Precision and accuracy of a new device (CNAP™) for continuous non-invasive arterial pressure monitoring: assessment during general anaesthesia

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Key points
- Continuous non-invasive arterial pressure measurement using the finger cuff method has shown comparable precision and accuracy to invasive arterial pressure measurement from radial artery catheter in patients undergoing general anaesthesia.
- It may be a useful alternative to invasive measurements when continuous arterial pressure monitoring is deemed important for patient care.

Background. Continuous non-invasive arterial pressure measured with CNAP™ (CNAP) has been shown to be superior to intermittent oscillometric measurements during procedural sedation and spinal anaesthesia. We assessed the performance of CNAP during general anaesthesia by analysis of agreement with invasive measurements of arterial pressure (AP).

Methods. Eighty-eight patients undergoing elective abdominal surgery, cardio-, or neurosurgery were included in the study. Systolic, diastolic, and mean AP measured by an intra-arterial catheter in the radial artery (IAP) were compared with those obtained by CNAP from the same arm. Data were analysed to determine the precision (i.e. measurement error) and accuracy (i.e. systematic error) of beat-to-beat CNAP values with respect to IAP. Also, we compared the frequency of fast changes in AP (FCAP) and hypotension (IOH) by both methods.

Results. CNAP precision of 4.5, 3.1, and 3.2 mm Hg (systolic, diastolic, and mean AP, respectively) was not significantly different from IAP precision, and CNAP accuracy was +6.7, −5.6, and −1.6 mm Hg. The frequency of AP pairs having a difference within the calculated limits of agreement was 81%, 64%, and 76% for systolic, diastolic, and mean AP, respectively. The calculated limits of agreement were ±17.6, ±11.4, and ±12.0 mm, Hg, respectively. CNAP and IAP detected simultaneously to 82.1% FCAP and to 84.6% IOH.

Conclusions. CNAP provides real-time estimates of arterial pressure comparable with those generated by an invasive intra-arterial catheter system during general anaesthesia.

Accepted for publication: 20 April 2010

Prevention of hypotension during anaesthesia is a major goal of perioperative anaesthetic care. Intraoperative hypotension (IOH) may precede cardiovascular events and may increase 1 yr postoperative mortality. Since the haemodynamic effect of commonly used anaesthetics occurs within a few minutes, acute changes in arterial pressure (AP) may not be detected in time by intermittent oscillometric measurements. Recently, continuous non-invasive AP measurements generated by a new device called CNAP™ (CNSystems Medizintechnik AG, Graz, Austria) has been shown to be superior to intermittent oscillometric measurements by a better detection of fast changes in AP (FCAP) and IOH episodes during sedation for interventional endoscopy and spinal anaesthesia for Caesarean section. On the basis of the volume clamp method, this device monitors blood flow into the finger and translates blood flow oscillations sensed by the encircling finger cuff into continuous pulse pressure waveforms and beat-to-beat values of AP.

At present, continuous beat-to-beat AP monitoring is usually performed invasively by an intra-arterial catheter, which is associated with injury, expense, and required skill to acquire the data. Therefore, the aim of the present study was to investigate whether CNAP™ generated AP waveform would provide real-time estimates of systolic, diastolic, and mean AP comparable with those generated by an invasive intra-arterial catheter system during different surgical procedures under general anaesthesia. Our primary investigation goal was to test the hypothesis that the two methods of AP measurement are interchangeable with respect to defined limits of agreement. Further, we also investigated whether the observed AP differences between...
methods are related to the magnitude or the measurement time of AP and whether FCAP and IOH are detected by both methods in a comparable manner.

Methods
This study was approved by the University Hospital of Erlangen research ethics committee (Ref: 3697). Patients receiving general anaesthesia for abdominal surgery (AS), cardiology (CS), or neurosurgery (NS) between February 2008 and March 2009 were included in this prospective study. Adult patients were eligible if they had an ASA status I–III with a clinical need for invasive arterial pressure measurement (IAP) monitoring in the supine intraoperative position, no advanced dysfunction of peripheral perfusion (i.e. arterial peripheral artery occlusive disease, Raynaud’s syndrome), no arteriovenous shunts for haemodialysis, or no vascular surgery of the upper extremities. All patients gave written consent.

