CARDIOdiagnostics
A division of SOMNOmedics

Compendium

The SOMNOmedics Pulse Transit Time (PTT) Method – Blood Pressure Measurement Reinvented

- non-invasive
- continous
- cuffless

SOMNOmedics GmbH
Am Sonnenstuhl 63
D-97236 Randersacker
Germany

Tel.: +49 931 359094-0
Fax: +49 931 359094-49

www.somnomedics.eu
info@somnomedics.de

FOREWORD

Now more than ever medical technology must be oriented to the latest medical research and the increased needs of doctors and patients. In particular, the rapidly developing field of sleep medicine requires ground-breaking, forward-thinking solutions.

We began in sleep medicine and see ourselves as specialists in polysomnography and cardio-respiratory screenings. Thanks to our experience of more than 20 years, we have also been able to tap into the fields of cardiology and neurology. Today we offer sophisticated solutions for diagnostic long-term EEGs, long-term ECGs and ambulatory blood pressure (BP) measurements.

The SOMNOmedics PTT Method for BP Measurement

A unique feature in our products is the continuous BP measurement based on the PTT method, which we developed and patented in 2006. This innovative technology sets new standards both in terms of patient comfort and the quality of the results. The blood pressure is continuously calculated based on the recording of the pulse transit time (PTT), for which only an ECG and finger plethysmogram are required. Patients are no longer disturbed by the inflation of the cuff. The PTT method of BP measurement is integrated into our polysomnography and polygraphy systems. For ambulatory, long-term BP measurement the SOMNOtouch™ NIBP is available.

With this compendium, we are pleased to give you, as a doctor, healthcare provider or interested patient, an insight into the basics of the PTT method and to show possible applications of the SOMNOtouch™ NIBP.

Validation

In the time since the continuous systolic BP measurement based on PTT analysis was patented, a number of studies have been published that demonstrate the validity of this pioneering method.

We have prepared summaries of these publications to give you a brief overview of each. For a more detailed report of the results, we refer to the originally authored and published articles.

CONTENT

1. LONG-TERM BLOOD PRESSURE MEASUREMENTS

Arterial hypertension (high blood pressure) is a very common disease - affecting about 30% of the world's population [1]. High blood pressure is one of the main risk factors for cardiovascular diseases such as coronary heart disease, heart attack, stroke and peripheral artery disease. Often, however, arterial hypertension is a symptomless condition, making detection of this disease more difficult.

The current European guidelines (ESH/ESC Guidelines 2018) suggest, in addition to the formerly recommended office blood pressure (BP) measurements, the broader use of out-of-office BP measurements as an option to diagnose hypertension, to detect white-coat or masked hypertension and to monitor BP control [2]. Out-of-office BP measurements can be either done by ambulatory 24 h blood pressure measurement (ABPM) or home blood pressure measurement (HBPM).

A 24 h ABPM records a patient's BP levels under conditions that are more representative of daily life and therefore offers useful information about the diurnal BP pattern. It also provides a much larger number of BP measurements than the "snapshot" yielded by office BP. The resulting BP values can be summarized into 24 h mean values and can also be divided into time windows, e.g. day and night.

Increasing evidence suggests that night-time ambulatory BP is a more sensitive predictor of cardiovascular outcomes than daytime BP. In the 11-year follow-up of the PAMELA study (n = 2051 subjects), the prognostic value of ambulatory and office BP was assessed. At different initial BP values, a 10 mmHg BP increase leads to a several-times-greater increase in risk of cardiovascular mortality if BP measurements are based on night values compared to office measurements ([3], Figure 1).

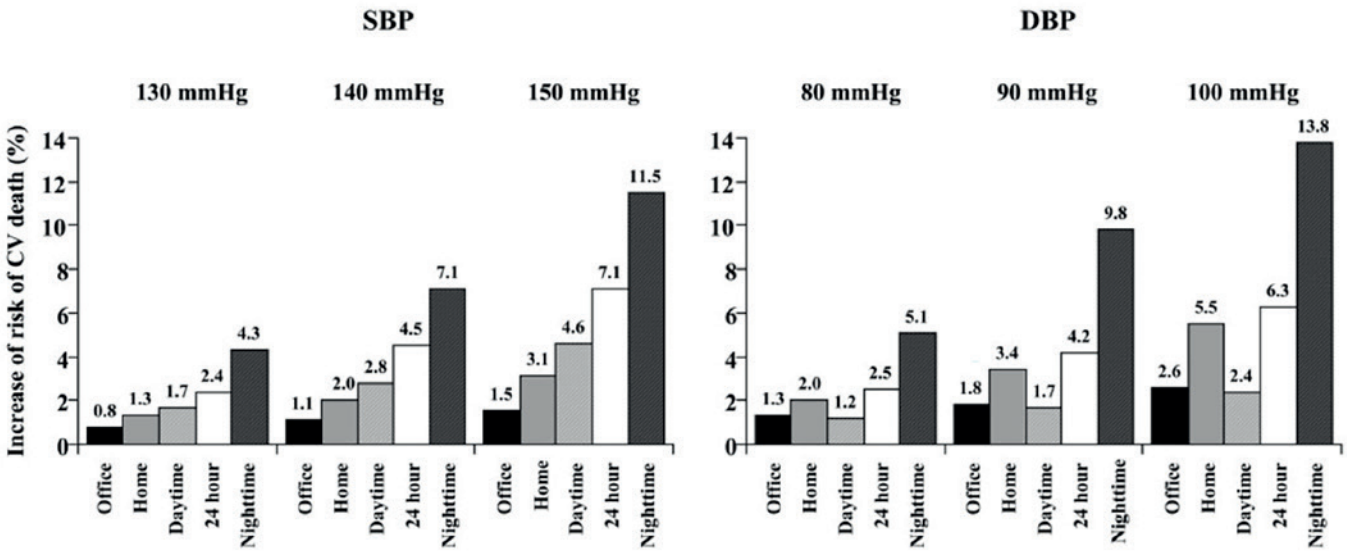


Figure 1 Increase in risk of cardiovascular (CV) mortality (Source: Sega et al., 2005 [3]).
Office, home and ambulatory BP values at various initial BP values were assessed. Clearly evident is the increased information content of nocturnal BP values.

Normally, in healthy persons, BP drops during night by 10% to 20% of daytime average (dipper; [4]). Patients in whom the nocturnal BP drop is less pronounced (non-dipper) or in whom BP even rises during night (inverted dipper) have an increased cardiovascular risk in cardiovascular morbidity and mortality. It is only possible to record this important BP behaviour at night with a 24 h ABPM.

Additionally, ABPM allows the exclusion of a so-called office hypertension („white-coat hypertension"). Here, high BP levels are only measured in a medical environment like in the clinic or office, while self-measurement or ABPM show normal values. White-coat hypertension is seen in 30 - 40% of patients in which BP is elevated in office [2].

Furthermore, ABPM can help to detect masked hypertension, the classic form of stress-induced hypertension. Normal values (< 140/90 mmHg) are seen in office measurements, but BP values in everyday life or at work are higher (about 15% of patients with normal office BP; [2]).

ABPM also offer advantages for therapy control of patients under anti-hypertensive medication. The outcome of the ABPM can be used to judge whether there is any necessity to optimize the treatment.

2. LONG-TERM BLOOD PRESSURE MEASUREMENTS ACCORDING TO RIVA-ROCCI – IS THE METHOD STATE-OF-THE-ART?

The cuff-based method for measuring BP was introduced in 1896 by Scipione Riva-Rocci. To this day, long-term BP measurements are usually carried out with automated devices based on this method.

Using this method, measurements are taken four times per hour during day and twice per hour during night (10 pm- 6 am).

The established cuff devices are to be used under following conditions:

1) The measurement should be performed after 5 minutes at rest.
2) Patients should be in a relaxed sitting position with their back supported.
3) The legs should not be crossed.
4) The arm should be relaxed during the measurement and placed on a firm surface.
5) The cuff should be at heart level.

However, for 24 h BP measurements these requirements cannot always be met:

- The patients should follow their daily routine. However, this would mean that they cannot possibly be still during the recording. Therefore, criteria 1, 2, 3, 4 and 5 are not necessarily fulfilled.
- A 24 h measurement also includes the sleep period that is spent in lying down. During sleep, body position changes about 1.5 times/h. Hence, criteria 2 and 5 cannot be met for the sleep period. The deviation due to the hydrostatic effect by body position changes can be up to +/- 15 mmHg for cuff measurements, (Figure 2).

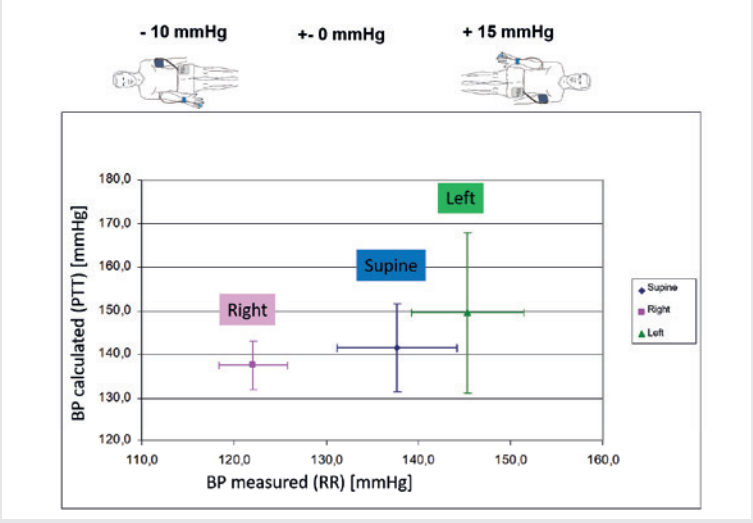


Figure 2 BP values (for RR and PTT measurements) according to body position (Source: SOMNOmedics).

Mean BP values with associated standard deviations are shown. There were significant differences between right and supine position as well as left and right position for measurements according to RR. In contrast, there were no significant differences for the BP by PTT measurement in different body positions.

Further drawbacks of cuff devices for 24 h BP measurements:

- Due to the discontinuous measurement, real maximum and minimum BP values may not be recorded.
- Sleep disorders: cuff inflation causes arousals or awakening reactions (affecting 18% of nocturnal readings), which can result in deviations of up to +/- 30 mmHg.
- Most automatic devices are not validated for BP measurement during arrhythmias.
- There is no correlation to individual sleep times. Sleep time is predefined from 10 pm until 6 am. BP values during possible wake stages in this time interval are automatically assigned to the sleep phase.
- The inflation of the cuff is perceived as annoying. In many patients this leads to an aversion to 24 h ABPM. This is particularly the case when measurements need to be repeated.
- Inaccurate measurements due to physical activity during the pumping process are not detected.

3. CONTINUOUS, NON-REACTIVE BP MEASUREMENT USING PULSE TRANSIT TIME (PTT)

3.1 The PTT-BP Relationship

The PTT (pulse transit time) describes the time a pulse pressure wave needs to cover the distance between two points within the arterial system – in our case from the left ventricle of the heart (defined by the R-peak of the ECG) to the fingertip (detected by plethysmography).

By using the distance (d = running distance from the heart to the fingertip) the pulse wave velocity (PWV) can be determined from the PTT:

$$PWV = \frac{d}{PTT}$$

PWV directly depends on the elasticity modulus (also stiffness) of the blood vessel (E):

$$PWV = f(E)$$

The elasticity of a vessel is in turn influenced by the BP:

$$E = f(BP)$$

The BP influences the elastic properties of the vessel. It can be seen as an analogy to a motorcycle tire: this has a larger elasticity modulus when inflated (it is therefore stiffer), while it is much softer when un-pressurized, and thus has a lower elasticity modulus.

Summarized, we get following relationship:

$$PTT \sim \frac{1}{PWV} \sim \frac{1}{E} \sim \frac{1}{BP}$$

The higher the wall tension (= stiff vessels) the faster the PWV as compared to a low wall tension (= smooth vessels). Figurately speaking, in a stiff pipe the pulse wave propagates faster than in a soft tube. Consequently, in stiff vessels a short PTT and a high BP and, conversely, in smooth vessels a long PTT and low BP is present:

High PWV ▶ short PTT
stiff vessels
high BP

Low PWV ▶ long PTT
smooth vesels
low BP

3.2 Recording BP using the PTT Method

The calculation of systolic (SBP) and diastolic blood pressure (DBP) is based on a non-linear correlation between BP (in mmHg) and PTT (in ms) [5]. The PTT method is patented [6] and clinically validated, e.g. according the ESH International Protocol revision 2010 [7].

Measuring the PTT is a simple method for determining a person's blood pressure. As such, the interval between the R-wave of the ECG and the arrival of the corresponding pulse wave at the peripheral site (the finger) is measured. The turning point of the finger pulse curve is taken as indicator for the arrival of the pulse wave

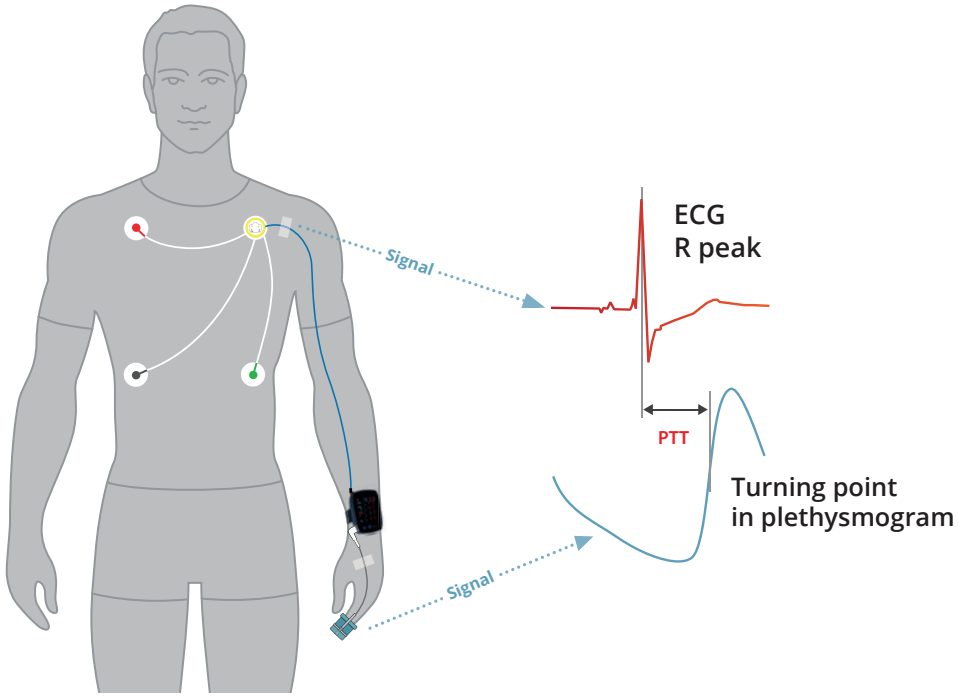


Figure 3 Measurement of the PTT with the SOMNOtouch™ NIBP (Source: SOMNOmedics).

The relation between PWV and SBP follows a non-linear function ([5] and see Figure 4). As explained in the previous section, PWV and PTT depend on the elasticity of the blood vessels. The elasticity is also influenced by the vessel history (e.g., age, diabetes, etc.) and by the current BP.

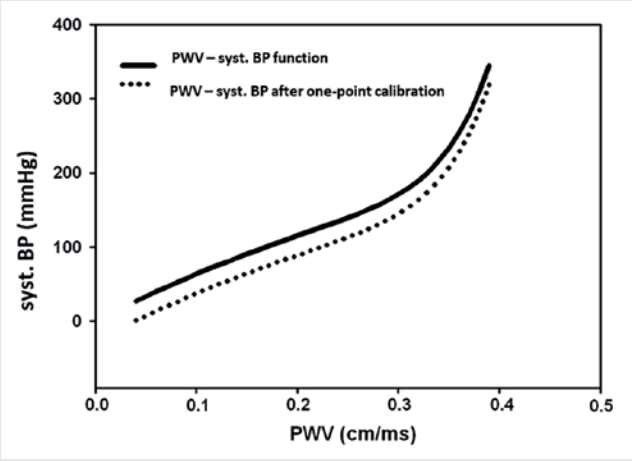


Figure 4 BP-PWV function (Source: Gesche et al., 2012 [5]).

Without (solid line) and with (dashed line) correction after one-point calibration.

With a one-point calibration during the ongoing measurement, the current BP and the vessel properties are recorded and the BP-PWV relation is individually corrected. By adding the patient's body size (to determine the running distance of the pulse wave), an accurate SBP and DBP value can be calculated for each PTT value.

