CARDIO diagnostics
A division of SOMNOmedics

Blood Pressure Measurement using PTT

Compendium

Non-invasive | continuous | non-reactive

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CONTENT

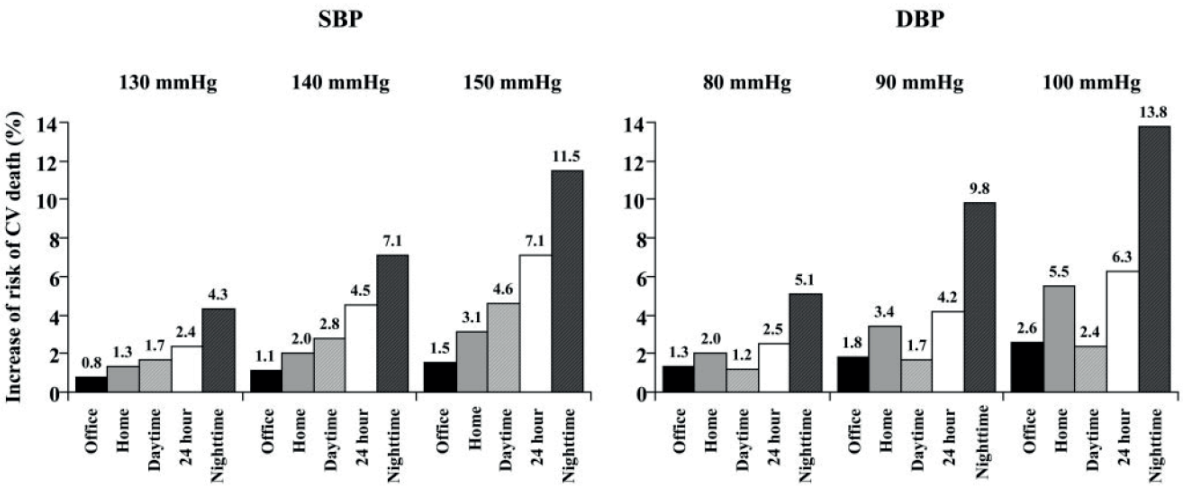
1. LONG-TERM BLOOD PRESSURE MEASUREMENTS

Arterial hypertension (high blood pressure) is a very common disease - affecting approximately 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 the disease more difficult.

The current European guidelines (ESH / ESC Guidelines 2018) recommend, in addition to the formerly recommended in-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 24h ambulatory blood pressure measurement (ABPM) or home blood pressure measurement (HBPM).

A 24h ABPM records a patient's BP levels under conditions which are more representive 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 an in-office BP. The resulting BP values can be summarized into 24h mean values and can 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 in-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 in-office measurements (3 - see figure below). Thus, by recording the nocturnal BP, the cardiovascular risk can be better analysed.



Increase in 11-year risk of cardiovascular (CV) mortality for 10-mm Hg increase in office, home and ambulatory BP at various initial BP values. Clearly evident is the increased information content of nocturnal BP values (from 3).

Normally, in a healthy person, the BP during the night can drop by between 10% to 20% of the daytime average BP (Dipper; 4). Patients in whom the nocturnal BP drop is less pronounced (Non-Dipper) or in whom BP even rises during the night (Inverted Dipper) have an increase in cardiovascular morbidity and mortality. It is only possible to record this important BP behavior at night with a 24h ABPM measurement.

Additionally, ABPM allows the exclusion of the so-called in-office hypertension ("white-coat hypertension"). Here, high levels of BP are only measured in a medical environment like the clinic or office, while self-measurement or ABPM show normal values. White-coat hypertension is seen in 30-40% of patients (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 increased (about 15% of patients with normal office BP; 2).

ABPM also offers 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 BP MEASUREMENTS ACCORDING TO RIVA-ROCCI – IS THE METHOD STATE-OF-THE-ART?

