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*Research article*

# Body surface and body core temperatures and their associations to haemodynamics: The BOSTON-I-study: Validation of a thermodilution catheter (PiCCO) to measure body core temperature and comparison of body surface temperatures to thermodilution-derived Cardiac Index

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**Abstract:** Assessment of peripheral perfusion and comparison of surface and body core temperature (BST; BCT) are diagnostic cornerstones of critical care. Infrared non-contact thermometers facilitate the accurate measurement of BST. Additionally, a corrected measurement of BST on the forehead provides an estimate of BCT (BCT_Forehead). In clinical routine BCT is measured by ear thermometers (BCT_Ear). The PiCCO-device (PiCCO: Pulse contour analysis) provides thermodilution-derived Cardiac Index (CI_TD) using an arterial catheter with a thermistor tip in the distal aorta. Therefore, the PiCCO-catheter might be used for *continuous* BCT-measurement (BCT_PiCCO) in addition to *intermittent* CI-measurement. To the best of our knowledge, BCT_PiCCO has not been validated compared to standard techniques of BCT-measurement including measurement of urinary bladder temperature (BCT_Bladder). Therefore, we compared BCT_PiCCO to BCT_Ear and BCT_Bladder in 52 patients equipped with the PiCCO-device (Pulsion; Germany). Furthermore, this setting allowed to compare different BSTs and their differences to BCT with CI_TD. BCT_PiCCO, BCT_Ear (ThermoScan; Braun), BCT_Bladder (UROSID; ASID BONZ), BCT_Forehead and BSTs (Thermofocus; Tecnimed) were measured four times within 24h. BSTs were determined on the great toe, finger pad and forearm. Immediately afterwards TPTD was performed to obtain CI_TD. 32 (62%) male, 20 (38%) female patients; APACHE-II 23.8 ± 8.3. Bland-Altman-analysis demonstrated low bias and percentage error (PE) values for the comparisons of BCT_PiCCO vs. BCT_Bladder (bias 0.05 ± 0.27 °Celsius; PE = 1.4%), BCT_PiCCO vs. BCT_Ear (bias 0.08 ± 0.38 °Celsius; PE = 2.0%) and BCT_Ear vs. BCT_Bladder (bias 0.04 ± 0.42 °Celsius; PE = 2.2). While BCT_PiCCO, BCT_Ear and BCT_Bladder can be considered interchangeable, Bland-Altman-analyses of BCT_Forehead vs. BCT_PiCCO (bias = −0.63 ± 0.75 ° Celsius; PE = 3.9%) Celsisus, BCT_Ear (bias = −0.58 ± 0.68 ° Celsius; PE = 3.6%) and BCT_Bladder (bias = −0.55 ± 0.74 ° Celsius; PE = 3.9%) demonstrate a substantial underestimation of BCT by BCT_Forehead. BSTs and differences between BCT and BST (DCST) significantly correlated with CI_TD with r-values between 0.230 and 0.307 and p-values between 0.002 and $p < 0.001$. The strongest association with CI_TD was found for BST_forearm (r = 0.307; $p < 0.001$). In a multivariate analysis regarding CI_TD and including biometric data, BSTs and and their differences to core-temperatures (DCST), only higher temperatures on the forearm and the great toe, young age, low height and male gender were independently associated with CI_TD. The estimate of CI based on this model (CI_estimated) correlated with CI_TD (r = 0.594; $p < 0.001$). CI_estimated provided large ROC-areas under the curve (AUC) regarding the critical thresholds of CI_TD ≤ 2.5 L/min/m$^2$ (AUC = 0.862) and CI_TD ≥ 5.0 L/min/m$^2$ (AUC = 0.782). 1.) BCT_PiCCO, BCT_Ear and BCT_Bladder are interchangeable. 2.) BCT_Forehead significantly underestimates BCT by about 0.5 ° Celsius. 3.) All measured BSTs and DCSTs were significantly associated with CI_TD. 4.) CI_estimated is promising, in particular for the prediction of critical thresholds of CI.

**Keywords:** body core temperature; body surface temperature; toe temperature; infrared thermometer; Cardiac Index; transpulmonary thermodilution; PiCCO; urinary bladder thermistor; thermofocus

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**Abbreviations:** APACHE-II: Acute Physiology And Chronic Health Evaluation; AUC: Area under the curve; BCT: Body core temperature; BCT_Bladder: Body core temperature derived from thermistor in the urinary bladder; BCT_Ear: Body core temperature measured with ear thermometer; BCT_Forehead: Body core temperature calculated from infrared thermometer measurement of BST on the forehead; BCT_PiCCO: Body core temperature measured with PiCCO; BST: Body surface temperature; BST_Forehead: Body surface temperature estimated by measurement of the forehead temperature**;** CI: Cardiac index; CI_estimated: Estimate of cardiac index derived from multivariate regression; CI_TD: Cardiac index derived from thermodilution; CO: Cardiac output; DCST: Difference of core and surface temperature; EVLW(I): Extravascular lung water (index); GEDV(I): Global end-diastolic volume (index); ICU: Intensive care unit; PE: Percentage error; PiCCO: Pulse contour cardiac output; ROC: Receiver-operating characteristics; TPTD: Transpulmonary thermodilution.

