Continuous blood pressure estimation using ECG and PPG in the operating theatre

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Abstract
In a significant portion of surgeries, blood pressure (BP) is often measured non-invasively in an intermittent manner. This practice has a risk of missing clinically-relevant BP changes between two adjacent intermittent BP measurements. This study proposes a method to continuously estimate systolic blood pressure (SBP) based on previous intermittent SBP measurements and electrocardiography (ECG) - and photoplethysmography (PPG) - derived features. Continuous ABP, ECG, and PPG signals were acquired from 23 patients undergoing major surgery. After extracting nine features from PPG and ECG signals, we dynamically selected features upon each intermittent measurement (every 10 minutes) of SBP based on feature robustness and the principle of correlation feature selection. Finally, a multiple linear regression model was built to combine these features in order to estimate SBP every 30 seconds. Compared to reference SBP, the proposed method achieved a mean of difference at 0.07 mmHg, a standard deviation of difference at 7.92 mmHg, and a correlation coefficient at 0.89. This study presents the feasibility of continuously estimating SBP with clinically-acceptable accuracy during surgery with the aid of non-invasive intermittent BP measurements.
1. Introduction

Hemodynamic monitoring is of great importance for patients in the operating theatre. The monitoring of blood pressure (BP) is routinely implemented by either cuff-based intermittent measurement or invasive continuous measurement with a catheter. In a significant portion of operations, BP is intermittently measured with a brachial cuff. Despite the advantage of convenience and non-invasiveness, these intermittent measurements have the risk of missing clinically-relevant BP changes. Thus, this method is not preferred in major surgery with the risk of rapid changes in hemodynamics.

However, catheterization has been associated with the risk of adverse effects including distal ischemia, bleeding, thrombosis, and infection, which can result in increased morbidity and costs. These drawbacks of existing BP monitoring methods have prompted researchers to pursue non-invasive continuous solutions of ABP monitoring. Besides technologies such as the vascular unloading method or tonometry that both require specialized and additional equipment, photoplethysmography (PPG) has emerged as a candidate technology for this pursuit as well. By using PPG-derived features, systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) can be estimated via regression models.

The most widely-studied feature for SBP estimation is pulse arrival time (PAT). It is defined as the time delay between an R peak in the electrocardiography (ECG) signal and a fiducial point in the PPG signal. PAT is often inversely related to the pulse wave velocity – the velocity a pulse propagates along vessels. Increased BP induces decreased elasticity of arteries, leading to an increased pulse wave velocity and therefore decreased PAT. In addition to PAT, other PPG-derived features have also been investigated, including those extracted from morphology, the first derivative, second derivative, and spectrum. Although the associated physiological basis is not fully understood, several features have shown significant correlations with blood pressure.

Despite these extensive studies of PPG-derived methods, these methods still warrant improvements in the clinical context. It is therefore an interesting and relevant attempt to investigate how to utilize previous intermittent measurements to strengthen the estimation model, as models inferring blood pressure often show improved performance in the presence of calibration and recalibration. In view of the clinical relevance of SBP, in this work, we propose an SBP estimation method using ECG- and PPG-derived features and the information from previous intermittent measurements. In this model, dynamic feature selection was employed based on feature robustness and the principle of correlation feature selection (CFS).

2. Materials and methods

2.1. Patients

The study was reviewed and approved by the regional medical ethics committee (METC Brabant, The Netherlands, NL48421.028.14-P1409). With written informed consent, a heterogeneous group of 29 patients scheduled for major surgery was enrolled. Characteristics of patients are shown in table 3.1.
2.2. Protocol

Anesthesia was induced by propofol (2mg/kg), sufentanil (0.5mcg/kg), and rocuronium (0.6mg/kg), and maintained by means of continuous infusion.

