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Cuffless Estimation of Systolic Blood Pressure for Short Effort Bicycle Tests: The Prominent Role of the Pre-Ejection Period

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Abstract— **This paper investigates the specific contributions of the pre-ejection period (PEP) and pulse transit time (PTT) for blood pressure estimation based on the pulse wave methodology. We show that in short-term physical stress tests, PEP dominates PTT variations raising the question of a suitable blood pressure calibration. A model using a generalized pulse wave velocity achieves acceptable accuracy for systolic blood pressure estimation, given our experimental conditions.**

Keywords: pulse transit-time, pre-ejection period, blood pressure regulation, physical stress, blood pressure calibration.

I. INTRODUCTION

BLOOD pressure (BP) is one of the most important physiological parameters relevant for medical diagnostics, prevention as well as therapy strategies. Given the prevalence of hypertension, there is a clear demand of the medical community to dispose of a better blood pressure monitoring during day and night, aiming at improved hypertension diagnostics and blood pressure management. For these applications the measurement of the pulse wave velocity (PWV) or pulse transit time (PTT) has been identified as a promising approach, which offers conceptually the opportunity to derive arterial blood pressure at a beat level without applying an external pressure. There is a long research history dealing with this methodology [4,5] and one major challenge is finding an appropriate calibration procedure [1,13]. Recent results of a large evaluation over more than 6 weeks show good agreement with values provided by a standard sphygmo-manometric occlusive arm-cuff, under well-controlled conditions at rest [12]. However, a blood pressure calibration must be proven reliable in tracking BP variations caused by significant or even dramatic changes in the subject's general cardio-vascular status e.g. variations of the ambient temperature, movements, physical or mental stress, the consequences of various pathologies (fever, cardiac-arrhythmia, hypertension, oedema or dehydration) or the influence of medications including vaso-active drugs.

This paper deals with pulse transit time (PTT) variations and blood pressure calibrations related to short-term physical stress exercises at two activity levels. In this way we simulate normal life activities like short walks, going up or down stairs. We start by presenting the basic principles of blood pressure calibration including the underlying blood pressure regulation. For the most popular sensor configuration with an ECG as proximal signal and a photo-plethysmographic (PPG) sensor located at a peripheral site like the finger, we clarify the specific roles of the pre-ejection period (PEP) and PTT of relevance for interpreting the actually measured pulse arrival time (PAT). This time is defined as the time-delay between the R-peak of the QRS wave from the ECG and the arrival of the arterial pulse wave at the periphery and comprises the sum of PEP and PTT, both representing different underlying cardio-vascular mechanisms [5-7,9,10]. Based on data gathered in a trial with healthy volunteers performing a short physical effort test we investigated the relationship of PEP and PTT and evaluated several strategies for systolic blood pressure estimation via PAT measurements.

II. EXPERIMENTAL PROTOCOLS, SET-UPS AND DATA ANALYSIS

A. *Experimental Design*

18 healthy volunteers (4 female, 14 male) have been asked to perform a short term physical effort test inducing significant changes of their blood pressure. All persons were non-smokers and had no known heart or other diseases. The biometric characteristics of the test were as follows (average, minimum, maximum):

TABLE I: STATISTICS OF THE BIOMETRIC PARAMETERS OF THE 18 VOLUNTEERS (AVERAGE, MIN, MAX)

age [y]	**Size [m]**	**BMI**	**Arm length [m]**
∅ 33 23; 51	∅ 1.78 1.56; 1.92	∅ 23.4 18.5; 28.8	∅ 0.72 0.62; 0.81

The test protocol with a bicycle ergometer consisted of the following phases:

- 3 minutes at rest
- physical exercise: 2 minutes at 70 W
- 4 minutes at rest
- physical exercise: 2 minutes at 150 W
- 6 minutes at rest

During the experiments, the following vital signals have been collected: the electrocardiogram (ECG, Einthoven-II), the index finger photoplethysmogram (PPG, Philips finger clip sensor), the thorax impedance (IMP), the right arm impedance plethysmogram (IPG), the subject's posture as well as activity level (by a 3-axis acceleration sensor) and the blood pressure (by oscillometry). Except for the blood pressure, all signals were sampled at 200 Hz. The ECG, PPG and activity signals have been recorded by a self-developed data acquisition system. The thorax impedance was acquired using a "NICCOMO" patient monitor (Medis, [14]) and the blood pressure was measured with a Philips Intellivue MP50 monitor.

