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Posted Date: 20 February 2023

doi: 10.20944/preprints202302.0338.v1

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Intraoperative Beat-to-Beat Pulse Transit Time (PTT) Monitoring via Non-Invasive Piezoelectric/Piezocapacitive Peripheral Sensors Can Predict changes in Invasively Acquired Blood Pressure in High-Risk Surgical Patients

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Abstract: Background: Non-invasive acquistion of beat-to-beat pulse transit time (PTT) via piezoelectric/piezocapacitive sensors (PES/PCS) may expand perioperative hemodynamic monitoring. This study evaluated the ability for PTT via PES/PCS to correlate with systolic, diastolic, and mean invasive blood pressure (SBP_{IBP}, DBP_{IBP}, and MAP_{IBP}) and to detect SBP_{IBP} fluctuations. Methods: PES/PCS and IBP measurements were performed in 20 patients undergoing abdominal, urological, and cardiac surgery. A Pearson's correlation analysis (r) between 1/PTT and IBP was performed. The predictive ability of 1/PTT with changes in SBP_{IBP} was determined by area under the curve (reported as AUC, sensitivity, specificity). Results: Significant correlations between 1/PTT and SBP_{IBP} were found for PES (r=0.64) and PCS (r=0.55) ($p<0.01$), as well as MAP_{IBP}/DBP_{IBP} for PES (r=0.6/0.55) and PCS (r=0.5/0.45) ($p<0.05$). A 7% decrease in $1/PTT_{PES}$ predicted a 30% SBP_{IBP} decrease(0.82, 0.76, 0.76), while a 5.6% increase predicted a 30% SBP_{IBP} increase (0.75, 0.7, 0.68). A 6.6% decrease in $1/PTT_{PCS}$ detected a 30% SBP_{IBP} decrease (0.81, 0.72, 0.8), while a 4.8% $1/PTT_{PCS}$ increase detected a 30% SBP_{IBP} increase (0.73, 0.64, 0.68). Conclusions: Non-invasive beat-to-beat PTT via PES/PCS demonstrated significant correlations with IBP and detected significant changes in SBP_{IBP}. Thus PES/PCS as a novel sensor technology may augment intraoperative hemodynamic monitoring during major surgery.

Keywords: piezoelectric; piezocapacitive; pulse transit time; non-invasive hemodynamics; Intraoperative blood pressure; anesthesiology

1. Introduction

Perioperative hemodynamic optimization, particularly optimal blood pressure (BP) management and early-onset BP fluctuation detection is vital for perioperative outcomes[1–4]. Tracking beat-to-beat BP can be achieved either through invasive or non-invasive methods[5]. A critical prerequisite for such sensors is the capability to record reliable arterial pulse waves (PWs). From these, a pulse transit time (PTT) can be extrapolated, which may serve as a non-invasive surrogate marker for arterial BP on a beat-to-beat basis[6]. PTT presents as an ideal bio-signal, as it encompasses the pulse arrival time and pre-ejection period, as well as functioning as an excellent peripheral surrogate BP marker[7].

 doi:10.20944/preprints202302.0338.v1

Tracking PTT through PW analysis can be accomplished via vascular unloading technique utilizing optical or ultrasound based sensors via pulse plethysmography (PPG). While these techniques have their respective advantages, they may be associated with patient discomfort, high cost, potential optical sensor problems such as light interference, as well as accuracy issues[8,9]. Further issues include the limited amount of clinically valid data generated from the perioperative period, where reliable, non-invasive solutions for continuous beat-to-beat BP tracking are needed.

An emerging sensor technology that can non-invasively track peripheral PW's is dual piezoelectric (PES)/piezocapacity (PCS) film sensors. These sensors function in the following manner: incoming PWs induce a sensor deformation, thereby leading to electric depolarization in proportion to pressure[10]. This depolarization is then transformed into a readable arterial PW, *(signal transduction method*)[11]. The piezocapacitive portion of the sensor transduces this pressure change into a capacitance change (*relative change in pressure*)[12], with a lower pressure sensitivity[13]. The piezoelectric portion directly converts pressure signals into electrical signals with high pressure sensitivity (absolute change in pressure)[13]. Combined, this dual sensor system can detect both relative and absolute change in pressure, delivering 2 distinct waveforms.

Data is however lacking regarding the applicability of PES/PCS to track PTT in the perioperative period amongst high-risk surgical patients. It also remains unclear if PTT obtained from these types of sensors could correlate with invasively acquired blood pressure (IBP). Another critical point of investigation is to determine if beat to beat PTT via PES/PCS could detect early onset BP fluctuations. The goal of this study was thus to deploy non-invasive PES/PCS to determine valid PW morphology (PW_{PES}/PW_{PCS}) and compare them to PW_{IBP}. In addition, PTT via PES/PCS was evaluated to determine correlations with invasively acquired systolic, diastolic, and mean BP (SBP_{IBP}, DBP_{IBP}, MAP_{IBP}), as well as their potential to predict intraoperative SBP_{IBP} fluctuations.

2. Methods

Study design

This study was designed as a prospective observational study and performed at the Charité – Universitätsmedizin Berlin. All procedures involving humans were in accordance with the ethical standards of the institutional research committee and with the 1964 Declaration of Helsinki and its later amendments. The study was approved by the local ethics committee (EA1/155/17) and registered at ClinicalTrials.gov (NCT 03263988). Informed written consent was obtained from all study patients.

