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Device-guided slow breathing with direct biofeedback of pulse wave velocity – acute effects on pulse arrival time and self-measured blood pressure

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Background **There isevidence that device-guided slow breathing using biofeedback acutely reduces blood pressure (BP) and pulse wave velocity [i.e. increased pulse arrival time (PAT)].**

Objectives **The objectives of the study presented here were to test whether the results of changes observed in PAT in earlier studies are reproducible over 1 week and how changes in pulse wave velocity/PAT translate into absolute self-measured BP changes.**

Methods **Patients with a systolic BP 130–160 mmHg or treated essential hypertension (21 females/23 males) were trained to perform unattended device-guided slow breathing exercises for 10 min daily over 5 days. Furthermore, they were skilled to perform self-measurement of BP before and after the breathing exercise using a validated upper-arm device.**

Results **Office BP at screening [median (1, 3. Q)] was 137 (132, 142)/83 (79, 87) mmHg. We observed a significant ($P<0.05$) increase in PAT of 5 ms (SD 12.5 ms) on average after 10 min of guided breathing and an additional 1 ms ($P<0.05$, SD 8 ms) during the following 5 min of spontaneous breathing compared to baseline. PAT before the exercise remained constant over 5 days paralleled by constant self-measured BP before the exercise. Device-guided breathing was associated with a significant reduction of self-measured SBP of 5 mmHg ($P<0.01$, SD 8 mmHg). Data furthermore demonstrated that these changes were highly reproducible over 1 week.**

Conclusions **Device-guided slow breathing and biofeedback lead to reproducible and favorable changes (increase) in PAT and SBP (decrease).** ***Blood Press Monit*** **28: 52–58 Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc.**

Blood Pressure Monitoring 2023, **28**:52–58

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Received 27 July 2022 **Accepted** 23 October 2022.

Introduction

There is multifold evidence that essential hypertension is accompanied by increased activity of the sympathetic nervous system [1,2]. Additionally, autonomic dysfunction, characterized by an imbalance of sympathovagal function, was predictive of incident hypertension in the Atherosclerosis Risk in Communities Study study [3]. Therefore, device-based invasive therapeutic interventions modifying sympathetic activity to reduce blood pressure (BP) like renal denervation or carotid baroreflex activation are intensively investigated and the role of the sympathetic nervous system in hypertension [4] gets currently revisited.

Alternatively, noninvasive methods such as device-guided slow breathing [5] have been proposed to reduce sympathetic activity and BP. According to Mathani *et al.* [6] device-guided slow breathing has a net BP-lowering effect in the order of 3–4 mmHg SBP. Up to now the effect of device-guided breathing could mainly be monitored by the conventional office or ambulatory BP measurement. Furthermore, the acute effects of device-guided breathing in commercially available devices could not be visualized by biofeedback of BP.

In this work, we propose that a promising approach to improve the efficacy of device-guided slow breathing is the utilization of biofeedback based on pulse arrival time or pulse wave velocity. Decreases in BP directly lead to reductions in pulse wave velocity [7] and hence to an increase in pulse arrival time (PAT), which can easily be measured via 1-lead ECG and finger plethysmography. We have recently shown the feasibility of such a solution in a cohort of essential hypertensives [8] by the means of a pilot study.

The objectives of the study presented here were trifold: (1) we aimed to test whether the results of changes observed in PAT of the prior pilot study are reproducible in a different cohort, (2) how do changes in pulse wave

DOI: 10.1097/MBP.0000000000000628

velocity and PAT transform to self-measured absolute BP values and (3) reproducibility of BP reductions induced by slow breathing using PAT feedback during repeated measurements over 1 week.

Methods and materials

Cohort

Initial medical workup included medical history about 2 days before potential inclusion to the study, included three manual office BP readings by a trained operator using a mercury sphygmomanometer sequentially on the alternate upper arm (right, left, right). On the basis of that we enrolled volunteers and patients with high normal or grade I hypertension (SBP > 129 mmHg) or the presence of antihypertensive treatment without existing cardiovascular morbidities besides diagnosed hypertension. The ultimate inclusion criterion was the willingness to give informed consent after patient training and education. Furthermore, demographic data were assessed.

The study protocol was approved by the ethics committee of the Medical Association of Westphalia-Lippe and the University of Münster ('Ethik-Kommission der Ärztekammer Westfalen-Lippe und der Westfälischen Wilhelms-Universität Münster'), and all patients gave informed consent to participate in the study.