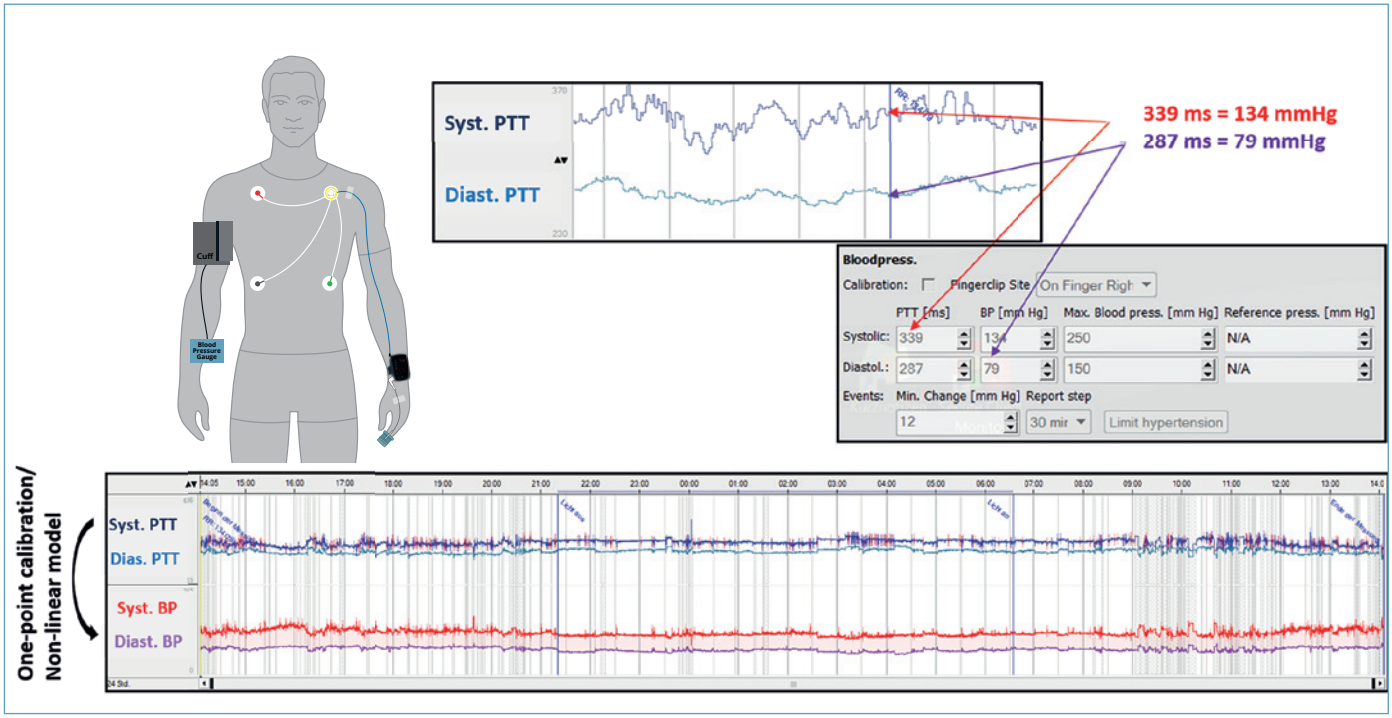


Figure 5 One-point calibration (Source: SOMNOmedics).
Beat-to-beat determination of SBP and DBP by one-point calibration from systolic and diastolic PTT.

4. THE SOMNOtouch™ NIBP

The SOMNOtouch™ NIBP is an ambulatory BP device for continuous, non-invasive and non-reactive determination of SBP and DBP with a recording duration of up to 24 hours.

By simultaneously recording the ECG and finger plethysmogram (including oxygen saturation), the PTT can be calculated by the software.

The exact values for SBP and DBP are displayed on the colour touch screen display.

Figure 6 The SOMNOtouch™ NIBP device and application of sensors (Source: SOMNOmedics).

More than just an ambulatory BP recording device

- Syst./diast. BP, beat-to-beat
- 3-channel ECG
- SpO_2, pulse rate
- Plethysmogram
- Body position
- Activity (sleep/wake estimation)

The marker button enables the patient to document important events like stress, dizziness, medication intake, etc.

Motoric activity and body position of the patient are recorded with the internal movement sensors of the SOMNOtouch™ NIBP, allowing a valid sleep/wake analysis [8]. Therefore, the actual sleep time ("Time in Bed") and, consequently, the dipping behaviour can be determined more precisely. In addition, the patient can be instructed to press the marker button "lights off" when going to sleep and "lights on" when getting up.

By recording this activity, it is possible to distinguish between physical and psychogenic BP increases during the day.

5. AREAS OF APPLICATION FOR THE SOMNOtouch™ NIBP

The SOMNOtouch™ NIBP enables three routine examinations to be performed simultaneously with one device:

- 24 h ambulatory BP measurement
- Long-term ECG
- Oximetry

The simultaneous recording of different vital parameters provides a more precise pathophysiological profile of the patient in one procedure. It has the additional benefit of reducing costs as well as minimising stress for the patient.

5.1 24 h Ambulatory BP Measurement

With the SOMNOtouch™ NIBP a continuous, systolic and diastolic BP (in mmHg) reading over 24 h can be performed.

In general, BP represents a highly fluctuating vital parameter which should not be examined separately from other vital parameters. The SOMNOtouch™ NIBP enables the user to record and analyse various parameters simultaneously.

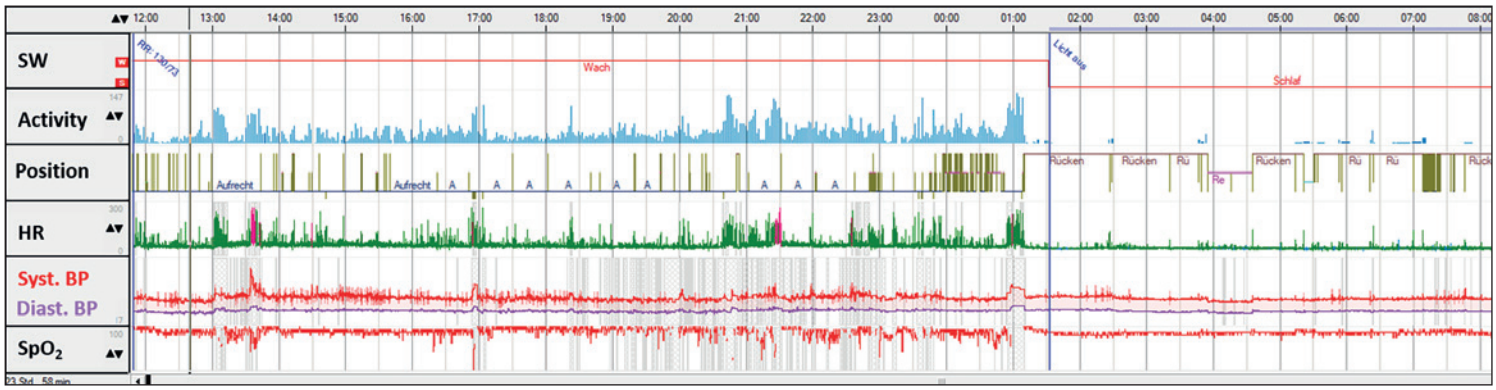


Figure 7 Example of a 24 h ambulatory BP recording performed with the SOMNOtouch™ NIBP (Source: SOMNOmedics).

BP Analysis during the Daytime

Simultaneous recording of BP and motoric activity allows for a differentiation of BP increases due to physical or mental stress.

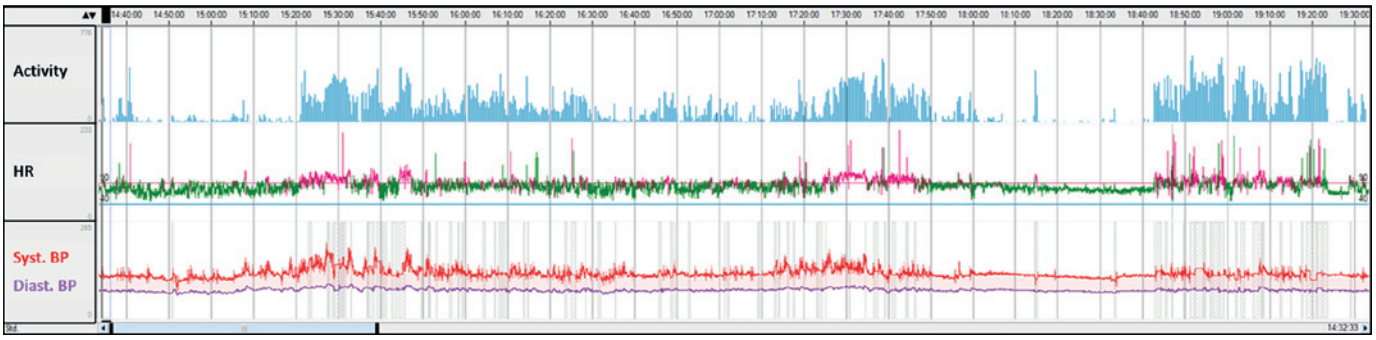


Figure 8 BP analysis during the daytime (Source: SOMNOmedics).
Increase of heart rate (HR) and BP (Syst./Diast.) due to motoric activity.

BP Analysis during Sleep

With the help of the sleep/wake analysis [8], BP values can be assigned to periods of sleep or wake and can be considered for analysis.

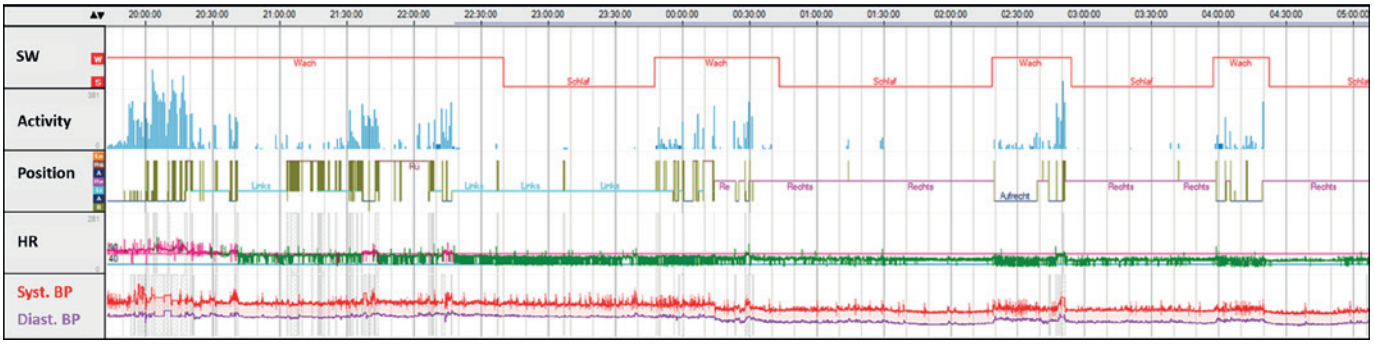


Figure 9 BP analysis during sleep (Source: SOMNOmedics).
Sleep/wake determination via recorded activity and body position. Example measurement of a patient with several wake phases during night, which are associated with BP increases.

The circadian rhythm of BP has a high relevance from a clinical point of view. Normally, BP drops during sleep by 10 to 20% (dipper). A smaller drop (non-dipper) or even an increase (inverted dipper) leads to a higher cardiovascular risk. In this patient group, a more frequent occurrence of end organ damage and an increased apoplexy frequency has been reported [9].

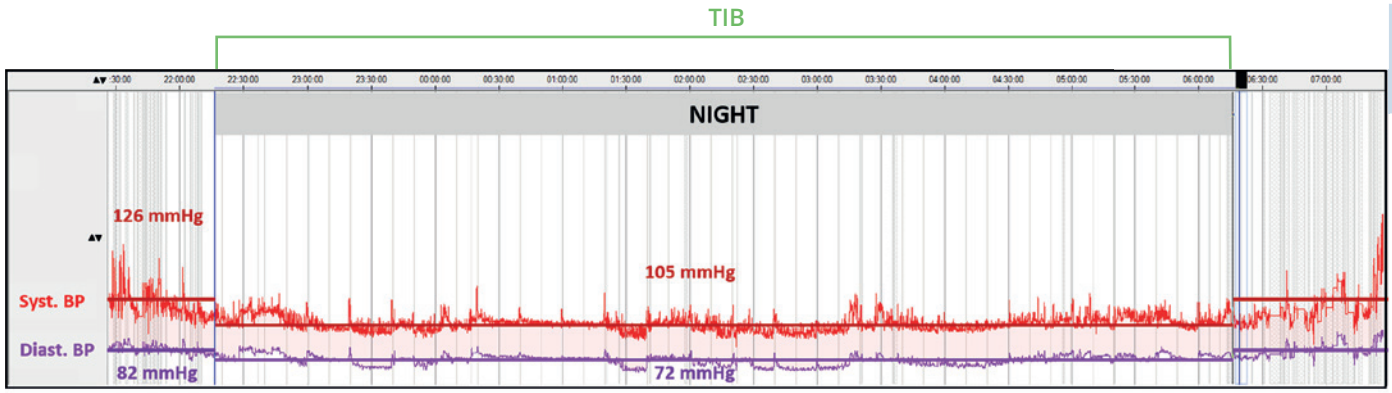


Figure 10 Example measurement dipper (Source: SOMNOmedics).
Drop of BP during night for a dipper (SBP -16.7%, DBP -12.2%).

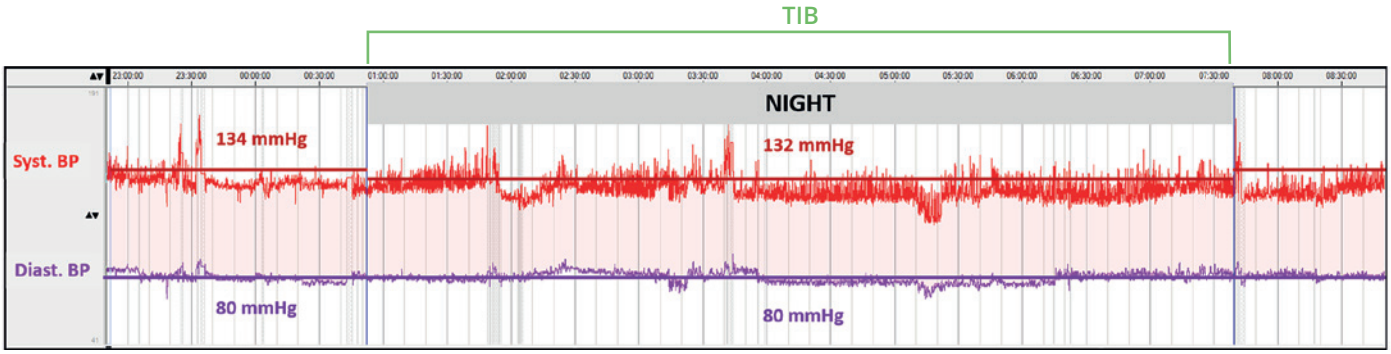


Figure 11 Example measurement non-dipper (Source: SOMNOmedics).
Nocturnal BP behaviour for a non-dipper (SBP -1.5%, DBP +/- 0%).

The day/night drop of BP can be shown visually (above) or statistically (see section "Blood Pressure Report" on page 24).

Classification of Dipper/Non-Dipper Patterns

Normal Dipper	A nocturnal BP drop of 10% to 20% from daytime level
Non-Dipper	A nocturnal BP drop of < 10% from daytime level
Inverted Dipper	Increase of BP level at night
Extreme Dipper	Nocturnal BP drop of > 20% from daytime level

Clinical Relevance: Nocturnal Blood Pressure Fluctuations (NBPF) and Superposition

Nocturnal blood pressure fluctuations measured by using pulse transit time in patients with severe obstructive sleep apnea syndrome.

Gehring, J., et al. (2018), Sleep Breath, 22(2): p. 337-343.

Due to the high "time" resolution (beat-to-beat) of the PTT method, fluctuating BP changes can be detected.

Obviously, respiratory disturbances of sleep such as apnea, hypopnea, snoring, but also periodic leg movements (PLM) provoke not consciously perceived arousal reactions, each time causing co-activation of sympathetic and parasympathetic nervous system and short-term systolic blood pressure increases (= nocturnal BP fluctuations, NBPFs).

The obstructive sleep apnea syndrome (OSAS) is highly correlated with arterial hypertension and cardiovascular diseases. OSAS occurs with a frequency of 3 - 4% in the population. Of the OSAS patients, 50 - 80% suffer from hypertension. A better knowledge of night-time BP behaviour leads to a better understanding of the pathophysiology of hypertension in OSA patients but may also support diagnosis and therapy of hypertension in this high-risk group. The non-invasive BP determination using PTT enables a non-reactive, continuous BP recording during sleep. In the study of Gehring et al., night-time SBP was investigated beat-to-beat using the PTT method [10].

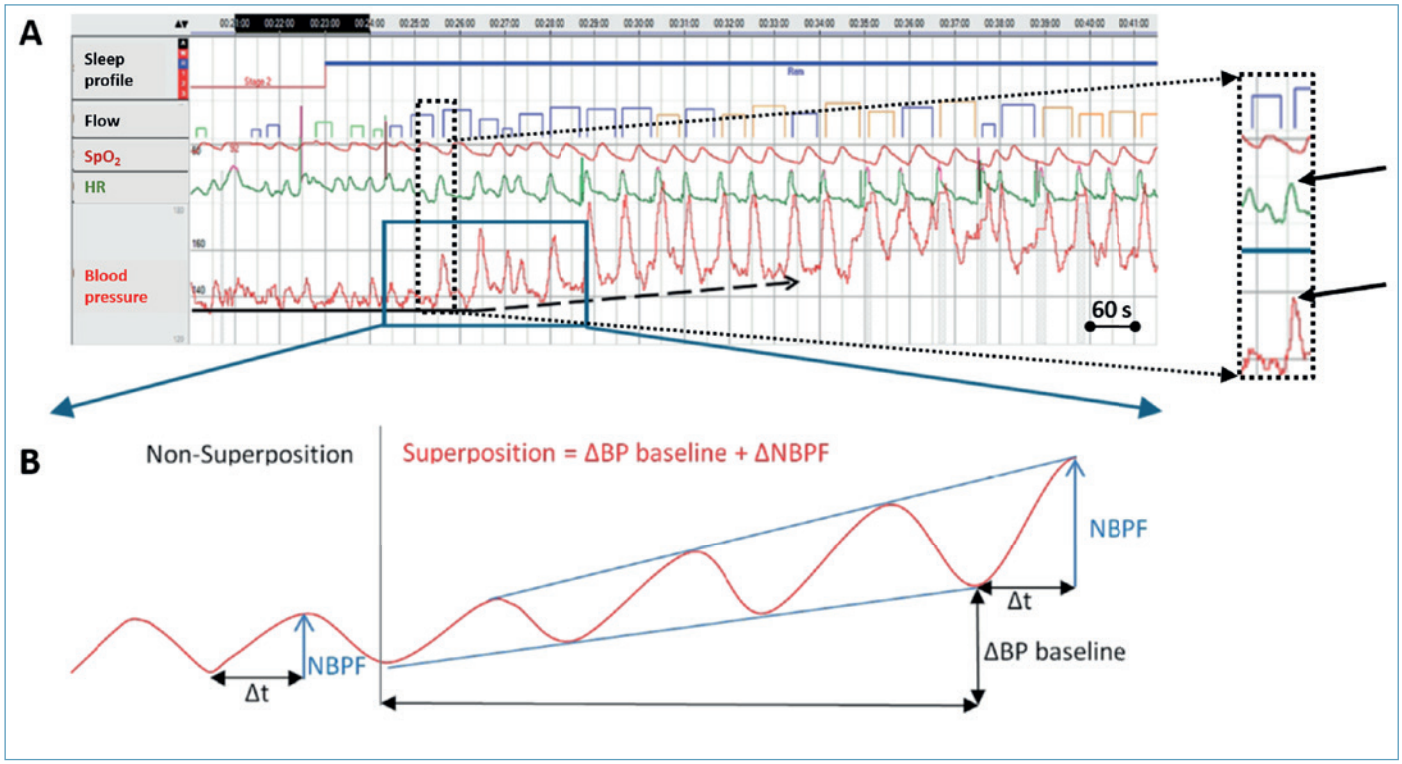


Figure 12 NBPFs and Superposition (Source: SOMNOmedics).
(A) Sequence of obstructive apneas during NON-REM and REM transition (signal track Flow; blue: apnea, green: hypopnea, yellow: mixed apnea). At the end of apneas, there is a transient increase of HR (green) and SBP (Bloodpress., red); shown enlarged on the right (in dashed box). (B) Superposition periods are characterized by rise of SBP baseline (ΔBP baseline) and an increased amplitude of NBPFs (↑NBPF). Non-Superposition periods are defined by the lack of SBP baseline elevation during NBPF.