B. Data Analysis

Data streams coming from different set-ups were synchronized via the acquired ECG signals, which gave an accuracy in time of about ±3 ms between the different streams. The NICCOMO monitor provided the pre-ejection period (PEP) and several other cardiac related parameters like left ventricular ejection time (LVET) and stroke volume (SV). The pulse arrival time (PAT) has been defined as the time delay between the R-peak of the ECG, detected by a modified Pan-Tompkins algorithm, and the pulse-foot of the PPG-signal. This last point can be accurately determined from the tangent to the uprising pulse and has been shown to be robust regarding reflections and other signal artefacts. A parameter subset of heart rate, PAT, and PEP for a specific blood pressure measurement was extracted as the average values in an 10 - 15 s window around each blood pressure measurement. The pulse transit time (PTT) was calculated as the difference of the PAT and the PEP. The data processing and analysis has been carried out with Matlab.

III. BLOOD PRESSURE CALIBRATION PRINCIPLES

A. Theoretical Background

Functional relations between blood pressure and pulse wave velocity for BP calibrations are often justified using the Moens-Korteweg equation, in which the PWV is basically an indicator of vessel wall elasticity through

$$PWV = \frac{distance}{PTT} = \sqrt{\frac{Eh}{\rho 2r}}, \qquad (1)$$

ρ being the blood density, r the vessel radius, h the wall thickness and E the Young elasticity modulus of the wall [2][1]. Indeed it is assumed that ρ, r and h undergo small changes, the main variations coming from the elasticity [3]:

$$E = E_0 e^{\alpha P}, \alpha \approx 0.017\, mmHg^{-1} \qquad (2)$$

This experimental relation provides also the link between the PWV and blood pressure (P) variations. A calibration step is necessary to scale the PTT to BP conversion, the other parameters (α, E_0, h, r) being clearly subject-dependent and quite difficult to measure directly. Calibration functions can be derived from the combination of the Hughes equation and Moens-Korteweg equation, which leads to:

a logarithmic dependency of the form [11,12]:

$$P = A \ln PTT + B \qquad (3)$$

a quadratic relationship by linearizing the exponential as $E \sim E_0(1+\alpha P)$ [12]:

$$P = A(1/PTT)^2 + B \qquad (4)$$

This framework does not provide a clear solution as to how the systolic and diastolic phases should be handled. In these models the characteristics of the arterial tonus, inherently modelled by the coefficients α and E_0, affect the fitting parameters. However, blood pressure is regulated by at least four other factors representing the patient's cardio-vascular status: 1. the cardiac output, 2. the rate of ventricle contractility related to systolic intervals PEP & LVET (left ventricle ejection time) [9], 3. the total peripheral resistance (TPR) [9,11] and 4. the return of venous blood insuring the filling of the right ventricle and determining the cardiac preload. Most of these factors are often assumed to be constant under well-defined conditions, typically at rest.

B. Practical Measurement Setup

Equation (1) has been derived under quite restrictive assumptions of a homogeneous arterial segment, which requires in practice two pulse detectors to be accurately positioned on the arterial tree. The most popular measurement technique involves a one-lead ECG and a PPG clip at a finger, toe or ear, because the ECG is more easily accessible. The R peak of the QRS wave provides the start time of each heartbeat and the foot of the PPG volume pulse gives the arrival time. However this leads to the estimation of a Pulse Arrival-Time (PAT) made up of two parts:

$$PAT = PEP + PTT \qquad (5)$$

Here the pre-ejection period (PEP) is the duration of the iso-volumetric ventricle contraction up to the aortic valve opening (AVO) while the second term is the true transit time of the pulse along the arterial wall over a long non-homogeneous vascular path. Only the PTT values relate to the arterial wave propagation modelled by Moens-Korteweg equation, PEP being a non-constant additive delay, which changes rapidly in response to stress, emotion and physical effort [5-7, 9,10].

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[1] The Bramwell-Hill equation results from inserting the expression of volume compliance $\gamma = 2r / Eh$.

IV. RESULTS

A. *Typical Experimental Observations*

Fig. 1 show the variations of the Heart Rate, PAT, PEP, systolic and diastolic blood pressure (SBP, DBP) of a 25 year-old well trained male during the different phases of an experiment. At the beginning the subject has a PAT of 220 ms and a PEP of 90 ms. During the experiment, significant changes of the systolic blood pressure are induced, whereas the diastolic blood pressures remains almost constant compared to the blood pressure measurement accuracy. The maximal heart rate is 134 min^{-1}. For this specific subject, during the first activity phase and the following resting period the PEP changes jointly with the PAT (δ PAT$_{max}$=-55 ms) and almost no PTT variation is observed. PAT and PEP reach their base levels again after a first recovery period of 4 min. In the second activity phase the maximum PEP variation is roughly the same of the first phase, but the PAT is smaller indicating a significant contribution by δPTT of about -20 ms, but this δPTT disappears quickly in the second recovery phase. Then PEP and PAT evolve in parallel reaching their base levels within 5 minutes.