## 1. Introduction

Based on technologies such as pulse contour analysis and transpulmonary thermodilution (TPTD), the last two decades brought substantial advances in hemodynamic monitoring. Nevertheless, clinical examination including the assessment of body core temperature (BCT), body surface temperature (BST) and their difference (Delta-Core-Surface-Temperature; DCST) are diagnostic cornerstones of critical care [1–3]. BCT outside a small normal range from 36 ° to 38 ° has been defined as a diagnostic criterion of sepsis and systemic inflammatory response syndrome [4]. Considering this small normal range, accurate measurement of temperature is crucial. Despite conflicting data on their accuracy predominantly in pediatric patients [5–8], infrared thermometers to assess the tympanic temperature in the ear (BCT_Ear) are commonly used for *intermittent* measurement of BCTs in ICU-patients [9]. Due to potentially rapid changes in BCT in critically ill patients, continuous measurement of BCT is appealing, e.g. during cooling after resuscitation [10]. Measurement of urinary bladder temperature using a thermistor equipped Foley-catheter is among the options for continuous measurement of BCT_Bladder [11–15], in particular in patients at need for urinary bladder catheterization.

TPTD is based on subtle analysis of the changes of temperature in the distal aorta after injection of a bolus of 15mL of ice-cold saline [16]. Therefore, a specific arterial catheter is introduced via the femoral artery. In addition to a conventional arterial access for blood withdrawal and measurement of arterial blood pressure, this catheter also includes a thermistor to measure changes in temperature after the injection of cold indicator solution. Changes in temperature over time after indicator injection allow for the calculation of cardiac output (CO), of the preload marker global end-diastolic volume (GEDV [17]) and of extravascular lung water (EVLW [18]), a marker of pulmonary oedema. According to the manufacturer´s recommendation, this procedure should be repeated after intervals of 8h. Due to the central position of the thermistor and continuous display of absolute temperatures, the PiCCO-device (PiCCO: Pulse Contour cardiac output) could be suitable for continuous measurement of BCT. Except one study comparing measurements of BCT by PiCCO to a similar method in the pulmonary artery [19], continuous assessment of BCT by PiCCO (BCT_PiCCO) has never been validated to different standard methods of BCT-measurement.

The "Thermofocus" (Tecnimed; Varese; Italy) is a non-contact infrared thermometer to measure BSTs and to estimate BCT based on measurement of BST at the forehead (BCT_Forehead).

In addition to use the Thermofocus to estimate BCT, also accurate measurement of BST is of interest in critically ill, since several studies have shown a significant association of BST with CO [1,3,20–27]. However, to the best of our knowledge, the association of CO with BSTs measured with Thermofocus has not been investigated.

Therefore, our study had two major aims:

1.) Validation of continuous measurement of BCT with the PiCCO-catheter (BCT_PiCCO) compared to assessment of BCT by tympanic temperature (BCT_Ear) and a urinary bladder thermistor (BCT_Bladder).

2.) Since an arterial PiCCO catheter in place allows for measurement of cardiac index (CI_TD), we also compared BSTs measured with Thermofocus to CI_TD derived by TPTD with the PiCCO.

## 2. Materials and methods

This study was conducted in an eight-bed-intensive care unit (ICU) of a university hospital. It was approved by the local ethics committee (Ethikkommission der Technischen Universität München 3049/11s). Due to the observational design and the use of clinical routine methods, the need of informed consent was waived. The study has been registered (ISRCTN17182512).

In 52 ICU-patients BCT was measured four times within one day using a PiCCO-catheter (BCT_PiCCO; PV2025L20-catheter, Pulsiocath, Pulsion Medical Systems, Munich, Germany), a thermistor-tipped urinary catheter (BCT_Bladder; "UROSID"; ASID BONZ; Herrenberg; Germany) and an ear thermometer (BCT_Ear; "Thermoscan"; Braun; Melsungen; Germany). Additionally, BSTs were determined on the great toe, finger pad, forearm and forehead using an infrared non contact thermometer ("Thermofocus"; Tecnimed; Verese; Italy). For the measurement on the forehead the “forehead button” was used which results in display of an estimate of BCT based on BST on the forehead. Immediately afterwards, TPTD was performed (triplicate measurement with 15mL ice-cold saline 0.9%) as described previously [16,28]. Based on the TPTD-curves cardiac index CI, global end-diastolic index GEDVI and extravascular lung water index EVLWI were calculated by a PiCCO-2-device (Pulsion Medical systems SE; Feldkirchen; Germany.

There were two major endpoints of the study:

To compare BCT_PiCCO to BTC_Ear, BCT_Bladder and BCT_Forehead, we used Wilcoxon-test for paired samples and Bland-Altman-analysis.

To investigate the association of BSTs and biometric data (age, gender, weight, height) with CI_TD we used correlation (Spearman), Wilcoxon-test for paired samples, multivariate linear regression analysis (backward selection) and reveiver-operating-characteristic areas under the curve (ROC-AUC).

Non-parametric statistics (Wilcoxon-test) were preferred in general, since Kolmogorov-Smirnov-test failed to prove normal distribution for several parameters (including BCT_Bladder and BCT_Forehead).

The power calculation was based on the number of patients required to detect a mean-difference of at least 0.5 ° Celsius in a population with a mean gold-standard body core temperature of 37 $\pm$ 1.25 ° Celsius.

Based on pilot data in our ICU we assumed a true mean of 37 $\pm$ 1.25 ° Celsius and a 0-hypothesis mean of 36.5 ° Celsius. A number of n = 49 would provide a p-value of $p < 0.05$ and a statistical power of 80%. Assuming a drop-out-rate of 5%, we included a total of n = 52 patients.

All statistical analyses were performed with IBM SPSS 26.