Blood pressure self-measurement and device-guided breathing

All participants enrolled in the study got detailed introduction and training on the user devices and the protocol, because the device-guided breathing exercise as well as the BP self-measurement later took place unattended in a quiet room. BP self-measurement was intended before starting and directly after finishing the device-guided breathing exercise.

Participants were trained to perform three subsequent automated oscillometric BP readings using a validated device (OMRON M500 Intelli IT, Omron Healthcare Europe, Hoofddorp, Netherlands.). Each reading was followed by a 1-min break to relieve the upper arm. Readings were stored automatically by the device.

Every breathing exercise session consisted of 10 min paced breathing phase followed by 5 min of spontaneous breathing (cooling phase). The breathing was paced by a mobile phone app (Fig. 1) visualizing the individual preset breathing frequency by an animated balloon which rises during the desired inhalation and falls during the desired exhalation. According to the literature, six breathing cycles per minute have been expected to be optimal [9]. Several probands were not able to follow such a slow pace in a relaxed manner during training. Therefore, these participants got individualized breathing frequencies for the exercise in a range between six and eight cycles per minute. Direct feedback was given to the user by a color change of the balloon from yellow to green when the PAT increased by five or more milliseconds as well as numerical values. Change of PAT was measured by the smartPWA (AIT Austrian Institute of Technology, Vienna, Austria) device using ECG and index finger photoplethysmography.

smartPWA sensor device

The smart Pulse Wave Analysis (smartPWA) device is a medical-grade bio-signal acquisition sensor device according to European Medical Device Regulation, especially developed and built by the AIT Austrian Institute of Technology (Vienna, Austria). The device is intended to be held by the user with both hands, like a gamepad, as shown Fig. 1. It uses three conductive surface areas that are touched by the user with both thumbs and left index finger to acquire a standard Einthoven I lead ECG. Furthermore, the user's right index finger touches an optical sensor for photoplethysmography to measure blood volume changes in the finger's microvascular bed.

Communication with a smartphone or tablet computer is established via Bluetooth low energy and the measured signals are streamed continuously to a mobile app for further data processing. The data processing procedure is described in detail in [8].

Feature calculation

From the recorded ECG and photoplethysmography signals, several features are calculated on a beat-by-beat basis. They are continuously averaged using a sliding 3-min moving average to remove short-term fluctuations of the features. The extracted features are the heart rate (HR) and respiratory sinus arrhythmia (RSA) from the ECG [8,10–13].