All patients were premedicated with 7.5 mg midazolam and were allowed to drink fluids up to 2 h before surgery. In the induction room, a 18 G cannula (BD Angiocath™, Becton Dickinson, Heidelberg, Germany) was inserted in a peripheral vein for the infusion of anaesthetic drugs and for infusion therapy (Ringer’s lactate solution of 2–10 ml kg⁻¹ h⁻¹). Standard monitoring with electrocardiography and pulse oximetry was attached and connected with a Dräger Infinity Delta monitor (Dräger Medical Systems, Inc., Danvers, MA, USA). A 20 G arterial line (Leader Cath, Vygon, Aachen, Germany) was usually inserted into the left radial artery after local skin infiltration with 0.5–1 ml mepivacain 1% and connected to a transducer (xtrans²⁰, CODAN pvb Critical Care GmbH, Forstinning, Germany) by a low-volume, non-compliant length of tubing (CODAN pvb Critical Care GmbH) after careful de-airing. The quality of the waveform (sharp upslope and downslope) was inspected and the arterial signal was zero-referenced and the pressure dome was placed at the height of the midaxillary position. The IAP and the oscillometric upper-arm arterial pressure (NIAP) were monitored throughout the study period. The general anaesthetic procedure was performed by the attending anaesthesiologist in accordance with the standard procedures of our department.

The CNAP™ monitoring system consists of reusable finger cuffs, the cuff controller, and the CNAP™ pod which interfaces into the patient monitor. The finger cuffs are available in three sizes (i.e. small, medium, and large) and consist of two semi-rigid cylinders covering two adjacent fingers between digits II–IV. Inflatable cuffs, sensors, and electronics are inside the semi-rigid cylinders. The adequately sized finger cuff was connected to the cuff controller that contains the pneumatic control unit for the inflatable parts of the finger cuff. The finger cuff was applied ipsilaterally to the radial artery catheter. A 2.5 m long cable leads from the cuff controller to the CNAP™ pod (Version 2.9.14) that evaluates the continuous non-invasive AP curve. The continuously changing finger cuff pressure is measured with a pressure transducer XFGM050 (Fujicura Ltd, Tokyo, Japan).

The analogue signal of the CNAP™ pod was displayed on another Dräger Infinity Delta monitor (Dräger Medical Systems, Inc.) that also controlled a standard oscillometric upper-arm cuff for scaling purposes. Continuous non-invasive AP (CNAP) is obtained by applying pressure via the finger cuffs such that the blood volume flowing through the finger arteries is held constant (i.e. volume-clamping). The finger arterial pressure was scaled to central AP every 15 min by a scaling function with NIAP values as arguments. After applying this scaling operation, CNAP values correspond to the values measured at the brachial artery. The NIAP measurements were performed on the same arm with the arterial catheter and CNAP™ finger cuff. The analogue signals of the ECG, IAP, and CNAP were simultaneously derived from the patient monitors, digitized at 100 samples per second (12 bit per kHz), and interfaced via USB ports (V. 2.0) into a laptop computer along with synchronized information regarding NIAP measurements and blood sampling episodes for further offline analysis.

Data processing
Episodes of NIAP measurement and blood sampling were first excluded from the digitized data of ECG, IAP, and CNAP. Subsequently, the onset and duration of each QRS complex in the ECG and the onset and duration of each pulse beat in the IAP, and of each pulse beat in the CNAP were identified by robust open-source algorithms. After automated rejection of artifact-contaminated pulse beats, QRS-triggered pairs of IAP and CNAP pulse beats were extracted from the time period of skin incision to skin suture in each patient. During cardiopulmonary bypass, no QRS activity was present, and thus, this time period was excluded from further analysis. From each selected IAP and CNAP pulse beat, the systolic AP value was calculated as the pressure value of the pulse beat occurring at the first zero crossing of the first derivative of the pulse beat. The diastolic AP value was calculated as the minimum value of the pulse beat occurring between the onset of the pulse beat and the systolic AP value. The mean AP value was calculated by the sum between diastolic AP value plus 5 and one-third of the difference between systolic and diastolic AP value.

FCAP was defined as absolute differences between the end and start point of a linear regression line on systolic AP during intraoperative time episodes of 3 min length that were >20 mm Hg. IOH was defined as the median value of systolic AP lower than 100, 90, 80, and 70 mm Hg during intraoperative time episodes of 5 min length. The analysis of agreement between methods was performed with 2000 pairs of QRS-triggered IAP and CNAP randomly selected from each patient. The random selection of AP pairs followed a uniform distribution during the investigated surgical procedure in each patient.

Statistical Analysis
The Association for the Advancement of Medical Instrumentation ANSI/AAMI SP10 considers a mean difference of ±5
mm Hg between the test device and the reference method as a clinically acceptable disagreement. Using a t-test and assuming equal standard deviations (SDs) for IAP and CNAP of 15 mm Hg (derived from a previous pilot study during CS), we would have to include at least 75 patients to detect a difference in AP of 5 mm Hg with 80% power and a significance level of 5%.