## 3. Results

### *3.1. Patients characteristics*

Table 1 shows the patients characteristics.

**Table 1.** Patients characteristics.

| Patients | n = 52 |
|---|---|
| Gender | n = 32 (62%) male; n = 20 (38%) female |
| Age [years] | 63 $\pm$ 11 |
| Height [cm] | 172 $\pm$ 9 |
| Weight [kg] | 74 $\pm$ 17 |
| APACHE-II-score | 23.8 $\pm$ 8.3 |
| Aetiology | 19 (37%) Cirrhosis or acute liver failure |
| | 14 (27%) Pneumonia; Acute respiratory distress syndrome |
| | 9 (17%) Sepsis |
| | 4 (7%) Cardiogenic shock |
| | 3 (6%) Gastrointestinal bleeding |
| | 3 (6%) CNS-affections |
| Mechanical ventilation | 34 (65%) |
| Vasopressor therapy | 27 (52%) |

### 3.2. Comparison of BCTs

BCT_PiCCO (r = 0.912 vs. BCT_Bladder and r = 0.966 vs. BCT_Ear, BCT_Ear (r = 0.912 vs. BCT_Bladder) correlated with high significance ($p < 0.001$ for all comparisons). The coefficient of correlation was substantially lower for the correlations of BCT_Forehead vs. BCT_PiCCO (r = 0.649), BCT_Forehead vs. BCT_Ear (r = 0.706) and BCT_Forehead vs. BCT_Bladder (r = 0.757; $p < 0.001$ for all correlations).

BCT_PiCCO (37.15 ± 1.16 ° Celsius; p = 0.125 vs. BCT_Ear and p = 0.663 vs. BCT_Bladder), BCT_Ear (37.10 ± 1.16 ° Celsius; p = 0.863 vs. BCT_Bladder) and BCT_Bladder (37.06 ± 1.17 ° Celsius) were not significantly different (Figure 1).

However, BCT_Forehead (36.52 ± 0.90 ° Celsius) was significantly lower compared to BCT_PiCCO ($p < 0.001$), BCT_Ear ($p < 0.001$) and BCT_Bladder ($p < 0.001$).

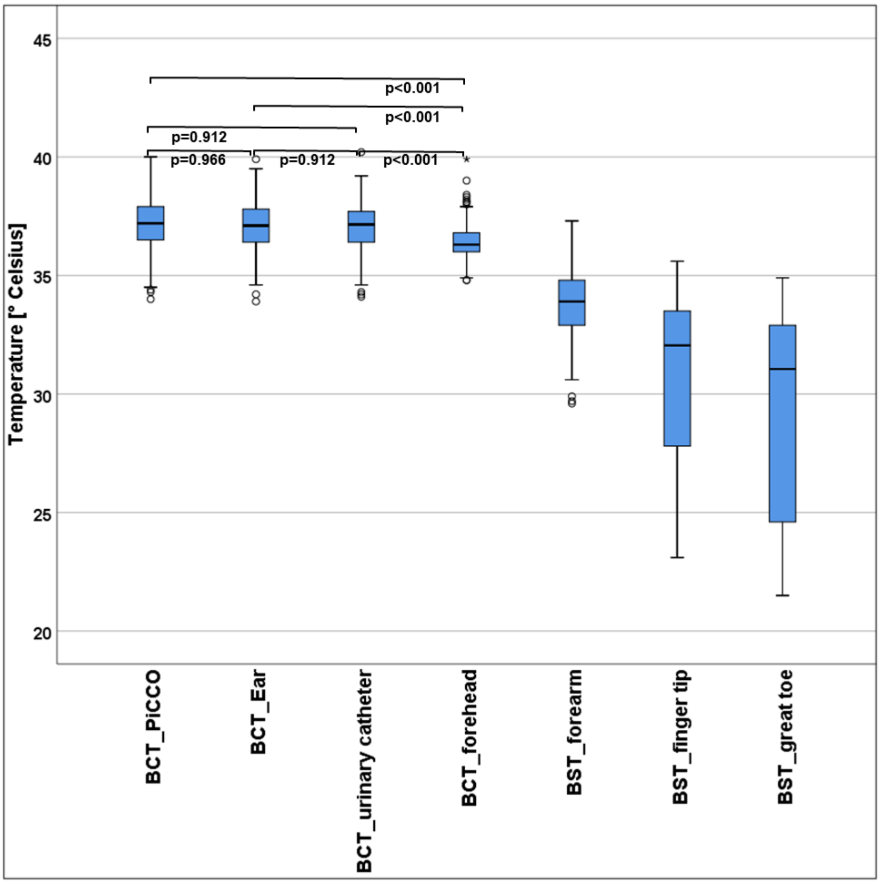


**Figure 1.** Boxplots comparing different body core temperature (BCT) and body surface temperatures (BST).

Bland-Altman-analysis demonstrated low bias and percentage error (PE) values for the comparisons of BCT_PiCCO vs. BCT_Bladder (bias 0.05 ± 0.27 ° Celsius; PE = 1.4%; Figure 2), BCT_PiCCO vs. BCT_Ear (bias 0.08 ± 0.38 ° Celsius; PE = 2.0%; Figure 3) and BCT_Ear vs. BCT_Bladder (bias 0.04 ± 0.42 ° Celsius; PE = 2.2%; Figure 4).