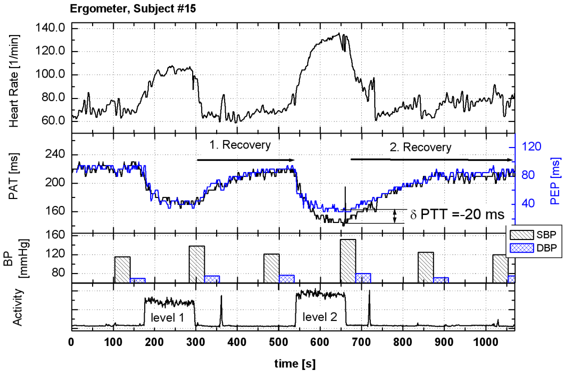

Fig. 1. Bicycle test of a 25 years old male; 1st: HR(t); 2nd: PAT(t) and the PEP(t), the PEP evolution follows closely the PAT; 3rd: SBP and DBP measurements; 4th: the subject's activity during the different phases

Fig. 2 shows the same HR, PAT, PEP and activity parameters for another 34 year-old subject, who does not regularly perform sport. In this case, during both activity phases and following resting phases, there are contributions of δPEP as well as δPTT. For the activity level 1 there is a δPTT=-15 ms and for the second level δPTT=-30 ms. The base levels of PAT and PEP from the beginning are not reached back in the recovery phases indicating a longer recuperation time.

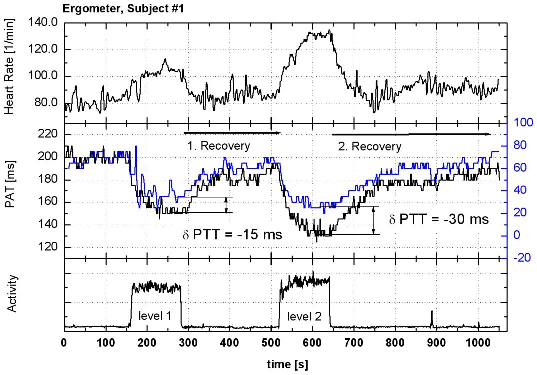

Fig. 2. bicycle test of a 34 years old male; 1st: HR(t); 2nd: PAT(t) and the PEP(t); 3rd: the activity of the subject during the different phases

B. *General Observations*

These two examples of the PEP-PTT variations represent typical observations of our experiments. The PAT variations provoked by the activity phases show an expected PEP decrease with the HR increase accompanied with positive or negative δPTT indicating the vascular response consecutive to the physical stress.

$$|\,\delta\, PEP\,| \geq |\,\delta\, PTT\,| \qquad (6)$$

This fact implies a much stronger influence of the PEP on PAT measurements for this specific procedure. We also analysed the correlations between SBP, DBP, PEP, PTT and PAT for our data set. Correlations coefficients greater than 0.8 for more than 90 % of the subjects have been observed for: SBP vs PAT and SBP vs PEP. Therefore we investigated only the systolic blood pressure calibrations based on PAT, PEP and PTT measurements.

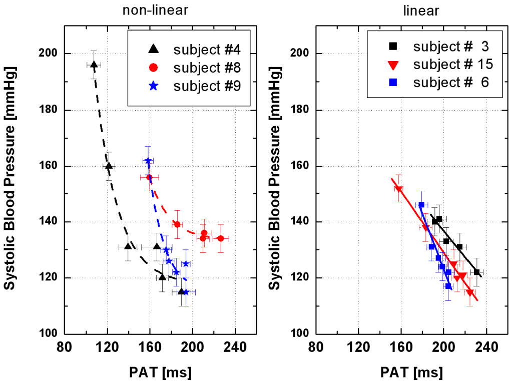

Fig. 3. Linear and non-linear dependency of SBP and PAT shown for several subjects

Fig. 3 shows two plots of systolic blood pressures versus the measured PAT for several subjects having different characteristics. On the left diagram SBP-PAT relations are obviously non-linear whereas on the right linear dependencies are visible. An analysis of the PEP changes indicates that the non-linearity comes from the PEP physiological lower bound. Interestingly all subjects with a linear relation have regular sport activities and reach a significantly lower maximal SBP than the subjects in the left diagram, which might indicate a faster adaptation of arterial elasticities for trained persons.