Study inclusion and exclusion criteria

All adult patients admitted for elective major abdominal and urological surgery, as well as cardiac (including cardiopulmonary bypass [CPB]), under general anesthesia were screened for study inclusion. Exclusion criteria were defined as follows: pregnancy, atrial fibrillation or other severe heart rhythm disorders, presence of cardiac pacemakers, arteriovenous fistulas at the upper extremities, body mass index > 35kg/m^2, impossibility of placing the PES/PEC around the index finger, a difference in blood pressure measured between both arms > 12 mmHg, severe heart valve disease, left ventricular ejection fraction (LVEF) < 35%, tricuspid annular plane systolic excursion (TAPSE) < 16 mm or necessity of any type of left ventricular assist device or the inability to give informed consent.

Study protocol

Upon arrival in the anesthesia induction area, standard monitoring was initiated, which included a 3-lead electrocardiogram (ECG), pulse oximetry monitoring, and initial non-invasive oscillmetric blood pressure monitoring. All patients underwent general anaesthesia, which was performed according to local standard operating procedure (SOP). Patients undergoing major abdominal or urologic surgery, anesthesia were induced with Fentanyl (1-2 µg kg^{-1}), Propofol (1-2 mg kg^{-1}) and Cisatracurium (0.15 mg kg^{-1}). Anaesthesia was maintained to the discretion of the

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attending anaesthesiologist with Sevoflurane or Propofol as well as intermittent boli of Fentanyl and Cisatracurium as needed. If clinically indicated, a peridural catheter was placed (TH8-12), infusing a solution of 0.2% Ropivicaine (6-8ml/hour). For patients undergoing cardiac surgery, induction was performed with Propofol (1-2 mg/kg), Sufentanil (0.1-0.5 µcg/kg) and cis-atricurium (0.1 mg/kg). Before CPB, anesthesia was maintained with Sevoflurane (approximate 1.0 MAC) and a continuous infusion of Sufentanil (0.2-0.5 µg/kg/hr) and on-CPB pump with Propofol (6mg/kg/hr) for regulatory reasons. Ventilation was performed via pressure controlled ventilation (PCV) with the goal of maintaining an end-tidal $C0_2$ ($etC0_2$) between 35-40 mmHg.

For IBP monitoring, an arterial catheter was placed in the left radial artery via Seldinger technique and recorded on a beat-to-beat basis. General intraoperative hemodynamic management in all patients was aimed at maintaining mean arterial pressure (MAP) ≥65 mmHg via the judicious administration of vasoactive medications or intravenous balanced crystalloid fluids.

PES/PEC sensors were affixed to the patient's right index finger after induction in order to reduce artifacts, and measurements were started after signal quality was checked. Data from these sensors were collected from this point onwards till end of surgery.

The PES/PEC sensor system used were developed and manufactured by SectorCon (SectorCon Ingenieurgesellschaft mbH, Berlin, Germany). The dual sensors are composed of piezoelectric and piezocapacitive sections, both displaying 2 unique PW's with different properties (low/high frequency tracking absolute/relative pressure changes). They are capable of measuring a pressure range of -5 to 50 kPa, with a sample rate of 250Hz. PW (millivolt). PW's and PTT were recorded and captured via a hand-held device developed by the same company, with a separate ECG cable. The PW amplitude is reported as arbitrary units (a.u.) PTT was defined as milliseconds, using the 3-lead ECG as a reference. In total, 2 unique PWs and 2 PTTs on a beat-to-beat basis were recorded and analyzed. Data were converted to an ASCII file for offline analysis. An example of a PES/PEC sensor is depicted in Figure 1 and the data collection device is depicted in Figure 2.

Figure 1. Example of dual PES/PCS sensor affixed to the index finger.

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Figure 2. Data collection device for PES/PCS system.

Data Analysis

PW_{PES}/PW_{PCS} were analyzed in the following steps in order to determine the frequency of reliable PW morphology:

1.) Detect R-Peaks in the ECG using a Hilbert transformation based algorithm[14] and use them as the defining point for the start of a new beat-to-beat PW.

2.) Calculate the mean PW from the non-invasive sensors and the correlation p of each beat-to-beat PW to the mean PW. The area under the PW is defined as its magnitude (mag). A PW was marked as an outlier if one of the following two conditions are not met:

- $\varrho > 0.85$
- The absolute relative difference in magnitude to the mean PW (Δmag) is below 0.5

3.) PTT is defined as the time from the R-Peak to the steepest increase of the PW

4.) This procedure results in a PTT time series with missing values which are interpolated using the 4th order weighted essentially non-oscillatory (WENO4) technique[15].

This was performed for each patient and for all non-invasive and invasive PW's (Figure 3). Patient specific examples of PW analysis are shown in Figures 4 and 5.

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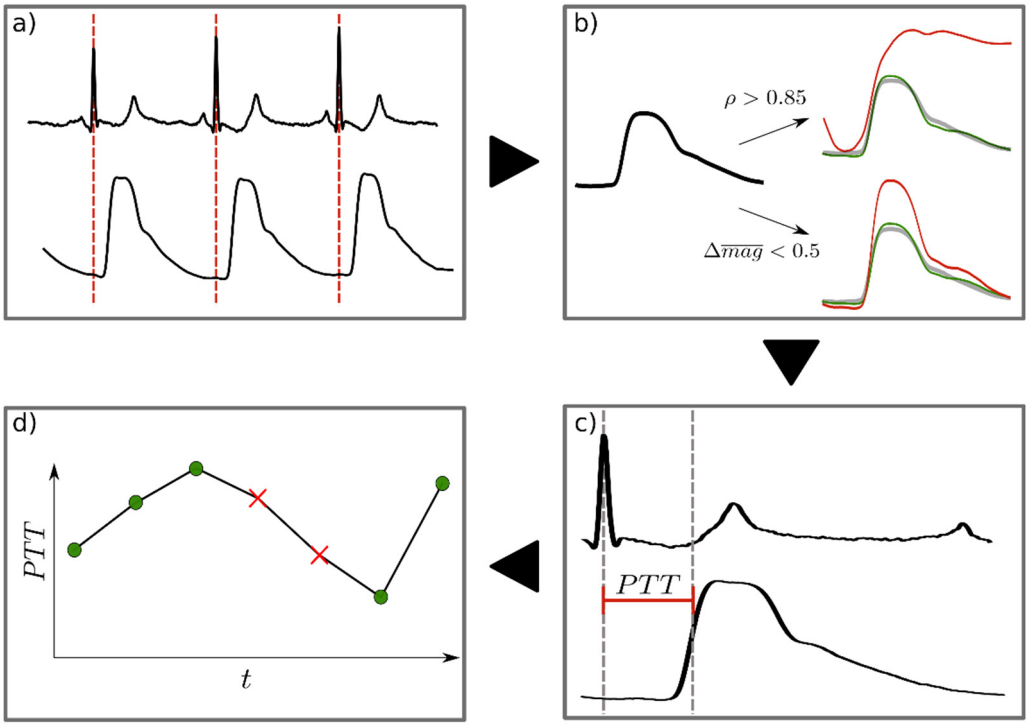