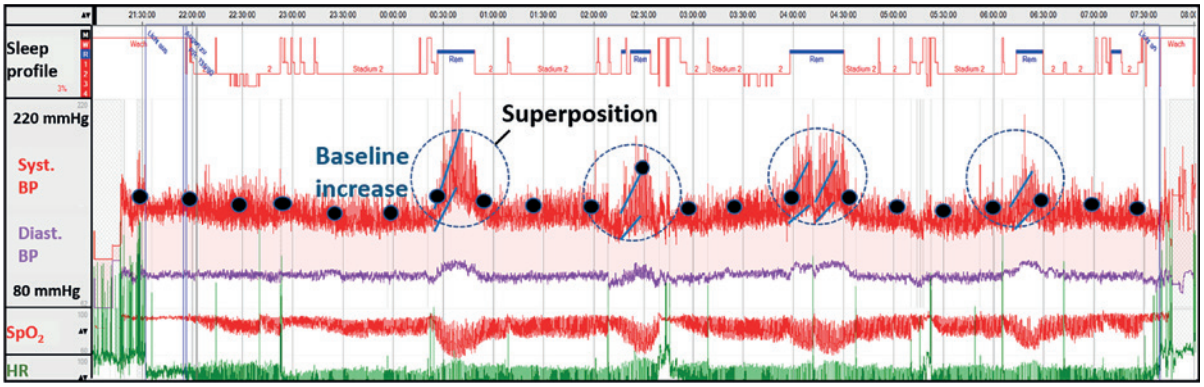


Figure 13 Example measurement of a patient (Source: SOMNOmedics).
Hypertensive periods during REM sleep caused by apneas. The duration of REM periods is < 30 min. Which could lead to a reason why maximum BP values are often not detected with a conventional cuff measurement (represented by black dots).

Ninety-seven patients with the diagnosis of OSAS (apnea-hypopnea index (AHI) ≥ 30) were included in the study. A polysomnography (SOMNOscreen™ plus) of night sleep was performed and physiological data were analysed according to AASM. SBP values were determined automatically beat-to-beat with the DOMINO software based on a non-linear pulse wave velocity-SBP function in combination with an initial BP calibration.

Apnea/hypopnea-induced nocturnal blood pressure fluctuations (NBPFs) were detected. Furthermore, NBPFs in combination with a steady increase in SBP baseline were observed: This newly discovered phenomenon, defined by SBP baseline elevations ≥ 10 mmHg, is called "Superposition". Periods of „Superposition" were analysed in comparison to periods of „Non-Superposition".

In all patients, periods of obstructive apnea were accompanied with NBPFs meaning that BP transiently increased at the end of each apnoeic period. Forty-eight patients showed the phenomenon of superposition. A total of 84 periods of superpositions were detected in this group. They occurred mainly during REM sleep (76%) and in the last third of the night (40%).

The mean duration of superposition periods was 17 +/- 7 minutes. The mean change of the basal BP in these phases was 16.7 +/- 6.7 mmHg. The maximum SBP during superposition periods was higher (204 +/- 32.1 mmHg) than during non-superposition (171.2 +/- 27.9 mmHg). Superposition periods were further associated with changes in respiratory parameters (AHI, apnea duration, time spent in apnea resp. respiration), oxygen saturation and heart rate.

This study demonstrates a new phenomenon, namely the superposition of nocturnal BP fluctuations (NBPF), leading to extreme high BP peaks. Only by using the non-reactive (no arousals due to cuff inflation) and continuous (no BP increase is missed due to the time interval between two measurements) BP measurement it was possible to detect these superposition periods. These BP elevations reflect sympathetic activation and might be important for the development of OSAS related hypertension. By the continuous and non-reactive BP measurement the prognosis, diagnosis, therapy, and follow-up of patients with OSAS or hypertension can be improved. So, for example, the treatment of OSA should be considered primarily when detecting apnea-indicated BP increases in order to reduce the cardiovascular risk to the patient.

Clinical Relevance: The Effect of CPAP Therapy on Nocturnal Blood Pressure Fluctuations

Effect of CPAP therapy on nocturnal blood pressure fluctuations, nocturnal blood pressure, and arterial stiffness in patients with coexisting cardiovascular diseases and obstructive sleep apnea.

Picard, F., et al. (2021), Sleep Breath, 25(1): 151-161.

Obstructive sleep apnea can induce dramatic nocturnal blood pressure fluctuations and can be associated with nocturnal hypertension and arterial stiffness. This study investigated the effect of short- and long-term continuous positive airway pressure therapy on NBPFs, nocturnal blood pressure, and arterial stiffness in patients with coexisting cardiovascular diseases (CVD) and OSA (CVD/OSA) [11].

Fifty-eight patients with CVD/OSA were investigated, 28 patients without OSA served as control. A full polysomnography (SOMNOscreen™ plus) was conducted at baseline, after the first night with CPAP therapy and after 6 months of continuous use of CPAP. Nocturnal blood pressure was determined by the PTT method, which allows the detection of NBPFs (defined as an increase of SBP > 12 mmHg within 30 s). Pulse wave analysis (PWA) and pulse wave velocity (PWV) was measured using SphygmoCor XCEL.

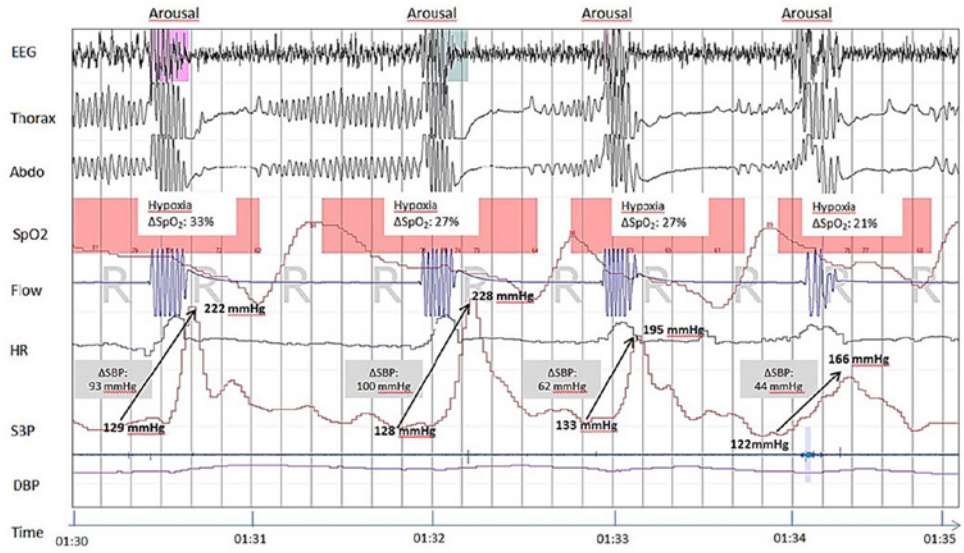


Figure 14 Polysomnographic recording (Source: Picard et al., 2021 [11]).
Respiratory-related NBPFs are shown by arrows. A significant reduction in airflow (flow) leads to a decline in oxygen saturation and rise in SBP. Dramatic increases of SBP up to 100 mmHg (ΔSBP) triggered by hypoxemia are possible.

Figure 14 shows an example of a polysomnography in which respiratory-related NBPFs predominate. Due to hypoxemia, there are dramatic increases in BP of up to 100 mmHg.

The mean values of nocturnal SBP as well as maximum nocturnal SBP were significantly higher in patients with CVD/OSA than in controls (CVD) (Figure 15 a and b). Long-term CPAP therapy significantly decreased mean nocturnal SBP, whereas maximum nocturnal SBP was already significantly decreased after the first night of CPAP therapy.

At baseline, patients with coexisting CVD/OSA had significantly more frequent NBPFs (overall and respiratory-related) compared with controls (Figure 15 c and d). NBPFs significantly decreased after only the first night, and an even stronger effect was seen after six months. CPAP therapy reduced the frequency of overall NBPFs by 30% and respiratory-related NBPFs by 87%.

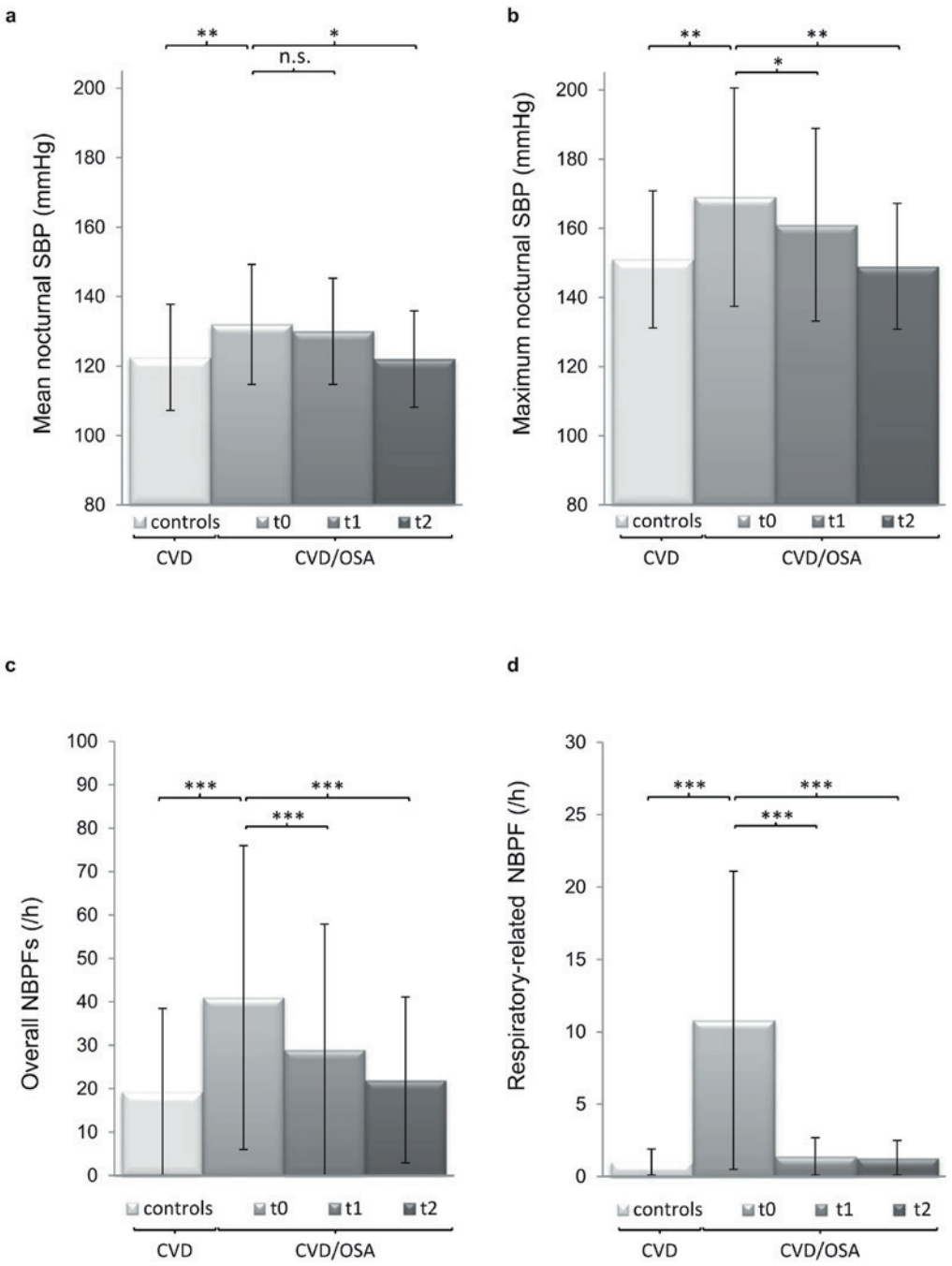


Figure 15 BP values of CVD (controls) and CVD/OSA patients (Source: Picard et al., 2021 [11]).
Different timepoints were investigated: baseline (t0), after first night of CPAP therapy (t1) and after six month of CPAP therapy (t2). Data are given as mean ±SD, * p<0.05; **p<0.01; ***p<0.001.

It is assumed that frequent NBPFs increase the maximum SBP and consequently lead to an increase in baseline SBP. This was now confirmed in this study: NBPFs (overall and respiratory-related) are associated with higher maximum and mean values of SBP. It was further shown that CPAP therapy reduced frequency of both overall and respiratory-related NBPFs. And as a consequence, this leads to an improvement of mean and maximum blood pressure. Another outcome of this study is that patients with more frequent NBPFs (CVD/OSA) have significantly higher PWV than controls (CVD). PWV, and thereby the arterial stiffness, was significantly reduced after the first night of CPAP therapy and even more after long-term therapy.

By using the PTT method for continuous BP determination, it could be demonstrated that patients with OSA have significantly higher NBPFs and NBPFs are associated with mean nocturnal SBP and arterial stiffness. CPAP therapy is of enormous importance for OSA patients and can contribute to reduce further cardiovascular events.

Clinical Relevance: Nocturnal Blood Pressure and Restless Leg Syndrome

Nocturnal systolic blood pressure is increased in restless leg syndrome.
Sieminsky and Partinen, 2016, Sleep Breath, 20: p. 1013-1019.

At rest or at night, patients with restless leg syndrome (RLS) feel uncomfortable sensations the lower limbs and an irresistible urge to move in the legs. RLS is one of the most common neurological diseases with a prevalence of 3 - 10%. About 80% of patients show an increased number of periodic leg movements (PLMS) during sleep [12]. The RLS can lead to sleep disorders and is associated with cardiovascular diseases including hypertension.

Figure 16 Example measurement of a patient with PLMS (Source: SOMNOmedics).
Periodic leg movements (highlighted by red boxes in signal trace PLM) cause NBPFs (short-term increases of SBP; shown enlarged on the right). There are no desaturations (SpO_2), respiratory events (Flow) or snoring (snore) as the cause of NBPFs (green box). If patients show a high number of PLM during sleep, this may lead to nocturnal hypertension.

To test the hypothesis that nocturnal BP is higher in patients with RLS than in subjects without this sleep disorder, 57 patients (30 RLS patients, 27 controls) were polysomnographically examined (SOMNOscreen™ plus) including beat-to-beat measurement by the PTT method [13]. Sleep architecture of RLS patients was disturbed (shorter sleep time, lower sleep efficiency, longer time of wake, higher index of periodic limb movements).

Mean values of daytime and wake BP did not differ between the groups. However, patients with RLS had a significant higher nocturnal SBP compared to the controls (124.4 ± 14.7 mmHg vs. 116.5 ± 15.6 mmHg). Furthermore, in the control group, nocturnal SBP values were significantly lower than values during day. In contrast, no dipping behaviour was found in the RLS group.

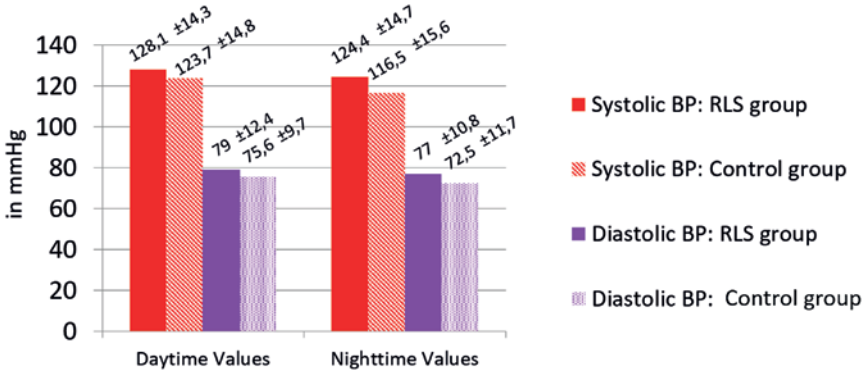


Figure 17 Values of BP in patients with RLS and controls (Diagram created with data in Table 3 from Sieminski and Partinen, 2016 [13]).

This study showed that patients with RLS have significantly higher BP values during the night and a non-dipping behaviour could be observed in this patient group. Patients with RLS require a close observation with regard to cardiovascular risk factors, i.e., 24 h ambulatory blood pressure measurements (ABPM).

Clinical Relevance: Vital Signs Prediction and Early Warning Score Calculation based on Continuous Monitoring of Hospitalised Patients

Validity of Vital Signs Prediction and Early Warning Score Calculation Based on Continuous Monitoring of Hospitalised Patients Using Wearable Technology.

Youssef Ali Amer, A., et al. (2020), Sensors (Basel), 2020.20(22).

According to the intended use, the SOMNOtouch™ NIBP is not approved as a monitoring device [14] and therefore must not be used clinically in this way. However, we would like to introduce you to the following study in which the SOMNOtouch™ NIBP was used for continuous monitoring of cardiological, post-operative and dialysis patients.

EWS (Early Warning Scores) are used in hospitals to control the condition of a patient. For this purpose, the vital signs (heart rate, respiration rate, systolic blood pressure, oxygen saturation, and temperature) are assessed, normally two to three times a day. Limitations are that they do not provide past trends or future predictions as well as the low frequency of the measurements. To overcome this, continuous monitoring of vital signs might be advantageous.

