

RESEARCH ARTICLE

Validation of the Next-Generation Caretaker Continuous Physiological Monitor Using Invasive Intra-Arterial Pressures in Abdominal Surgery Patients

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Abstract

Introduction

The reliable detection and, ultimately, prediction of hypotensive events in post-operative settings remains an unsolved problem, as patients are currently only monitored intermittently because of the lack of validated, non-invasive/non-intrusive and continuous physiological monitoring technologies.

With this goal in mind, the aim of this study was to validate a next-generation platform version of the currently FDA-cleared non-invasive Caretaker (CT) physiological monitor in the hemodynamically challenging environment of abdominal surgeries in comparison with blood pressures obtained from arterial catheters, evaluated against ANSI/AAMI/ISO 81060–2:2019 standards as well as against current non-invasive standard of care measurements provided by clinical-grade automatic oscillometric cuffs.

Methods

Comparison data from 41 major abdominal surgery patients at Cooper Hospital (Camden NJ) were analyzed in this IRB approved study. Each patient was monitored with a radial arterial catheter and CT using a finger cuff applied to the contralateral middle finger. Systolic and diastolic blood pressures continuously collected from the arterial catheter and CT were compared using Pearson correlation coefficients and Bland-Altman analysis. In addition, a trend analysis using 4Q plots was performed. Both the CT's continuous BP tracking and the CT's self-calibration capability were analyzed.

Results

The continuous data comparisons were performed with and without taking the CT recalibrations into account. With the recalibrations the mean differences and standard deviations (STDs) for systole and diastole were, respectively, -1.14 mmHg (13.82 mmHg) and -2.49 mmHg (9.42 mmHg), while the correlations were 0.80 and 0.78. Mean differences and STDs for an initial calibration and no subsequent recalibrations were, respectively for systole and diastole, -0.42 mmHg (16.73 mmHg) and -2.57 mmHg (10.36 mmHg), while the correlations were 0.64 and 0.67. For the CT's self-calibrations alone, correlations for systole and diastole were, respectively, 0.83 and 0.75, while corresponding mean differences (STD) were -3.19 mmHg (10.86 mmHg) and -2.41 mmHg (8.18 mmHg). For 41% of total surgery time, both systole and diastole were within 8 mmHg of the arterial catheter Gold Standard. The concordances for systolic and diastolic blood pressure changes on a 30-second time scale were 0.87 and 0.86. The same comparison analysis for the automatic cuff and the arterial catheter data yielded: correlations for systole and diastole: 0.69 and 0.61, mean differences and STDs: 2.48 mmHg (15.82 mmHg) and 0.65 mmHg (10.68 mmHg).

Conclusions

The results of this study are significant in that they validate the future use of the CT physiological monitor, which utilizes Pulse Decomposition Analysis (PDA), in the post-operative monitoring scenario both as a monitor to detect hypotensive events to facilitate clinical intervention as well as provide signal inputs that could enable anticipatory measures.

Introduction

The reliable detection of hypotensive events in post-operative settings remains an unsolved problem, as patients are currently only monitored intermittently because of the lack of validated, non-invasive/non-intrusive and continuous physiological monitoring technologies. Meanwhile, the relevance of detecting these events is increasingly recognized. A recent study involving recovering abdominal surgery patients showed that 25% of patients experienced at least one hypotension episode.¹ Almost 50% of patients experienced MAP<65 mmHg for at least 15 minutes that went undetected based on intermittent vital signs monitoring. Detection is critically important, however, because post-operative hypotension is strongly associated with subsequent morbidity and mortality, in particular a significant increase in myocardial injury and death after non-cardiac surgery.^{2,3} This is the case even without intraoperative hypotension episodes.⁴

The Caretaker (CT) is a continuous noninvasive physiological monitor (Caretaker Medical LLC, Charlottesville, Virginia) that is FDA-cleared for the measurement of heart rate, continuous noninvasive blood pressure, and respiration. The system and the underlying approach have been described in detail elsewhere.^{5,6} Briefly, the CT tracks central aortic BP via pulse analysis, specifically Pulse Decomposition Analysis (PDA), of the peripheral pulse at a site such as a finger. The approach is based on the concept that two central reflection sites are responsible for the shape of the pressure pulse envelope of the upper body.^{7,8,9} The two reflection sites, one located at the aortic juncture of thoracic and abdominal aortas, and the other at the iliac bifurcation, reflect the primary left ventricular ejection pulse to give rise to two additional, reflected, component pulses.

Within the pulse pressure envelope of each cardiac cycle these three component pulses arrive sequentially in the arterial periphery. The model of the spatio-temporal behavior of these three component pulses constitutes the PDA formalism that is used to monitor hemodynamic states and their changes. The fact that the PDA model is based on physical assumptions that coherently explain the structure of the pulse, as a result of which it is also readily testable, has led to increasing interest.^{10,11,12,13,14}

Hardware-wise, the device uses a low pressure [35–45 mmHg], pump-inflated, finger cuff that pneumatically couples arterial pulsations via a pressure line to a pressure sensor for detection and analysis. Physiological data is communicated wirelessly to a tablet-based user interface via Bluetooth or Wi-Fi. For this study, a next-generation platform version of the CT was used that features an enhanced pressure sensor, a faster pump, and significantly upgraded processing electronics and communication interfaces.

The PDA-based approach tracks changes in physiological parameters such as blood pressure. A calibration is required to initiate operation, which can be provided by inputting a blood pressure obtained externally, or by using the device's self-calibration feature. In this case the device performs an oscillometric pressure sweep, very similar to that of an upper-arm cuff, using the same finger cuff. The continuous sweep and simultaneous data acquisition completes in about 25 seconds, significantly faster than standard oscillometric technologies.

The aim of this study was to validate the non-invasive CT physiological monitor in the hemodynamically challenging environment of abdominal surgeries, by comparing its blood pressure calibration and tracking capability with intra-arterial pressures as well

as with non-invasive standard of care measurements provided by clinical-grade automatic oscillometric cuffs. With reference to the introduction, part of the analysis focused on tracking accuracy during hypotensive events.

