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Personalization of pulse arrival time based blood pressure surrogates through single spot check measurements

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Abstract*—*Objective: **We investigate the effect of selective single parameter personalization on the performance of multi-parameter models for pulse arrival time (PAT) based blood pressure (BP) surrogates. *Methods*: Our data set stems from 15 surgery patients, and we selected from each patient 5 segments of 30 min length each. We evaluate the root mean squared BP tracking error of the two models with and without single parameter personalization. We further compare the BP tracking performance to a surrogate-free sample-and-hold approach, e.g., as afforded by conventional non-invasive blood pressure (NIBP) oscillometry. *Results:* Parameter personalization is key to realizing a tracking performance benefit of PAT-based BP surrogates. The highest tracking error reduction of about 3.7 mmHg with respect to a sample-and-hold approach was reached with a personalized model which is linear in the pulse wave velocity domain. It achieves an estimation error of 7.8 mmHg with respect to a continuously measured invasive reference.**

***Clinical Relevance*—We give a performance analysis of PAT-based BP surrogates which are personalized to a patient with a single NIBP spot measurement. We show for surgery patients that patient-specific personalization enables continuous beat-to-beat BP monitoring over 30 min intervals with a average root mean squared error of less than 8 mmHg.**

I. Introduction

The clinical value of continuous arterial blood pressure (ABP) information of a patient is well recognized, and a much researched technical approach to non-invasive beat-to-beat BP measurements is rooted in the concepts of pulse arrival time (PAT), pulse transit time (PTT), and pulse wave velocity (PWV) [1]. In particular the PAT is often of great practical interest as a BP surrogate since it can be obtained unobtrusively from sensors that are already part of many standard clinical workflows in the intensive care units (ICU) and the operating room (OR), e.g., from the electrocardiogram (ECG) and a photoplethysmogram (PPG) sensor on the patient's finger.

A central point of ongoing research is the mathematical relationship between beat-to-beat $BP(t)$ and $PAT(t)$, and many models have been proposed. In this paper we consider a model of the form

$$PAT(t) = PEP + L \cdot f(BP(t), Q), \qquad (1)$$

where the PAT is the sum of a positive pre-ejection period (PEP) and a positive PTT term which factorizes into the travel path length L and BP-related function $f(\cdot, Q)$, with a set of parameters Q. The parameters PEP, L, and Q are patient-specific and, with the exception of L, considered relatively slowly time-varying so that they could require personalization and re-calibration. Notice, that the term $1/f(BP(t), Q)$ can also be thought of as the BP-dependent PWV.

A fully specified model of the form of (1) can then be used in reverse to estimate the beat-to-beat surrogate BP from the PAT

$$BP_{surr}(t, K, L) = f^{-1}\left(\frac{PAT(t) - PEP}{L}, Q\right) \qquad (2)$$

where $K = \{PEP, Q\}$ is the combined set of all slowly time-varying parameters.

Physical considerations [2] suggest that $f(\cdot, Q)$ is monotonically decreasing, i.e., that as the BP increases the PTT decreases (resp., the PWV increases), and we therefore choose to investigate the 3-parameter linear model of the form

$$PAT = k_1 + L \cdot (k_2 \cdot BP + k_3) \qquad (3)$$

with $K_{linPTT} = \{k_1, k_2, k_3\}$ and constraint $k_2 < 0$. Here, k_1 is a model for PEP and k_2 and k_3 for the BP-PTT relationship.

As an alternative we also consider the linear model in the PWV-domain

$$PAT = k_4 + \frac{L}{k_5 \cdot BP + k_6} \qquad (4)$$

with $K_{linPWV} = \{k_4, k_5, k_6\}$ and constraint $k_5 > 0$. Here we dropped the explicit time-dependency from the notation.

Considerable research effort has been devoted to BP surrogate parameter calibration techniques [3], and we expand in our article on the works of [4] and [5], which propose single-parameter offset adaptation in linear and non-linear models.

As in this prior work, we focus here solely on the scenario where the calibration data could be collected non-invasively and instantaneously, i.e., through a direct PAT observation immediately followed by a single oscillometric non-invasive blood pressure (NIBP) spot-check measurement, leading to a single pair of reference values $\{PAT_{ref}, BP_{ref}\}$. This reference value pair then allows for the direct calibration of any single one parameter from the set K, while the remaining parameters must be population-based and constant.