Table 3.1: Patient characteristics (n=29).

| Characteristic          | Value   |
|-------------------------|---------|
| Age [yr]                | 70.0 ± 8.9 |
| Gender (male/female)    | 23/6    |
| BMI [kg/m^2]            | 27.8 ± 9.7 |
| Height [cm]             | 172.3 ± 13.7 |
| Length of operation [hours] | 4.4 ± 1.4 |

Surgical procedures

| Urology:                |        |
| Bricker deviation       | 14     |
| Radical prostatectomy   | 3      |
| Cystectomy              | 1      |
| Pyeloplasty             | 1      |

| Vascular surgery:       |        |
| FEM-Fem bypass or crossover | 4     |
| EVAR removal and replacement | 3   |
| PTA Femoral Artery      | 1      |
| Recanalization Iliac artery | 1    |
| Carotid Endarterectomy  | 1      |

of propofol and sufentanil. The depth of anesthesia was assessed using bi-spectral index (BSI) with a target range of 40-55. The patients were ventilated in a volume-controlled, pressure-limited mode with tidal volume of 6-10 ml/kg at a frequency of 10-14/minute, and adjusted to maintain normocapnea. The positive end-expiratory pressure was set at 6 cm H_2O and adjusted as needed. Fluid management was at the discretion of the physician. During surgery, three signals were collected: invasive ABP signals (Philips Heartstart MRx monitor) by a radial arterial catheter, the finger PPG signal obtained at the right index finger (Philips M1191B), and the ECG signal (Philips Heartstart MRx monitor).

2.3. Feature extraction

We extracted nine features that have previously been proven to have significant relationship with BP. These features include PAT, the mean and variance of the first derivative in the systolic phase, PPG amplitude, stiffness index, and several features defined in the second derivative. They were categorized into four groups for the purpose of feature selection, as can be seen in table 3.2 and shown in figure 3.1. The criteria was based on a combination of physiological interpretation of these features and the robustness when extracting them. The first group refers to the time delay from combinations of ECG- and PPG-derived features. Here it comprises only PAT, which has been extensively studied and of which its physiological association with SBP has been established. It is, by far, one of the most relevant features for SBP estimation. The second group consists of features based on detected fiducial points in the first derivative and comprises PPG amplitude and the mean and variance of the first derivative in the systolic phase. The latter two features were determined after the pulse was normalized. They were found to contribute significantly to SBP estimation.
third group includes the pulse delay (PD), which found to be related to arterial stiffness by Millasseau et al.\textsuperscript{18}. PD was defined as the time delay between the first and second peak in a PPG pulse. In order to detect a second peak, it is necessary to detect the zero-crossing point in the first derivative. However, the patients in this study were elderly and the dicrotic notch, which results in the second peak, was often missing. In this case, a surrogate was often included from the zero-crossing point in the second derivative\textsuperscript{9}. Thus, PD was in Table 3.2: Extracted feature and their affiliated group.

| 1\textsuperscript{st} group | 2\textsuperscript{nd} group | 3\textsuperscript{rd} group | 4\textsuperscript{th} group |
|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| PAT                          | PPG amplitude                 | Pulse delay                   | c/a                           |
|                               | spmean                        |                               | e/a                           |
|                               | spvar                         |                               | norm a                       |
|                               |                               |                               | norm b                       |

\textbf{Figure 3.1:} Illustration of all features used in this study. The first panel (from top to bottom): ECG signal. The second panel: PPG signal. The third panel: the first derivative of the PPG signal. The fourth panel: the second derivative of the PPG signal. PAT: pulse arrival time. PD: pulse delay. AMP: PPG amplitude. SP: systolic phase. DP: diastolic phase. P1: The local maximum in the first derivative. P2: the local minimum in the first derivative.