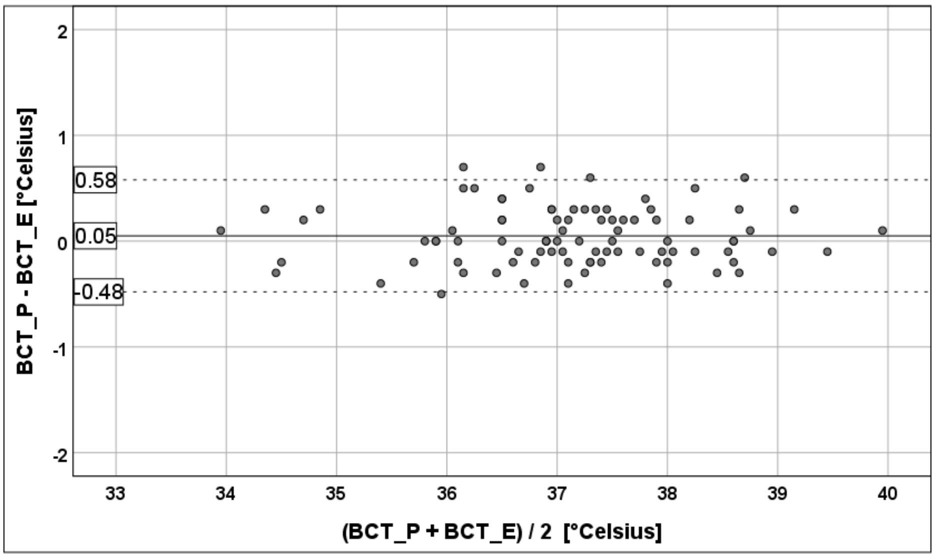


**Figure 2.** Bland-Altman-plot comparing body core temperature derived from PiCCO (BCT_P) to BCT_E (body core temperature derived from ear-thermometer). Percentage error = 1.4%. Dotted lines: Upper and lower limits of agreement.

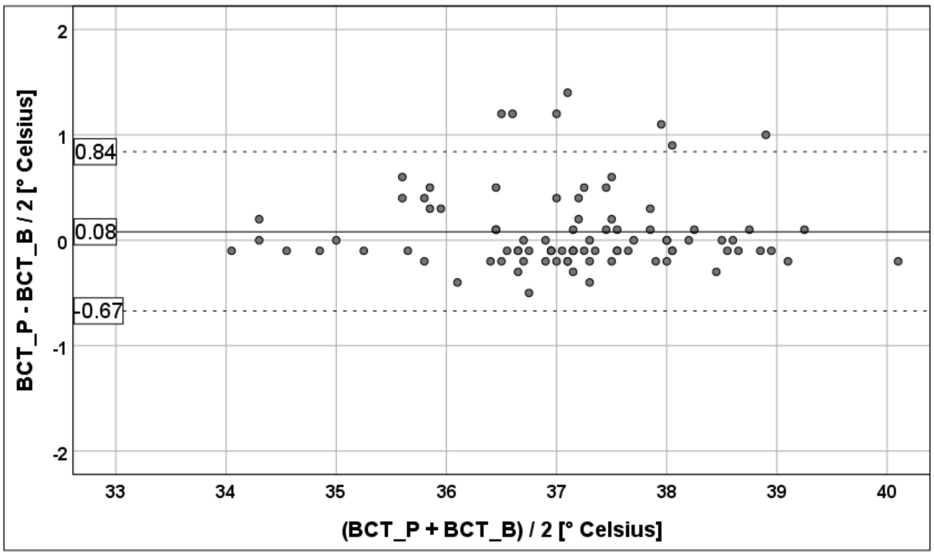


**Figure 3.** Bland-Altman-plot comparing body core temperature derived from PiCCO (BCT_P) to BCT_B (body core temperature derived from bladder-thermometer). Percentage error = 2.0%. Dotted lines: Upper and lower limits of agreement.

While BCT_PiCCO, BCT_Ear and BCT_Bladder can be considered interchangeable, Bland-Altman analyses of BCT_Forehead vs. BCT_PiCCO (bias = −0.63 ± 0.75 ° Celsius; PE = 3.9%), BCT_Ear (bias = −0.58 ± 0.68 ° Celsius; PE = 3.6%) and BCT_Bladder (bias = −0.55 ± 0.74 ° Celsius; PE = 3.9%) demonstrate a substantial underestimation of BCT by BCT_Forehead and a lower precision compared to BCT_PiCCO, BCT_Ear and BCT_Bladder (Figure 1; Figure 5).

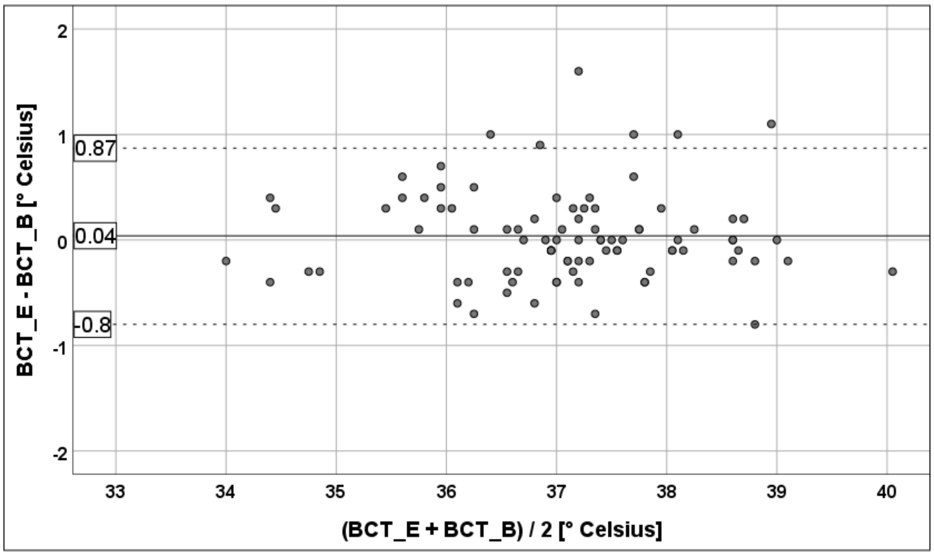


**Figure 4.** Bland-Altman-plot comparing BCT_E (body core temperature derived from ear-thermometer) to BCT_B (body core temperature derived from bladder-thermometer). Percentage error = 2.2%. Dotted lines: Upper and lower limits of agreement.