Methods

The Cooper Health System Institutional Review Board approved the study, and all subjects gave informed written consent. Data from forty one adult patients requiring hemodynamic monitoring during major open abdominal surgery were analyzed. Patients were not excluded due to other medical conditions. The type of surgeries was chosen because the blood pressure fluctuations and variability provided an opportunity to compare tracking accuracy under baseline and induced controlled dynamic conditions. Measurements were obtained during general anesthesia in these patients once the arterial catheter signal became available, usually within minutes after induction. The data was evaluated using the ANSI/AAMI/ISO 81060-2:2019-related standards of accuracy and precision,¹⁵ as well as current clinical standards in non-invasive blood pressure monitoring using automatic cuffs.

Anesthesia procedure

Patients were induced under general anesthesia by using propofol (2-4 mg/kg) and fentanyl (250ug). Tracheal intubation was facilitated by the administration of rocuronium (0.6 mg/kg). Mechanical ventilation was started using a volume controlled ventilator to maintain an adequate saturation and an end-tidal carbon dioxide of 35 mmHg. Inhalational anesthetic (Isoflurane) was added to maintain a BIS monitoring of 40-45. Vasoactive drugs were used to maintain a MAP greater than 60 mmHg based on the catheter value. Hemodynamic variables were measured from both devices for the entire procedure. The

MAP, systolic and diastolic blood pressures were continuously collected from the arterial catheter and CT and averaged over 10 s periods for both devices.

Invasive arterial pressure measurement

Standard arterial blood pressure monitoring was performed using a 20G intra-arterial catheter inserted in the radial artery under local anesthesia using ultra sound guidance. The catheter was connected to a disposable pressure transducer with standard low compliant tubing. The transducer was placed at heart level and zeroed to ambient pressure. The transducer data was digitized, processed, and collected using the Datex-Ohmeda S/5 Collect system (Datex-Ohmeda Division, Instrumentarium Corporation, Helsinki, Finland).

Non-invasive CareTaker arterial pulse signal recording

The arterial pressure pulse signal was continuously measured noninvasively using the CT device. In order not to interfere with Cooper procedures the device was placed on the OR patient's wrist during the procedure setup, with the finger cuff coupled to the middle member of the middle finger, and data transmission was verified, after which no further physical interaction with the device was possible. The patient's arms were then usually tucked underneath the patient's body as part of standard practice to facilitate the surgeon's access.

Operation of the device would commence after an initial blood pressure self-calibration procedure, lasting approximately 25 seconds, during which time the device scans the finger cuff's coupling pressure from 0 to 250 mmHg while collecting the pressure-modulated arterial pressure pulse signal at a 500 Hz acquisition rate. At the end of the pressure scan, systolic and diastolic blood pressures are calculated from the processed signal envelope. Thereafter, the device was

programmed to perform self-calibration scans at 5 minute intervals, operating in between in the continuous tracking mode with the finger cuff pressure collecting pulse data at a fixed baseline cuff pressure of between 20 and 45 mmHg. The coupling pressure for continuous operation is determined as part of the self-calibration procedure and held constant until the next procedure. Collected data were sent via Wi-Fi interface to an Android tablet for storage.

In most cases, the CT was placed on the arm contralateral to the one monitored with the radial arterial catheter. The automatic upper arm cuff was always placed on the arm contralateral to the arterial catheter

Data inclusion

Arterial catheter data were visually and algorithmically inspected and sections of obvious catheter failure, characterized by either continuous or spurious nonsensical readings, were excluded. Sections contaminated by excessive motion artifact such that the peak detection algorithm was no longer able to identify heart beats, were also excluded. In the case of the CT data, a custom signal/noise factor (SNF) was used to identify poor quality data sections, which were excluded. The factor is based on the ratio of the variances of the physiological signal band to the noise band and obtained using Fourier spectral analysis over an 8-s window with 1 s overlap. The frequency range of the band associated with the physiological signal was set to 1–10 Hz, based on data by the authors and results by others,¹⁶ while the noise band was set to the 100–250 Hz frequency range, which is subject to ambient noise but contains no signal relevant to the base band phenomena of the arterial pressure pulse or its propagation characteristics. Data sections with an SNF below 80 were excluded from the analysis.

Comparisons of methodologies

All comparisons between CT data, arterial catheter data, and automatic cuff data were post-processed. The beat-by-beat time alignment between CT data and arterial catheter data was established by analyzing inter-beat intervals (IBI) obtained from both data streams. For the time alignment between arterial catheter data and automatic cuff readings, the time stamps in the respective systems were used. For the CT, both the calibration data and the continuous tracking data were analyzed in comparisons with the arterial catheter readings. For the calibration data, the CT's readings were compared to 15 second averages of catheter readings prior to the CT's respective completion time. For the continuous data, comparisons were beat-to-beat. For the comparisons of the automatic cuff readings with the arterial catheter readings, catheter readings were averaged over a 30-second window prior the automatic cuff's respective completion time.

Statistical Analysis

For the comparisons of the CT data, both for the calibration and the continuous data, Pearson correlations and Bland-Altman plots were generated. The 95% confidence intervals were calculated for each plot. These analyses were repeated for low and normal to high blood pressure regimes, the demarcation being systole of 100 mmHg. Also examined were the percentage of time the CT measurements were in compliance with the currently applicable blood pressure standard, ANSI/AAMI/ISO 81060-2:2019.¹⁵

A trend comparison analysis of the CT and the arterial catheter data was performed.¹⁷ To facilitate visualization of the trend results, surface plots of 3D histograms were used to categorize trends with a resolution of 0.25 mmHg/second. Trending accuracy was examined over different time ranges. Zero change rates were excluded.