Fig. 1

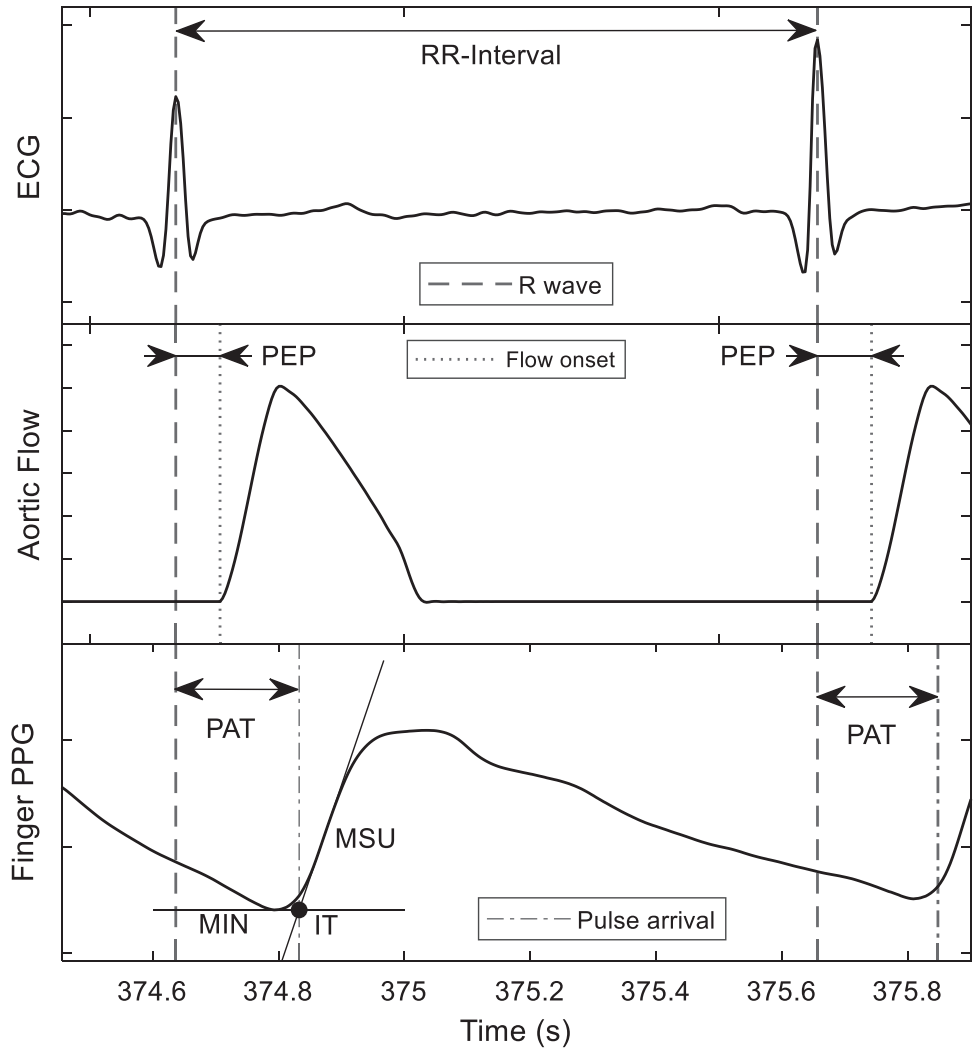
Screenshot of the Android App during the slow breathing exercise applying the smart PWA sensor device to acquire ECG and photoplethysmography and stream the biosignals to smartphone or tablet computer. PWA, pulse wave analysis.

PAT at the index finger measured with photoplethysmography and ECG is determined by ventricular and vascular properties and includes the pre-ejection period (PEP) of the left ventricle and the pulse wave travel itself. To determine the arrival time of the pulse wave (PAT), the method of intersecting tangents is used. First, the two tangents to the rising edge (maximum systolic upstroke) and the minimum (MIN) of the pulse wave signal are calculated. Second, the time corresponding to the intersection point of these tangents is calculated, representing the arrival time of the pulse wave. Finally, the PAT then is the time difference between the R wave of the ECG and the arrival time of the pulse, as shown in Fig. 2 [8,14].

Protocol

BP self-measurement and device-guided breathing exercises were performed on 5 subsequent days for any participant. Participants performed the sessions unattended, but before starting the medical investigator always checked settings for individual breathing frequency and participant data to ensure data consistency and protocol adherence. After 5 min of rest, probands started the BP self-measurement procedure, followed by the 10 min device-guided breathing exercise and 5 min cooling phase with spontaneous breathing. Finally, another BP self-measurement session was performed.

Fig. 2



Determination of the RR-interval and the pulse arrival time (PAT) using the simultaneous recording of electrocardiogram and pulse waves (Finger photoplethysmography). The fiducial point of the pulse waveform is detected by the intersecting tangents of the minimum (MIN) and the maximum systolic upstroke (MSU) of the waveform. Dashed lines mark the R waves in the ECG, Dash-dotted lines mark the arrival of the pulse wave. Intervals between those are the pulse arrival time (PAT) and the RR-interval, respectively. The aortic flow wave is shown to illustrate the pre-ejection period (PEP), marked with a dotted line.

Statistics

Analyses are presented using mean and SD for normally distributed data, otherwise median and first and third quartile is used. Kolmogorov–Smirnov–Lilliefors test was used to test for normal distribution of data. Pairwise comparisons between groups were done using Student's *T*-test for normally distributed data and Wilcoxon signed-rank test otherwise. For comparisons between three or more groups, repeated measures analysis of variance (rANOVA) and Holm–Bonferroni correction was used to avoid Alpha-error cumulation.

Results

Baseline

We enrolled 21 females and 23 males with a median (first and third quartile) office SBP of 137 (132, 143) mmHg and DBP of 83 (132, 143) mmHg in this study. The average age was 57.6 (SD 14.3) years. Table 1 provides a full baseline overview.