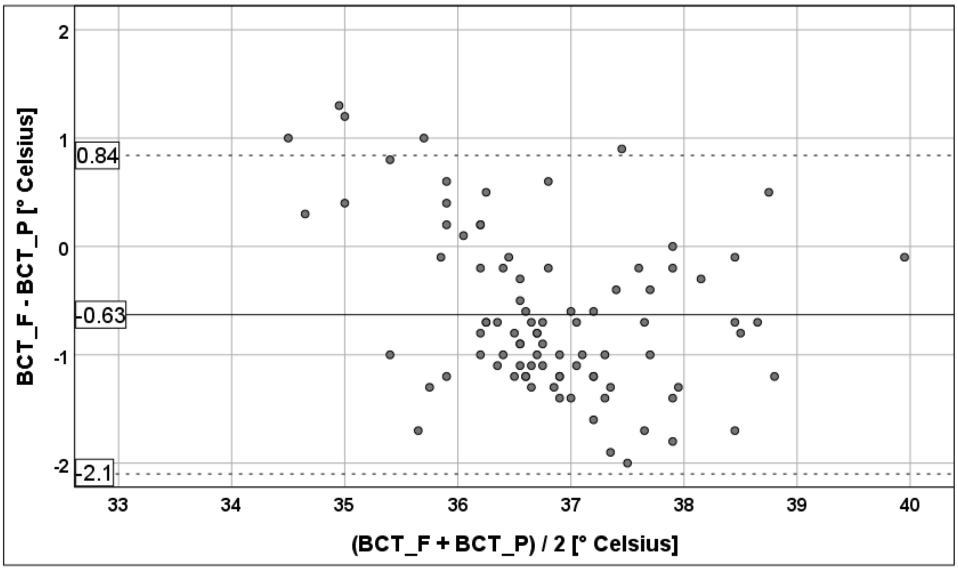


**Figure 5.** Bland-Altman-plot comparing BCT_F (body core temperature derived non-contact infrared thermometer (mesurement on the forehead) to BCT_P (body core temperature derived from PiCCO). Percentage error = 3.6%. Dotted lines: Upper and lower limits of agreement.

Interestingly, the differences of (BCT_Forehead-BCT_PiCCO), (BCT_Forehead-BCT_Ear) and (BCT_Forehead-BCT_Bladder) significantly correlated with BCT_PiCCO ($r = -0.530$; $p < 0.001$), BCT_Ear ($r = -0.565$; $p < 0.001$) and BCT_Bladder ($r = -0.525$; $p < 0.001$), respectively. This implicates that BCT_Forehead underestimates higher values and overestimates lower values of gold-standard measurements of BCT.

### 3.3. Body surface temperatures, biometrics and haemodynamics

As shown in Table 2, BSTs and differences between BCT and BST (DCST) significantly correlated with CI_TD with r-values between 0.230 and 0.307 and p-values between 0.002 and $p < 0.001$. The strongest association with CI_TD was found for BST_forearm ($r = 0.307$; $p < 0.001$).

In general, BSTs slightly better correlated with CI_TD than their differences to the core-temperature (DCST).

CI_TD was also sigificantly decreased with older age ($r = -0.284$; $p < 0.001$). However, there was no correlation of CI_TD with weight, height and gender.

**Table 2.** Correlation of body surface temperatures (BST) and their differences to the body core temperature (DCST) with cardiac index derived from transpulmonary thermodilution (CI_TD).

| Temperature | Coefficient of correlation vs. CI_TD | p-value |
|---|---|---|
| Finger | $r = 0.249$ | $p = 0.001$ |
| Forearm | $r = 0.307$ | $p < 0.001$ |
| Great toe | $r = 0.252$ | $p = 0.002$ |
| DCST_finger | $r = -0.230$ | $p = 0.002$ |
| DCST_forearm | $r = -0.230$ | $p = 0.002$ |
| DCST_great toe | $r = -0.258$ | $p < 0.001$ |

### 3.4. Multivariate analysis regarding CI_TD

In a multivariate analysis regarding CI_TD and including biometric data, BSTs and and their differences to core-temperatures (DCST), only higher temperatures on the forearm ($p < 0.001$) and the great toe ($p = 0.016$), young age ($p < 0.001$), low height ($p < 0.001$) and male gender ($p < 0.001$) were independently associated with CI_TD.

The estimate of CI (CI_estimated) based on this model significantly correlated with CI_TD ($r = 0.594$; $p < 0.001$; Figure 6)

Bland-Altman analysis demonstrated a low bias ($+0.03 \pm 0.98$ L/min/m²) and a percentage error of 45.9% (Figure 7).

### 3.5. Receiver-operating-characteristic (ROC) analysis

To evaluate the potential clinical usefulness of BSTs and CI_estimated, we performed ROC-analyses regarding critical thresholds of CI_TD.