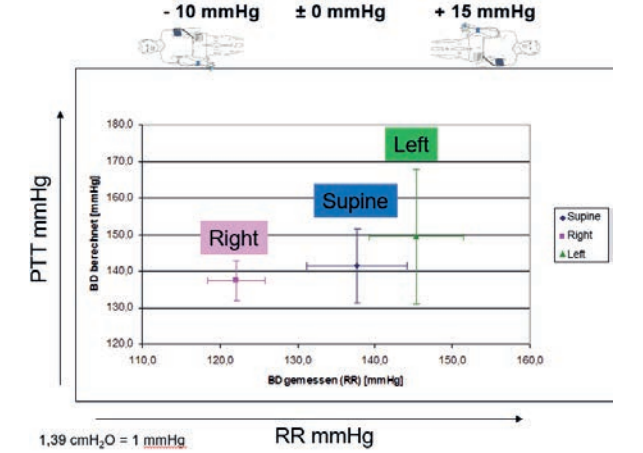
The cuff-based method for measuring BP was introduced in 1896 by Scipione Riva-Rocci. Until today, long-term BP measurements are usually carried out with automated devices based on this method. Thereby, recordings are taken four times per hour during the day and twice per hour during the night (10 pm - 6 am).

The established cuff devices were designed for the 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.

For 24h BP measurements these requirements can't be fulfilled:

- Patients follow their normal daily routine, i.e. they cannot stop moving during the recording (criteria 1, 2, 3, 4 and 5 not fullfilled)
- Patients do not sleep upright and the body position changes about 1.5 times/h during sleep (criteria 2 and 5). The deviation due to the hydrostatic effect can be up to +/- 15 mmHg for cuff measurements.



Mean BP values (for RR and PTT measurements) according to body position with associated standard deviations. 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 disadvantages of 24h BP measurement with cuff devices:

- Due to the discontinuous measurement, the real maximum and minimum BP values may not be recorded.
- Sleep distruptions: cuff inflation causes arousal 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 disturbing. In many patients this leads to an aversion to 24h ABPM measurements. This is particularly the case when the measurement needs to be repeated.
- Inaccurate measurements due to physical activity during the pumping process cannot be distinguished.

3. THE 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 the plethysmograph).

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:

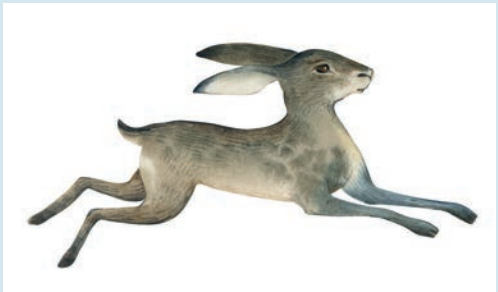
$$E = f(BP)$$

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

Summarized, we get following relationship:

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

The higher the wall tension (= stiff vessels) the higher the PWV 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.



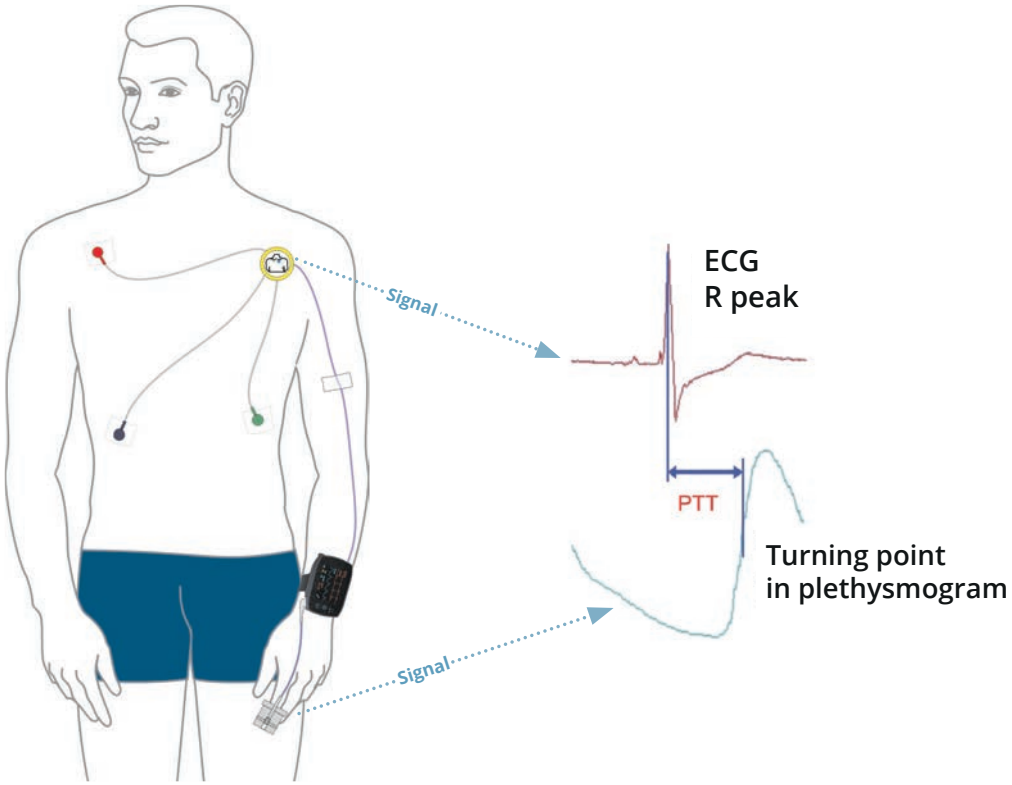
High PWV ▶ short PTT
stiff vessels
high BP