Figure 3. Flowchart for preprocessing PW Detection: a) The R-Peak in the ECG defines PW start. b) Mean PW was identified as a robust template for physiologically plausible PWs concerning morphology and magnitude. Each PW is then compared to a inter-patient specific template (green PW) for an automated deselection of non-optimal PW (e.g. due to movement noise). A PW is rejected if either its Pearson correlation with the template is below 0.85 or if the difference in normalized magnitude, (i.e the area under the curve [AUC]), is larger than 0.5 (red PW). All remaining PWs are defined as valid. c) For all valid PWs, the PTT is calculated as the time from R-Peak to the steepest increase in the PW. d) For R-Peaks where a PW was rejected, PTT values were imputed using a 4th order interpolation technique WENO4. This interpolation is justified as 95% of all gaps in the PTT signal, below 10 beats in length.

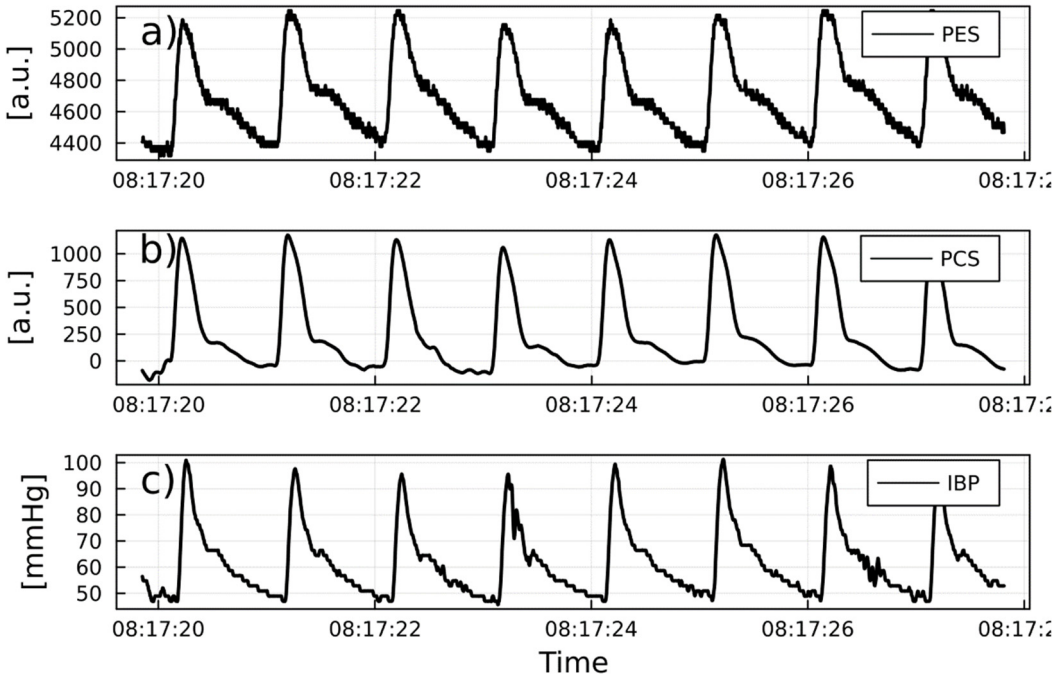

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Figure 4. a) Example of PW_{PCS}. b) Example of PW_{PES}. c) Example of PW_{IBP} from a cardiac surgery patient. PW_{PES} and PW_{PCS} reported as arbitrary units (a.u.). PW_{IBP} reported as mmHg.