As shown in Figure 8, CI_estimated (ROC-AUC = 0.862; $p < 0.001$) and the DCST_toe (ROC-AUC = 0.661; $p = 0.026$) significantly predicted a decreased CI_TD $\leq 2.5$ L/min/m². Similarly, CI_estimated significantly predicted an increased CI_TD $\geq 5$ L/min/m² (AUC = 0.782; $p < 0.001$; Figure 9).

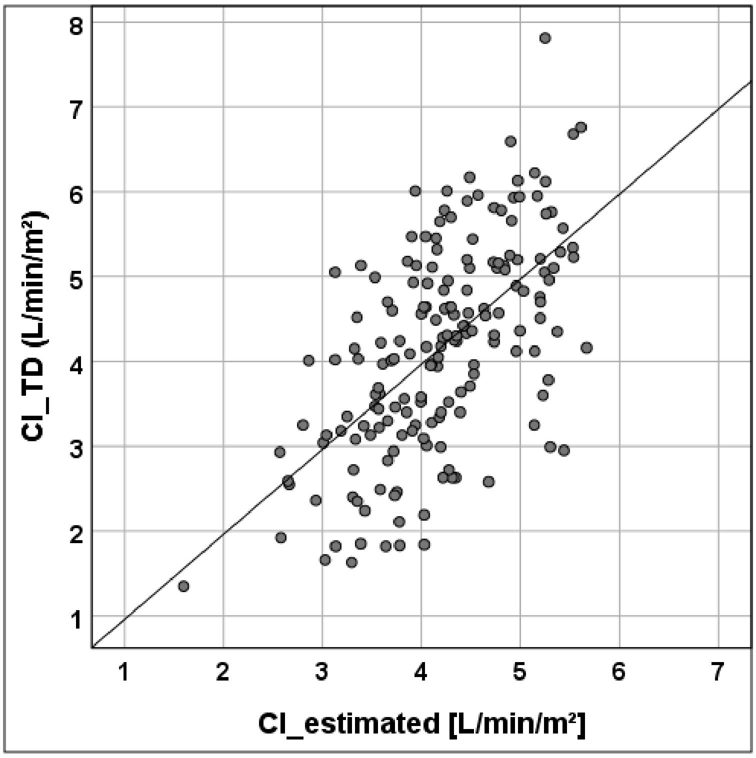


**Figure 6.** Correlation of estimated cardiac index CI_estimated with thermodilution-derived cardiac index CI_TD.

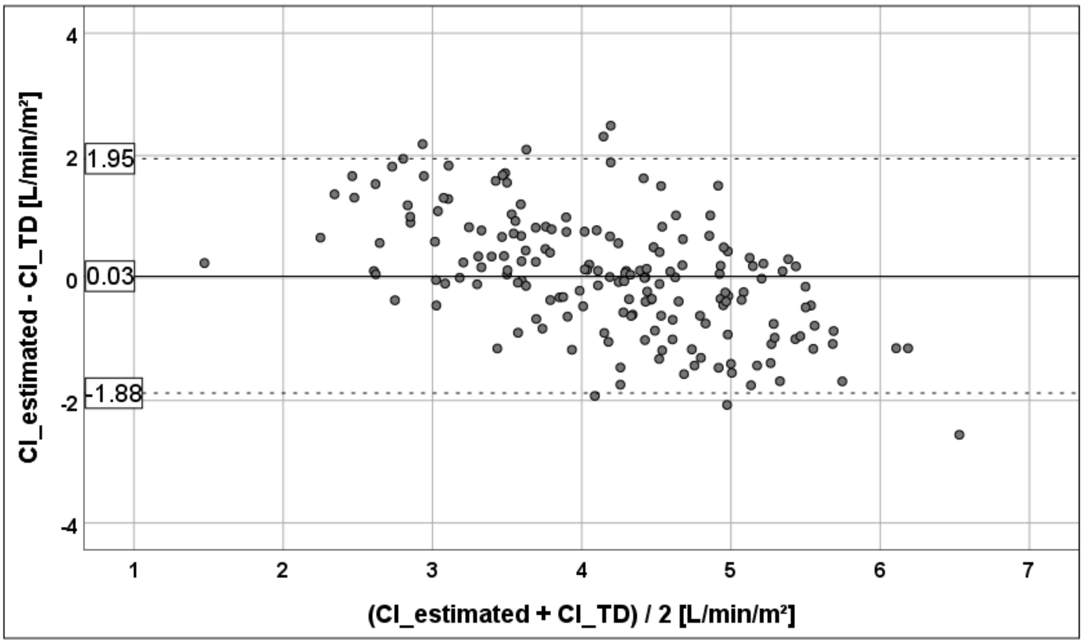


**Figure 7.** Bland-Altman plot comparing CI_estimated with CI_TD derived from transpulmonary thermodilution. Percetage error 44.9%. Dotted lines: Upper and lower limits of agreement. CI: Cardiac Index.