Low PWV ▶ long PTT
smooth vessels
low BP

3.2 Recording of BP using the PTT Method

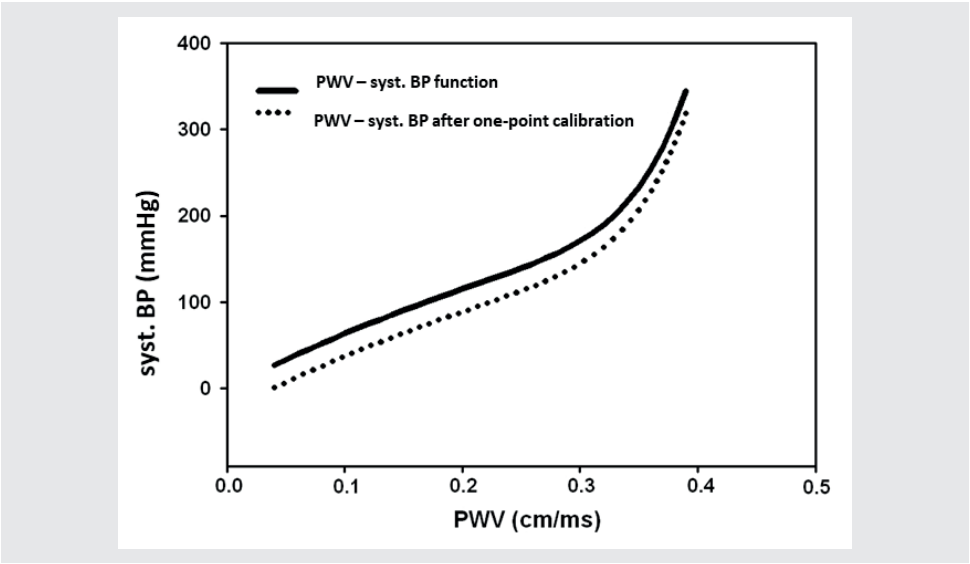
The calculation of systolic (SBP) and diastolic blood pressure (DBP) is based on a non-linear correlation between BP (in mmHg) and PTT (in ms) (5). The PTT method is patented (6) and clinically validated. A validation according the ESH International Protocol (revision 2010) is also available (7).

Measuring the PTT is a simple method for determining a persons 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 an indicator for the arrival of the pulse wave.