The aim of this study (EAGLE study, which was part of the Interreg EMR project WearIT4health on the development of wearables for hospitalised patients) was to (1) estimate statistical values of the vital signs components of the EWS at a high rate (one-minute segments) versus the conventional rate of 2-3 times per day and (2) to predict at least one-hour ahead statistical attributes of vital signs using a localised learning algorithm [15]. For this purpose, vital signs of patients (73 cardiology, 10 postsurgical, 7 dialysis) were continuously measured with the SOMNOtouch™ NIBP (including intercostal electromyography (EMG) to estimate respiration). The vital signs collected were heart rate (HR), systolic blood pressure (SBP), oxygen saturation (SpO_2), and respiration rate (RR).

This study found that a real-time implementation of EWS in clinical practice is possible. It shows the potential of wearable devices to continuously measure vital signs of hospitalised patients. Wearable technologies can provide a real-time estimation of the EWS and time-series prediction using a localized learning algorithm.

5.2 Long-term ECG (up to 24 h)

The SOMNOtouch™ NIBP records a 3 channel ECG with up to 6 leads (I, II, III according to Einthoven plus aVF, aVL and aVR according to Goldberger). Bradycardia, tachycardia and arrhythmia are recognized and displayed. By the integrated acceleration sensor, motoric activity can be compared to heart rate. With this, activity related arrhythmias can be detected and diagnosed.

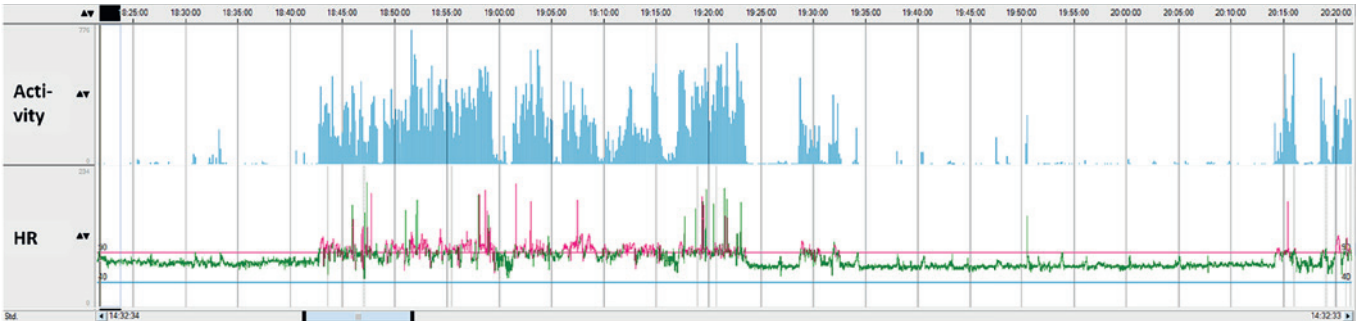


Figure 18 Comparison of activity and heart rate (Source: SOMNOmedics).
Increase of motoric activity (Act) with simultaneous rise of heart rate (HR).

Schiller Darwin2 OEM

For a detailed analysis of the recorded data, the fully integrated Schiller Darwin2 OEM, ECG long term arrhythmia analysis module can be used (software option at extra cost).

Figure 19 Screenshot of the Schiller Darwin2 software interface (Source: SOMNOmedics).

5.3 Extended Diagnosis

Oximetry

Using pulse oximetry, oxygen saturation, pulse and plethysmogram are recorded. Possible reasons for hypertension may be respiratory-related sleep disorders like obstructive sleep apnea syndrome (OSAS) [16]. OSA is a sleep-related breathing disorder which arises due to complete or partial collapse of the upper airways. This blockage causes a complete interruption (apnea) or a significant reduction of the airflow (hypopnea). Obstructions usually occur during REM sleep or in a supine position. Oxygen saturation decreases as a result of these obstructions. The body responds to the lack of oxygen with arousal reactions that are associated with activation of the sympathetic nervous system and thus with increases in BP and heart rate.

Further sleep related ventilation dysfunctions which can be identified by the oximetry are alveolar hypoventilation or a diffusion dysfunction (e.g., pneumonia). These are shown by a low SpO_2 basal saturation during night.

Desaturations can be detected by the continuous measurement of SpO_2. Due to the simultaneous recording of oxygen saturation and BP, desaturations respectively BP increases can be aligned.

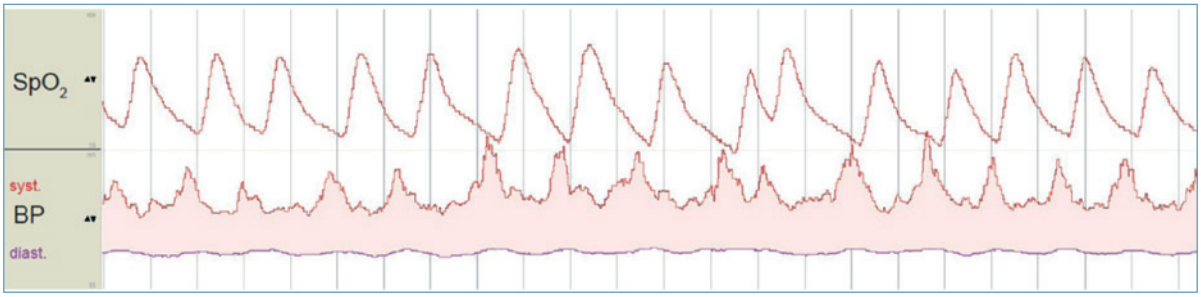
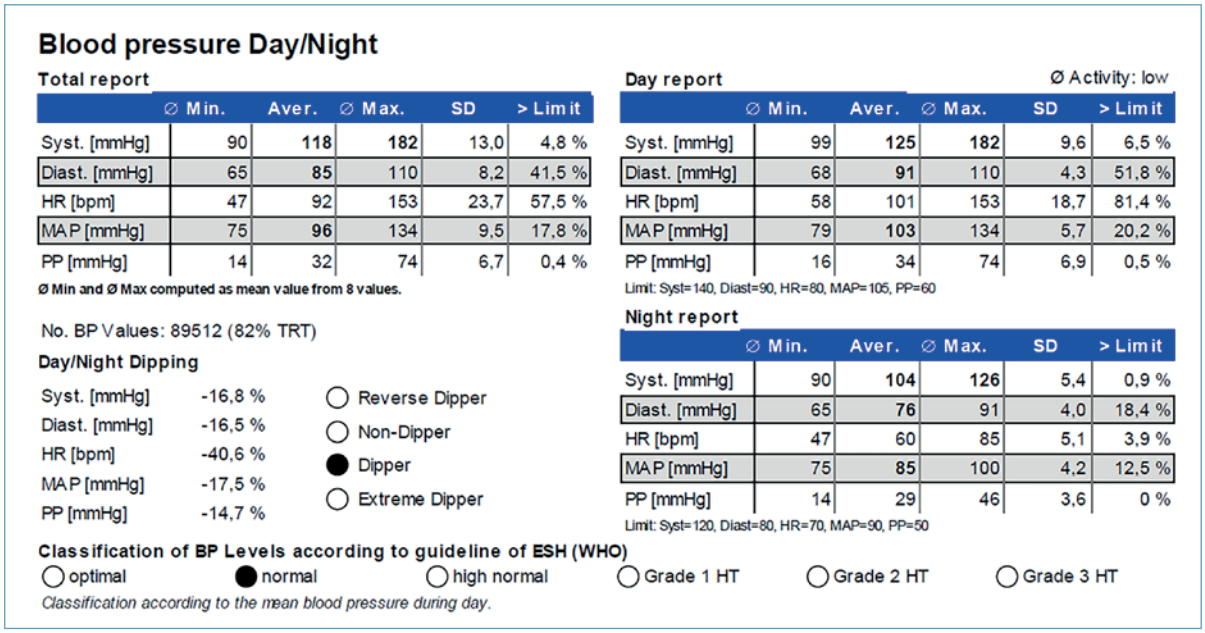


Figure 20 SpO_2 and BP (Source: SOMNOmedics).
Comparison of oxygen saturation (above) and BP (below) during a REM period of an OSAS patient. After each desaturation a BP increase can be seen.

6. REPORT

6.1 Blood Pressure Report

In addition to a visual analysis of the measurement, users also have the option to create, export and print out a comprehensive report. In the detailed 24 h BP report following information is included:



Blood pressure Day/Night

Total report

	∅ Min.	Aver.	∅ Max.	SD	> Limit
Syst. [mmHg]	90	118	182	13,0	4,8 %
Diast. [mmHg]	65	85	110	8,2	41,5 %
HR [bpm]	47	92	153	23,7	57,5 %
MAP [mmHg]	75	96	134	9,5	17,8 %
PP [mmHg]	14	32	74	6,7	0,4 %

Ø Min and Ø Max computed as mean value from 8 values.

No. BP Values: 89512 (82% TRT)

Day/Night Dipping

Syst. [mmHg]	-16,8 %
Diast. [mmHg]	-16,5 %
HR [bpm]	-40,6 %
MAP [mmHg]	-17,5 %
PP [mmHg]	-14,7 %

○ Reverse Dipper
○ Non-Dipper
● Dipper
○ Extreme Dipper

Day report Ø Activity: low

	∅ Min.	Aver.	∅ Max.	SD	> Limit
Syst. [mmHg]	99	125	182	9,6	6,5 %
Diast. [mmHg]	68	91	110	4,3	51,8 %
HR [bpm]	58	101	153	18,7	81,4 %
MAP [mmHg]	79	103	134	5,7	20,2 %
PP [mmHg]	16	34	74	6,9	0,5 %

Limit: Syst=140, Diast=90, HR=80, MAP=105, PP=60

Night report

	∅ Min.	Aver.	∅ Max.	SD	> Limit
Syst. [mmHg]	90	104	126	5,4	0,9 %
Diast. [mmHg]	65	76	91	4,0	18,4 %
HR [bpm]	47	60	85	5,1	3,9 %
MAP [mmHg]	75	85	100	4,2	12,5 %
PP [mmHg]	14	29	46	3,6	0 %

Limit: Syst=120, Diast=80, HR=70, MAP=90, PP=50

Classification of BP Levels according to guideline of ESH (WHO)

○ optimal ● normal ○ high normal ○ Grade 1 HT ○ Grade 2 HT ○ Grade 3 HT

Classification according to the mean blood pressure during day.

Figure 21 Blood pressure report 1 (Source: SOMNOmedics).

The overview table shows the minimum, maximum and mean values of syst. BP, diast. BP, heart rate (HR), mean arterial pressure (MAP) and pulse pressure (PP) for the whole recording (Total report), as well as for the day (Day report) and during TIB (Night report).

"> Limit" additionally shows the percentage of recording time, in which a parameter exceeds a defined limit (can be set by user).

Day/Night Dipping: shows the percentage change of systolic BP, diastolic BP, HR, MAP and PP during TIB compared to day values.

The dipping behaviour as well as classification of BP levels according to the guidelines applied are evident at first glance.

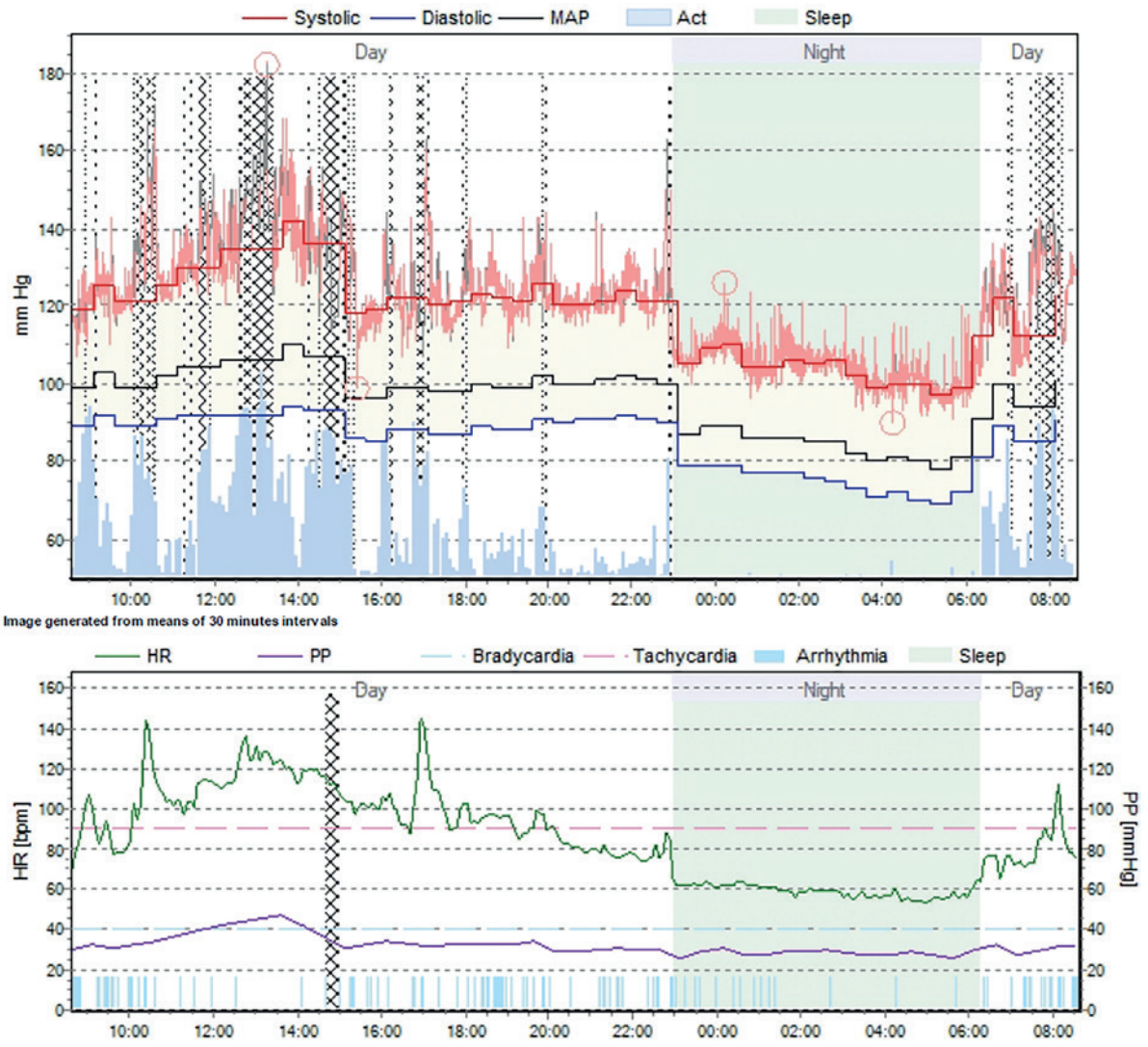


Figure 22 Blood pressure report 2 (Source: SOMNOmedics).

A graphical overview of the entire measurement is also displayed. The course of systolic and diastolic BP, mean arterial pressure (MAP), activity (Act) (upper part) as well as heart rate (HR) and pulse pressure (PP) (lower part) are clearly displayed over the entire measurement period. Arrhythmias are indicated and the sleep time (TIB) is highlighted as a light green panel behind the graph.

Conventional BP recording

No. BP Values: 89512 (82% TRT)

Time	∅ BP [mmHg]	BP [mmHg]	∅ HR [bpm]	HR [bpm]	∅ Activity [mg]	Desat.
18:00:00	127 / 89	128 / 88 (W)	102	104	138	-
18:15:00	123 / 89	122 / 89 (W)	94	96	21	-
18:30:00	123 / 89	A (W)	96	102	38	-
18:45:00	126 / 91	121 / 92 (W)	98	96	46	-
19:00:00	119 / 86	125 / 88 (W)	97	97	64	-
19:15:00	120 / 88	119 / 87 (W)	89	88	45	-
19:30:00	123 / 89	123 / 93 (W)	88	85	45	-
19:45:00	129 / 92	131 / 93 (W)	96	97	76	-
20:00:00	123 / 91	122 / 90 (W)	93	92	72	-
20:15:00	120 / 89	121 / 91 (W)	88	86	25	-
20:30:00	119 / 91	121 / 93 (W)	82	82	17	-
20:45:00	119 / 90	119 / 92 (W)	81	80	14	-
21:00:00	120 / 91	119 / 91 (W)	80	77	13	-
21:15:00	122 / 92	121 / 91 (W)	81	77	43	-
21:30:00	121 / 91	123 / 92 (W)	78	79	19	-
21:45:00	121 / 92	117 / 90 (W)	76	77	27	-
22:00:00	125 / 92	127 / 95 (W)	77	77	31	-
22:30:00	121 / 91	119 / 92 (W)	76	76	37	-
23:00:00	116 / 87	123 / 94 (W)	73	62	43	-
23:30:00	**106 / 79**	**108 / 80 (S)**	63	63	0	0 (0,0)
00:00:00	**110 / 79**	**108 / 79 (S)**	63	61	0	0 (0,0)
00:30:00	**109 / 78**	108 / 79 (S)	63	66	1	0 (0,0)
01:00:00	103 / 76	96 / 80 (S)	62	59	4	0 (0,0)
01:30:00	106 / 77	105 / 74 (S)	61	58	3	0 (0,0)
02:00:00	106 / 76	104 / 78 (S)	59	61	1	0 (0,0)
02:30:00	105 / 76	**110 / 78 (S)**	60	62	0	0 (0,0)
03:00:00	105 / 75	104 / 76 (S)	58	59	2	0 (0,0)
03:30:00	101 / 72	96 / 73 (S)	57	55	4	2 (4,0)
04:00:00	99 / 71	99 / 71 (S)	57	56	3	1 (2,0)
04:30:00	101 / 72	95 / 69 (S)	56	53	5	0 (0,0)
05:00:00	99 / 70	96 / 72 (S)	55	56	2	1 (2,0)
05:30:00	97 / 69	95 / 69 (S)	57	57	4	0 (0,0)
06:00:00	100 / 73	96 / 81 (S)	58	54	2	0 (0,0)
06:15:00	105 / 76	107 / 77 (S)	64	66	7	0 (0,0)
06:30:00	121 / 88	116 / 87 (W)	76	75	143	-
06:45:00	123 / 89	122 / 86 (W)	71	67	76	-
07:00:00	121 / 89	A (W)	75	84	159	-
07:15:00	109 / 83	107 / 80 (W)	73	74	45	-
07:30:00	116 / 88	A (W)	73	70	48	-
07:45:00	131 / 94	124 / 92 (W)	87	83	250	-
08:00:00	133 / 95	A (W)	91	80	172	-
08:15:00	118 / 88	115 / 85 (W)	96	91	153	-
08:30:00	126 / 92	130 / 93 (W)	78	84	40	-
∅ Day (6-22 o'clock)	124 / 90	125 / 90	98	97	113	
∅ Night (22-6 o'clock)	106 / 77	106 / 79	63	61	9	
∅ Record	118 / 86	120 / 88	91	90	92	

Ø BP [mmHg], Ø HR[bpm]: Mean of all single values in the respective interval
BP [mmHg], HR [bpm]: Value at the given time index
Ø Activity [mg]: Mean of all single values in the respective interval classified according to the thresholds from the Activity analysis
Desat.: Number (Index) of desaturations according to the thresholds from the SpO_2 analysis, if patient asleep
(W/S): Sleep/Wake state at the given time index
Green rows: Intervals the patient spent predominantly in sleep

Figure 23 Blood pressure report 3 (Source: SOMNOmedics).