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\textbf{2.4. Data Analysis}

Signal analysis was confined to the period of mechanical ventilation. For ABP and PPG signals, signal segments with low signal quality or with severe cardiac arrhythmia were
excluded by manual selection and a dedicated software program. This program, after identifying peaks and valleys for each pulse, computed three parameters. These were the distance between neighboring peaks, the distance between neighboring valleys and the amplitude of each pulse. For each parameter, if the difference between the present value and the extrema (maximum or minimum) in the past window of 30 seconds prior to that pulse was larger than the discrepancy between these maximum and minimum values, this pulse was excluded. For ECG signals, large signal segments with consistent invalid detected R peaks were removed manually. Note that an eligible segment requires three signals be of acceptable signal quality simultaneously. As a result, data from six patients were removed entirely. From the remaining 23 patients, 91.2 hours of data was found eligible for further analysis of PPV (9.8% data of the 23 patients was excluded due to poor signal quality or cardiac arrhythmia). Note that invalid pulses can also be excluded when deriving the feature values in the epoch of estimation, as explained in the next paragraph.

In this study, the epoch for SBP estimation was 30 seconds. All the extracted features and measured SBP were averaged using the values within the interquartile range (25% to 75%) in the epoch. The intermittent measurement of every 10 minute was simulated by the 30-second averaged SBP using this method at the time of the intermittent measurement. As our focus is to validate the algorithm and therefore we chose the stimulation of SBP in order not to induce additional errors when comparing cuff-based and catheter-based measurements. We chose the interval between intermittent measurements to be 10 minutes, as this is one option of the clinical practice.

The performance of the algorithm was evaluated by calculating agreement (Bland-Altman analysis), root mean square error (RMSE) and Pearson’s correlation coefficients in comparison with the reference SBP, derived from invasive ABP.

2.5. Feature selection and regression model

In this work, we propose method that includes a dynamic feature selection and regression model. We selected features at the time of each intermittent measurement (in this case every 10 minutes). With the selected features, we applied a regression model to combine the information of these features. This model was used to predict the SBP before the next intermittent measurement (i.e. provide SBP estimation every 30 seconds for the next 10 minutes). Upon the next intermittent measurement, both the features and regression model were updated.

The feature selection method for the first feature is given in figure 3.2. The procedure was implemented as follows. The most recent nine intermittent measurements (around 1.5 hours) and corresponding feature values were stored. Firstly, the absolute value of correlation coefficient (ACC) between PAT and SBP was computed based on these nine pairs of data. If the ACC was higher than 0.7, then PAT was chosen as the first feature. Otherwise, the correlation between SBP and the second group (features involving the detection of the fiducial
point in the first derivative) was assessed. If the maximum ACC between these features and SBP was higher than 0.7, we then performed a refined feature selection for the features with ACC higher than 0.7 (see figure 3.3). This refined feature selection was implemented by calculating the mean correlation coefficients after bootstrapping (1000 experiments with 10 samples per experiment) for each feature. The feature with highest mean ACC was selected. This was to prevent the spurious high correlation caused by several outliers, which did not indicate its predictive power for SBP estimation. In case that no features were found to have an ACC higher than 0.7 in the first and second group, the third and fourth groups were considered. The feature selection procedure for the third and fourth group was exactly the same as the second category. When no feature had an ACC higher than 0.7 in any of the category, we used the most recent SBP measurement as the estimation of SBP for the next 10 minutes. Note that we heuristically chose 0.7 because it is often associated with the boundary between strong and moderate correlation in practice.

After selecting the first feature, other features were included in the best feature subset (the features used to build the regression model) if they can provide complementary information to the first selected feature. This was realized by using correlation feature selection algorithm 25. The procedure is illustrated in figure 3.4. The merit indicating the strength of predicative power for a certain feature subset is given by

$$Merit = \frac{r_{sf1} + \cdots + r_{sfk}}{1 + (r_{f1f2} + \cdots + r_{fjf} + \cdots + r_{fkf1})}$$  \hfill (3.1)

where $r_{sf1}$ denotes ACC between $i$-th features and SBP, $r_{fjf}$ denotes ACC between $i$-th and $j$-th features, and $k$ is the number of features.

The new merits were calculated for the features already in the best feature subset combined with each newly-added feature and the highest merit among all calculated merits was identified. This highest merit was then compared with the stored best merit (the merit for the current best subset). If the current merit was larger than the stored one, the current feature was added to the best feature subset and the stored merit was overwritten by the new highest merit. Because we only used nine points to build the regression model, in order to avoid overfitting, we heuristically set the maximum number of features to be three.