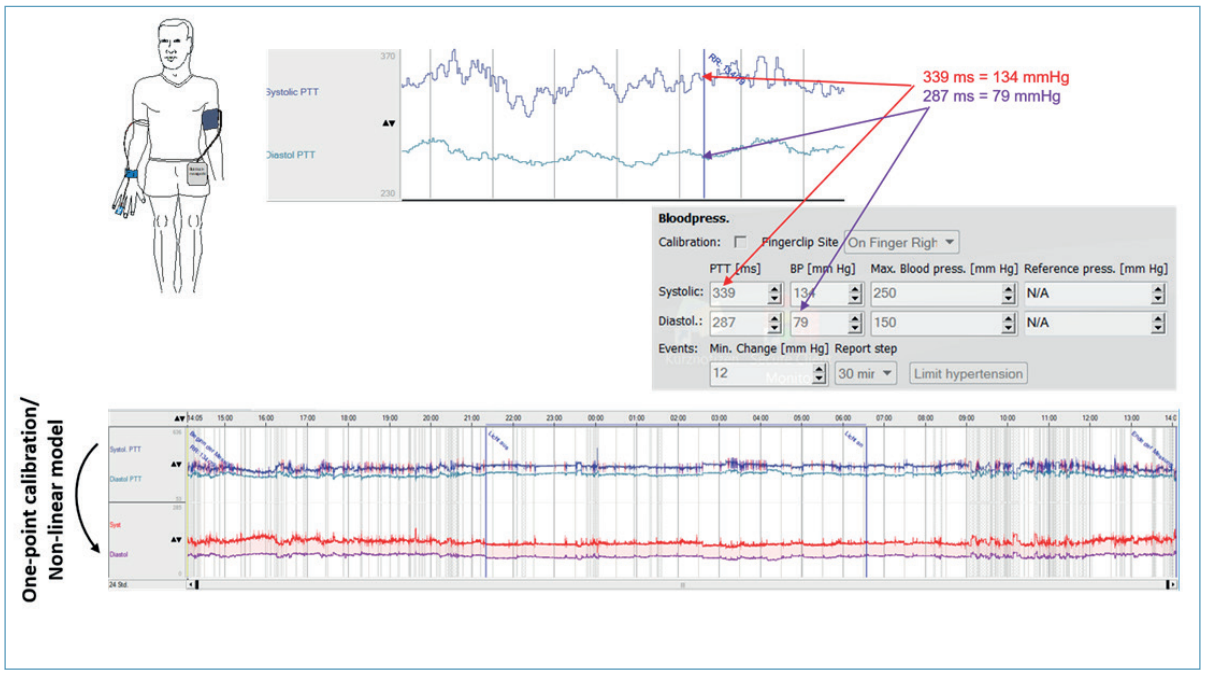


Measurement of the PTT with the SOMNOtouch™ NIBP.

The relation between PWV and SBP follows a non-linear function (5 and see figure right). 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.



A one-point calibration during the ongoing recording is used to correlate the PTT, the BP and the vessel properties. By adding the patient's height (to determine the running distance of the pulse wave), an accurate SBP and DBP value can be calculated for each PTT value.



Beat-to-Beat determination of SBP and DBP by one-point calibration from systolic and diastolic PTT.

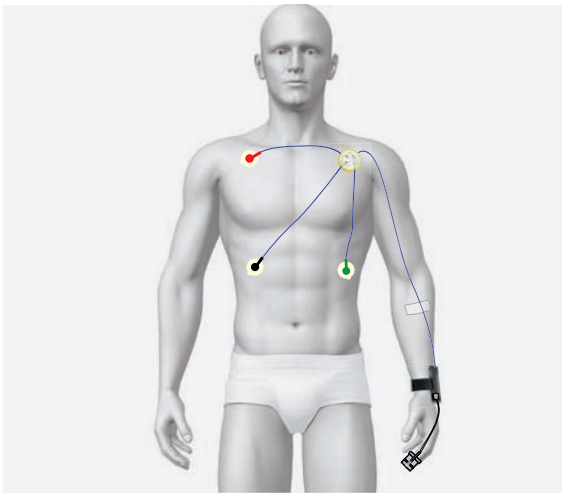
4. THE SOMNOtouch™ NIBP

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

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

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

The SOMNOtouch™ NIBP device.



Application of sensors for SOMNOtouch™ NIBP.

More than just an ambulant BP recording device

- Syst./diast. BP, beat-to-beat
- 3-channel ECG
- SpO_2, Pulse rate
- 12-Bit high-resolution plethysmography
- Body position
- Activity (sleep/wake estimation)

The marker button enables documentation of important events like stress, dizziness, medication intake, etc.

With the internal movement sensors in the SOMNOtouch™ NIBP, motoric activity and body position of the patient are recorded, 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 physiological and psychogenic BP increases during the day.