BP and HR values are also displayed in the form of a conventional BP report in intervals of 15 or 30 minutes. Additionally, the user gets information about the motoric activity (low, median and high activity; the thresholds can be customized in the activity analysis) and desaturations (only during sleep) in the respective measurement intervals. Desaturation events are detected when blood oxygen saturation is decreased > 4%. Sleep is highlighted in green.

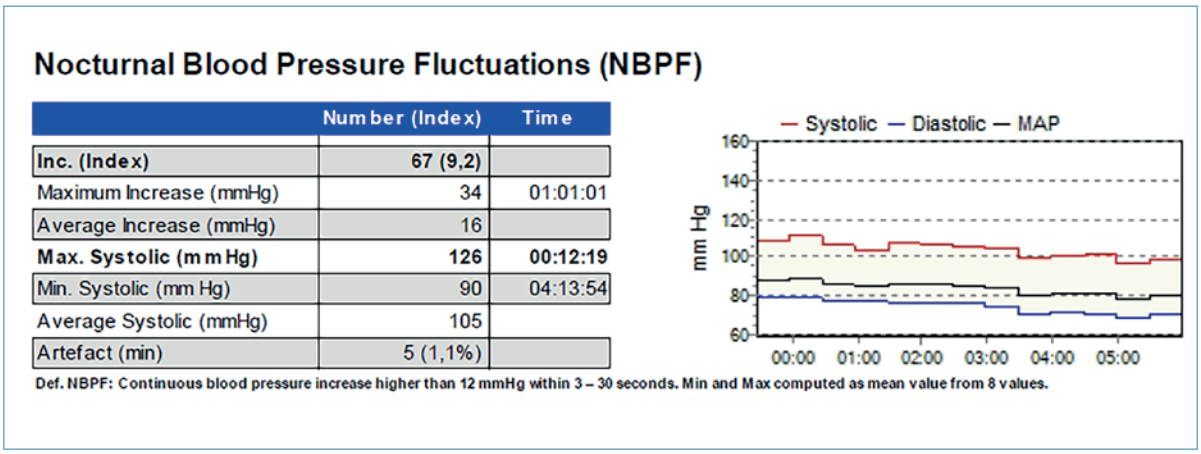


Figure 24 Blood pressure report 4 (Source: SOMNOmedics).

The NBPF™ (Nocturnal Blood Pressure Fluctuations) as an indicator for cardiac stress are shown. NBPF™ are defined as an increase of nocturnal BP of more than 12 mmHg within a timeframe of 3-30 seconds. Possible reasons for these short-time NBPF are periodic limb movement (PLM) or sleep-related breathing disorders (SRBD). The majority is caused by apneas, so it is recommended that a patient with a high number of NBPFs should undergo further cardiorespiratory screening.

6.2 Heart Rate Report

With the Heart Rate Report function in the software, users receive a tabular overview of the most important parameters of HR analysis as well as a graphical display of the HR distribution (%) for day, night and over the total analysis time.

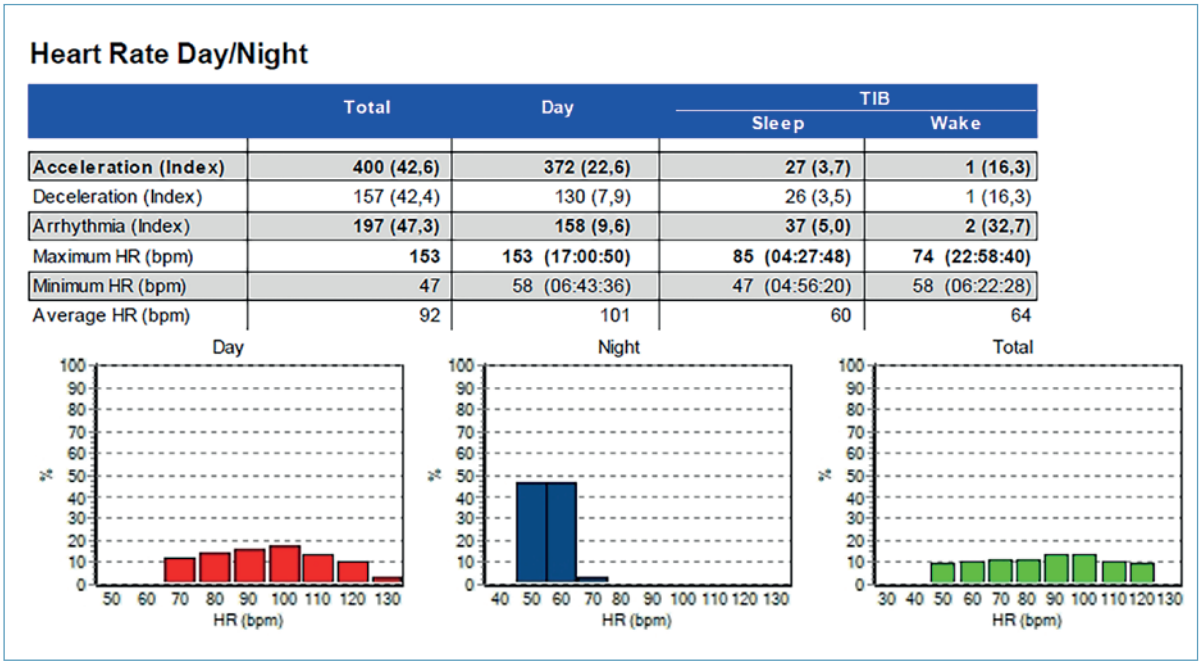
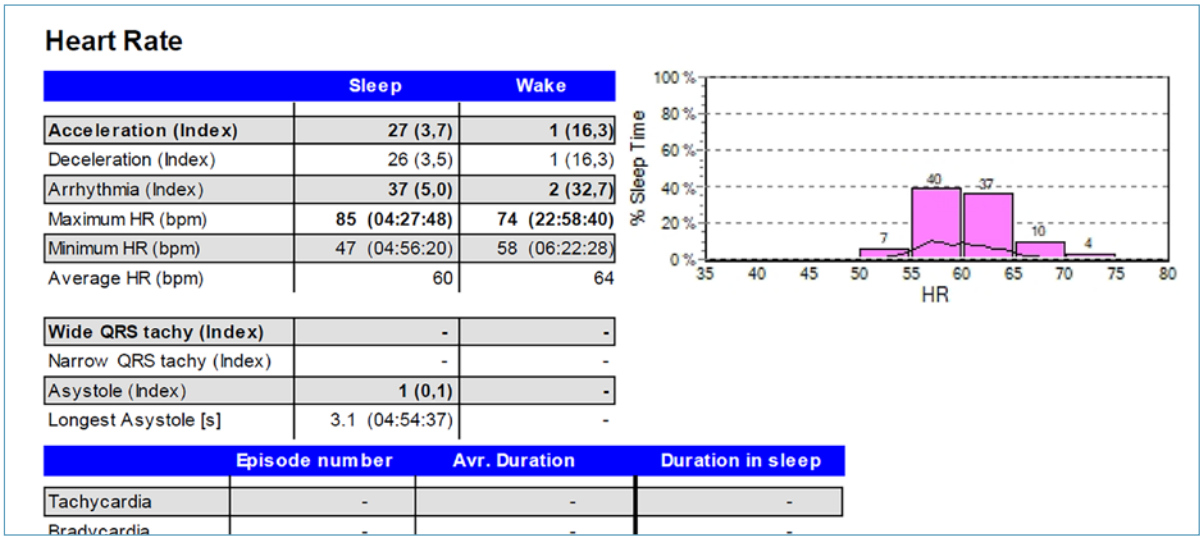


Figure 25 Heart rate report 1 (Source: SOMNOmedics).

When using the advanced Heart Rate Report, more parameters can be shown:



Heart Rate

	Sleep	Wake
Acceleration (Index)	27 (3,7)	1 (16,3)
Deceleration (Index)	26 (3,5)	1 (16,3)
Arrhythmia (Index)	37 (5,0)	2 (32,7)
Maximum HR (bpm)	85 (04:27:48)	74 (22:58:40)
Minimum HR (bpm)	47 (04:56:20)	58 (06:22:28)
Average HR (bpm)	60	64

Wide QRS tachy (Index)	-	-
Narrow QRS tachy (Index)	-	-
Asystole (Index)	1 (0,1)	-
Longest Asystole [s]	3.1 (04:54:37)	-

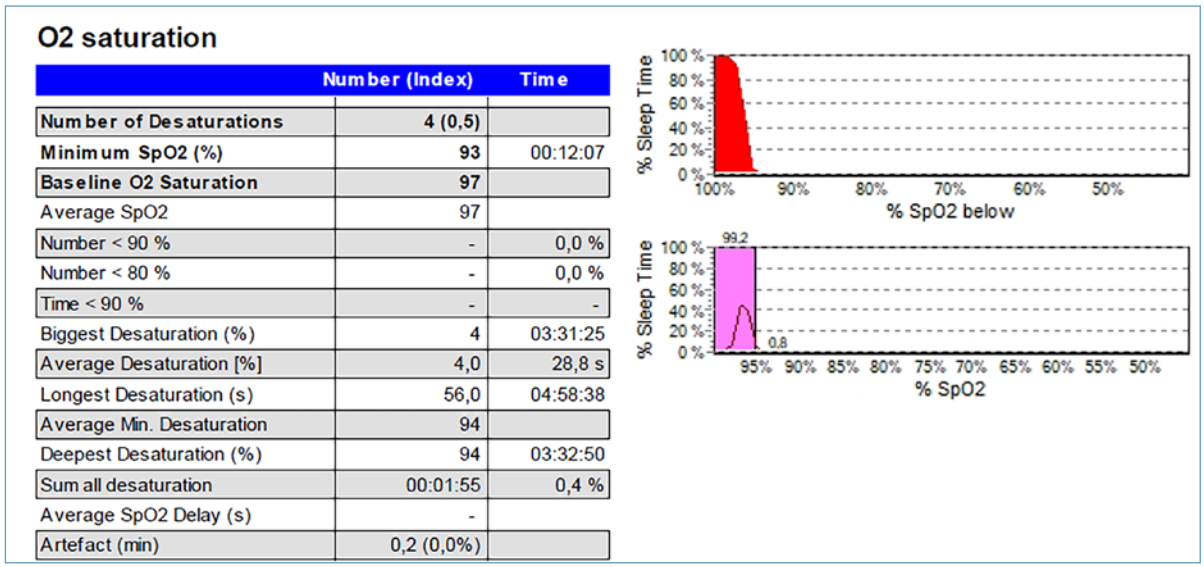
	Episode number	Avr. Duration	Duration in sleep
Tachycardia	-	-	-
Bradycardia	-	-	-

Figure 26 Heart rate report 2 (Source: SOMNOmedics).

Through acquisition of the ECG, especially the R-spike, the software calculates RR-intervals and is able to determine heart rate variability (HRV) and the sympathovagal balance thereof. These analyses can be displayed with the HRV Report/Stress Report or rather as Poincaré-Plot (not shown).

6.3 O_2-Report

With the report function, users get an overview of the SpO_2 analysis which provides detailed information about the respiratory status of the patient during the night.



O2 saturation

	Number (Index)	Time
Number of Desaturations	4 (0,5)	
Minimum SpO2 (%)	93	00:12:07
Baseline O2 Saturation	97	
Average SpO2	97	
Number < 90 %	-	0,0 %
Number < 80 %	-	0,0 %
Time < 90 %	-	-
Biggest Desaturation (%)	4	03:31:25
Average Desaturation [%]	4,0	28,8 s
Longest Desaturation (s)	56,0	04:58:38
Average Min. Desaturation	94	
Deepest Desaturation (%)	94	03:32:50
Sum all desaturation	00:01:55	0,4 %
Average SpO2 Delay (s)	-	
Artefact (min)	0,2 (0,0%)	

Figure 27 O_2 report (Source: SOMNOmedics).

Oxygen desaturation index: number of desaturations by at least 4% per hour of sleep.

7. ADVANTAGES OF THE SOMNOtouch™ NIBP COMPARED TO THE CUFF-BASED METHOD

Continuous, beat-to-beat:
Detects all minimum and maximum BP values and shows all information about BP during sleep. This allows conclusions to be drawn about the nocturnal blood pressure behaviour and to determine dipping/ non-dipping patients.

Non-reactive, cuffless and non-invasive:
- Maximum comfort for the patients: no disturbing pumping processes.
- No falsification of nocturnal BP values due to arousal reactions triggered by inflation of the cuff.

No influence of arrhythmias on the measurement method:
- Most automatic cuff devices are not validated for BP measurement in arrhythmias.
- The PTT method also provides reliable results in patients with underlying cardiological disorders.

Hydrostatic effect caused by changes of the body position is minimized.

Simultaneous recording of ECG, oxygen saturation and motoric activity:
- cardiogenic events are documented within the ECG, automatic ECG analysis
- desaturations are documented, evidence for apnea/hypopnea
- differentiation between physically and psychogenically caused hypertension

Internal sleep/wake-analysis [8]:
Actual sleep time (instead of the predefined night-time 10 pm - 6 am) is determined and BP values can be clearly mapped to sleep/wake states.

Comparison of cuff-based vs. PTT method		
mode	discontinuous	beat-to-beat
# measurements/ 24 h	80	86.400
Movements artefacts	15%	15%
Disturbance of sleep	18%	-
Arrhythmia	7%	-
Remaining BP values	48	73.440
Body position effect	high +/- 15 mmHg	low +/- 6 mmHg

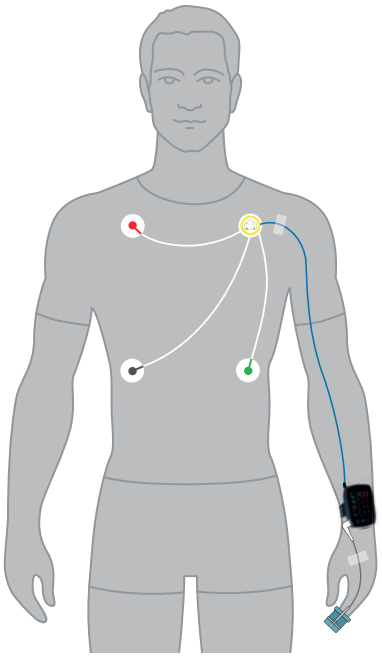
Table 1 Comparison of cuff-based vs. PTT method.

For the physician this means:
- The simultaneous, continuous recording of BP, ECG, oxygen saturation and activity allows a comparative analysis of these parameters and a better understanding of BP behaviour during day and night.
- The dipping behaviour of the BP can be reliably determined since the actual sleep time is determined.
- The SOMNOtouch™ NIBP can be used to diagnose white-coat hypertension, masked hypertension or orthostatic hypotension, and for therapy monitoring.

For the patient this means:
- A comfortable BP measurement, which can be frequently used.

8. APPLICATION NOTES AND TROUBLESHOOTING

8.1 Application of the SOMNOtouch™ NIBP



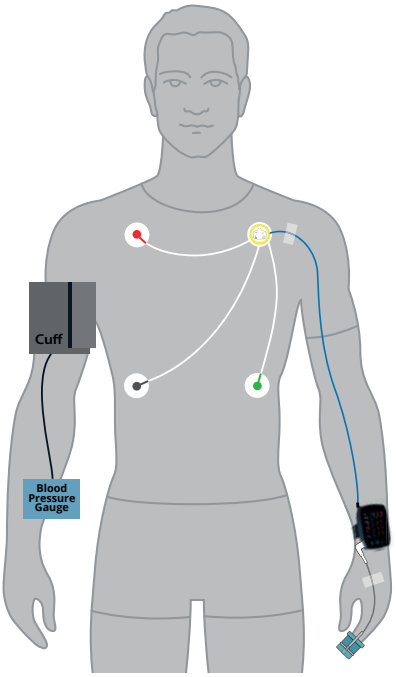
1. Attach the SOMNOtouch™ NIBP on the non-dominant wrist using the wristband.
2. Clean appropriate skin areas, connect ECG electrodes to snap electrodes and connect sensor to one of the free AUX ports.
3. Adhere the electrodes as bony as possible and close to the collarbone!
4. When using ECG with the yellow body position sensor: fix the yellow disk electrode with additional adhesive tape
5. Put the SpO_2 sensor on a finger (not the thumb) and connect it to the SOMNOtouch™ NIBP
6. Fix the cable of the sensor to the back of the hand with some medical tape for strain relief.

Figure 28 Application of the SOMNOtouch™ NIBP (Source: SOMNOmedics).

IMPORTANCE OF CALIBRATION

To calibrate the SOMNOtouch™ NIBP a single manual BP measurement is required during the ongoing measurement. To do this, place the cuff of an external BP monitor onto the opposite arm.

According to applicable guidelines during a BP measurement the patient should:



- be at rest for at least 5-10 minutes
- sit straight, relaxed and not cross legs
- not talk and not move
- put his arms on a table: the cuff should be at heart level
- It is important to choose the right cuff size.
- The correct application of the cuff must be ensured.