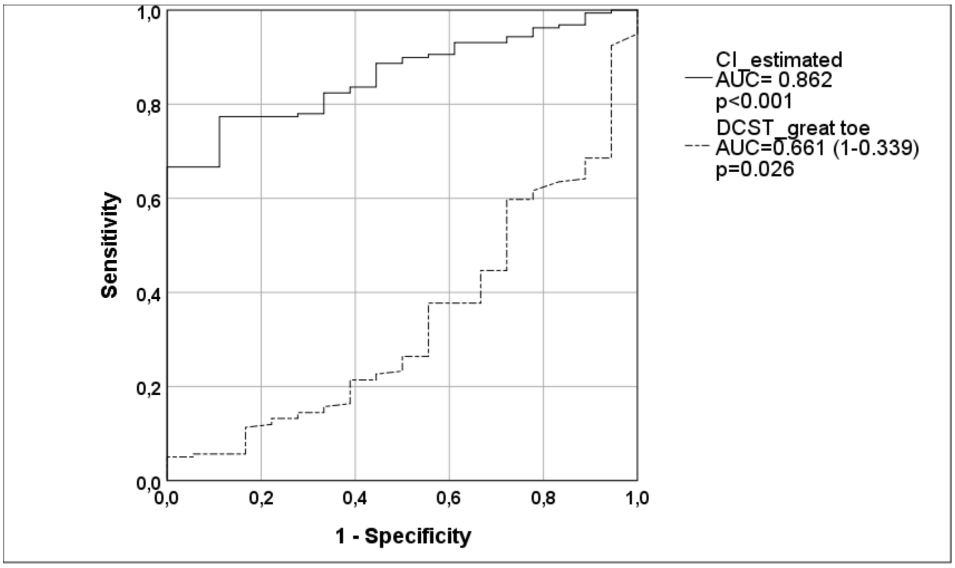


**Figure 8.** Receiver-operating-characeteristic area under the curve (ROC-AUC): Prediction of thermodilution-derived cardiac index CI_TD $\leq$ 2.5 L/min/m$^2$.

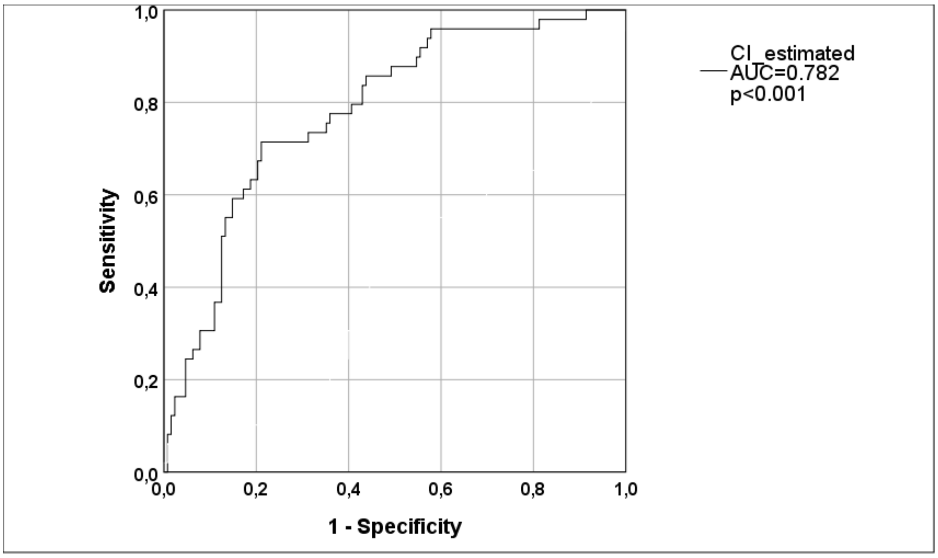


**Figure 9.** Receiver-operating-characeteristic area under the curve (ROC-AUC): Prediction of thermodilution-derived cardiac index CI_TD $\geq$ 5 L/min/m$^2$.

## 4. Discussion

Accurate assessment of BCT and BST is of high clinical importance for the diagnosis and differentiation of shock. There are several approaches to measure BCT including *intermittent* measurement of temperature in the ear [5,6,9], rectum and axilla [5,12]. With regard to hygienic issues, non-contact-infrared methods such as the Thermofocus are appealing to assess BCT [29–32]. Furthermore, thermistor-equipped urinary bladder catheters are used for *continuous* measurement of BCT [11,13].

To the best of our knowledge this study is the first evaluation of BCT measurement with the thermistor-equipped PiCCO-catheter to extravascular standard methods to derive BCT such as BCT_Ear, BCT_Bladder and BCT_Forehead. The study setting with the PiCCO-device in place providing accurate measurement of CI_TD also allowed for comparison of BSTs and DCSTs with CI_TD.

The findings of this study can be summarized as follows:

(1) BCT_PiCCO, BCT_Ear and BCT_Bladder are interchangeable
(2) By contrast, BCT_Forehead results in a substantial bias with an underestimation of BCTs by about 0.5 °Celsius compared to BCT_PiCCO, BCT_Ear and BCT_Bladder.
(3) All measured BSTs and DCSTs were significamntly associated with CI_TD.
(4) In our setting BSTs provided higher coefficients of correlation vs. CI_TD compared to DCSTs.
(5) Furthermore, CI_TD was significantly associated with biometric data, in particular with age.
(6) A simple linear regression model based on two BSTs and biometric data provided moderate to strong correlation with CI_TD with a low bias, but a substantial PE.
(7) CI_estimated based on this model provided large ROC-AUCs in predicting critical thresholds of CI_TD (CI_TD ≤ 2.5 L/min/m² and CI_TD ≥ 5 L/min/m²).