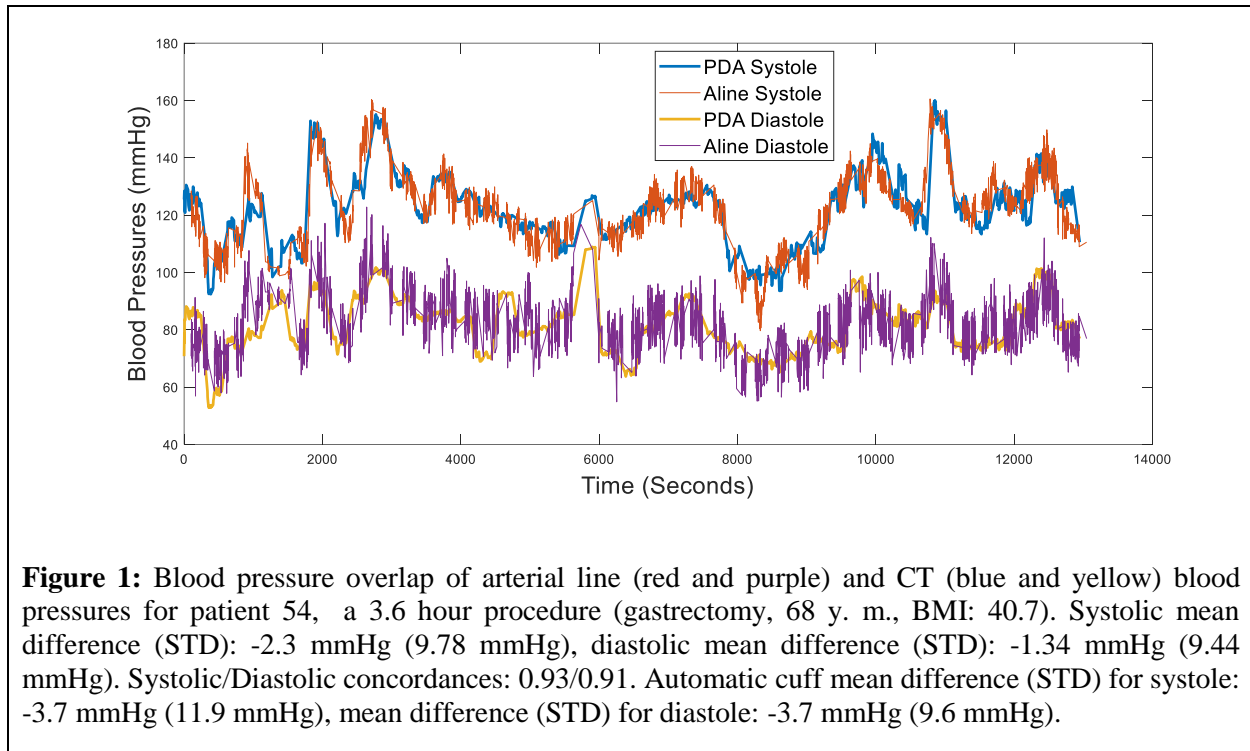
For the comparison of the automatic cuff and the arterial catheter data Pearson correlations and Bland-Altman analyses, with 95% confidence intervals, were generated. Linear regression lines showing the correlation are included on the correlation plots. Pitman's test was performed to assess the null hypothesis of no association of variance between both measurement methodologies.

A power analysis was not needed as the estimation of the difference between the technologies was the outcome of interest and, on average, almost 4,500 data points were matched per patient. The confidence intervals are reported to show the variability in the estimates. The final cohort size of 41 was determined primarily by patient availability and is 2.7 times larger than the required size of 15 patients using the ANSI/AAMI/ISO 81060-2:2019¹⁵ standard when an arterial catheter is used for comparison.

Results

A total of 55 patients were enrolled but complete sets of data for only 41 patients were available (m/f: 19/22, mean age: 64.9y (STD: 10.1 y), mean BMI: 28.8 (9.50)). Patient characteristics are compiled in **Table 1**. In 11 cases the arterial catheter data was not available, while in one case the Caretaker data was accidentally deleted and in three cases the CT was accidentally stopped early in the procedure due to operator error early in the study. For the comparison of continuous data a total of 184,395 matched data points were obtained, corresponding to approximately 113.5 surgical procedure hours. For the self-calibration evaluation, 1257 data comparisons were made. Across patients the mean of excluded data was 3.16% (STD: 5.87%, range 0 – 15%) while the median was 0%.

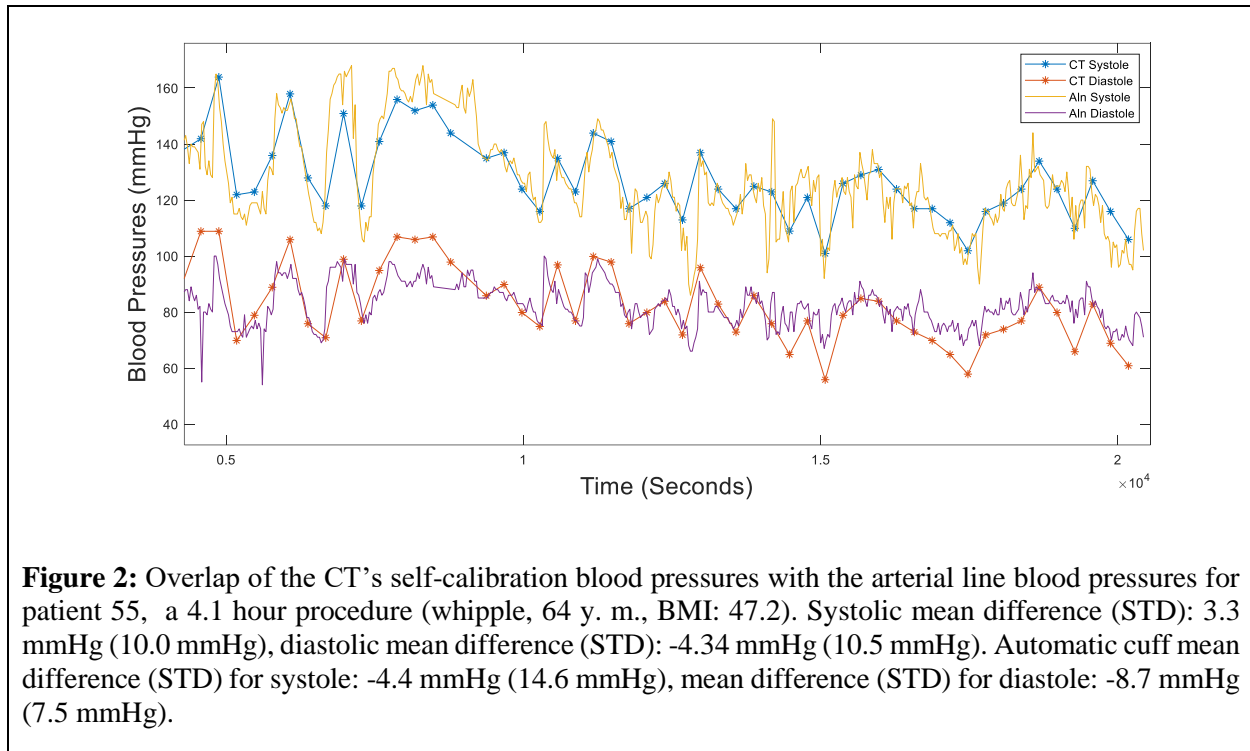
Characteristic	Mean (SD) or N (%)
Age – mean (STD) – yr.	64.8 (10.1)
Body Mass Index – mean (STD) – kg/m ²	28.8(9.5)
Male Sex – no. (%)	19 (46.3)
Procedure	
Whipple-related (%)	29.3
Laparoscopic procedures (%)	24.4
Other resections (%)	46.3