The accuracy of CNAP was assessed using analysis of bias and limits of agreement. Bias is the mean difference between CNAP and IAP, whereby differences were calculated by subtracting CNAP values from IAP values. Absolute differences between methods >50 mm Hg in systolic, diastolic, or mean AP were considered as outliers and excluded from further analysis. To define limits of agreement for interchangeability between IAP and CNAP, we first assessed the precision, i.e. the size of measurement error for each method separately as proposed in previous reports. This was estimated by the SD of repeated measurements of AP from 60 consecutive pulse beats in each patient, also called the within-subject SD and denoted as the sum of biases. The size of percentage measurement error was calculated by twice the within-subject SD divided by the population mean AP. IAP and CNAP beats were extracted independently of each other using the ECG complex as trigger information, so one can assume that the two measurement errors \( w_i \) are independent. Then, the size of the combined measurement error of the methods \( w_i = w_i + w_i \) can be calculated from the sum of the squared sizes of the measurement errors:

\[
\sqrt{w_i^2 + w_i^2}
\]

where \( i \) is the systolic, diastolic, or mean AP. Given no significant difference between the sizes of the measurement errors, one would accept the hypothesis of interchangeability between IAP and CNAP if the difference between methods is in 95% of observations within the limits of agreement of \( \pm 2.77 \) \( w_i + w_i \) that is, within the expected size of measurement error between two consecutive measurements in the same patient.

The dependence of AP bias from magnitude or time of AP measurement was assessed by the slope of the least-squares linear regression. The relative frequency of FCAP or IOH detected by each method was defined as the number of patients showing at least one episode of FCAP or IOH related to the total number of patients in the study population.

Normal distribution of data was assessed by Q–Q plots. AP differences between methods were analysed using a dependent t-test for paired measurements. Differences between more than two samples concerning AP or bias were analysed using analysis of variance for repeated measurements, and, if the test was positive, then a Bonferroni adjusted test for pairwise comparison of subgroups was performed. Differences between SDs were calculated using the F-test.

Construction of the data set was performed using Matlab (Version 2007a, The MathWorks, Natick, MA, USA). A priori sample calculations and statistical handling of the data set were performed using the SPSS statistical program (Version 15.0, SPSS Inc., Chicago, IL, USA) at a significance level of \( \alpha = 0.05 \), respectively. Results are presented as mean (SD) unless stated otherwise.

**Results**

Eighty-eight patients were enrolled into the study. In three patients, the AS procedure was interrupted due to inoperability, four patients were excluded due to technical problems, and three patients were excluded because of the presence of sustained cardiac arrhythmias. Thus, data from 78 patients (44 males and 34 females) undergoing AS (n=36), CS (n=21), and NS (n=21) were available for analysis (Table 1). AS procedures were in 42% bowel resections and in 20% pancreatectomies, trepanations were as frequent as 68% in neurosurgical procedures, and aortocoronary bypass procedures were performed in 78% of patients undergoing CS.
After data preprocessing, we obtained a total of 920,157 pairs of IAP and CNAP measurements. The mean percentages of artifacts per patient were 11% and 17% for IAP and CNAP (\(P=0.016\)), respectively. The individual artifact percentages correlated significantly between methods (Spearman’s \(r = 0.60\), \(P<0.001\)). 1.2% of the patients received a small finger cuff, 77% a medium one, and 21.8% a large one. The system set-up time of CNAP defined as the time between the start of the CNAP device and the occurrence of the first valid CNAP beat took on average 4 min.

Figure 1 shows the overall distribution of AP as measured by the invasive method. The precision of CNAP was not significantly different from that of IAP for systolic, diastolic, and mean AP, ranging from 7.5% to 9.0% and from 6.9% to 9.0% for CNAP and IAP, respectively (Table 2). The combined measurement errors of IAP and CNAP ranged from 10.2% to 12.8%. The calculated limits of agreement were \(\pm 17.6\) (31.5%), \(11.4\) (35.3%), and \(12.0\) (28.2) mm Hg for systolic, diastolic, and mean AP, respectively (Table 2).