From a practical perspective we deem such a NIBP spot-check calibration preferable to techniques requiring extensive co-operation of the patient, e.g., to facilitate posture changes to induce hydrostatic changes as in [6]. For the same reason we also do not consider calibration using information collected

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over time through multiple NIBP oscillometry measurements as in [7].

Our specific research questions in this article are:

1. What tracking performance can be achieved with an un-personalized PAT-based BP surrogate?
2. Given a single calibration measurement, which of the surrogate parameters should be personalized to achieve the best BP tracking performance, and how does it compare to NIBP-only sample-and-hold tracking?
3. Which of the tested PAT-BP models is preferred?

Given the space constraints of this article we limit our investigation to the tracking of the systolic BP, though the techniques are equally applicable to the diastolic or mean arterial pressure. Moreover, we isolate the additional accuracy limitations of NIBP oscillometry by using pressure data from an invasive arterial line for this conceptual study. Furthermore, we derive the PAT from the arterial line waveform to omit the added complexities of photoplethysmography, e.g., motion artifacts. Lastly, we give here no consideration to a causal implementation of the techniques.

II. Methods

A. Data collection

The MEC-U ethical committee approved our study (St. Antonius Ziekenhuis, Koekoekslaan 1, 3430 EM Nieuwegein, NL. Approval W19.046), and it was carried out at the Elisabeth-Tweesteden Ziekenhuis hospital in Tilburg, NL. All patients gave their written informed consent for the investigation.

The data set is a subset of the one we reported on in [8], and it was collected from $P = 15$ patients (9 females) during surgery in the OR with an arterial line as standard of care. Exclusion criteria were neuro-trauma, obesity (BMI > 40), pregnancy, delirium, and a significant language barrier that prevented the patient from understanding the informed consent. The patients of this study had an age range from 19 to 91 years (μ=55.2, σ=19.8), and a BMI from 17.3 to 31.7 kg/m^2 (μ=24.0, σ=3.7). The surgeries were vascular (5), and neuro (10).

We invasively acquired the ABP waveform from an Edwards Lifesciences TruWave disposable pressure transducer (Edwards Lifesciences, Irvine, CA) at the radial site and the 3-lead ECG signal with a Philips MP50 patient monitor (Philips Medizin Systeme, Böblingen, Germany) at a sampling rate of 125 Hz and 500 Hz, respectively. The data were recorded on a laptop with custom data logger software.

B. Data preparation

We selected per patient $S = 5$ segments of length 30 minutes with mostly artifact-free waveform data (see Figure 1 for an example). The systolic pressure peak for each heart beat (top panel, black dots) was manually annotated in the ABP waveform (light blue). Artifacts from the frequently occurring NIBP measurements on the same arm were omitted. In the center of the segment, 20 seconds worth of heart beats were marked as calibration beats (green dots), and their systolic ABP values were averaged to provide the calibration reference pressure BP_{ref} (red dot), which in practice could be obtained non-invasively using BP oscillometry.

In the ECG signal the R-peak was found for each beat and the PAT (Figure 1, bottom panel, black dots) was calculated to the 50% point of the rising edge of the ABP waveform. Also here we mark the center 20 seconds as calibration beats (green dots), whose PAT values are averaged to provide the calibration reference value PAT_{ref} (red dot).