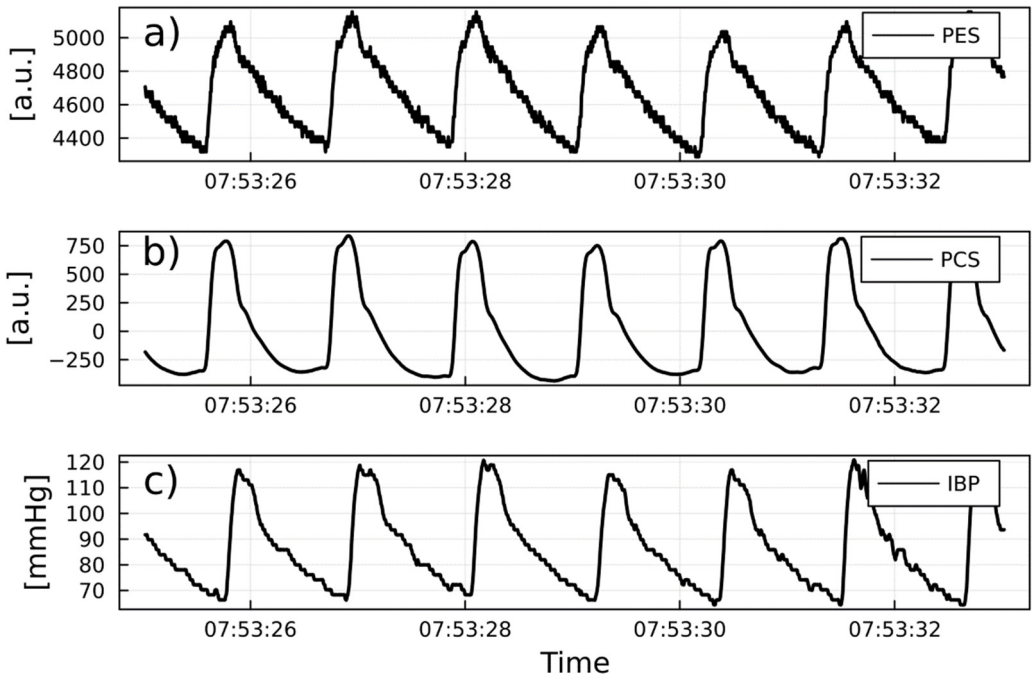

Figure 5. a) Example of PW_{PCS}. b) Example of PW_{PES}. c) Example of PW_{IBP} from a urological surgery patient. PW_{PES} and PW_{PCS} reported as arbitrary units (a.u.). PW_{IBP} reported as mmHg.

Statistical Analysis

For beat-to-beat correlations between IBP and 1/PTT (inverse of PTT) via PES/PCS, a Pearson's correlation coefficient tests (r) was performed. An area under the curve receiver operating curve (AUROC) was used to decipher the ability for PTT to detect fluctuations in intraoperative IBP. Significant fluctuations were defined as SBP_{IBP} either increasing or decreasing by more than 30% compared to the mean BP of each patient. As absolute PTT is specific to each individual, 1/PTT was converted to relative changes from start of measurement. The performance of the 1/PTT predictor via the AUROC analysis was adjusted to pinpoint the optimal cutoff based on maximizing sensitivity and specificity. PW reliability and correlation data are reported as median and inter-quartile range (IQR). Patient data is reported as mean with ± standard deviation (SD). Statistical analysis was performed using Julia programming language version 1.6.3 using the StatsBase library[16].

3. Results

Upon completion of the study data from 20 consecutive patients were analyzed. Patient characteristics, type of surgery and anesthesia are listed in Table 1.

Table 1. Patient demographics, bio-metrics, co-morbidities, type of surgery, length of surgery, and inoperative vasoactive medications. Values are reported as mean and ± standard deviation (SD).

Patient characteristics	
Gender (F/M)	12/8
Age (years)	62 ± 11.5
Height (cm)	170 ± 0.15

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Weight (kg)	78 ± 18
BMI (kg/m^2)	25 ± 8.2
BSA (m^2)	1.93 ± 0.3
ASA classification	
II	10
III	10
Co-morbidities	
Hypertension	10
Coronary artery disease	5
Diabetes Mellitus	4
Heart Failure	2
Chronic kidney disease	2
Hypothyroidism	2
Asthma	2
COPD	1
Type of surgery	
Cardiac (Coronary artery bypass grafting [CAB])	7
Abdominal (Whipple) (Pancreas resection) (Intestinal resection) (Hepatic resection)	7
Urological (nephritic) (cholecystectomy)	6
Average length of surgery (minutes)	
Cardiac	213 ± 30
Abdominal	214 ± 110
Urological	323 ± 23
Inoperative vasoactive medications	
Noradrenaline (infusion)	17
Dopamine (infusion)	2
Enoximone (infusion)	2
Caffeine/Theodrenaline (Bolus)	14
Atropine (Bolus)	6

PW reliability detection

Upon completion of the study, 92% (7.6) PW_{PES} and 93% (6.9) of all PW_{PCS} recorded from the inoperative period met reliability criteria as described in the methods section. In comparison, 97% (2.2) of all PW_{IBP} met reliability criteria.

1/PTT and IBP: correlations and predicitive capabilities

1/PTT revealed significant correlations between PES and SBP_{IBP} (r=0.64), DBP_{IBP} (r=0.55) and MAP_{IBP} (r=0.6). PCS exhibited significant correlations with SBP_{IBP} (r=0.55), DBP_{IBP} (r=0.45), and MAP_{IBP}

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(r=0.5) (Table 2). Figure 6 shows an example of the intraoperative course of 1/PTT with both PES/PEC sensors overlayed with SBP_{IBP}, DBP_{IBP}, and MAP_{IBP}. Boxplots highlighting the correlation data are shown in Figure 7.

AUROC curve analysis (Figure 8) showed that a 7% decrease in 1/PTTPES could predict a 30% decrease in SBPIBP (AUC 0.82, sensitivity 0.76, specificity 0.76), while a 5.6% increase predicted a 30% increase in SBPIBP (AUC 0.75 sensitivity 0.7 specificity 0.68). A 6.6% decrease in 1/PTTPCS could detect a 30% decrease in SBPIBP (AUC 0.81, sensitivity 0.72, specificity 0.8), while a 4.8% 1/PTT PCS increase could predict a 30% increase in SBPIBP (AUC 0.73, sensitivity 0.64, specificity 0.68).

Table 2. Correlation between 1/PTT via PES/PCS and SBP_{IBP}, DBP_{IBP}, and MAP_{IBP}. Median Pearson's correlation coefficient (r) and IQR are reported.