Table 1 Baseline as mean (SD) or median (first and third quartiles)

Parameter	Value
Age (years)	57.6 (14.3)
Gender (#/#)	21 females/23 males
Body height (cm)	173.4 (11.3)
Body weight (kg)	84.2 (16.6)
BMI	28.0 (5.0)
SBP (mmHg)	137 (132, 143)
DBP (mmHg)	83 (132, 143)

Pulse arrival time changes in cohort

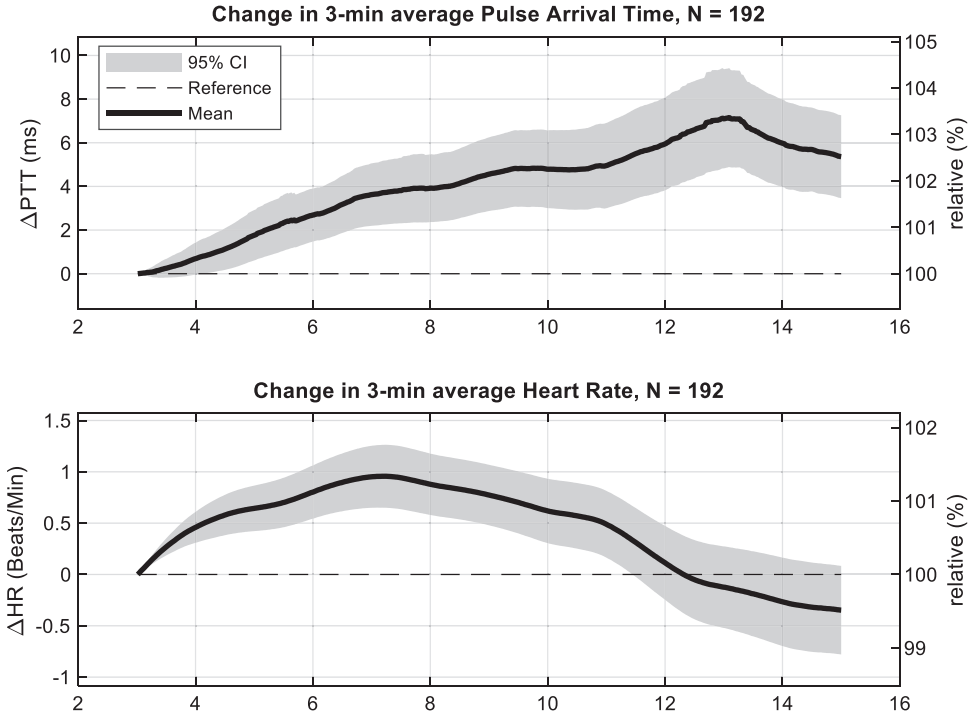
In order to confirm earlier findings in a different cohort we aggregated all available and valid readings of any patient and session and analyzed the change in PAT and HR during device-guided breathing. On the basis of 192 readings, we found a significant ($P<0.05$) increase in PAT of 5 ms (SD 12.5 ms) on average after 10 min of guided breathing and an additional 1 ms ($P<0.05$, SD 8 ms) during the following 5 min of spontaneous breathing compared to baseline (Fig. 3). Subsequently the maximum of PAT increase was reached in the cooling phase after paced breathing. HR was slightly increased during guided breathing with a climax at 7 min as illustrated in Fig. 3.

Absolute blood pressure changes in cohort

Cuff-based BP has been assessed at three distinct timepoints throughout the study. First, office measurement with a mercury sphygmomanometer by a medical professional at the initial medical workup and later automated BP self-measurements before and after each guided breathing exercise. In alignment with the results for PAT shown above all absolute BP values decreased significantly for each time point. Table 2 offers a brief numerical overview.

We observed a significant average decrease of 6 mmHg ($P<0.001$) in SBP between initial examination at

Fig. 3



Change (Δ) of PAT and HR over exercise time (min). HR, heart rate; PAT, pulse arrival time.

inclusion and oscillometric self-assessment before starting a breathing exercise (Table 2). This may be attributed to some white coat effect. Beyond this observation, we experienced on average another significant 5 mmHg ($P < 0.001$) decrease in SBP between oscillometric preassessment and postassessment as a direct response to the exercise (Table 2).