An accurate calibration is crucial for the PTT based BP measurement!

Figure 29 BP calibration (Source: SOMNOmedics).

8.2 Troubleshooting

In many cases you can easily solve any problems with the SOMNOtouch™ NIBP yourself. The following list shows you how to deal with the most common errors.

Problem	Possible cause	What to do?
Calibration not possible	Sensors not connected	Check, if sensors are connected (correctly)
	Signal quality not sufficient	ECG: Check the electrodes
		Pleth: warm up cold fingers, remove nail polish or artificial fingernails, use finger clip of right size
A recording cannot be transferred	Full hard disk	Archive all recordings and then delete them from the hard disk
		Has Windows logged off the network drive? Check in explorer if there is a red X near to the drive; if yes, open drive to reconnect
		Check your access rights to the hard disk, if needed, refer to system administrator
No BP was recorded	BP calibration was skipped by user	Please note that if the calibration is skipped, the validity of the blood pressure values in the analysis is not guaranteed. The time of calibration has to be selected by the user independently and the calibration measurement has to be performed at an appropriate point of time during the recording. Please use an appropriate marker to note the calibration in the later analysis
	Height of patient is not entered correctly	Check values
	Systolic or diastolic BP not entered correctly in the FW or SW	Check values
	BP was calibrated in area with artefacts	Relocate calibration time point minimally
One channel was not recorded	Montage not programmed correctly	Check montage and make sure the channel is selected
Report cannot be opened	There is no default printer under Windows	In the Windows printer settings, mark a printer as default
Error 002 on the display	Error of internal memory	Device must be returned for repair

Table 2 Troubleshooting.

If you need further support, you are welcome to contact us! Our service is free of charge and can be reached daily around the clock.

☎ +49 931 359094-994
@ service@somnomedics.de

9. VALIDATIONS OF THE PTT METHOD

The BP determination using the PTT method developed by SOMNOmedics was validated against other current methods:

- ✓ Validation according to the **ESH-IP 2010** protocol
- ✓ Against **cuff-based** method during **ergometry**
- ✓ Against **cuff-based** method over **24 hours**
- ✓ Against the **Penaz** method
- ✓ Against **intra-arterial** BP measurement

SOMNOtouch™ NIBP is listed on the dabl® Educational Trust website as a recommended device (http://www.dableducational.org/sphygmomanometers/devices_1_clinical.html#ClinTable).

Validations at a Glance

Study	Patient population	Objective	vs.	Major findings correlation	Mean disagreement
Bilo et al. (2015)	n = 33 Age: 25-78 BMI: 26.3	ESH–IP 2010 protocol	RR (cuff)	all validation requirements fulfilled SBP: r = 0.973 DBP: r = 0.976	SBP: 0.44 ± 6.1 mmHg DBP: 0.33 ± 3.4 mmHg
Gesche et al. (2011)	n = 50 young, healthy	Ergometry Increased load (0.5 – 2.5 W/kg) BP range: 110 – 230 mmHg	RR (cuff)	SBP: r = 0.83 (n = 267)	0 mmHg ± 19.8 mmHg
Dick et al. (unpublished)	n = 21	Ergometry	RR (cuff)	SBP: r = 0.96 DBP: r = 0.74	SBP: 4 ± 8 mmHg DBP: -3 ± 8 mmHg
Hulpke-Wette et al. (2018, poster)	n = 27 (100 planned) Age: 5 - 18	24 hours contralateral arm	RR (cuff)	SBP: r = 0.8 DBP: r = 0.7 (n = 228)	2.2 mmHg; +22/-17 mmHg 4.8 mmHg; +22/-12 mmHg
Zachwieja et al. (2020)	n = 30 Age: 10 - 18 primary hypertension or high normal	24 hours contralateral arm	RR (cuff)	SBP: r = 0.85 DBP: r = 0.64	SBP: 4.09 mmHg; +12.1/-20.3 DBP: 1.7 mmHg; +18.4/-21.8
Becker et al. (2020)	n = 36 healthy (10), HFrEF (12), PAH (14)	under simulation of sleep- disordered breathing	RR (cuff)	SBP: 111.3 ± 15.1 mmHg (RR), 110.0 ± 14.7 mmHg (PTT) DBP: 69.9 ± 12.2 mmHg (RR), 69.9 ± 14.2 mmHg (PTT)	SBP: 1.3 mmHg; +19.8/-22.4 DBP: 0.1 mmHg; +19.4/-19.2
Zagrada et al. (2019)	n = 57; Age: 11.4 ± 4.9; normal ward n = 9; Age: 9.8 ± 6.8; ICU	24 hours	RR (cuff) invasive	RR: SBP: r = 0.787 DBP: r = 0.634 inv: SBP: r = 0.894 DBP: r = 0.496	RR: 4-6 mmHg inv: 2 mmHg (SBP) -0.1 mmHg (DBP)
Hennig et al. (2012)	n = 11 OSAS	during sleep, nocturnal BP fluctuations (apnea induced)	Penaz (Portapres)	BP changes: 28.7 mmHg (PTT) 28.2 mmHg (Portapres)	13.7 mmHg (confidence interval)
Patzak et al. (2015)	n = 12 healthy	Dobutamin 5, 10, 20 µg/kg BP range > 230 mmHg	invasive	SBP: r = 0.947 (n = 107) DBP: r = 0.419 (n = 108)	1 mmHg ± 19 mmHg 5 mmHg ± 18 mmHg
Bartsch et al. (2010)	n = 40 non-hypotensive (10), hypotensive (8), arrhythmia (22)	Intensive Care, 60 min	invasive	No significant differences of SBP and DBP values	

Table 3 Overview validation studies.

9.1 Validation of the SOMNOtouch™ NIBP according to the ESH (European Society of Hypertension) International Protocol

Validation of the Somnotouch-NIBP noninvasive continuous blood pressure monitor according to the European Society of Hypertension International Protocol revision 2010.

Bilo, G., et al. (2015), Blood Press Monit, 20(5): p. 291-4.

The study protocol was based on the European Society of Hypertension International Protocol (ESH-IP) revision 2010 for the validation of blood pressure measuring devices in adults [17].

According to the requirements of the ESH-IP, the study included 33 patients (mean age 63.5 (25 - 78); BMI 26.3 ± 16.0 kg/m^2; arm circumference 27.6 (20 - 32) cm; 22 M/11 F) from low, medium and high BP strata [7].

Validation of the device was performed according to ESH-IP adapted to the distinct characteristics of the device. In particular, as the device requires initial calibration with cuff measurement, a 15-minute interval between calibration and validation measurements was introduced to verify calibration maintenance.

All validation requirements of the ESH-IP were fulfilled (see Table 4).

Requirement ESH-IP	≤ 5 mmHg	≤ 10 mmHg	≤ 15 mmHg	2/3 ≤ 5 mmHg**	0/3 ≤ 5 mHg***	Result
required	73 or 65*	87 or 81*	96 or 93*	≥ 24	≤ 3	
SBP - achieved	75	90	96	28	2	PASS
DBP - achieved	90	99	99	31	1	PASS

Table 4 Validation results (Source: based on Bilo et al., 2015 [7])

* two out of three required for the first threshold; three out of three required for the second threshold
** number of subjects with two out of three differences ≤ 5mmHg
*** number of subjects with none of the differences ≤ 5mmHg

The number of absolute differences between device and observers within 5, 10, and 15 mmHg was 75/99, 90/99, and 96/99, respectively, for SBP and 90/99, 99/99, and 99/99, respectively, for DBP.

For SBP, a strong correlation of 0.973 with a device-observer disagreement of 0.44 +/- 6.1 mmHg was detected (see Figure 30, left). For DBP, a strong correlation of 0.976 with a device-observer disagreement of 0.33 +/- 3.4 mmHg was detected (see Figure 30, right).

The SOMNOtouch™ NIBP fulfils all the ESH-IP 2010 validity requirements and passed all validation grades for both SBP and DBP levels. The SOMNOtouch™ NIBP represents a potentially useful option for cuffless BP monitoring with lesser interference with nocturnal sleep compared with traditional cuff-based BP monitoring methods.

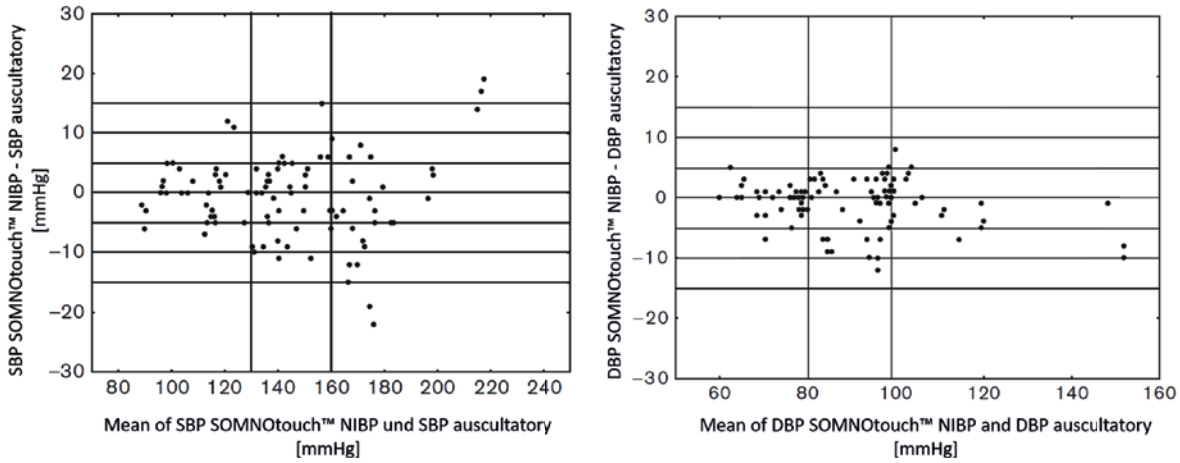


Figure 30 Scatter Plots (Source: Bilo et al., 2015 [7]).
Comparison of SOMNOtouch™ NIBP and auscultatory measurements for SBP (left) and DBP (right).

9.2 Comparison of the PTT Method against **CUFF-BASED Method** during ERGOMETRY

Continuous blood pressure measurement by using the pulse transit time: comparison to a cuff-based method.
Gesche, H., et al. (2012), Eur J Appl Physiol, 112(1): p. 309-15.

The gold standard for non-invasive BP recording is the cuff-based method of Riva-Rocci. In order to validate the PTT based method, SBP values were compared to that simultaneously obtained by the cuff-based method in 50 healthy subjects [5]. To induce a rise in BP, the volunteers performed an exercise test in which the load was stepwise increased (five steps, from 0.5 W/kg body mass [BM] to 2.5 W/kg BM).

The values of the PTT method and the cuff-based method significantly correlated (r = 0.83, n = 267). The limits of agreement in the Bland-Altman plot were +/- 19.8 mmHg.

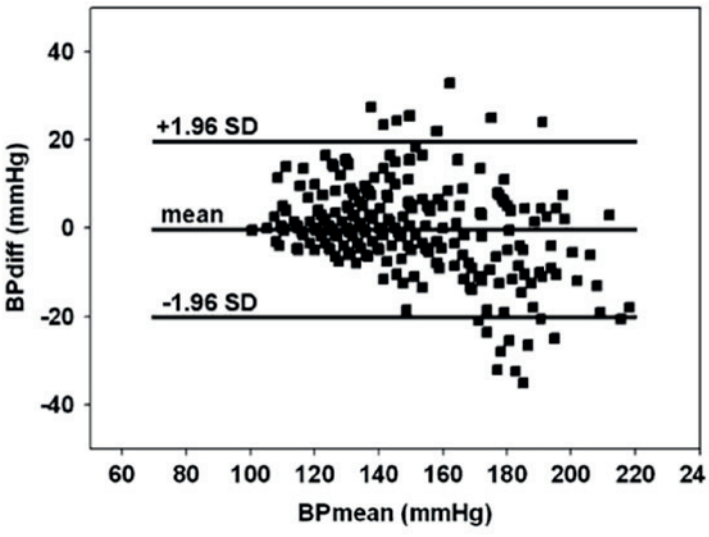


Figure 31 Bland-Altman Plot PTT vs. RR (Source: Gesche et al., 2012 [5]).

93.5% of data pairs are inside the "limits of agreement". The outliers are based on artefacts caused by movement during intense exercise.

Validation of an ambulatory blood pressure recorder using pulse transit time and a one point calibration to determine non-invasive systolic and diastolic blood pressure.
Dick, R., et al., unpublished.

SBP as well as DBP values derived from the PTT method were compared to that from a cuff-based method [18].

A standard exercise test was performed with 21 subjects (age: 54 +/- 11 years; BMI: 27.4 +/- 4.2 kg/m²). Five of them did the test under medication (beta-blocker, AT_2-blocker, calcium antagonists and ACE inhibitors). The values of the PTT method are highly correlated to that of the cuff-based method. For SBP, a correlation of 0.96 with a mean deviation of 4 mmHg and a standard deviation of 8 mmHg was detected. For DBP, a correlation of 0.74 with a mean deviation of -3 mmHg and a standard deviation of 8 mmHg was detected. Oral medication did not influence the results and no adverse events have been observed during exercise testing.

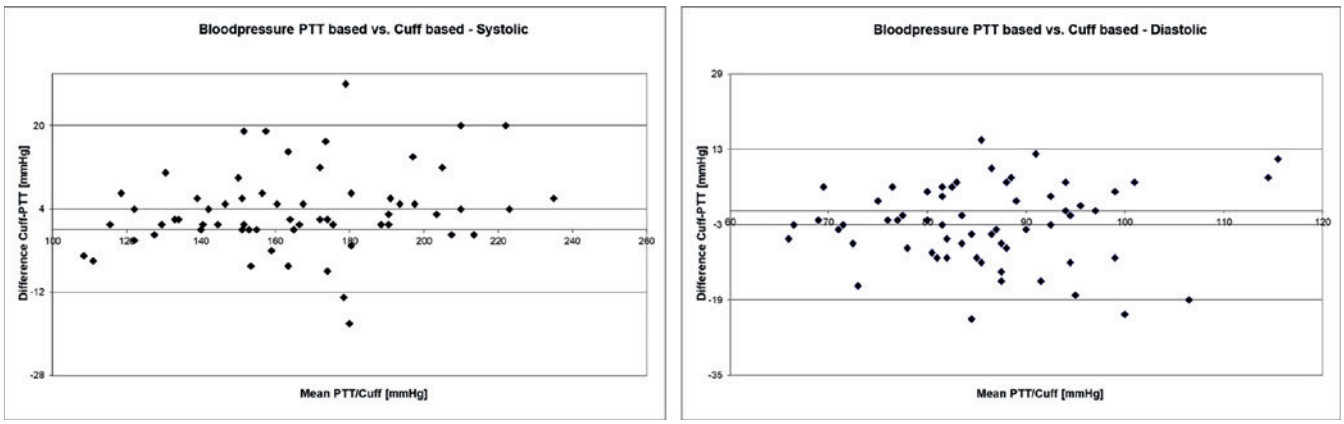


Figure 32 Bland-Altman plots (Source: Dick et al., unpublished [18]).
Comparison of SOMNOwatch™ plus and cuff-based measurements for SBP (left) and DBP (right).

9.3 Comparison of the PTT Method against **CUFF-BASED Method: over 24 HOURS**

Cuff-less blood pressure measurement using the pulse transit time - a comparison to cuff-based oscillometric 24 hour blood pressure measurement in children.
Hulpke-Wette, M. et al., preliminary data presented at the ESH 2018 congress.

Previous studies in adults have shown a good agreement between conventional ABPM and the PTT method for determination of BP.

In this study, both methods are compared over 24 hours in children (100 planned, 5-18 years) [19].

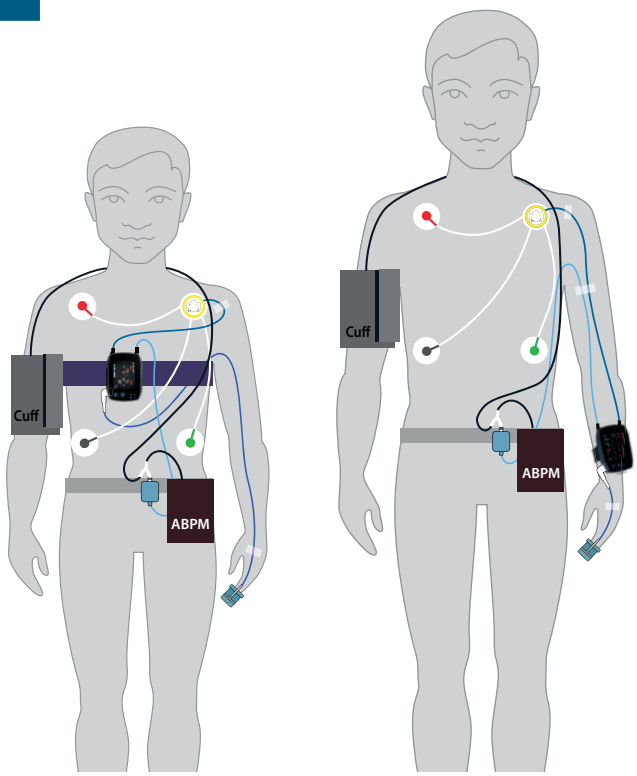


Figure 33 Application in children (Source: SOMNOmedics).
5 - 12 years: application at thorax via belt; 13 - 18 years: application at wrist.

The SOMNOtouch™ NIBP and a cuff device are worn at the same time on the contralateral arm. The application of the SOMNOtouch™ NIBP is dependent on the age of the children:

SBP and DBP are determined over 24 hours using an ABPM device at intervals of 2 times/h during daytime (7-21 h) and 1 time/h during night-time (21-7 h) and simultaneously beat-to-beat by the PTT method. Additionally, motoric activity, body position, oxygen saturation and cuff pressure are recorded.

To date, SBP and DBP were measured in 27 children (6 females, mean age 10.7 +/- 2.6 years, 152.7 +/- 15.6 cm, 48.7 +/- 17.4 kg). All questionable recordings of cuff measurements due to arrythmia, activity or arousals during sleep as well as artefacts in cuff inflation/deflation were excluded from analysis.