After determining the best subset, a linear regression model was built by using SBP and features from the most recent nine intermittent measurements. The regression coefficients for each feature was determined collectively in this linear fitting. After acquiring the coefficients for each feature, the offset was determined when fitting the most recent intermittent measurement. This aimed to ensure that the model fitted perfectly with the most recent measurement.

2.6. Comparison with two methods

To further evaluate the performance of the proposed method, we compared it with two methods. These two methods also provided SBP estimation every 30 seconds. In the first method, SBP was continuously estimated using the most recent intermittent SBP measurement until a new SBP intermittent measurement was acquired. This is essentially the zero-order hold of the most recent measurement, which is in line with what current clinical practice implies.
Thus, the first method was termed zero-order hold. In the second method, the model was built using the most recent nine intermittent measurements. Particularly, the regression coefficient for PAT was estimated by these nine intermittent measurements, while the offset was determined using the most recent measurement. The second method was therefore termed PAT-only. This method was equivalent to the first step in the proposed method. This method was used to assess the effect of features derived exclusively from PPG.

2.7. Statistical Analysis

To statistically quantify the comparison between our proposed method and the two methods, we applied Friedman’s one-way test on the RMSE and correlation coefficients. The Friedman’s test was followed by pairwise comparisons, which were implemented using the sign test. The p values were corrected according to the Bonferroni method using the number of comparisons (in this case 3). A p < 0.05 was regarded statistically significant.

3. Results

The SBP estimation performance for all the considered methods (zero-order hold, PAT-only, and the proposed method) can be found in table 3.3. All the results in table 3.3 are based on pooled data from all patients. It can be seen that the proposed method outperformed zero-order hold and PAT-only methods in the SD of the difference in the Bland-Altman analysis. The proposed method also showed higher correlation coefficients with reference SBP when compared to other two methods. Figure 3.5 shows an example on the performance comparison of the considered methods. It is shown that the proposed method approached better the value and trend of measured SBP compared to the other two methods. Figure 3.6 gives the boxplot of the estimation performance of these three methods for each patient. It is demonstrated that the proposed method performed significantly better compared to these two methods in both RMSE and correlation coefficients. After the correction by Bonferroni method in which the p values were increased by 3 times, all the p values were still smaller than 0.05, indicating that the statistically significant differences still held. Particularly, the median difference in the RMSE was 1.11 mmHg between the PAT-only and the proposed method and 4.32 mmHg between the zero-order hold and the proposed method. The median difference was 0.05 in the correlation coefficients between the proposed method and PAT-only method and 0.21 between the proposed method and the zero-order hold.
All the features values and SBP for the previous 9 intermittent measurements

Calculate the correlation coefficient $r$ between PAT and SBP

$\text{abs}(r) > 0.7$

$\text{Y}$

Put PAT in the best subset

$\text{N}$

Calculate the correlation coefficient $r$ for features in the 2nd group (see table 3.2)

Max $\text{abs}(r) > 0.7$

$\text{Y}$

Put features with $\text{abs}(r) > 0.7$ in the refined feature selection (see figure 3.3)

$\text{N}$

Calculate the correlation coefficient $r$ for features in the 3rd group (see table 3.2)

Max $\text{abs}(r) > 0.7$

$\text{Y}$

Put features with $\text{abs}(r) > 0.7$ in the refined feature selection (see figure 3.3)

$\text{N}$

Calculate the correlation coefficient $r$ for features in the 4th group (see table 3.2)

Max $\text{abs}(r) > 0.7$

$\text{Y}$

Put features with $\text{abs}(r) > 0.7$ in the refined feature selection (see figure 3.3)

$\text{N}$

Take the most recent measurement as the estimation

Figure 3.2: The flowchart for selecting the first feature.
The statistics of selected features for the proposed method is presented in table 3.4. It is shown that three features were selected in a majority of cases and PAT was often chosen as one of these three features. Next to best feature subsets comprising three features, best feature subset comprising one feature was chosen to build the regression model, where PAT was the most selected feature. In very few cases, two features were selected to build the regression model.