Accurate and precise measurement of changes in blood temperature by a PiCCO-thermistor has been shown previously, since accurate measurement of changes of the blood temperature induced by a 15mL-bolus of ice-cold saline is the main principle of TPTD to derive CI and other parameters such as GEDVI and EVLWI [33]. According to the principles of trasnspulmonary thermodilution, the difference in temperature between central blood (femoral artery; distal aorta) and the ice-cold saline represents the indicator which is used for indicator dilution. Accurate measurement of CI, GEDVI and EVLWI by TPTD has been shown in numerous studies. At least two studies suggest that measurements are even accurate, when the amount of indicator is reduced by using room-temperature injectate instead of ice-cold saline [28,34].

The use of the thermistor-equipped arterial PiCCO-catheter for continuous measurement of BCT is an appealing concept for several reasons: Its position in the distal aorta is anatomically as close to the body core as possible. Although the purpose of the thermistor is intermittent TPTD, BCT is continuously displayed at the PiCCO-monitor. Considering additional costs for thermistors in urinary bladder catheters, measurement of BCT with the PiCCO-catheter saves additional costs and avoids additional contact with potential contamination or invasiveness. It might be usefull in particular in high risk ICU-patients at risk of fast changes in temperatures related to disease (fever) or therapeutic measures including extracorporeal organ support or deliberate cooling after resuscitation [19].

BCT_Bladder and BCT_E have been validated before, but not extensively in the ICU-setting. Therefore, interchangeability of BCT_Bladder, BCT_Ear and BCT_PiCCO in critically ill patients is a clinically relevant finding.

The use of non-contact infrared thermometers such as Thermofocus is appealing for several reasons. The non-contact measurement provides the least invasive and the most hygienic approach to estimate BCT (BCT_Forehead) and to measure BST with very low costs. BCT_Forehead is based on measurement of BST on the forehead which is corrected by a proprietary algorithm to estimate BCT. However, our data show that BCT_Forehead systematically understimates BCT measured by other techniques (BCT_PiCCO, BCT_Ear, BCT_Bladder). Correlation analyses demonstrate that the underestimation increases with higher values of BCT measured by other techniques. While this questions the use of BCT_Ear by Thermofocus in ICU-patients at present, a systematic increase in the bias with higher values of BCT suggests a potential for correcting the algorithm. Furthermore, the ICU-setting and a frequent use of vasopressors might be a particular difficult setting for this technology.

By contrast, BCT_Bladder was accurate and precise vs. BCT_PiCCO and BCT_Ear. Although, specific urinary bladder catheters for measurement of BCT_Bladder are associated with additional costs and a certain invasiveness, they can be considerd as gold-standard for *continuous* measurement of BCT in patients without a thermistor-equipped vascular access to central blood vessels like the distal aorta or the pulmonary artery.

Our data suggest that accurate measurement of BSTs to estimate CI might be the main application of non-contact infrared thermometers in ICU-patients. The association of BSTs with CI_TD in our study confirms previous data with other technologies including continuous measurement with probes. To the best of our knowledge, the combination of BSTs with biometric data to improve prediction of CI has never been investigated before. Our resulting model CI_estimated had an excellent bias, but a certain imprecision as suggested by PE-values above 30%. Nevertheless, the predictive capacities are remarcable regarding the easiness of use, its low expenses and a PE at least comparable to invasive and/or expensive devices such as FloTrac [35], ProAqt [36,37] and ClearSight [38].

Furthermore, CI_estimated provided large ROC-AUCs regarding critical thresholds of CI.

Interestingly, we found no better associations of DCSTs with CI_TD compared to BSTs. However, it has to be kept in mind that all patients were investigated in an air-conditioned ICU with constant room temperatures around 21 ° Celsius. DCSTs might be potentially advantageous in other situations such as pre-clinic scenarios and cooling.

### *4.1. Strengths of the study*

The experimental setting with the thermistor-equipped PiCCO-catheter and thermistor-equipped urinary bladder catheters in place allowed for two major endpoints of the study, i.e. validation of BCT_PiCCO as well as comparison of PiCCO-derived haemodynamics to BSTs. This provided the novelties to use the PiCCO to derive BCT and to combine BSTs with biometric data to predict CI_TD.

### *4.2. Limitations*

This was a single center study with a limited number of patients. Furthermore, more than a third of our patients suffered from liver disorders, which is not the usual proportion in a multidisciplinary ICU. Therefore, we recalculated our main data after elimination of the patients with liver failure.

The main analyses in this subgroup provided data comparable to the totality of patients (data not shown). Additional analyses also including the use of vasopressors might further improve regression formulas for estimation of CI, since the use of vasoactive drugs might modulate the association of CI and BSTs. E.g. BST on the great toe was independently associated with high CI_TD as well as with low dosages of noradrenaline and adrenaline (data not shown).

Further analyses including independent evaluation and validation cohorts are required to validate CI_estimated. Finally, future studies should directly compare CI_estimated with other, more invasive and expensive technologies based on pulse contour analysis, bio-impedance and other techniques.

## 5. Conclusions

(1) BCT_PiCCO, BCT_Ear and BCT_Bladder are interchangeable.
(2) BCT_Forehead results in a significant bias with an underestimation of BCTs by about 0.5 ° Celsius.
(3) All measured BSTs and DCSTs were significantly associated with CI_TD.
(4) Combination of BSTs and biometric data to estimate CI_TD is promising, in particular for the prediction of critical thresholds of CI.

## Acknowledgments

Wolfgang Huber collaborates with Pulsion Medical Systems SE, Feldkirchen, Germany as member of the Medical Advisory Board.

Wolfgang Huber holds a patent on estimating cardiac index (PCT/EP2017/054044).

## Conflict of interest

All other authors have no conflict of interest to disclose.

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