Sources compared	Pearson Correlation (median and IQR)
SBP_{IBP} vs.$1/PTT_{PES}$	0.64 (0.32)
SBP_{IBP} vs. $1//PTT_{PCS}$	0.55 (0.28)
DBP_{IBP} vs. $1/PTT_{PES}$	0.55 (0.36)
DBP_{IBP} vs. $1/PTT_{PCS}$	0.45 (0.40)
MAP_{IBP} vs. $1/PTT_{PES}$	0.6 (0.31)
MAP_{IBP} vs. $1/PTT_{PCS}$	0.5 (0.27)

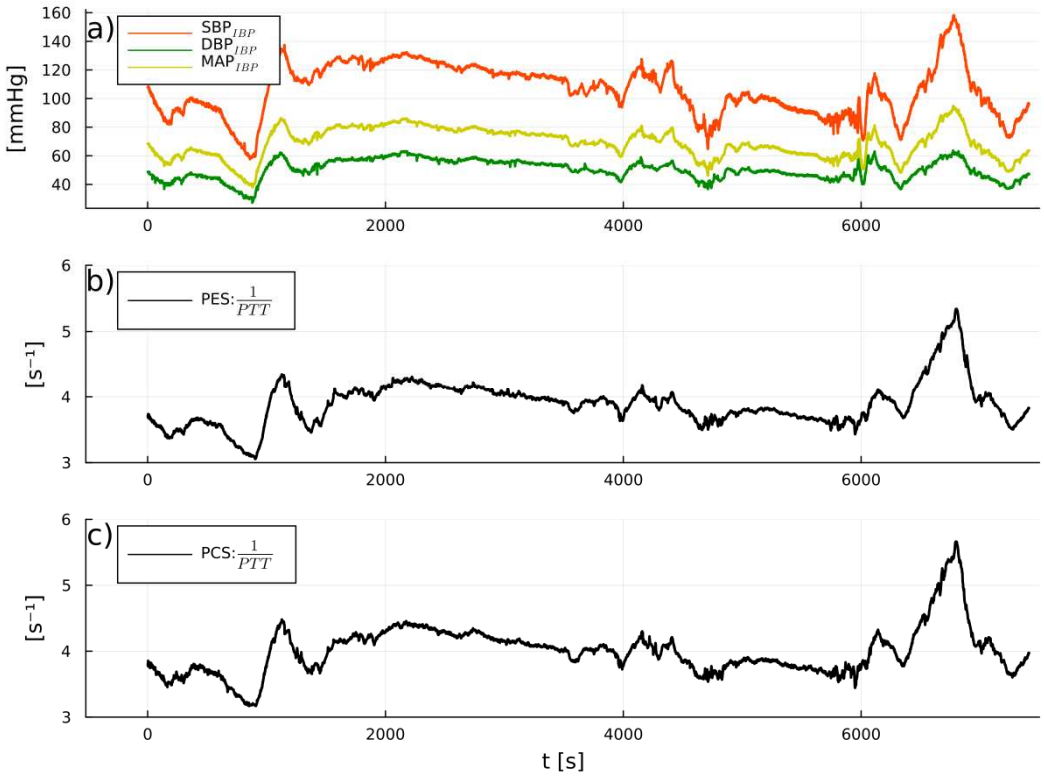

Figure 6. Example of intraoperative IBP: a), PTT_{SBP} red, PTT_{DBP} green, and PTT_{MAP} yellow. b), $1/PTT_{PCS}$. c), $1/PTT_{PES}$.].

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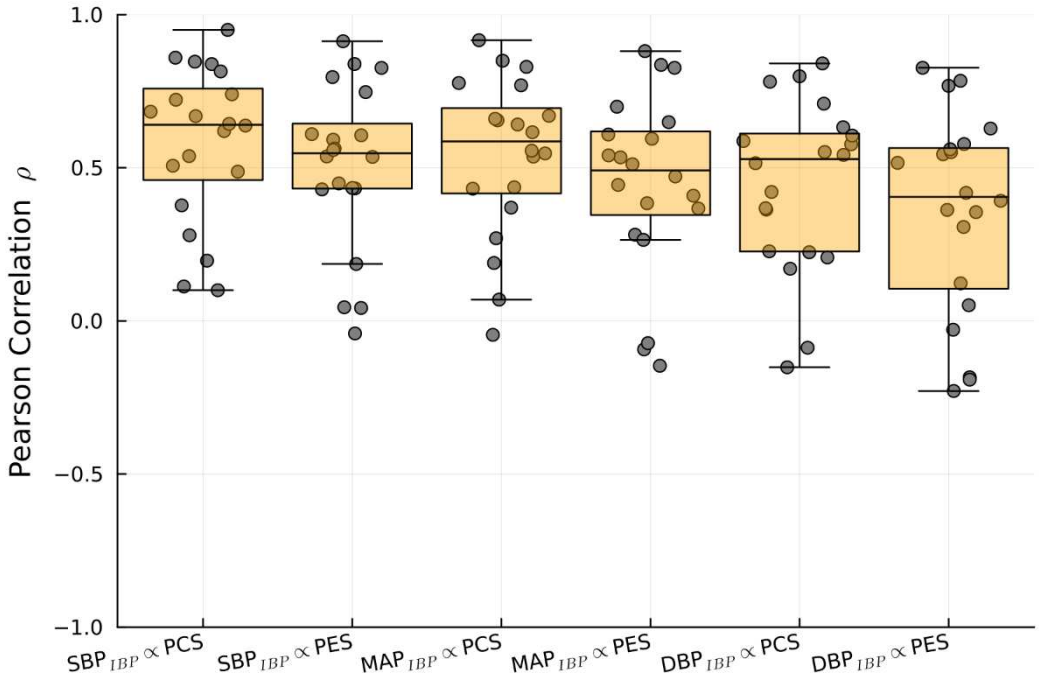

Figure 7. Boxplot of the Pearson correlation between SBP_{IBP}, MAP_{IBP}, and DBP_{IBP} with $1/PTT_{PES}$ and $1/PTT_{PCS}$.