4. Discussion

In this study, we propose a novel method utilizing the previous intermittent SBP measurements and ECG- and PPG-derived features to build a regression model for continuous SBP estimation (every 30 seconds). Based on the physiological understanding of these features and robustness when extracting them, we selected the first feature (the most important feature). Next, we selected the features that provided complementary information based on correlation feature selection. The results show that the proposed method outperformed the existing zero-order hold method and PAT-only method.
**Figure 3.4:** The selection strategy for the second and third features.

**Table 3.3:** The SBP estimation performance for zero-order hold, PAT-only, and the proposed method.

|                  | Zero-order hold | PAT-only  | Proposed |
|------------------|-----------------|-----------|----------|
| RMSE (mmHg)      | 12.97           | 10.06     | 7.92     |
| Bland-Altman analysis (Bias ± SD) [mmHg] | 0.07 ± 12.97 | -0.27 ± 10.06 | 0.07 ± 7.92 |
| Correlation Coefficients | 0.71           | 0.83      | 0.89     |
In a significant portion of operations, invasive beat-to-beat blood pressure monitoring is not necessary and blood pressure is only intermittently measured using a brachial cuff. Although non-invasive and convenient, this may hinder clinicians from observing clinically-relevant changes in the blood pressure in the interval between intermittent blood pressure measurements. It is therefore important and valuable to also monitor the blood pressure between adjacent intermittent measurements. In this study, we achieved this goal by building an ECG- and PPG-based regression model that can provide SBP estimation every 30 seconds. Furthermore, we demonstrated that the proposed model yielded estimation that was in a good agreement and well correlated with the invasive reference SBP. The SD of difference was within the acceptable threshold of 8.
Figure 3.6 Boxplots of performance comparison between zero-order hold method, PAT-only method and, the proposed method. (a) Comparison on the RMSE. (b) Comparison on the correlation coefficients. The uncorrected p values from sign test are presented on the solid line.

mmHg according to the Association for the Advancement of Medical Instrumentation.  

A few features have been applied to estimate SBP in the existing literature. The extraction of some of these features is more sensitive to noise when detecting fiducial points has to be done in higher derivatives. This is because the relevant signal is often attenuated in the higher derivative, while noise is often largely preserved. In this study, we designed a method where features

| Feature                   | Occurrence frequency | Top 3 occurrence                  |
|---------------------------|----------------------|----------------------------------|
| One feature               | 19.1%                | PAT                              |
|                           |                      | PPG amplitude                    |
|                           |                      | spvar                            |
| Two features              | 1.5%                 | e/a, PAT                         |
|                           |                      | spvar, PAT                       |
|                           |                      | PPG amplitude, PAT               |
were categorized based on the used derivatives when extracting these features. After selecting the best feature based on this consideration, additional features were chosen based on the idea that a relevant feature should correlate reasonably well with SBP while not inducing redundancy in the presence of existing features. The results show that PAT is most likely to be selected. This is in accordance with literature, as PAT is often shown to be correlated well with BP and has a physiological basis. In addition to PAT, other features such as sp\text{var} and e/a in the second derivative are often chosen, which is in line with the finding in our previous work \(^7\).

Our study has several limitations. First, several parameters such as the number of measurements used to build the regression model were determined heuristically. With the acquisition of more data, these parameters can be further optimized and an improvement in the estimation performance can be expected. Second, in other clinical scenarios with non-sedated patients, a fixed measurement-interval of 10 minutes might be uncomfortable for some patients. In those scenarios, future research might be dedicated to devising smart triggering strategy where the BP measurement is only triggered when the estimation algorithm is likely to fail. By doing this, we can maximize the interval between each measurement.

In conclusion, this study presents a novel method that is capable of estimating SBP between the intermittent measurements of blood pressure. This method outperformed the zero-order hold and PAT-only methods.
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