Blood pressure and pulse arrival time changes over 1 week

Subgroup analysis by day-wise aggregation of data was performed to investigate the reproducibility and direct effects of both the assessment settings as well as the breathing exercise over 5 days. SBP, as well as PAT, proved to be stable and concordant measures over the period of 5 days as illustrated in Table 3. ANOVA was performed for both variables and showed no significant differences in mean values at every different measurement day for SBP ($P = 0.9666$) and PAT ($P = 0.9152$). For both parameters, no differences over 5 days were noted (Table 3).

The desired significant BP lowering effect of the breathing exercise was observed every day to a similar extent (Fig. 4). Furthermore, Fig. 4 shows the according change in the PAT per day. A certain mirror effect due to the inverse relationship between the change in BP and PAT is evident.

Discussion

In summary, this work confirmed our earlier findings from a pilot trial that a simple method for device-guided breathing and biofeedback leads to favorable changes (increase) in PAT. Beyond this confirmation, we showed that these changes are highly reproducible over 1 week. In addition, we demonstrated that this increase in PAT is associated with a significant reduction of SBP beyond the white coat effect using oscillometric self-measurement before and postbreathing exercise, which is in line with underlying physical laws describing the association of PAT and SBP. Finally, our data suggest that baseline results for BP and PAT remain stable and desired effects of breathing exercises even improve over repeated sessions for given measurement conditions.

We showed earlier [8] that noninvasively assessed PAT using a one-lead ECG combined with a finger photoplethysmography seems to be a suitable surrogate for SBP changes induced by slow breathing and biofeedback, although systems that report back biofeedback via pulse wave velocity or PAT were first described in 1976 [7,15]. In line with our findings, a study with different paced respiratory rates (14-7/min) showed a progressive increase in PAT with increasingly slower breathing accompanied by harmonization of respiratory rates with the Mayer waves [16]. The changes in PAT in our study induced by the respiratory exercise were highly reproducible over a week and therefore warrant further use.

In our previous study [8], we found that in 27 out of 30 (90%) of the supervised guided breathing exercises, adherence to the breathing rate could be confirmed using RSA. Fully consistent with this, 201 of the 215 (93%) unsupervised guided breathing exercises in the current study showed an RSA that matched the guided breathing rate.

The BP-related findings are also in line with data found in the literature and furthermore, our data enriches the knowledge base, because none of these earlier studies had both PAT and oscillometric BP self-measurement. The net BP reduction (without white coat effect), measured unobserved by the patients themselves with a validated oscillometric upper arm device, was 5 mmHg systolic. The maximum effect may be even greater, since the oscillometric BP measurements were not carried out until 5 min after the end of the exercise, at a time when the maximum effect on the PAT was already over. Interestingly the PAT during the cooling phase, that is, during spontaneous breathing, even increased by 1 ms additionally which may indicate that hemodynamic changes induced by device guided breathing persist for a certain period.

In earlier studies, a drop in SBP has already been reported after 2 min of slow breathing in normotensives and hypertensives, with an office BP drop between 3.4 and 9.6 mmHg [17,18]. Li *et al.* compared the acute effects of paced breathing over 5 min each with frequencies of 16 vs. 8 breaths per minute [19]. The 60 untreated hypertensives in his study with an initial BP of 150/92 mmHg, responded with obvious and significant differences in SBP and DBP to slow breathing compared to faster respiration [19].

We observed a slight increase in HR during guided breathing which was also observed in earlier studies [20,21]. Notwithstanding, other studies did not observe an effect on HR or even observed a decrease in HR [9,17,19].