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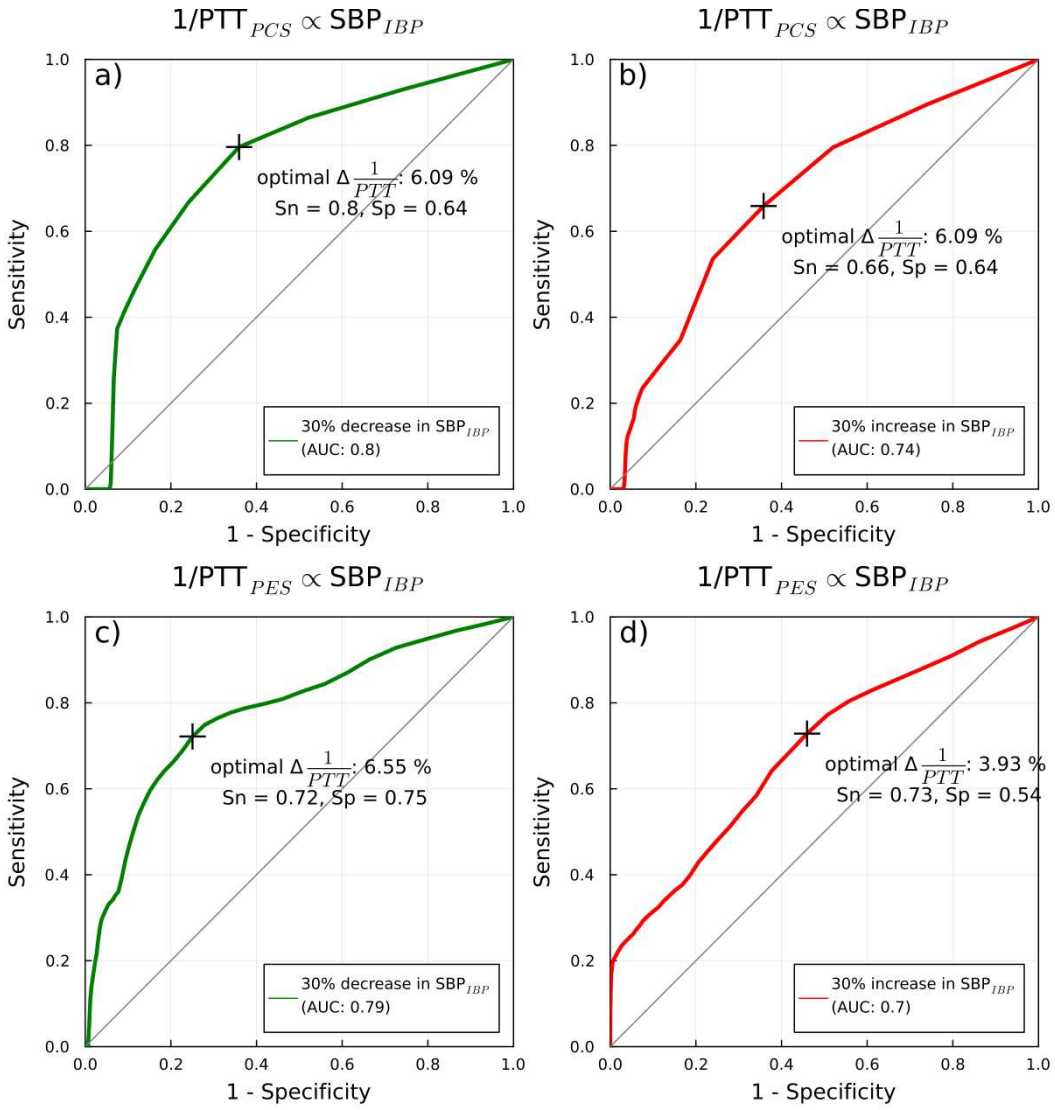

Figure 8. AUROC curves detailing 1/PTT changes detected with PES/PCS sensors with changes in SBP_{IBP}. a), Delta of $1/PTT_{PCS}$ with decrease in SBP_{IBP}. b), Delta of $1/PTT_{PCS}$ with increase in SBP_{IBP}. c), Delta of $1/PTT_{PES}$ with decrease in SBP_{IBP}. d), Delta of $1/PTT_{PCS}$ with increase in SBP_{IBP}.

4. Discussion

This study demonstrated that novel PES/PEC sensors exhibited a >90% reliable intraoperative PW detection rate amongst patients undergoing major abdominal, urological and cardiac surgery. A significant correlation between intraoperative SBP_{IBP} with both $1/PTT_{PES}$ and $1/PTT_{PCS}$ was also observed, while significant, albeit lower correlations were found for DBP_{IBP} and MAP_{IBP}, which is in line with previous studies[17]. Additionally, an approximate 7% change in $1/PTT_{PES}$ and $1/PTT_{PCS}$ sensors could predict a 30% change in intraoperative SBP_{IBP} fluctuations. The only other comparable study of this nature found that a 15% change in PTT could predict a 30% change in SBP_{IBP} via PPG sensors[17]. Thus, the results of this monocentric study promote the potential for beat-to-beat PTT tracking via PES/PCS as an innovative non-invasive sensor technology that may augment future intraoperative hemodynamic monitoring.