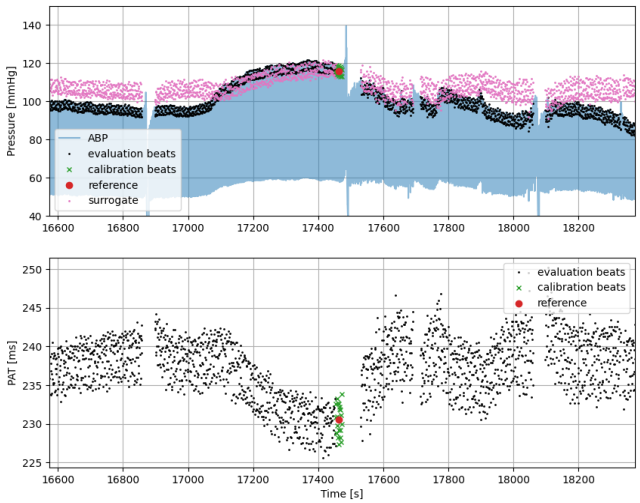

Figure 1 Waveform segment example. Top: continuous ABP waveform (light blue) with marked systolic pressure peaks (black - evaluation beats, green - calibration beats), red - reference point (BP_{ref}=116mmHg), pink - BP surrogate (lin. PTT model with L=0.8m, k_1=157ms, k_2=-1.0ms/m/mmHg, k_3=207ms/m, RMSE=9.6mmHg). Bottom: beat-by-beat pulse arrival time (black - evaluation beats, green – calibration beats), red – reference point (PAT_{ref}=231ms).

C. Experiments

We perform all experiments in a leave-one-patient-out fashion, i.e., we consider always one of the 15 patients as the test patient P_{test} and the other 14 patients as the training population P_{train}, from whom we derive any necessary population model parameters.

As a performance metric we evaluate for each test recording the root mean squared error (RMSE) between the ground truth BP_{eval} of the evaluation beats (black dots in Figure 1, top panel), and the surrogate BP_{surr} (pink dots).

1) Baseline – NIBP sample-and-hold

As a first baseline we employ a simple sample-and-hold strategy, i.e., we consider the reference BP measurement BP_{ref} of a segment of a test patient as surrogate for all evaluation beats of that segment. This personalized single parameter method "M1" does not employ any PAT-based information, and it is to represent the current state-of-the-art BP monitoring practice with fixed-interval oscillometry.

M1: $$BP_{surr} = BP_{ref} \quad (5)$$

2) Linear PTT model

We apply for each test patient an un-personalized linear PTT surrogate model "M2" according to (*2*) and (*3*).

M2: $$BP_{surr}(PAT(t), K_{linPTT}, L) = \frac{1}{k_2^*}\left(\frac{PAT(t) - k_1^*}{L} - k_3^*\right) \quad (6)$$

The parameter set $\{k_1^*, k_2^*, k_3^*\}$ is obtained from the training patients' data by minimizing the surrogate RMSE for all evaluation beats $t \in T$ of all segments $s \in S$ of all training patients $p \in P_{train}$:

$$\{k_1^*, k_2^*, k_3^*\} = \underset{k_1,k_2,k_3}{\operatorname{argmin}} \sum_{\forall p,s,t} \left(BP_{eval}^{p,s}(t) - BP_{surr}(\, PAT^{p,s}(t), K_{linPAT}, L^p)\right)^2 \quad (7)$$

Here, L^p is the travel path length (arm length) of patient p, and $BP_{eval}^{p,s}(t)$ and $PAT^{p,s}(t)$ are the evaluation beats' BP and PAT values of segment s of patient p, respectively. The three-dimensional linear least-squares optimization problem of (*7*) can be solved in closed form, and the obtained parameter values are then using in a PAT-based BP surrogate for the left-out test patient.

As outlined above, the central idea of this paper is the personalization of the BP surrogate to a patient through a spot check measurement, and we illustrate this process now with the example of personalizing the parameter k_1 of (*6*).

Here, using the training patients' data, we have to find the optimum population-based un-personalized parameters k_2^* and k_3^*, for the k_1-personalized surrogate BP. This can be achieved by solving an optimization problem similar to (*7*) but where each signal segment receives its own optimum value $k_1^{p,s\,*}$ while we still have a single optimum k_2^* and k_3^* for the entire training population

$$\{k_1^{PxS,*}, k_2^*, k_3^*\} = \underset{k_1^{PxS},k_2,k_3}{\operatorname{argmin}} \sum_{\forall p,s,t} \left(BP_{eval}^{p,s}(t) - BP_{surr}(\, PAT^{p,s}(t), \{k_1^{p,s}, k_2, k_3\}, L^p)\right)^2 \quad (8)$$

This is a 72-dimensional optimization problem as we search for 14·5=70 k_1^*-values, as well as the optimum population values for k_2^* and k_3^*. For convenience, we solve this numerically using the Levenberg-Marquardt method with the constraints listed above and the starting values k_1 of half the smallest PAT value in the training data, k_2=50 ms/m/mmHg, and k_3=0 ms/m.