As an example of an overlap of significantly varying continuous blood pressures obtained with the CT and the arterial catheter, we present the results for patient 54 in **Figure 1**. The procedure and comparison statistics are presented in the figure caption, as are the performance statistics of the automatic arm cuff. In the case of this patient the CT was set to recalibrate every 5 minutes. **Figure 2** presents the same information for an overlap example of just the CT re-calibration blood pressure values with the arterial catheter data for patient 55.

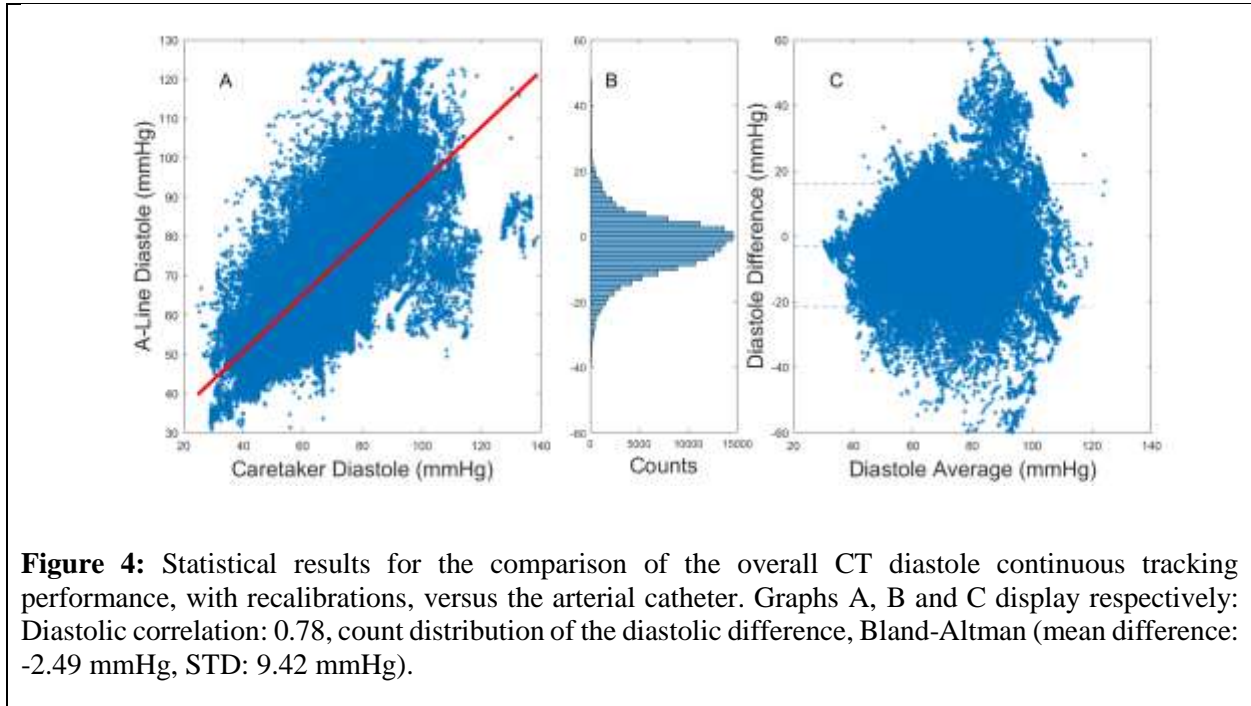
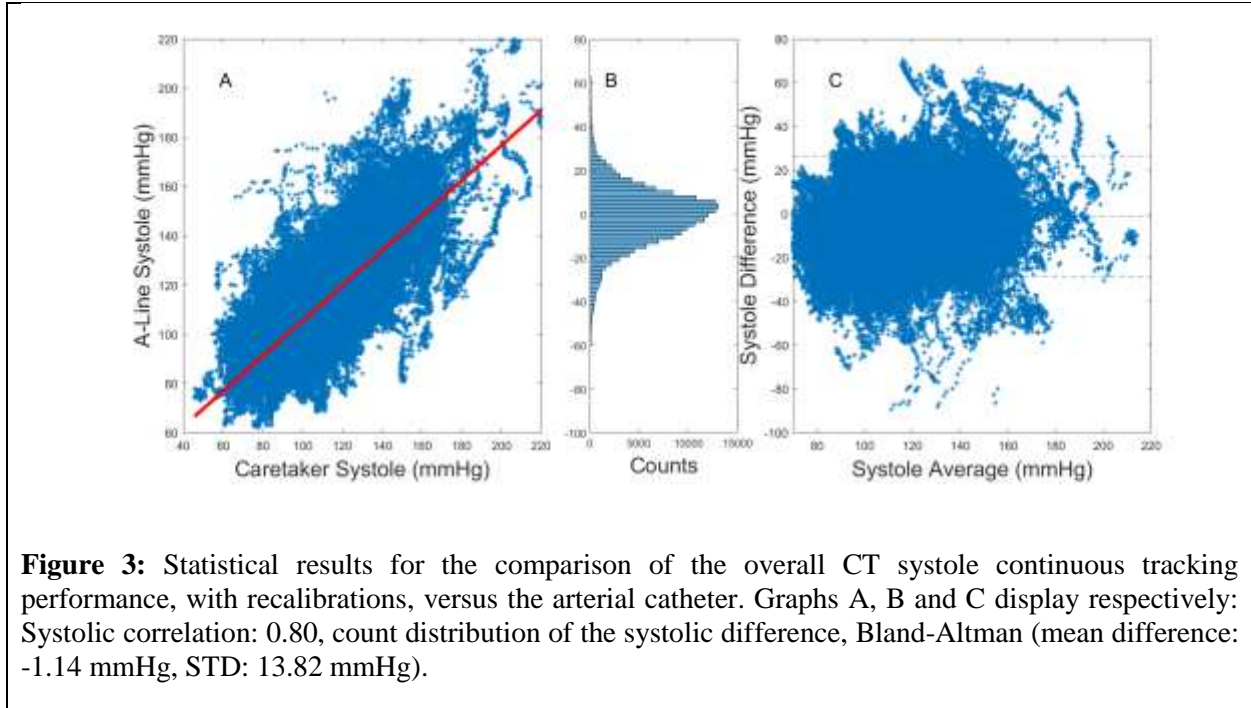
The overall continuous data comparisons were performed with and without taking the CT recalibrations into account, meaning in the latter case that results depended entirely