The CNAP systolic AP was consistently lower and the CNAP diastolic AP was consistently higher than IAP systolic and diastolic AP, yielding to a systolic bias of +6.7 mm Hg and a diastolic bias of −5.6 mm Hg, respectively. The CNAP mean AP was also consistently higher than IAP mean AP, yielding to a bias of −1.6 mm Hg. Considering the standard errors given in Table 3, the bias for mean AP would lie between −4.4 and −1.2 mm Hg (bias ±1.96*SE) for 95% of investigations, and thus decreases within the recommended range of ±5 mm Hg for clinical agreement between the test and the reference method. The frequency of AP pairs having a difference within the calculated limits of agreement was 81%, 64%, and 76% for systolic, diastolic, and mean AP, respectively (Table 3). No significant differences in performance were present between measurements with medium and large finger cuffs; the one patient with small cuff was not considered. Figure 2 shows the difference vs average of the systolic, diastolic, and mean AP between CNAP and IAP along with the defined limits of agreement.

AP differences were weakly dependent on the magnitude of AP, as indicated by the slope of the least-squares linear regression that was significantly different from zero (\(P<0.01\)), i.e. 0.18, 0.15, and 0.12 for systolic, diastolic, and mean AP, respectively. No relationship between AP differences and the time of AP measurement could be identified. The incidence of detected FCAP was similar for both methods. IOH lower than 90 mm Hg was present more frequently with CNAP as with IAP (Table 4).

**Discussion**

In this study, we investigated whether CNAP measurements are equivalent to invasive measurements of AP generated by an intra-arterial catheter system (IAP) during different surgical procedures under general anaesthesia. The precision of CNAP was not significantly different from that of IAP. Furthermore, the occurrence of measurement artifacts was similar for both methods. The proportion of AP differences between methods that decrease within the calculated limits of agreement was lower than the one expected for statistical method equivalence. No relationship between AP differences and the measurement time of AP was present. CNAP detected as frequent as IAP episodes of FCAP and more frequent IOH. The time for obtaining the first valid CNAP measurement was comparable with the time for obtaining the first IAP measurement.
In clinical practice, a new monitoring technique is acceptable for clinical use if both its applicability and performance are comparable with those of an established method. The intra-arterial measurement of AP from radial or brachial artery is still the method of choice when continuous AP monitoring during predictable intraoperative haemodynamic instability is required. Nevertheless, given the fact that CNAP is a reliable device to assess the arterial AP continuously, there is a wide range of possible clinical applications. Its non-invasiveness facilitates its use for any operation with a need to assess, document, and maintain haemodynamic stability.

The clinical use of CNAP is restricted to a setting without the need for arterial blood gas measurements. During operations like endoscopic surgery to the paranasal sinuses, orthognathic surgery or operations involving the skull, arterial pressure within a certain range is mandatory to prevent bleeding but still maintain adequate organ perfusion. Arterial blood gas analysis is not required on a regular basis. Patients with such operations might benefit from the use of CNAP, as non-invasive continuous AP assessment might uncover AP alterations earlier than the NIAP measurement.

The performance of CNAP was assessed by quantifying its precision and accuracy. The CNAP precision was assessed separately for systolic, diastolic, and mean AP by calculating the within-subject SD of repeated measurements on the same subject. Since AP changes during the measurement period may increase the size of the measurement error, we considered time periods of ~1 min as short enough to obtain constant AP values and long enough to be representative for continuous AP measurements during general anaesthesia. The observed measurement percentage error of 7–9% for CNAP is in agreement with the reported percentage error for physiological measurements of ~10%. Furthermore, the size of the measurement error of CNAP was not significantly different from that of IAP.

The currently available recommendations for evaluation of the accuracy of non-invasive AP monitoring devices consider the mean difference and the SD of differences between the test and the reference method or express agreement in terms of percentage of differences that decrease within certain thresholds. Importantly, they consider intermittent rather than continuous AP devices. Further, they do not consider a potential measurement error of the reference method. Thus, these evaluation protocols may partly not be applicable to continuous non-invasive AP measurements. Consequently, we evaluated the accuracy of CNAP considering the proportion of differences in IAP that decreases within the calculated limits of agreement. Considering the combined precision of CNAP and IAP, we obtained as limits of agreement ±17.6, ±11.4, and ±12.0 mm Hg for systolic, diastolic, and mean AP, respectively. The observed frequency of AP differences within these limits was found to be lower than 95%, as it would be expected for method equivalency.
Fig 2 Difference vs average of systolic (a), diastolic (b), and mean (c) AP between non-invasive (CNAP) and invasive (IAP) measurements along with calculated limits of agreement as horizontal dashed lines.
Since CNAP provides reconstructed brachial AP and the invasive AP measurements were performed in the radial artery, the observed bias may be explained by the inherent physiological difference between brachial and radial artery AP. The systolic AP in the radial artery increases as a result of wave reflection, whereas the diastolic AP decreases due to resistance to flow, which is reflected by the systolic and diastolic bias of our study (Table 3). This systematic bias is also considered by the FDA-standard for intermittent oscillometric sphygmomanometers in a meta-analysis that reported absolute differences of 0.68–13.4 and 0.8–18 mm Hg for systolic and diastolic AP, respectively.14 The observed 6.7 and –5.6 mm Hg for systolic and diastolic bias with this investigation, respectively, lie within these ranges.