With the training population-based optimum values for k_2^* and k_3^* at hand, and the reference measurements $\{PAT_{ref}, BP_{ref}\}$ of a test patient, we can now eliminate k_1

$$k_1 = PAT_{ref} - L \cdot (k_2^* \cdot BP_{ref} + k_3^*) \quad (9)$$

and complete (*6*), thereby forcing the surrogate BP time series through the reference BP point. In this particular case the parameter k_3^* drops out and we arrive at the k_1-personalized linear PAT surrogate model "M3":

M3: $$BP_{surr} = \frac{PAT - PAT_{ref}}{L \cdot k_2^*} + BP_{ref} \quad (10)$$

The development of personalized models for other parameters in the linear PTT model follows along the same lines, i.e., the personalization of parameter k_2 in (*6*) through the reference measurement

$$k_2 = \frac{1}{BP_{ref}}\left(\frac{PAT_{ref} - k_1}{L} - k_3\right) \quad (11)$$

requires first finding training population-based k_1^* and k_3^* that are optimal under k_2-personalization

$$\{k_1^*, k_2^{PxS,*}, k_3^*\} = \underset{k_1,k_2^{PxS},k_3}{\operatorname{argmin}} \sum_{\forall p,s,t} \left(BP_{eval}^{p,s}(t) - BP_{surr}(\, PAT^{p,s}(t), \{k_1, k_2^{p,s}, k_3\}, L^p)\right)^2 \quad (12)$$

and leads to surrogate model "M4":

M4: $$BP_{surr} = \frac{PAT - k_1^* - L \cdot k_3^*}{PAT_{ref} - k_1^* - L \cdot k_3^*} BP_{ref} \quad (13)$$

Finally, the personalization of the parameter k_3 in Eq. (*6*)

$$k_3 = \frac{PAT_{ref} - k_1}{L} - k_2 \cdot BP_{ref} \quad (14)$$

leads to

$$BP_{surr} = \frac{PAT - PAT_{ref}}{L \cdot k_2^*} + BP_{ref} \quad (15)$$

which is identical to model "M3", and does not need to be considered separately.

As a performance bound we also compute the optimal linear model "M5" for each test data segment by fitting a linear model directly to the evaluation BP_{eval} and PAT data points. This model is, of course, not available in practice since it would require continuous BP data to create. However, it does provide a bound on the best achievable predictive capabilities of the linear PTT surrogate model of form (*3*).

3) Linear PWV model

We start by re-writing equations (*2*) and (*4*) as

$$BP_{surr}(PAT(t), K_{linPWV}, L) = \frac{1}{k_5} \cdot \left(\frac{L}{PAT(t) - k_4} - k_6\right). \quad (16)$$

As a safeguard against the denominator "$PAT - k_3$" becoming zero during evaluation or parameter optimization we modify this model by introducing the differentiable softplus function

$$\mathrm{sp}_\gamma(x) = \gamma \cdot \log\left(1 + \exp\left(\frac{x}{\gamma}\right)\right) \quad (17)$$

in denominator, and a small constant term ε which leads to

$$BP_{surr}(PAT(t), K_{linPWV}, L) = \frac{1}{k_5} \cdot \left(\frac{L}{\mathrm{sp}_\gamma(PAT - k_4) + \varepsilon} - k_6\right) \quad (18)$$

and we choose $\gamma = \varepsilon = 1ms$.

In the same spirit as in previous section we derive for each patient an un-personalized model "M6", the models "M7", "M8", and "M9" for the personalization of the parameters k_4, k_5, and k_6, respectively, as well as the optimum bound model "M10."

III. Results

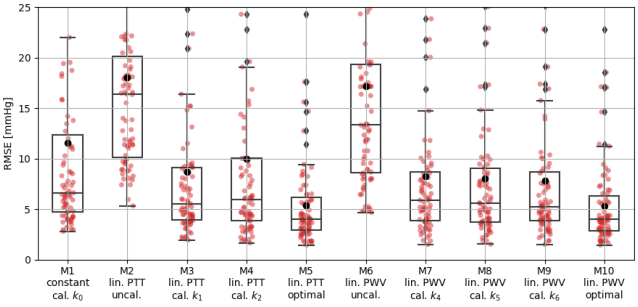

Figure 2 BP estimation RMSE performance of the blood pressure surrogate for the 10 models. For each model we have 45 data points (from 15 patients with 5 segments each; marked with red dots), the box plot, and the average RMSE (black dots).