Prior PES/PEC research

A critical prerequisite to determine valid PTT is to detect and deliver a reliable PW morphology. Previous studies with piezo-based sensors have been able to detect reliable PW's amongst healthy volunteers[18,19], volunteers with arrythmias[20],and hypertensive volunteers[13]. In a clinical

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setting, Clemente et al., also demonstrated a reliable beat-to-beat PW detection rate in a small cohort of ICU patients[21]. All of these mentioned studies detected a reliable piezosensor based PW detection rate of >90%, which our study was also able to confirm. Not only did the PES/PCS system in our study detect a >90% PW_{PES}/PW_{PCS} rate, but was also able to achieve this in a rigorous perioperative environment from high-risk surgical patients, in which rapid changes in BP occur frequently.

Disrupting perioperative factors such as electro-cauterization, extreme BP fluctuations, positional changes, intraabdominal pressure, and changes in vascular tone due to bleeding, pain and vasoactive medications contribute to a challenging environment for testing novel non-invasive sensors. Despite this, a >90% PES_{PW}/PCS_{PW} validity was detected, compared to a 97% validity being determined for PW_{IBP}. This difference is most likely due to the above-mentioned factors, with electric cauterization being the primary cause for invalid PES_{PW}/PCS_{PW}. Despite these factors, the PES/PSC sensors were able to decipher a beat-to-beat PT for all valid PW's, which has also been verified amongst ambulatory hypertensive patients[22]. One other technical challenge of the PES/PCS sensors, is the correct amount of external pressure needed to obtain optimal PW measurement. The optimal contact pressure for piezosensors is in the range of 1.6-2 Newtons[13], and too little, or too much application pressure can diminish the PW signal amplitude. The advantage of these sensors is the ability for the PCS portion to register the amount of pressure applied, thereby acting as a PW quality control mechanism, which was verified in this study. Future studies comparing PES/PCS with PPG based sensors to determine PW reliability, correlations, and predictive capabilities in the perioperative are needed to verify these findings.

PTT: correlation and predictive capabilities

While no study has examined correlations between piezo-sensor based PTT and IBP, as well the ability for piezo-based PTT to predict IBP fluctuations in the perioperative environment, there are a handful of comparable PPG studies of this nature. Two studies have provided evidence that piezo-sensor derived PTT shows a significant correlation and accuracy with PTT obtained from PPG devices[10,23]. Regarding correlations between non-invasively acquired PTT and BP, PTT demonstrates a good correlation with SBP, while correlations between MAP and DBP vary[24–26]. One study demonstrated a significant correlation between PTT and SBP during the administration of vasoactive medications which is highly relevant for the perioperative environment, as vasoactive medications are frequently being administered to stabilize hemodynamic status[27]. The only directly comparable study examining non-invasively acquired PTT amongst hypertensive kidney transplant patients in the perioperative setting, found a good correlation between PTT and SBP_{IBP}, while moderate correlations were found with MAP_{IBP} and DBP_{IBP}[17]. The major differences to our study, is the technique used to measure PTT (PCS/PES vs PPG) and the time period of measurement (intraoperative vs induction). Kim et al., also found a greater level of correlation for SBP (R=>0.8), MAP (R=0.8), and DBP (R=0.6), which were higher than the correlations demonstrated by PES/PCS in this study. This is most likely due to the time frame that these correlations were recorded (induction period vs post-induction period), where disruptive intraoperative factors are minimal. Despite these differences, our study confirms this correlation trend.

Another clinical study tracking PTT during post spinal anesthesia demonstrated a good correlation between PTT with non-invasively acquired MAP, while no information was given about correlations between SBP and DBP[28]. Retrospective analysis from >500 patients experiencing rapid declines in SBP in a non-perioperative setting showed a correlation between PTT with SBP of r=-0.91[29]. The significant correlation between PTT and SBP were attributed to SBP being influenced by both cardiac activity and vascular tone[27]. In that same study, the authors found no correlation between PTT and DBP and MAP. The reason for this being that both DBP and MAP are indicators of vascular stiffness, which diminishes the correlation with PTT. The reason why stronger correlations

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are found between PTT and SBP may be due to pressure and velocity factors, as well as the influence of the incoming pressure wave registered hemodynamic sensors. The systolic cycle involves the forward propulsion of blood (velocity) which exerts a pressure gradient (pressure), cumulating as a pressure wave, as opposed to DBP and MAP[30]. Our study however found moderate correlations between PTT with MAP_{IBP} and DBP_{IBP}, which supports the findings of Kim et al., and refutes the findings of Payne et al,. These significant correlations could be due to the residual effects of the pulse reflection wave during DBP, thereby influencing MAP[17].

Our patient cohort consisted of high-risk patients with co-morbidities, which could have impacted PTT measurements. The existence of cardiovascular co-morbidities may impact the relationship between PTT and systemic BP, as the structural changes to the myocardium and vascular architecture may alter PW propagation[31]. Other clinical studies have found that the relationship between PTT and systemic BP is not affected amongst patients with hypertension[17,28]. Another study examining hemodialysis patients undergoing simulated fluid shifts via lower body negative pressure (LBNP), found that distally measured PTT showed a very good correlation during acute decreases in systemic BP[32]. What is interesting in this study, is that despite the presence of high-risk patients with co-morbidities, significant correlations between PTT and IBP were found, suggesting that this type of hemodynamic monitoring is quite feasible, even amongst patients with existing cardiac dysfunction.