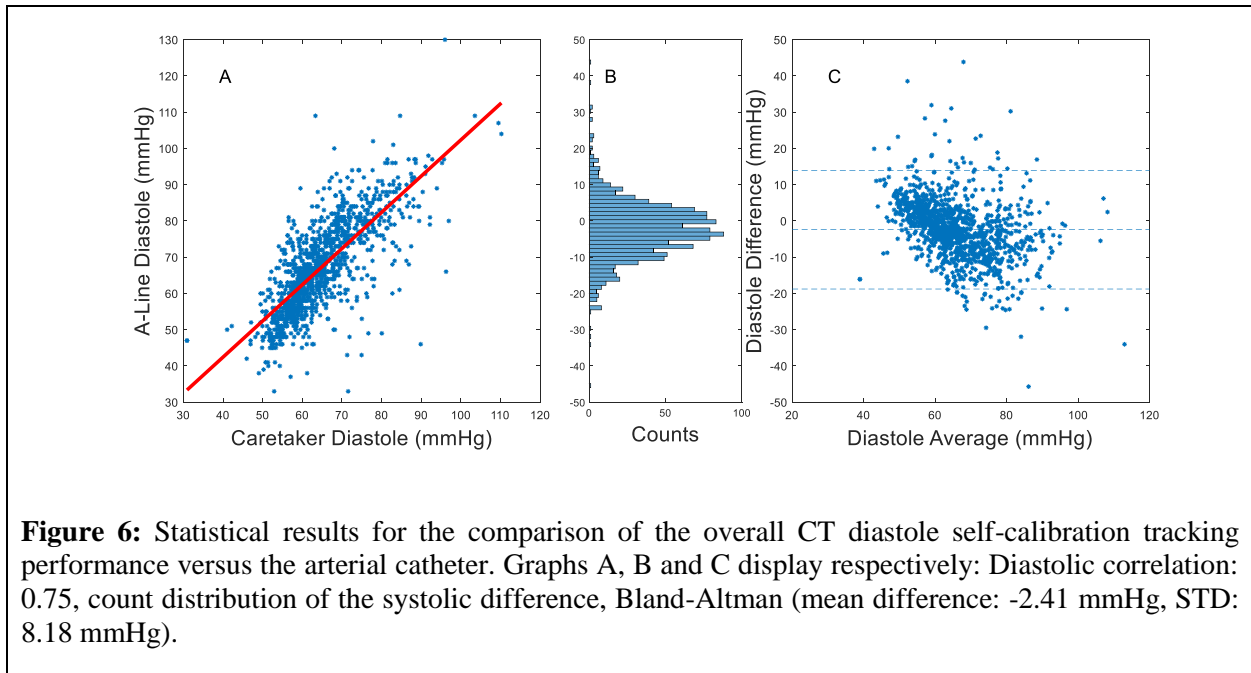
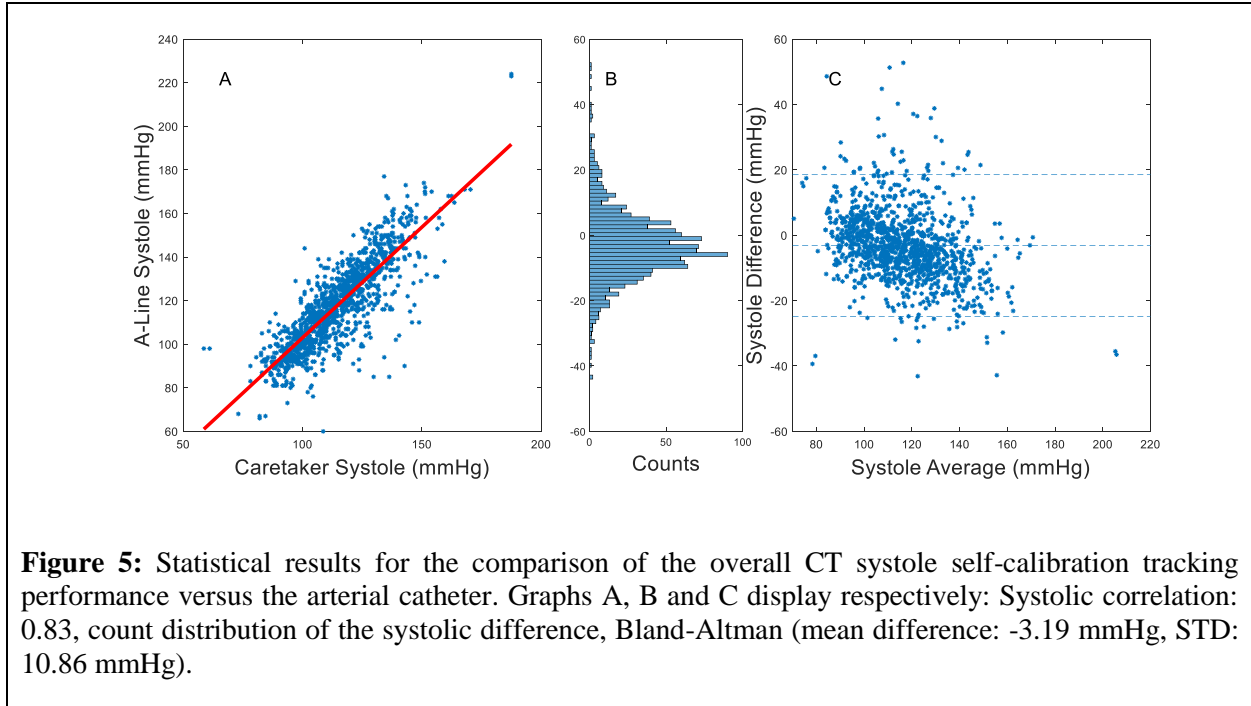
on the CT's tracking capability with no corrections. With the recalibrations the mean differences and standard deviations (STDs) for systole and diastole were, respectively, -1.14 mmHg (13.82 mmHg) and -2.49 mmHg (9.42 mmHg), while the correlations were 0.80 and 0.78. Correlation, count distributions, and Bland-Altman plots for systole and diastole are presented in **Figure 3 a-c** and **Figure 4 a-c**, respectively. Mean differences and STDs for an initial calibration and no subsequent recalibrations were, respectively for systole and diastole, -0.42 mmHg (16.73 mmHg) and -2.57 mmHg (10.36 mmHg), while the correlations were 0.64 and 0.67. No trends are seen in the Bland-Altman figures.