Preliminary results revealed a linear correlation of both methods in children (r = 0.8 for SBP, r = 0.7 for DBP, n = 228). Limits of agreement in Bland-Altman plot were +22 and -17 mmHg, with a mean difference of 2.2 mmHg, for SBP, resp. +22 and -12 mmHg, with a mean difference 4.9 mmHg, for DBP (see Figure 34).

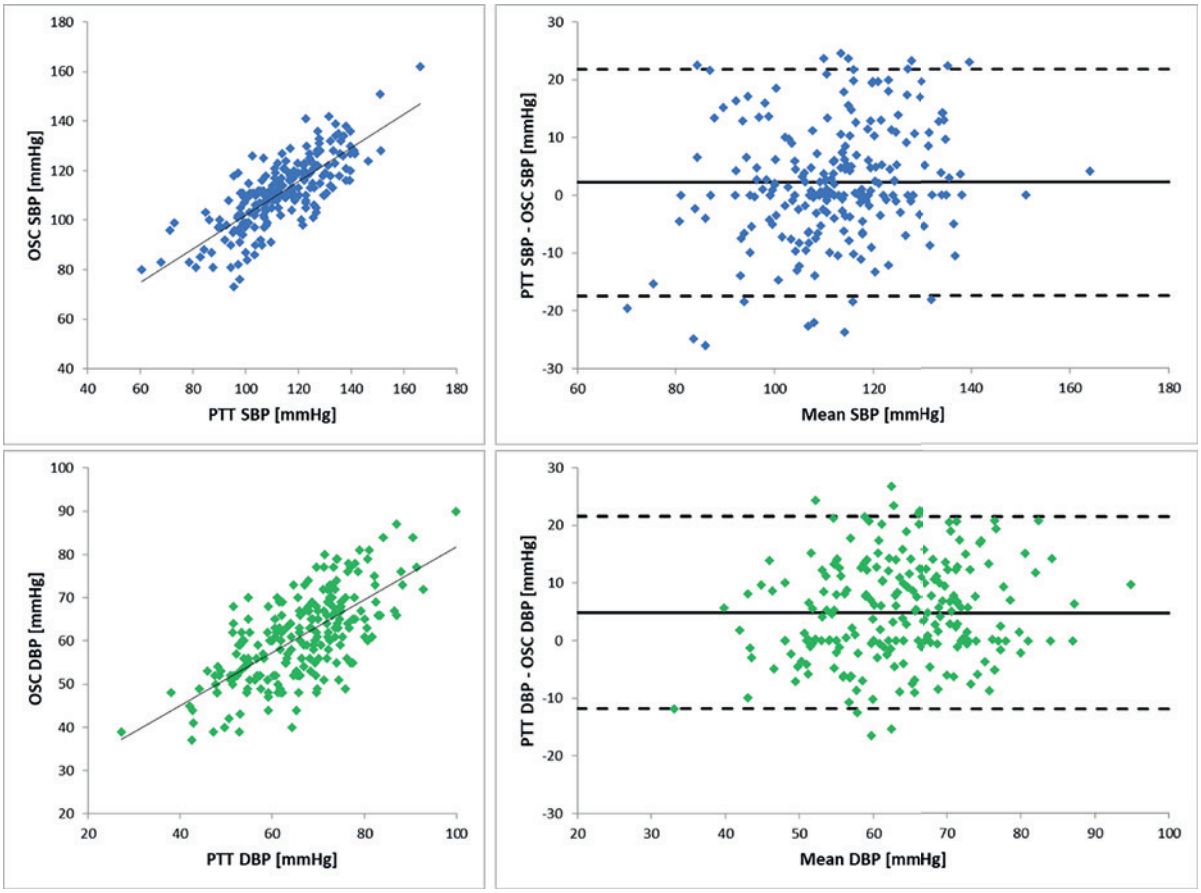


Figure 34 Scatter plots and Bland-Altman plots (Source: Hulpke-Wette et al., 2018 [19])
Comparison of SOMNOtouch™ NIBP and cuff-based measurements for SBP (blue) and DBP (green).

Our preliminary results imply that PTT and ABPM-based BP values are closely correlated in children during a 24 h measurement if invalid recordings were excluded. Despite the generally high activity of children, the PTT method provides considerably more BP values than the cuff-based method.

Comparison of cuff-based and cuffless continuous blood pressure measurements in children and adolescents.
Zachwieja, J., et al. (2020), Clin Exp Hypertens, 42(6): p. 512-18.

Common cuff devices are relatively large devices that are neither convenient nor practical during normal everyday routines, especially for children. Children find it difficult to accept the repetitive inflation processes of the cuff devices, and the resulting arousal reactions during night can falsify nocturnal BP values. In addition, cuff devices measure discontinuously, so that short-term BP fluctuations cannot be assessed.

The aim of this study was to compare BP values obtained by the PTT method with those of a standard upper arm device in children over 24 hours [20]. For this purpose, blood pressure was measured simultaneously with the SOMNOtouch™ NIBP on the left arm and with an ABPM device on the right arm (n = 30; age 10-18 years; primary hypertension or high normal). A second calibration of the SOMNOtouch™ NIBP was carried out with a cuff value in the morning still during TIB.

The 24 h mean values with the cuff device were 123.47 ± 14.91 mmHg for SBD and 66.88 ± 11.86 mmHg for DBD. With the SOMNOtouch™ NIBP, a 24 h mean of 127.48 ± 15.98 mmHg for SBP and 68.52 ± 12.36 mmHg for DBP was determined. The limits of agreement in the Bland-Altman plot were +12.11 and -20.29 mmHg for SBP, with a mean difference of 4.09 mmHg, and for DBP +18.39 and -21.78 mmHg, with a mean difference of 1.7 mmHg (see Figure 35). There were significant positive correlations between the cuff and the NIBP measurements (SBP r = 0.85489; DBP r = 0.63868).

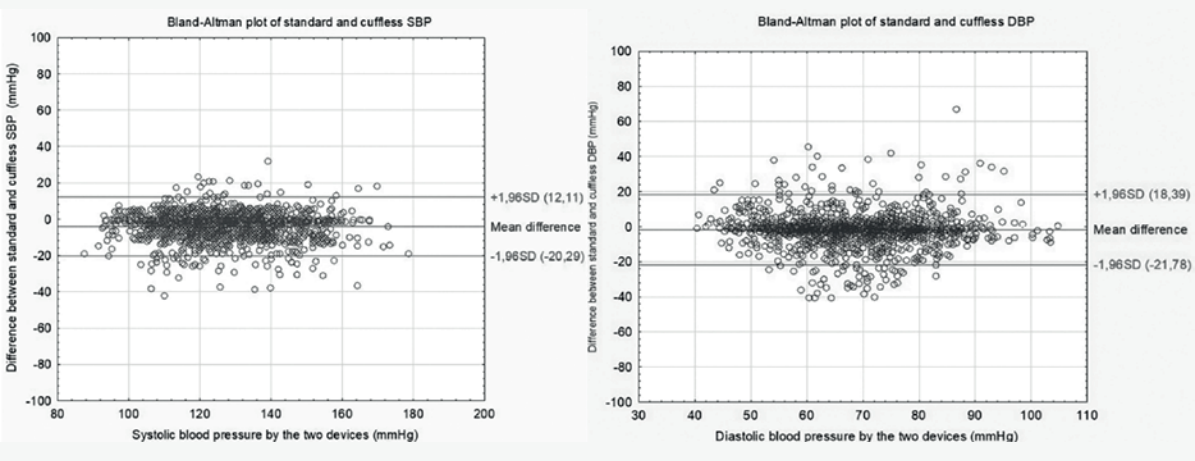


Figure 35 Bland-Altman plots for SBP (left) and DBP (right) (Source: Zachwieja et al., 2020 [20]).

With the cuffless method, values were 4.09 ± 8.27 mmHg (SBP) and 1.7 ± 10.25 mmHg (DBP) higher. The higher values are presumably due to the larger proportion of measured values during physical activity and the larger number of values in general that are obtained with the PTT method. The authors think that the PTT method is a promising tool for measuring 24 h BP values and that the development of cuffless BP measurement systems offers new solutions in numerous medical situations.

9.4 Comparison of the PTT Method against CUFF-BASED Method: during Different Breathing Maneuvers

Validity of transit time-based blood pressure measurements in patients with and without heart failure or pulmonary arterial hypertension across different breathing maneuvers.

Becker, S., et al. (2020), Sleep Breath, Mar;24(1):221-230.

The PTT method for BP monitoring is beneficial for sleep laboratories by not disturbing the patients and causing no arousals from sleep. The aim of this study was to assess the validity of the PTT method under sleep laboratory-like condition, especially in patients with heart failure with reduced ejection fraction (HFrEF) and with pulmonary arterial hypertension (PAH), as well as during simulation of sleep-disordered breathing (SDB) [21].

Ten healthy volunteers, 15 patients with HFrEF and 14 patients PAH were included in this study. Each study subject performed under non-invasive hemodynamic and respiratory monitoring five different breathing maneuvers to mimic SDB. BP was measured over 1 h both oscillometrically at least every 15 minutes with the Task Force Monitor™ and continuously by the PTT method (SOMNOscreen™ plus).

For the whole recording an oscillometric-based SBP of 111.3 ± 15.1 mmHg and a PTT-based SBP of 110.0 ± 14.7 mmHg was determined. Values obtained for DBP were 69.9 ± 12.2 mmHg and 69.9 ± 14.2 mmHg, respectively. The limits of agreement in the Bland-Altman plot were 19.8 and -22.4 mmHg with a mean difference between both methods of -1.3 ± 10.8 mmHg for SBP, and 19.4 and -19.2 mmHg with a mean difference of 0.1 ± 9.8 mmHg for DBP (see Figure 36).

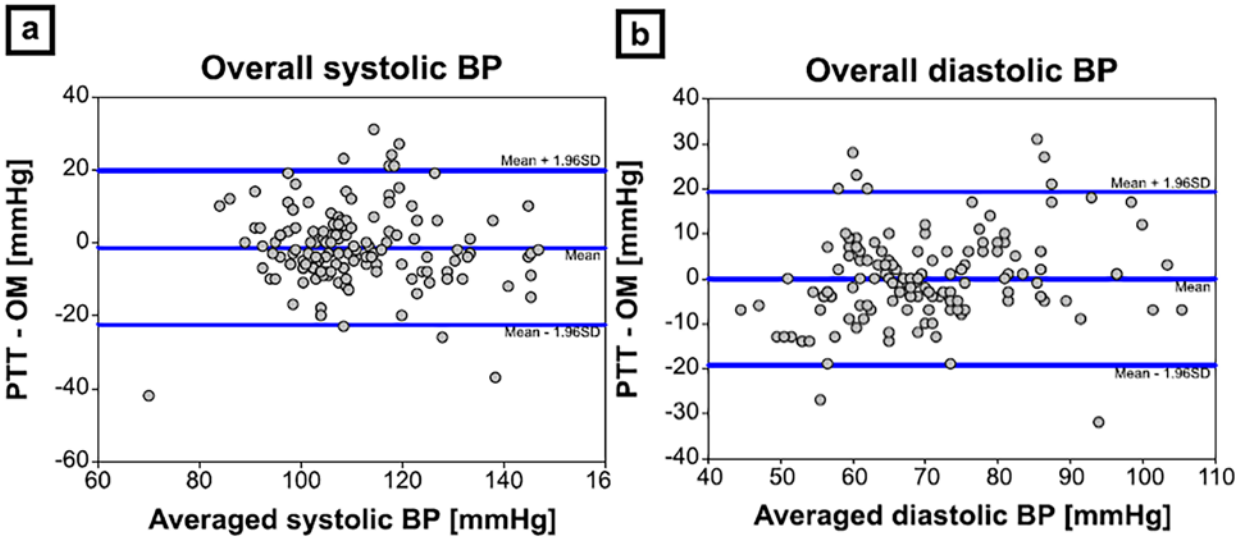


Figure 36 Bland-Altman plots for SBP (a) and DBP (b) over the whole recording (Source: Becker et al., 2020 [21]).

Furthermore, SBP and DBP values obtained by oscillometric and PTT-based BP measurement did not vary significantly before, during and after the different breathing maneuvers (data not shown). Additionally, differences between both methods were similar in volunteers, in HFrEF and in PAH patients (data not shown).

This study shows that the PTT-based BP monitoring provides clinically acceptable BP readings in the overall group as well as in the subgroups of healthy subjects and patients with HFrEF or PAH. In addition, it could be demonstrated that the PTT method delivers reliable BP values during both regular and SBD-like breathing patterns.

9.5 Comparison of the PTT Method against CUFF-BASED Method and INTRA-ARTERIAL Measurement

Continuous non-invasive blood pressure measurement using pulse wave transit time in children and adolescents (translated from German).

Zagrada, E., et al. (2019), Klin Padiatr, Mar;231(2):67-73.

The auscultatory measurement according to Riva-Rocci and Korotkow is the standard method of BP measurement, also in paediatric patients. In practice, however, the automatic oscillometric measurement of arterial BP is usually used for reasons of handling. Experience shows that children react to cuff-based BP measurements with defensive reactions and are, in the case of 24 h BP measurements, more easily woken up during sleep by inflation of the cuff. The continuous, non-invasive BP measurement using the PTT method therefore seems to be of particular interest for children.

The aim of this study was to compare in children and adolescents the continuous BP measurement using the PTT method with the oscillometric long-term BP measurement as well as the intra-arterial (i.a.) BP measurement at an intensive care unit [22].

In 57 patients (11.4 ± 4.9 years), BP was measured simultaneously over 24 hours using the PTT method (SOMNOtouch™ NIBP) and oscillometrically with the custo screen 300 device (custo med GmbH, Ottobrunn). Values measured with the PTT method were 4-6 mmHg higher. However, there was only a significant difference between both devices for values during night and mean arterial pressure for the complete measurement. The correlations for the total measurement were 0.787 for the SBD and 0.634 for the DBD.

In a further nine patients in an intensive care unit (9.8 ± 6.8 years), a comparison between the PTT method and the intra-arterial BP measurement was carried out. The total mean values by comparing the PTT method versus i.a. method were 115 ± 27.2 mmHg and 113 ± 24.8 mmHg for SBP and 58.4 ± 14.4 mmHg and 58.5 ± 13.0 mmHg for DBP, meaning differences between the PTT method and i.a. measurement of only 2 mmHg for SBP or -0.1 mmHg for DBD. The correlations were r = 0.894 (SBP) and r = 0.496 (DBP).

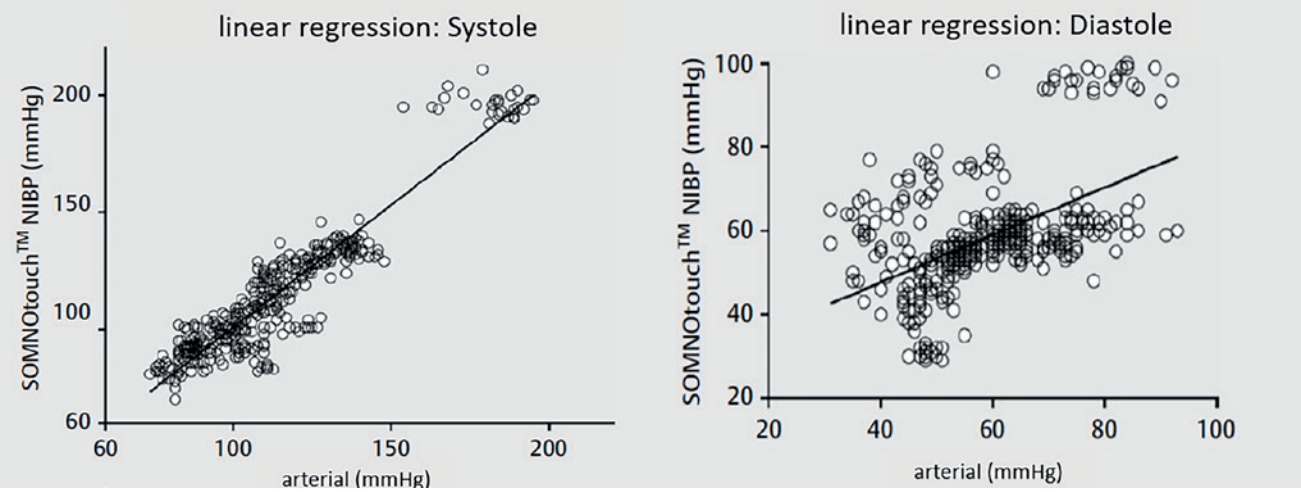


Figure 37 Scatter plots PTT vs. i.a. BP measurement for SBP (left) and DBP (right) (Source: based on Zagrada et al., 2019 [22]).

Compared to long-term measurements in children and adolescents, the PTT method provides good correlations with the reference measurements and appears to be a useful method, especially at rest, to measure blood pressure in children. The advantage of this method is that the children are not woken up when they are asleep by inflation of the cuff and that the continuous measurement enables constant recording. Thus, all BP fluctuations during the day and night are gathered.

9.6 Comparison of the PTT Method against **PENAZ Method**

Measurement of apnea related blood pressure changes using pulse transit time and Penaz principle (translated from German).
Hennig A, et al. (2012), Atemwegs- und Lungenerkrankungen, 38(11): p. 447–454.

A causative relationship between arterial hypertension and obstructive sleep apnea (OSA) is evident. Cuff-based BP recordings are inappropriate for evaluating BP during sleep. The physiological reaction (arousals due to cuff pumping) and the time interval between two recordings influence the results and important events will be missed, respectively. In order to show that the PTT method is suitable for measuring respiratory induced fluctuations of the BP, especially in apnea patients, the PTT method was validated against the Portapres system from the company FMS [23]. Eleven patients with diagnosis of sleep apnea were polysomnographically investigated. The SBP was recorded for 8 hours using the PTT method and the Penaz method.