Table 2 Averaged blood pressure values as median (Q1, Q3) mmHg

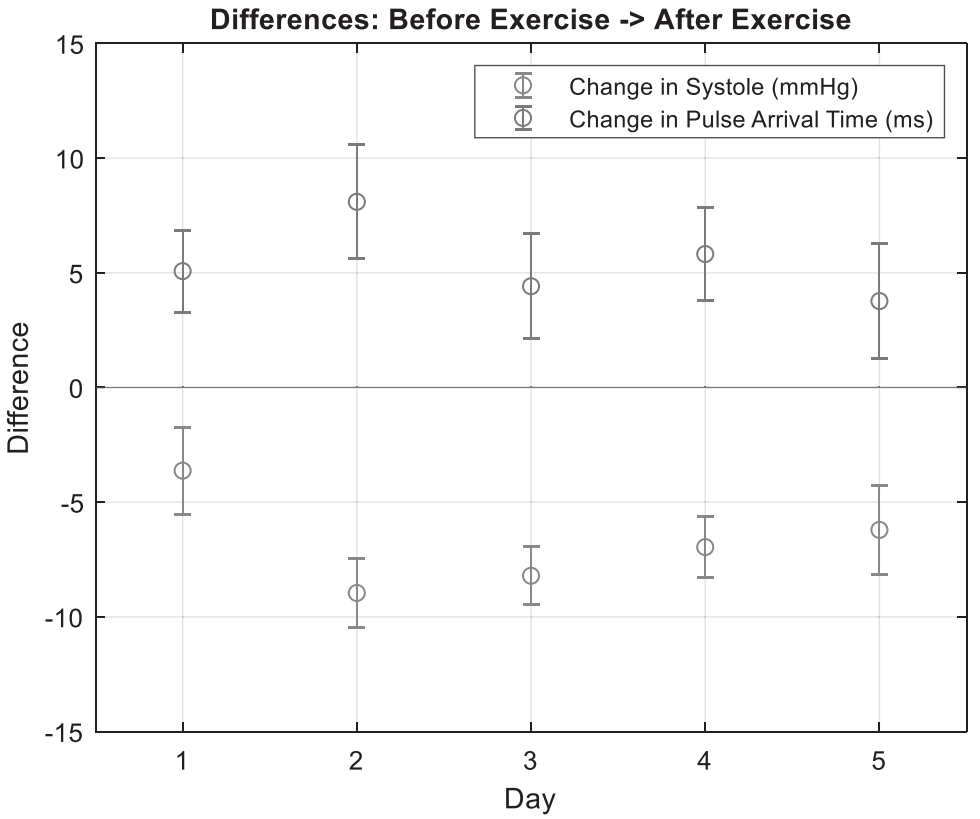
	Systole, mmHg	Diastole, mmHg	*N*
1.Initial medical work-up	137 (132, 143)	83 (79, 87)	171
2.Prebreathing exercise	131 (124, 140)	81 (74, 86)	171
3.Postbreathing exercise	126 (119, 134)	78 (73, 85)	171

Table 3 Baseline readings for SBP and pulse arrival time before starting the guided breathing exercise

	Day 1	Day 2	Day 3	Day 4	Day 5
SBP (mmHg)	131.2 (16.8)	133.7 (13.8)	132.9 (13.7)	133.4 (14.3)	133.2 (13.0)
PAT (ms)	213.5 (22.7)	214.1 (23.3)	212.8 (21.6)	215.5 (20.2)	217.7 (21.6)

PAT, pulse arrival time.

Fig. 4



Change in blood pressure and pulse arrival time during breathing exercise, over 5 days, as mean and SE.

Our findings are not limited to pathological patterns, these acute effects on BP, accompanied by changes in HR (variability) and reductions in sympathetic muscle nerve activity, were also observed in healthy normotensives [20–22]. Bernardi's research group described similar antihypertensive effects in slow, device-guided breathing as well as in meditative praying and yoga mantras accompanied by improved baroreflex sensitivity and rhythmization of breathing, BP, and cerebral blood flow [9,23]. In comparison to commercially available devices, the measurement of PAT during device-guided breathing allows direct biofeedback to the user potentially enhancing the effect of the exercise.

A minor limitation of this study is that using the ECG signal to determine the start time of the pulse wave is not ideal from a physiological point of view, as this means that the PEP is also included in the measurement. The reader may note that there is no clear consensus in the literature on what factors affect PEP although recent publications [24–26] suggest only a moderate influence of PEP on PAT and BP changes. However, considering the resulting simplification of the measurement methodology and the present results, this limitation seems justifiable.

In conclusion, our findings confirm the results of the previous pilot study [8] to a high degree and demonstrate that the favorable increase in PAT is consistent over several days. Furthermore, our results confirm the assumption that this increase in PAT is closely related to a real decrease in BP, as postulated previously. While most patients experienced a significant short-term improvement in PAT and associated BP, no adverse effects were observed. The ease of use of the measurement makes this method ideal for home use and self-monitoring and warrants future studies.

Acknowledgements

This research was funded by the State of Lower Austria with co-financing from the European Regional Development Fund (ERDF/EFRE) – Project 'smart-PWA'/WST3-F-5030665/002-2017 and Project DigiPit/WST3-F-5030665/010-2021.

Conflicts of interest

There are no conflicts of interest.

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