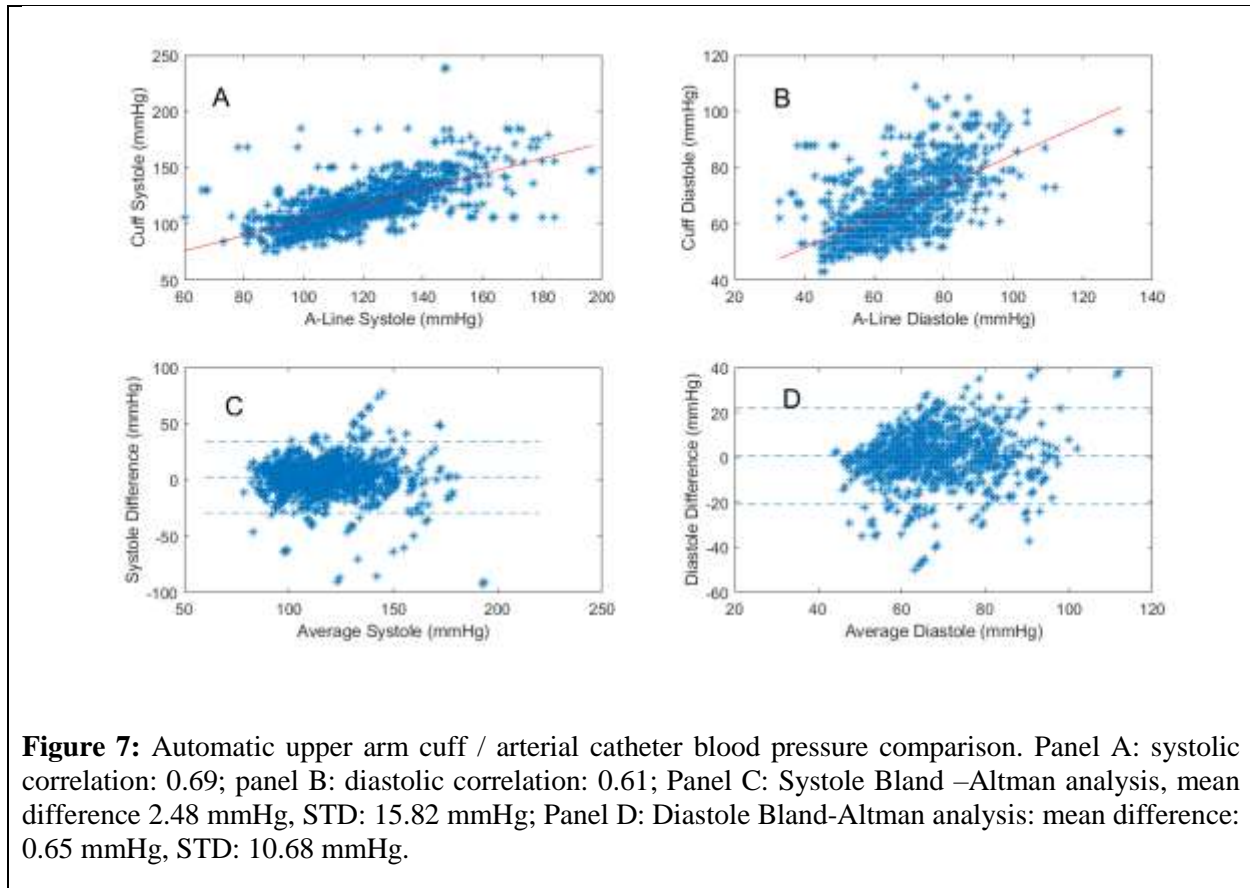


The calibration and re-calibration data were analyzed separately in comparison to the arterial catheter data. Correlations for systole and diastole were, respectively, 0.83 and 0.75, while corresponding mean differences (STD) were -3.19 mmHg (10.86 mmHg) and -2.41 mmHg (8.18 mmHg). The results, respectively for systole and diastole, are presented in **Figure 5 a-c** and **Figure 6a-c**.