The ability for PTT to predict significant intraoperative BP fluctuations is a major advantage of this particular bio-signal. There exist a handful of clinical studies highlighting the potential for PTT to detect significant BP fluctuations. The most relevant study by Kim et al., found that a 15% change in 1/PTT could predict a 30% change in systolic blood pressure during anesthesia induction[17]. During obstetric spinal anesthesia, beat-to-beat changes in PTT could detect significant blood pressure changes in normotensive and hypertensive women[28,33]. Our study supports these findings, albeit, a lower 1/PTT change (approximately 7%) could detect 30% changes in IBP, compared to 15%. This could be due to differences in sensor technology, and could suggest the piezo sensors may be more sensitive to subtle changes in peripheral vascular tone than PPG sensors. The 30% cut-off showed the highest sensitivity and specificity, while reducing this cut-off to 10-20% changes in SBP significantly reduced the sensitivity and specificity. Other studies have determined a PTT cut-off of 15% to detect a >30% change in IBP[17], and a 20% change in intraoperative PTT could detect 10% changes in oscillometric MAP amongst women undergoing cesarean section[33]. Significant fluctuation in intraoperative BP, particularly >30% decreases in SBP can lead to critical reductions in organ perfusion to myocardial tissue and renal tissue leading to organ damage[34,35], as well as increases in post-operative mortality[36]and morbidity[37]. Thus, a >30% change in BP seems to be a clinically relevant cut-off point. Prior findings have demonstrated that PTT shows a higher propensity over RR-Interval for predicting autonomic responses to nociceptive stimulation and fluctuations in anesthestic depth[38]. PTT has also been shown to reliably indicate an effective axillary block via the loss of vasomotor tone. This was indicated by an increase in 12 ms 3 minutes after block with a sensitivity of 87% and specificity of 71%[39]. The results of our study, suggest that smaller percentage changes in PTT can provide predictive information about BP fluctuations, however, the sensitivity is dependent upon the BP cut-off. Further studies are needed to determine ideal cut-off BP limits. The ability for PTT to serve as an early indicator of systemic blood pressure fluctuations has shown promise in theoretical models[40], however there are only a handful of monocentric clinical trials that support this. Finally, all of the above mentioned studies utilized PTT recorded with PPG methods. While both deploy different modalities of PW recognition, both are comparable with each-other with regard to reliability. Thus, the results of this study highlight the ability for PTT via PES/PCS to detect significant SBP_{IBP}, DBP_{IBP}, and MAP_{IBP} correlations, as well as the ability for these sensors to track intraoperative BP fluctuations. Finally, both techniques show no difference with regards to measuring vascular tone.

Limitations

The primary limitation of the study was a small heterogenous group of surgical patients receiving either inhalative (Sevoflurane) or intravenous (Propofol) anesthesia. While it is theorized that propofol may exhibit greater peripheral arterial distension, no significant differences between propofol versus sevoflurane based anesthesia on PTT have been found[41]. The majority of patients in our cohort received vasopressor therapy and volume administration during surgery. Vasopressor therapy directly increases in systemic vascular resistance, which has been shown to not have an effect on overall PTT[42]. Volume administration and its impact on PTT has to our knowledge not been studied. The effects of both interventions on PTT as well as PTT correlations and predictive capabilities in this study may or may not have impacted our results. Further studies examining the effects vasopressor and volume therapy have on PTT need to be performed. Another limitation was the omission of PTT measurements during anesthesia induction, as well as not performing a simultaneous measurement using PPG, in which a Bland-Altmann plot could have been performed. While both techniques can record PW/PTT, the methodology differs (pressure vs. Infrared). Prior non-clinical studies have shown that both techniques are similar with regards to respiratory rate tracking via finger probe[43–46]. Both techniques showed no major difference for HR, HRV, and PW tracking amongst a cohort of healthy volunteers. Further investigations have indicated that both systems can reliably detect SBP and DBP derived from finger PWs. Finally, a statistically significant correlation between 1/PTT and IBP may not be suitable for an individuals prediction of BP values, but it can serve as a prerequisite for these type of predictions to be made possible.

Summary and future applications

This study deployed novel PES/PCS to track intraoperative beat-to-beat PW's, and PTT from a hetergenous cohort of patients undergoing major surgery. The results determined a >90% beat-to-beat PW reliability detection rate. PTT from these sensors showed a higher significant correlation with SBP_{IBP} on a beat-to-beat basis over DBP_{IBP} and MAP_{IBP}. Finally, PTT from PES/PCS demonstrated the ability to detect early onset SBP_{IBP} fluctuations with a high degree of sensitivity and specificity, thus offering critically valuable hemodynamic information. The major advantage of PES/PCS sensors, compared to PPG technology, is the ability to utilise these sensors on different sites other than the finger, as a PW can be detected with the proper applied pressure. Future studies will involve the use of applying these sensors on various areas of the body in order to assess a multi-dimensional level of hemodynamic status, as opposed to being solely regulated to the distal extremities.

Author Contributions: RFT performed the study. MN composed the manuscript. MP performed primary statistical analysis and graphic design. JK and NW assisted in statistical analysis. CB and PB revised the manuscript. RK and PK designed and supplied the hardware and software. ST designed and implemented the study. All authors have read and agreed to the published version of the manuscript.

Funding: This project was partially funded by German Government sponsored ZIM (Zentralen Innovationsprograms Mittelstand) program (Grant number 4279701AW6).

Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki, and approved by the local Ethics Committee of Charité – Universitätsmedizin Berlin (EA1/155/17 and date of approval).

Informed Consent Statement: Written informed consent was obtained from all patients involved in the study to publish this paper.

Conflicts of Interest: RFT has received funding from Deutsche Herzstiftung (German Heart Foundation) and DZHK (German Centre for Cardiovascular Research). MN, MP, JK, CB, PB, and NW report no conflict of interest. RK and PK work for SectorCon-Ingenieurgesellschaft mbH, Berlin, Germany, and had no role in the final conclusions derived from this research. ST received funding for experimental research as well as honoraria for lectures from Edwards, Orion Pharma, Amomed, Cytosorbents, Philips, and Smith & Nephews outside this work.

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