C. Blood Pressure Calibration Models

Our observations indicate that the blood pressure calibration concepts derived by equations (2), (3) for the pulse transit time, may not be suitable for PAT measurements, because they require a constant PEP.

For BP calibration, a generalized pulse wave velocity (pPWV), defined as the ratio of a subject's arm length L and the PAT, came out as the most suitable choice:

$$pPWV = \frac{L}{PEP + PTT} < \frac{L}{PTT} \qquad (7)$$

The pPWV is always smaller than the true PWV. In Fig. 4 the SBP-pPWV dependency is shown for several test persons. Most of the SBP range is well fitted by a linear dependency with some larger discrepancies at higher SBP values. We investigated various heuristic calibration models the results of which are presented in Table II. The intraRMSE (root mean square error) depicts the average model quality with separately optimized parameters for each subject whereas the interRMSE parameter represents a model with a constant sensitivity factor A – averaged over all subjects - and the parameter B individually adapted for each person.

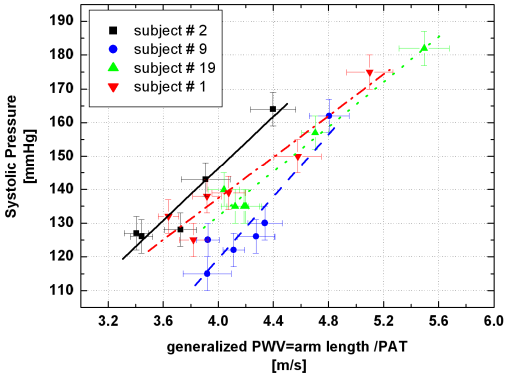

Fig. 4. Systolic Blood Pressure vs. generalized PWV that is defined by the ratio of a subject's arm length with PAT

TABLE II: INVESTIGATED HEURISTIC CALIBRATION MODELS

Calibration function	**Intra RMSE [mmHg]**	**Inter RMSE [mmHg]**
SBP=A*lnPAT+B	4.4	7.5
SBP=A*L/PAT+B	3.9	6.9
SBP=A*$(L/PAT)^2$+B	3.6 (2)	7.3

A linear dependency of the squared pPWV achieves the best results for interRSME case. The sensitivity parameter A could not be related to other biometric data than the arm length, but an average A value gives acceptable results if the parameter B is adjusted based on a single cuff calibration measurement. A correlation plot (Fig 5) of the estimated SBP versus the reference SBP demonstrates a good agreement up to 170 mmHg, but higher SBP are not modelled accurately. The sensitivity parameter A results in a SBP variation of about 1 mmHg per 1 ms, which requires therefore a rigorous calibration procedure, because PEP appears to vary at rest up to ±10 ms.

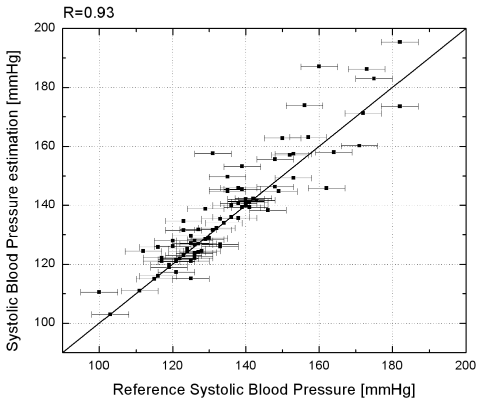

Fig 5. Correlation plot of the estimated SBP vs reference SBP using a quadratic SBP-pPWV calibration model (averaged sensitivity factor A and subject dependent B); RMSE= 7.3 mmHg

V. CONCLUSION

Our experiments show that, when short physical efforts affect the systolic blood pressure, the pre-ejection period has a clearly higher influence on PAT measurements than the PTT. This raised the question of an appropriate blood pressure calibration methodology, because the true pulse wave velocity is not available. Therefore, a heuristic linear calibration function has been designed based on a generalized PWV. This gives acceptable estimations and requires only a single blood pressure measurement for calibration at rest. Current work investigates the influence of other parameters like SV, CO and LVET on blood pressure calibrations. A practical test of the validity of a BP calibration appears to be an important challenge for deploying the pulse wave methodology in real life conditions.

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