The results for the same comparison analysis for the automatic cuff and the arterial catheter data (correlations for systole and diastole: 0.69 and 0.61, mean differences and STDs: 2.48 mmHg (15.82 mmHg) and 0.65 mmHg (10.68 mmHg) are presented in **Figure 7**. Pitman's tests for systole and diastole failed to reach statistical significance (respectively, $p=0.135$ and $p=0.137$).







Tracking accuracies in different blood pressure regimes were examined by repeating the statistical analyses for systolic blood pressures below and above 100 mmHg. For systole < 100 mmHg, the correlations for systole and diastole were, respectively: 0.62 and 0.64, mean differences and STDs: 0.90 mmHg (12.20 mmHg) and -0.70 mmHg (7.96 mmHg). For systole > 100 mmHg the corresponding values were: 0.72 and 0.73, mean differences and STDs: -1.77 mmHg (14.22 mmHg) and -3.04 mmHg (9.78 mmHg).

Also examined was the percentage of time that STDs for systole and diastole were within the 8 mmHg criterion associated with the ANSI/AAMI/ISO 81060–2:2019 standard. The corresponding values for

systole and diastole, respectively, were 50.0% and 69.2%, while for both simultaneously the percentage was 41.0%. The mean (STD) systolic pressure, as determined using arterial catheter data, for, respectively, the within/outside 8 mmHg STD was 114.7 mmHg (19.5 mmHg) and 117.4 mmHg (21.1 mmHg).

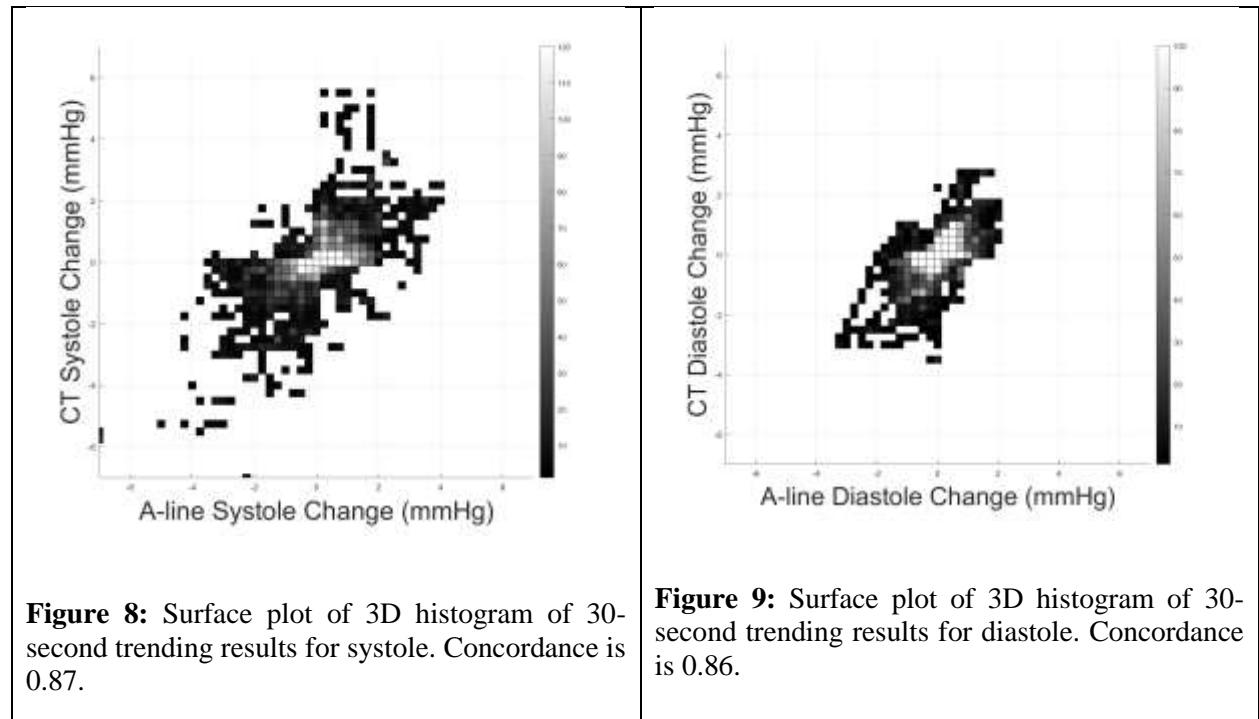
A trend comparison analysis of the continuous data on different time scales was performed. The methodology used here follows the approach outlined by Saugel.¹⁷ The CT and arterial catheter blood pressure data were averaged over time windows from 10 to 30 seconds and matched rates, i.e. mmHg/sec, were calculated by obtaining the ratio of blood pressure and time differences

of adjacent systole and diastole data points. Zero change rates were excluded.

Time average (seconds)	Systolic concordance	Diastolic concordance
30	0.87	0.86
20	0.83	0.82
10	0.75	0.74

The level of concordance was calculated by taking the ratio of the proportion of data points in the quadrants representing direction of change agreement to all data points. The concordances for systole and diastole for the different time scales are listed in **Table 2**. The 30-second time scale trending results for, respectively, systole and diastole, are presented as surface plots of 3D histograms in **Figure 8** and **Figure 9**. The resolution of the histograms is 0.25 mmHg/second in both dimensions. The counts for each two-

dimensional bin are represented as a grayscale intensity. The concordances for systolic and diastolic blood pressure changes on a 30-second time scale were 0.87 and 0.86, respectively. For the systolic trend the angular bias relative to unity slope, i.e. a 45-degree diagonal, was -16.4° , the corresponding angular bias for the diastolic trend was -14.3° . Overall trend results did not change significantly whether recalibrations were included or not.