The achieved performance of the 10 models is visualized in Figure 2, and the numerical values are listed in Table 1. The best performing personalized linear PTT model is "M3", with personalized k_1 (μ=86.7x10^{-3}, σ=29.7 x10^{-3}) s, and the population based k_2^* (μ=-1.05x10^{-3}, σ=0.12x10^{-3}) s/m/mmHg, where mean μ and standard deviation σ are computed over the leave-one-patient-out runs. This model achieves an average estimation RMSE of 8.7 mmHg.

Table 1 Surrogate BP estimation performance for the 10 models.

Model / RMSE [mmHg]	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10
Mean	11.5	18	8.7	10	5.3	17.2	8.2	8	7.8	5.3
STD	12.6	11.9	8.9	10.7	4.2	12.7	8.2	7.3	7.4	4.1
Min	2.8	5.3	1.9	1.6	1.4	4.7	1.5	1.5	1.5	1.4
Median	6.6	16.4	5.5	5.9	4	13.3	5.9	5.6	5.2	4
Max	65.1	64.9	46.4	46.4	24.3	65.5	47.5	39.4	39.1	22.8

The best performing linear PWV model is "M9" , with the personalized parameter k_6 (μ=1.82, σ=0.41) m/s and the population parameters k_4^* (μ=3.4x10^{-8}, σ=1.4x10^{-8}) s, and k_5^* (μ=10.9 x10^{-3}, σ=0.39x10^{-3}) m/s/mmHg. This model achieves an average estimation RMSE of 7.8 mmHg.

IV. Discussion

We find that the un-personalized PAT-based surrogate models "M2" (RMSE=18 mmHg) and "M6" (RMSE=17.2 mmHg) perform significantly worse than the surrogate-free sample-and-hold method "M1" (RMSE=11.5 mmHg), which is somewhat indicative of current clinical practice using NIBP alone. The performance loss is 6.5 mmHg and 5.7 mmHg, respectively, and these effects are highly statistically significant with $p<10^{-5}$ and $p<10^{-3}$. Here it is better not to use a PAT-based surrogate at all.

With single parameter personalization by means of a one-time reference BP measurement the situation changes drastically, and all personalized PAT-based surrogate models "M3, "M4," and "M7" – "M9" outperform the sample-and-hold approach of "M1" significantly ($p<0.05$).

The best personalized linear PTT model "M3" reduces the estimation error to 8.7 mmHg. The best personalized linear PWV model "M9," on the other hand, achieves an even lower estimation RMSE of 7.8 mmHg.

The choice of how to personalize a model, i.e., which parameter to adapt, can also matter significantly. The two personalized linear PAT models "M3" and "M4" differ by 1.3 mmHg in performance ($p=0.01$), and we conclude that it is better to personalize the k_1 parameter than the k_2 parameter.

Similarly, the linear PWV models "M7" – "M9" differ in their achieved performance by up to 0.4 mmHg though their differences are not statistically significant. We can therefore give no strong recommendation as to which of the parameters $\{k_4, k_5, k_6\}$ to personalize.

We can also see that large room for improvement exist for both model types since the inherent limitation of the surrogate with linear PTT and linear PWV models is 5.3 mmHg as evidenced by the hypothetical models "M5" and "M10". We can, however, not devise how to establish these optimum models for a patient in a non-invasive fashion.

Lastly, we want to remind the reader that all our computational experiments were conducted under somewhat idealized conditions because we excluded the influence of the limited accuracy of the NIBP oscillometry as well as any complexity arising from the use of the PPG signal to measure PAT in practice. Hence, the practically achievable performance will naturally be worse than what we report here.

The BP tracking performance can, however, always be improved by shortening the tracking time horizons, i.e., by re-calibrating more frequently. The price for this solution is then a reduction in patient comfort.

V. Conclusion

Our experiments with BP and PAT data from the OR indicate that model parameter personalization is key to realizing a tracking performance benefit of PAT-based BP surrogates. The highest tracking error reduction of about 3.7 mmHg with respect to a current state-of-the-art sample-and-hold approach over a 30 minute time window was achieved through one-parameter personalization of a linear PWV-to-BP model. This model achieves a tracking error of 7.8 mmHg.

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