBPs (Figure 1B).

With regard to DBP, the SphygmoCor XCEL considerably overestimated central and brachial values, but the SDs were relatively small (central DBP: 13.4±6.4 mmHg; brachial DBP: 11.7±6.9 mmHg) (Table 2). The DBP scatter plots of noninvasive versus invasive measurements showed that the slopes were smaller than 1.0, but the intercepts were near zero for both central and brachial DBPs (Figure S1A). The *r* values were 0.83 for central DBP and 0.80 for brachial DBP. Bland-Altman plots did not show a clear trend as they did for SBP (Figure S1B).

The underestimation of SBP and overestimation of DBP account for the additive underestimation of PP for both central and brachial artery (Table 2). The PP scatter plots of noninvasive versus invasive measurements showed that the slopes were larger than 1.0, but the intercepts were near zero for both central and brachial PPs (Figure 2A). The *r* values were 0.89 for central PP and 0.90 for brachial PP, being similarly high to those of SBP. The corresponding Bland-Altman plots showed similar upward slopes to those found in SBP (Figure 2B).

**Relationships between input error and output error**

Figure 3 demonstrates the correlation between output error and input error. Output errors in SBP and PP (differences between invasively- and noninvasively-measured central

SBPs or PPs) highly correlated with their corresponding input errors (differences between invasively- and noninvasively-measured brachial SBPs or PPs), suggesting that the accuracy for central SBP and PP estimation was mainly impaired by the calibration error derived from the oscillometric method.

## DISCUSSION

To the best of our knowledge, this is the first study validating the SphygmoCor XCEL against well-established invasive techniques. We found that the cuff measurement error in brachial SBP and PP (i.e., input error) impaired the accuracy of the estimated central SBP and PP (i.e., output error); these results suggest that, in the SphygmoCor XCEL, input errors are transferred to output errors, which is a common problem to the tonometric device: the SphygmoCor CP. We noted strong significant correlations between measurements obtained via invasive catheter and the values estimated via the SphygmoCor XCEL,which warrants future investigations to determine the clinical validity of this device.

Two early studies reported that the SphygmoCor XCEL provided comparable estimation of central SBP to the SphygmoCor CP.[11,12] Although this present study also showed that the mean bias of the noninvasively-measured central SBP was within the acceptable limit (<5 mmHg)[18] in comparison with invasive measurement, we found a systemic bias in estimated central SBP as indicated by the large slope of the regression line. A similar bias observed in estimated brachial SBP and the strong correlation between the output errors and the input errors ($r = 0.80$, $P<0.01$) leaded us to conclude that this bias was mainly due to the input errors (i.e.calibration errors). Although the accuracy of central

BP estimation by GTF largely depends on the accuracy of calibration,[13-16] noninvasive brachial BP estimation is coexistent with a consistent error.[15,19-21] This finding and our results indicate the systemic bias of estimated central SBP with this device is a common rather than device-specific issue among noninvasive devices including SphygmoCor CP and XCEL.

The considerable underestimation of central PP noted in the present study (approximately 19 mmHg) was within the limits reported in literature; specifically, in almost all devices that rely on the oscillometric method, input errors consisting of underestimation of brachial SBP and overestimation of brachial DBP lead to the underestimation of central PP (output errors).[5,13,15] Moreover, as expected, the error in central PP estimation was largely determined by the error in cuff-derived brachial PP, as was the case with the estimation of central SBP.

While the accuracy of the SphygmoCor XCEL in estimating central SBP and PP was impaired by calibration errors, the usefulness of the device should be judged also based on its diagnostic and predictive ability. This device was shown to provide comparable estimation of central BP with the tonometric SphygmoCor device,[11,12] the clinical validity of which has been well established in several studies.[1,22,23] Furthermore, we found that estimated central SBP and PP strongly correlated with invasively measured

values, which warrants future studies investigating the diagnostic and predictive ability of the SphygmoCor XCEL.

Although the SDs of the mean bias for the noninvasive estimates of central SBP and PP were above the acceptable limit (<8 mmHg), the Bland-Altman plots of SBP and PP suggested that the large SDs were considerably due to the upward trend of the regression lines, which resulted in increased SD as the range of BP widened. Since the scattering of values along the regression line was narrow, we speculated that the large SDs were due to the systemic bias of the brachial BP rather than the lack of precision of the SphygmoCor XCEL.

Our findings must be considered within the context of the strengths and limitations of our study. A major strength of the present study was that the validation of the SphygmoCor XCEL as a clinically valuable device for estimating central BP was performed against a well-established invasive technique that relies on a high-fidelity BP measuring system. In addition, the simultaneous measurement of brachial BP via invasive (direct) methods allowed us to assess the magnitude and source of the error in central BP estimation. On the other hand, our study included patients who underwent coronary angiography, resulting in a high prevalence of high-risk patients. This represents a limitation of the study, because such patients often take vasoactives that might affect the

accuracy and precision of noninvasive central BP estimation.

**Perspectives**

As brachial cuff-based oscillometric devices can be used in an operator-independent manner, it is expected that their application for estimation of central BP will become routine in clinical practice. We present the validation of such a device, the SphygmoCor XCEL, against a well-established invasive technique for high-fidelity measurement of central BP. We found that the estimated values strongly correlate with the values obtained by the invasive approach, and concluded that the SphygmoCor XCEL is likely to provide reliable estimates of the central SBP and PP for use in daily clinical practice. However, as limited clinical data are available regarding this device, further study is warranted to assess the diagnostic and predictive ability of the central SBP and PP estimated using the SphygmoCor XCEL.

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**Conflicts of Interest/Disclosure Statement**

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The other authors have no conflicts to report.

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**Figure legends**

**Figure 1.** Scatterplots (A) and Bland-Altman plots (B) of SBP measured using an invasive catheter vs. using the SphygmoCor XCEL device.

**A.** The dotted lines indicate the identity line. The regression lines were drawn as solid lines.

**B.** Horizontal lines at the mean value (solid lines) and plus and minus two standard deviations (dotted lines) were drawn. The regression lines were drawn as solid lines. SBP, systolic blood pressure; c, central; b, brachial; inv, measured with an invasive catheter; xcel, measured with the SphygmoCor XCEL; SD, standard deviation.

**Figure 2.** Scatterplots (A) and Bland-Altman plots (B) of PP measured using an invasive catheter derived vs. using the SphygmoCor XCEL device.

**A.** The dotted lines indicate the identity line. The regression lines were drawn as solid lines.

**B.** Horizontal lines at the mean value (solid lines) and plus and minus two standard deviations (dotted lines) were drawn. The regression lines were drawn as solid lines. PP, pulse pressure; c, central; b, brachial; inv, measured with invasive catheter; xcel, measured with the SphygmoCor XCEL; SD, standard deviation.

**Figure 3.** Scatterplots of output vs. input errors in the estimation of central SBP and PP. The dotted lines indicated the identity line. The regression lines were drawn as solid lines.

SBP, systolic blood pressure; PP, pulse pressure; c, central; b, brachial; inv, measured with invasive catheter; xcel, measured with the SphygmoCor XCEL.

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