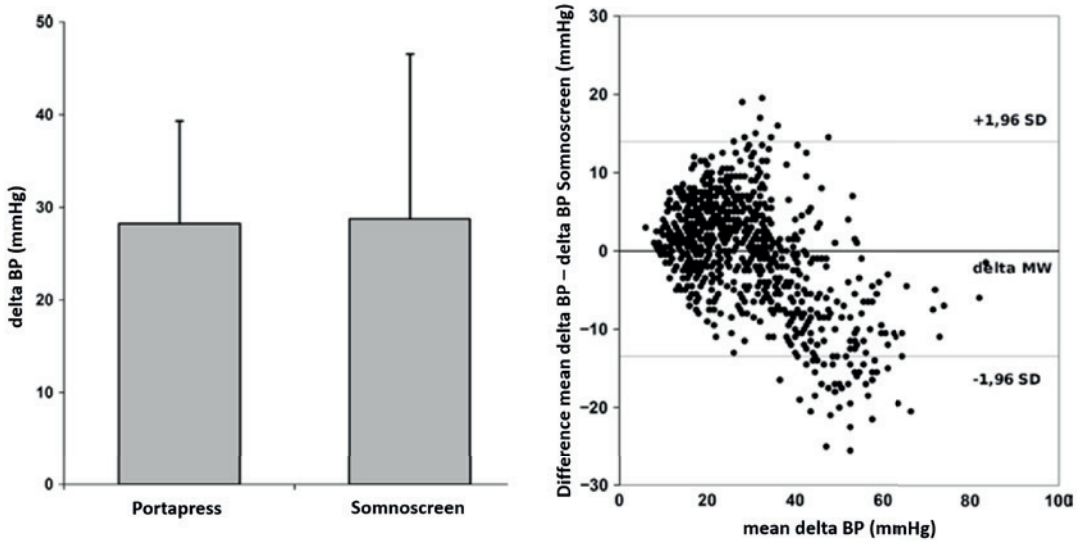


Figure 38 Apnea-induced BP changes (Source: based on Hennig et al., 2012 [23]).
Mean values (left) measured with the Portapres system and SOMNOscreen™ plus and comparison of both methods by Bland-Altman plot (right).

Both techniques similarly identified respiratory related (apnea and hypopnea) BP changes. Mean values of apnea-induced BP increases were 28.2 mmHg for Portapres and 28.7 mmHg for the PTT method (see Figure 38, left). The confidence interval was 13.7 mmHg (see Figure 38, right).

It could be shown that apnea/hypopnea goes along with transient elevations of BP, which could be reliably detected by the PTT method. The differences between the PTT method and the Portapres system are clinically acceptably.

9.7 Comparison of the PTT Method against INVASIVE Blood Pressure Recording: DOBUTAMINE

Continuous blood pressure measurement using the pulse transit time: Comparison to intra-arterial measurement.
Patzak, A., et al. (2015), Blood Press, 24(4): p. 217-21.

The continuous, non-invasive BP measurement based on PTT was validated by comparing it to intra-arterial BP measurement [24].

The intra-arterial measurement of BP is the gold standard and is often used in intensive care units (ICU). The BP of patients in an ICU should be kept constant. This raises a problem when trying to compare a new method with the gold standard. To create high BP ranges that are necessary for the estimation of the correlation, 12 healthy subjects received dobutamine intravenously in the following dosages: 5, 10 and 20 µg/kg body weight. The positive inotropic effect of dobutamine leads to an increase of BP up to 200 mmHg with only a slight effect on heart rate. Arterial BP was determined in parallel with the PTT method and the intra-arterial method.

Correlation analysis revealed a highly significant relation between the PTT method and the intra-arterial measurement for SBP (r = 0.947; n = 107). The mean difference between both methods for SBP was 0.78 mmHg and the limits of agreement were +/- 18.9 mmHg.

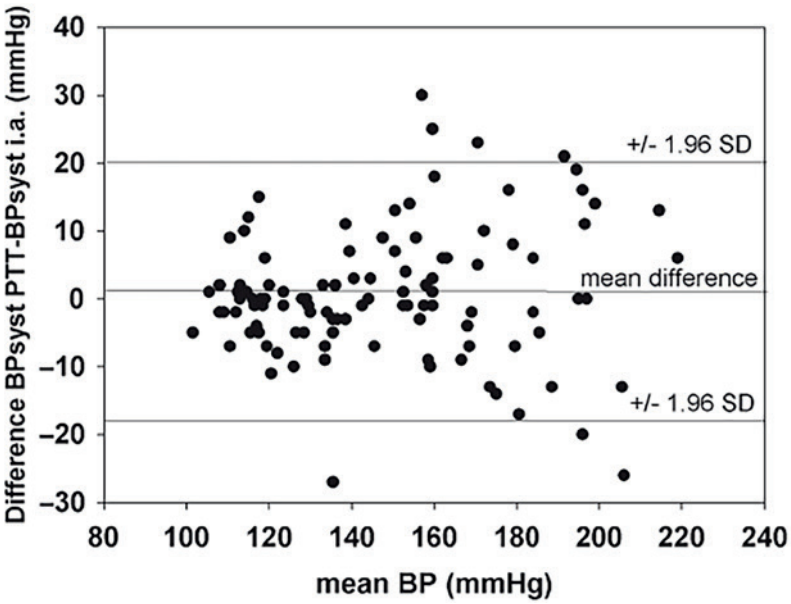


Figure 39 Bland-Altmann plot of SBP of all patients (n =107) (Source: Patzak et al., 2015 [24]).

9.8 Comparison of the PTT Method against INVASIVE Blood Pressure Recording: CARDIAC INTENSIVE CARE UNIT

Validation of continuous blood pressure measurements by pulse transit time: a comparison with invasive measurements in a cardiac intensive care unit (translated from German).

Bartsch, S., et al. (2010), Dtsch Med Wochenschr, 135(48): p. 2406-12.

In order to show that the PTT method is also suitable for patients with cardiac pathology, three different populations in a cardiologic intensive care unit were examined (n = 40, 29 males; mean age 68.7 +/- 15 years) [25]. They were separated into the following groups: Group 1: patients without hypotension and without arrythmia (n = 10); Group 2: hypotensive patients (n = 8); Group 3: Patients with arrythmia absoluta (by atrial fibrillation and/or complete bundle block; n = 22). In a period of 60 minutes the PTT method was compared to the invasive method. Values were analysed and compared in 30-second intervals (9600 values for each method).

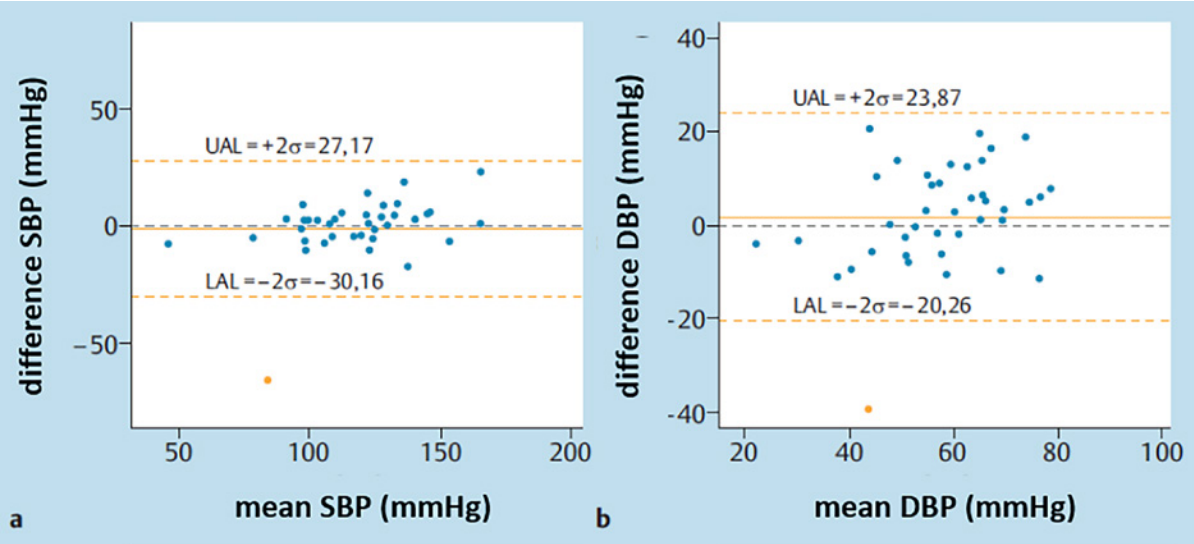


Figure 40 Bland-Altman plot of SBP and DBP values for the whole group (Source: based on Bartsch et al. 2010 [25]).

There were no significant differences between recorded SBP and DBP values in subpopulations and the total population. The method using the PTT provided a smaller number of analysable data compared to the gold standard.

The PTT method can provide reliable values over a period of at least one hour in cardiology patients in whom the R-peak in the ECG and sufficient blood ejection from the heart can be detected.

10. TECHNICAL DATA

SOMNOtouch™ NIBP

Recording of the following parameters:

- SBP and DBP
- ECG
- SpO_2
- finger pulse waveform (plethysmogram)
- motoric activity
- body position
- patient marker

Technical Specifications

Data collection
Data transfer via USB, 12 Bit signal resolution.
Individually adjustable sample rate from 1 Hz to 512 Hz

Data storage
Internal data storage, 512 MB capacity.
Charging and data transfer via docking station

Size and weight
74 x 55 x 16 mm, 58 g (incl. battery)

Display
High resolution, colour touch display (320 x 240) pixels

Power supply
Li-Ion battery (rechargeable), up to 24 hours recording duration

Analysis software
DOMINO light

SOMNOtouch™ NIBP in docking station

12. LIST OF ABBREVIATIONS

Act	-	Motoric Activity
ABPM	-	Ambulatory Blood Pressure Measurement
BM	-	Body Mass
BP	-	Blood Pressure
CPAP	-	Continuous Positive Airway Pressure
DBP	-	Diastolic Blood Pressure
ECG	-	Electrocardiogram
HR	-	Heart Rate
HRV	-	Heart Rate Variability
MAP	-	Mean Arterial Pressure
NBPF	-	Nocturnal Blood Pressure Fluctuation
OSAS	-	Obstructive Sleep Apnea Syndrome
PP	-	Pulse Pressure
PTT	-	Pulse Transit Time
PWV	-	Pulse Wave Velocity
RLS	-	Restless Legs Syndrome
SDB	-	Sleep-Disordered Breathing
SBP	-	Systolic Blood Pressure
SOT	-	SOMNOtouch™
SVB	-	Sympathovagal Balance
TIB	-	Time in Bed

13. REFERENCES

1. Mills, K.T., J.D. Bundy, T.N. Kelly, J.E. Reed, P.M. Kearney, K. Reynolds, J. Chen and J. He, Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. Circulation, 2016. 134(6): p. 441-50.
2. Williams, B., G. Mancia, W. Spiering, E. Agabiti Rosei, M. Azizi, M. Burnier, D.L. Clement, A. Coca, G. de Simone, A. Dominiczak, T. Kahan, F. Mahfoud, J. Redon, L. Ruilope, A. Zanchetti, M. Kerins, S.E. Kjeldsen, R. Kreutz, S. Laurent, G.Y.H. Lip, R. McManus, K. Narkiewicz, F. Ruschitzka, R.E. Schmieder, E. Shlyakhto, C. Tsioufis, V. Aboyans, I. Desormais and M. Authors/Task Force, 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. J Hypertens, 2018. 36(10): p. 1953-2041.
3. Sega, R., R. Facchetti, M. Bombelli, G. Cesana, G. Corrao, G. Grassi and G. Mancia, Prognostic value of ambulatory and home blood pressures compared with office blood pressure in the general population: follow-up results from the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study. Circulation, 2005. 111(14): p. 1777-83.
4. O'Brien, E., G. Parati, G. Stergiou, R. Asmar, L. Beilin, G. Bilo, D. Clement, A. de la Sierra, P. de Leeuw, E. Dolan, R. Fagard, J. Graves, G.A. Head, Y. Imai, K. Kario, E. Lurbe, J.M. Mallion, G. Mancia, T. Mengden, M. Myers, G. Ogedegbe, T. Ohkubo, S. Omboni, P. Palatini, J. Redon, L.M. Ruilope, A. Shennan, J.A. Staessen, G. vanMontfrans, P. Verdecchia, B. Waeber, J. Wang, A. Zanchetti, Y. Zhang and M. European Society of Hypertension Working Group on Blood Pressure, European Society of Hypertension position paper on ambulatory blood pressure monitoring. J Hypertens, 2013. 31(9): p. 1731-68.
5. Gesche, H., D. Grosskurth, G. Kuchler and A. Patzak, Continuous blood pressure measurement by using the pulse transit time: comparison to a cuff-based method. Eur J Appl Physiol, 2012. 112(1): p. 309-15.
6. Patent numbers DE 102005014048.3-35, EP 20060001181.4-1526, US 11/364 174 US 2006/0217616 A1, 7374542.
7. Bilo, G., C. Zorzi, J.E. Ochoa Munera, C. Torlasco, V. Giuli and G. Parati, Validation of the Somnotouch-NIBP noninvasive continuous blood pressure monitor according to the European Society of Hypertension International Protocol revision 2010. Blood Press Monit, 2015. 20(5): p. 291-4.
8. Dick, R., T. Penzel, I. Fietze, M. Partinen, H. Hein and J. Schulz, AASM standards of practice compliant validation of actigraphic sleep analysis from SOMNOwatch versus polysomnographic sleep diagnostics shows high conformity also among subjects with sleep disordered breathing. Physiol Meas, 2010. 31(12): p. 1623-33.
9. Schrader, J., Nächtlicher Blutdruckabfall. Management Hypertonie Journal by Fax, 2001. 12.
10. Gehring, J., H. Gesche, G. Drewniok, G. Kuchler and A. Patzak, Nocturnal blood pressure fluctuations measured by using pulse transit time in patients with severe obstructive sleep apnea syndrome. Sleep Breath, 2018. 22(2): p. 337-343.
11. Picard, F., P. Panagiotidou, L. Weinig, M. Steffen, A.B. Tammen and R.M. Klein, Effect of CPAP therapy on nocturnal blood pressure fluctuations, nocturnal blood pressure, and arterial stiffness in patients with coexisting cardiovascular diseases and obstructive sleep apnea. Sleep Breath, 2021. 25(1): p. 151-161.
12. Trenkwalder, C., Restless-Legs-Syndrom (RLS) und Periodic Limb Movement Disorder (PLMD). DGN Leitlinien für Diagnostik und Therapie in der Neurologie. 2012.
13. Sieminski, M. and M. Partinen, Nocturnal systolic blood pressure is increased in restless legs syndrome. Sleep Breath, 2016. 20(3): p. 1013-9.
14. SOMNOmedics, Instruction Manual SOMNOtouch™NIBP. 2020. Rev. 9.
15. Youssef Ali Amer, A., F. Wouters, J. Vranken, D. de Korte-de Boer, V. Smit-Fun, P. Duflot, M.H. Beaupain, P. Vandervoort, S. Luca, J.M. Aerts and B. Vanrumste, Vital Signs Prediction and Early Warning Score Calculation Based on Continuous Monitoring of Hospitalised Patients Using Wearable Technology. Sensors (Basel), 2020. 20(22).
16. Parish, J.M. and V.K. Somers, Obstructive sleep apnea and cardiovascular disease. Mayo Clin Proc, 2004. 79(8): p. 1036-46.
17. O'Brien, E., N. Atkins, G. Stergiou, N. Karpettas, G. Parati, R. Asmar, Y. Imai, J. Wang, T. Mengden, A. Shennan and H. Working Group on Blood Pressure Monitoring of the European Society of, European Society of Hypertension International Protocol revision 2010 for the validation of blood pressure measuring devices in adults. Blood Press Monit, 2010. 15(1): p. 23-38.
18. Dick, R., Validation of the ambulatory blood pressure recorder SOMNOwatch™ plus using pulse transit time and a one-point calibration to determine non-invasive blood pressure. unpublished.
19. Hulpke-Wette, M., Göhler, A., Hofmann, E., Küchler, G., Cuff-less blood pressure measurement using the pulse transit time - a comparison to cuff-based oscillometric 24 hour blood pressure measurement in children. Journal of Hypertension, 2018. 36(p e73).
20. Zachwieja, J., A. Neyman-Bartkowiak, A. Rabiega, M. Wojciechowska, M. Barabasz, A. Musielak, M. Silska-Dittmar and D. Ostalska-Nowicka, Comparison of cuff-based and cuffless continuous blood pressure measurements in children and adolescents. Clin Exp Hypertens, 2020. 42(6): p. 512-518.
21. Becker, S., J. Spiesshoefer, T. Brix, I. Tuleta, M. Mohr, M. Emdin, M. Boentert and A. Giannoni, Validity of transit time–based blood pressure measurements in patients with and without heart failure or pulmonary arterial hypertension across different breathing maneuvers. Sleep and Breathing, 2020. 24(1): p. 221-230.
22. Zagrada, E., T. Krickau and W. Rascher, [Continuous Non-Invasive Blood Pressure Measurement Using Pulse Transit Time in Children and Adolescents]. Klin Padiatr, 2019. 231(2): p. 67-73.
23. Hennig, A.G., H.; Fietze, I.; Penzel, T.; Glos, M.; Patzak, A., [Measurement of apnea related blood pressure changes using pulse transit time and Penaz principle]. Atemwegs- und Lungenkrankheiten, 2012. Jahrgang 38: p. 1–8.
24. Patzak, A., Y. Mendoza, H. Gesche and M. Konermann, Continuous blood pressure measurement using the pulse transit time: Comparison to intra-arterial measurement. Blood Press, 2015. 24(4): p. 217-21.
25. Bartsch, S., D. Ostojic, H. Schmalgemeier, T. Bitter, N. Westerheide, S. Eckert, D. Horstkotte and O. Oldenburg, [Validation of continuous blood pressure measurements by pulse transit time: a comparison with invasive measurements in a cardiac intensive care unit]. Dtsch Med Wochenschr, 2010. 135(48): p. 2406-12.

14. LIST OF FIGURES

15. LIST OF TABLES

NOTES

NOTES

NOTES

IMPRINT

Address:
SOMNOmedics GmbH
Am Sonnenstuhl 63
97236 Randersacker
D-Germany

Contact:
Tel.: +49 (931) 359094-0
Fax: +49 (931) 359094-49
E-Mail: info@somnomedics.de

CEO: Dr. Gert Küchler

Texts: Dr. Elisabeth Hofmann

5.24_05-2022_EN_Rev_6

CE 0297