Discussion

This study's principal finding is that the CT continuous physiological monitor demonstrated overall very good agreement with invasively measured arterial blood pressure. The results show agreement with the 81060 standard over a significant fraction of time, very good trending, and performance within current standard clinical non-invasive monitoring performance levels, as evidenced by the automatic cuff results. But the CT's significant added benefit is providing continuous hemodynamic information, which is of particular importance with regard to the intended focus on the detection of hypotension. Further emphasizing the CT's relevance in this clinical application are the comparison results that isolated performance in that blood pressure regime.

It is also important to put the comparisons of these results with the 81060 standard in perspective. The standard was developed for spot-check BP measurements under stable conditions, neither of which are given here. Instead, the comparisons of this study were intentionally made under hemodynamically highly challenging conditions, with multiple patients experiencing episodes with blood pressure transitions from hypotension to extreme hypertension within minutes. The performance of the clinical-grade automatic arm cuff further reinforces the challenge non-invasive blood pressure measurements environment represent, as its readings did not comply with the 81060 standard for a single complete patient procedure. In fact, for patient 03 the automatic arm cuff had to be moved to the thigh after failing to obtain a single upper-arm reading.

The presented blood pressure comparison results between CT and arterial catheter are

encouraging, particularly when considering the challenges that are associated with 1. Monitoring blood pressure non-invasively in general, 2. Comparing blood pressures measured at different measuring sites, and 3. Utilizing surrogate measures as opposed to direct measurements of blood pressure.

Regarding the first point, less than optimal comparison results have been amply documented in comparison studies between the clinical standard in non-invasive blood pressure measurements, the upper arm cuff, and arterial catheter Gold Standard when considering the 81060 standard.^{18 19} Those studies concluded that tighter device standards are needed, in part because there is no standardization in processing algorithms, most of which are proprietary.²⁰ However, the problem is certainly not entirely related to technical shortcomings but is also very much related to the broad range of variances in human physiology.

As to the comparison of blood pressures obtained from different physiological monitoring sites, the lack of generally applicable defined functional forms relating them has been well documented.^{21 22 23} Indeed, the most recent study [21] revealed the lack of a consistent general relationship even just between systole measured invasively at the brachial and radial arteries in a cohort of 180 subjects, in other words with the same arterial catheter at two different measurement sites. While 43% of subjects presented with differences of <5mmHg, the remainder presented with differences in both sign, i.e. brachial systole was higher than radial (11%) which is an unexpected result, and magnitude, i.e. radial systole > 10 mmHg (19%) and >15 mmHg (13%).

Finally there are the additional problems associated with monitoring indirect, surrogate measures to track blood pressure, such as pulse transit time or pulse analysis, mainly because neither provide measures that depend on blood pressure changes only.^{24 25}

²⁶ Instead, surrogate measures are subject to other hemodynamically relevant parameters, such as heart rate or arterial stiffness that can mask blood pressure-related effects. A benefit of the PDA formalism is that it proposes a reasonably comprehensive physiologically-based explanation of the structure of the arterial pulse that seeks to model the interplay of these overlapping effects. This is different from approaches that seek to correlate features on the pulse, such as for example the inversions associated with the renal reflection known as the second systolic peak, with hemodynamic variables.^{27 28} The problem with the latter approach is that such features cannot be counted on to persist permanently across the continuum of inter- and intra-subject physiological states. One benefit of modeling underlying mechanisms, i.e. the spatio-temporal interplay of the component pulses of the pulse envelope, is that the disappearance of features under certain hemodynamic circumstances can be algorithmically prepared for. For these reasons PDA's grounding in physiological assumptions makes the model attractive.

All of these considerations suggest that there may be a natural "lower limit" to the degree to which non-invasive blood pressure monitors can match the results obtained invasively, particularly across large patient groups with commensurately varied physiologies and pathologies, and under highly variable hemodynamic conditions.

These considerations and the fact that there is always the possibility that surrogate measures will not track blood pressure with sufficient accuracy during episodes of extreme hemodynamic changes, make the 25-second self-calibration feature of the CT more significant. Under such circumstances it is this feature that provides the fallback option of fast, traditional and trustable oscillometry-derived measurements, which potentially could be triggered repeatedly until a hemodynamically more stable state is again reached to resume beat-by-beat tracking based on PDA-based pulse analysis. Sustained rapid changes in arterial stiffness as well as heart rate could be a trigger condition for such a temporary operation mode and is the focus of current work.

The primary limitation of this study relates to time recordings of unequal lengths for different patients, resulting in unequal weighing of patients' data in the different analyses. These were associated with the accommodations necessary to perform research within the clinical workflow of invasive abdominal surgeries.

Conclusion

We have presented blood pressure value and trend comparison results of the Next-generation Caretaker physiological monitor against invasively obtained blood pressures in the highly dynamic clinical environment of abdominal surgeries. Blood pressures spanned a clinically meaningful range, from severe hypotension to extreme hypertension, with at times rapid transitions from one physiological state to the other. Performance of the Caretaker matched that of current clinical-grade non-invasive blood pressure monitoring, but with the significant advantage of providing continuous vital

signs, and was within AAMI compliance standards, despite the inapplicability of the measurement setting, over 40% of the time simultaneously for both systole and diastole.

Future studies and analyses will focus on the Caretaker's usability in clinical settings where the prediction and detection of hypotension is of significant interest, particularly in post-operative settings, where patients currently are only monitored intermittently because of the lack of validated, non-invasive/non-intrusive and

continuous physiological monitoring technologies that could supply the input to predictive algorithms. While work will continue to further improve the CT's tracking algorithm performance, the emphasis will shift to identification and down-selection of predictive patterns in combinations of vital signs, such as heart rate variability (HRV), arterial stiffness (AS), and blood pressure variability (BPV), as well as pulse analysis parameters derived from the CT pulse signal. The encouraging results of this study provide the basis for that advanced development.

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