Furthermore, the observed bias for mean AP lies within the range of ±5 mm Hg for clinically acceptable agreement as recommended by the Association for the Advancement of Medical Instrumentation ANSI/AAMI SP10.

As shown in previous investigations,22 the measurement accuracy of a method can be increased by averaging a certain number of single, repeated measurements on the same subject. But, the amount of averaging continuous AP values varies considerably in the literature, where averages over 10, 30, or more values are reported.23 24 Since the time over which a continuous AP measurement should be averaged is not defined in guidelines,14 25 and objective criteria are difficult to establish for clinical settings, we preferred to perform the evaluation of the CNAP accuracy on non-averaged, single measurements of AP. This may have additionally increased the bias and may have artificially caused the observed weak correlation between AP differences and the magnitude of AP, since the AP continually changed between skin incision and skin suture.

Currently, commercially available devices for continuous non-invasive arterial pressure measurement are based on arterial tonometry (T-line Tensysmeter, Tensys Medical, Inc., San Diego, CA, USA) and on volume clamp method (Finapres, Finometer, Portapres, Nexfin, Datex-Ohmeda, Louisville, KY, USA). Investigations performed with the T-line Tensysmeter reported clinically acceptable results,23 26 but the challenge to obtaining accurate pressure values by tonometry is to find the optimal position over the artery to apply the sensor. Earlier comparative studies performed with the Finapres device reported an unreliable reflection of invasive AP in anaesthetized adults27 that may have been caused by an increase in venous blood volume distal to the finger cuff and by rapid contractions and dilations of finger arteries in relation to psychological, physical, and chemical stress (i.e. heat, cold, orthostasis, blood loss, and catecholamines). In order to reduce these limitations, the CNAP device switches repeatedly between two adjacent finger cuffs that are controlled by concentrically interlocking loops for rapid detection of blood flow oscillation.6 These technological advancements may have contributed to the high agreement between CNAP and IAP in frequency of occurrence and amount of FCAP (Table 4). Regarding IOH, CNAP showed a higher frequency of episodes than IAP. Nevertheless, the frequency of FCAP and IOH simultaneously detected by both methods was high even in patients undergoing CS (Table 4). These patients had the highest ASA physical status and amount of co-morbidities and they also showed a higher variability of systolic, diastolic, and mean AP that was probably caused by massive fluid resuscitation, observed cardiac arrhythmias, and catecholamine therapy usually given after separation from cardiopulmonary bypass.
One possible limitation of our study design may be the choice of radial artery as a reference for invasive AP measurement. At our institution, continuous AP monitoring in patients with predicted haemodynamic instability is usually performed by an intra-arterial catheter system placed into the left or right radial artery. CNAP measurements represent AP at the brachial artery because of the calibration with upper-arm oscillometric measurements. Although the comparison between CNAP and invasive AP in the brachial artery would have been more close to an ideal study design, we decided not to perform the invasive AP measurements at this arterial site because of the complications associated with arterial puncture and the inflating and deflating of the upper-arm cuff on the same arm and near the intra-arterial catheter.

In conclusion, the systolic, diastolic, and mean CNAP measurements were not statistically equivalent to simultaneous AP measurements of the radial artery catheter. However, the observed AP differences between methods could be explained by physiological differences between radial and brachial AP measurements and the preprocessing technique of the data. Furthermore, the measurement errors and the frequencies of simultaneously detected FCAP and IOH were similar for both methods. The bias for mean AP and the frequencies of simultaneously detected FCAP and IOH were similar for both methods. The bias for mean AP decreases within the recommended, clinically acceptable range. These findings indicate that CNAP provides real-time estimates of arterial pressure comparable with those generated by an invasive intra-arterial catheter system during general anaesthesia.

Acknowledgement
The authors would like to thank Dr A. Ackermann for the management of clinical data.

Conflict of interest
None declared.

Funding
C.J. received a research grant from CNSystems AG, Graz, Austria, and hardware support from Draeger Medical Systems, Inc., Danvers, MA, USA.

References
14. ANSI/AAMI. American national standard for manual, electronic, or automated sphygmomanometers. Association for the Advancement of Medical Instrumentation, 2002