5. AREAS OF APPLICATION FOR THE SOMNOtouch™ NIBP

The SOMNOtouch™ NIBP allows three simultaneously routine examinations:

- 24h 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 24h Ambulatory BP Measurement

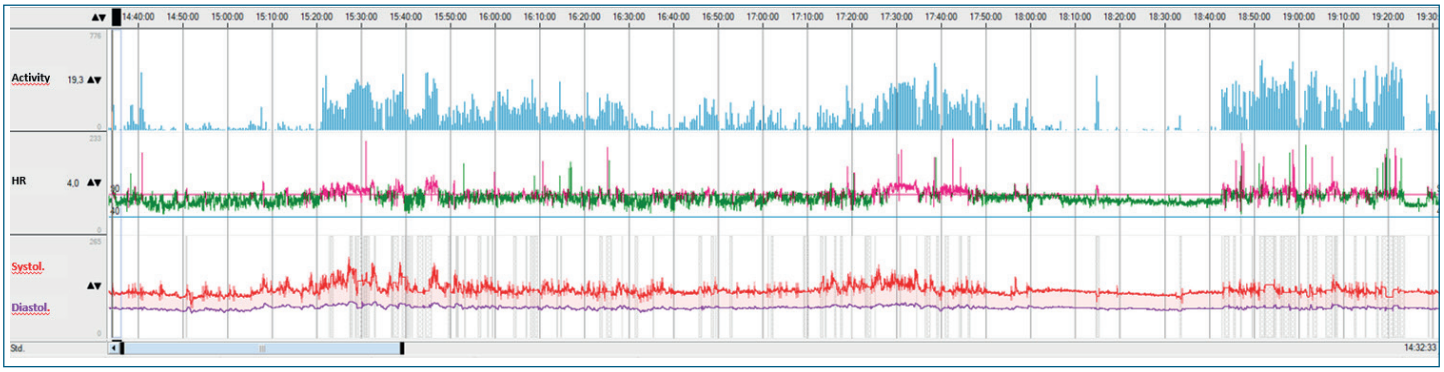
With the SOMNOtouch™ NIBP a continuous, beat-to-beat, systolic and diastolic BP reading over 24h can be performed.

In general, the 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.

Example of a 24h ambulatory BP recording performed with the SOMNOtouch™ NIBP.

Blood Pressure Analysis during Daytime

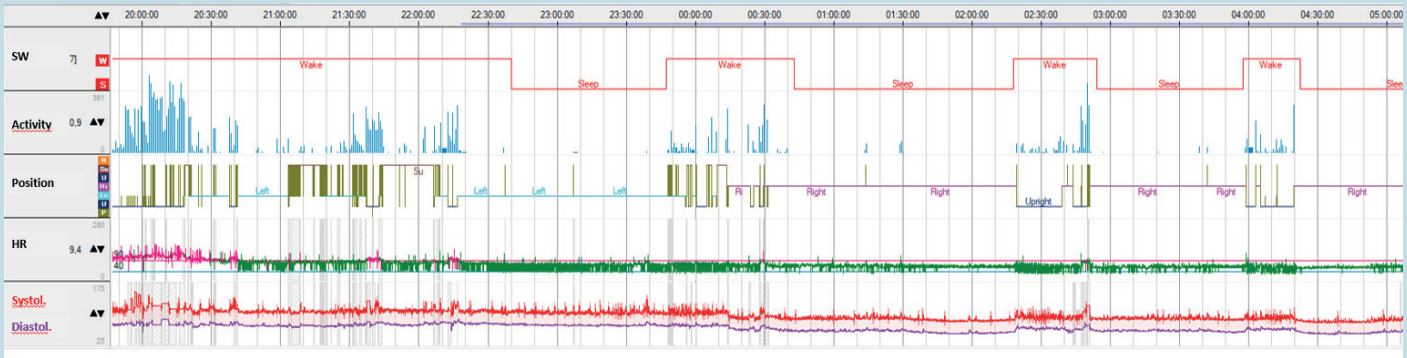
Simultaneous recording of BP and motoric activity allows a differentiation between physically and psychogenically triggered BP increases.



Increase of heart rate (HR) and BP (Systolic/Diastolic) due to motoric activity.

Blood Pressure analysis during Sleep

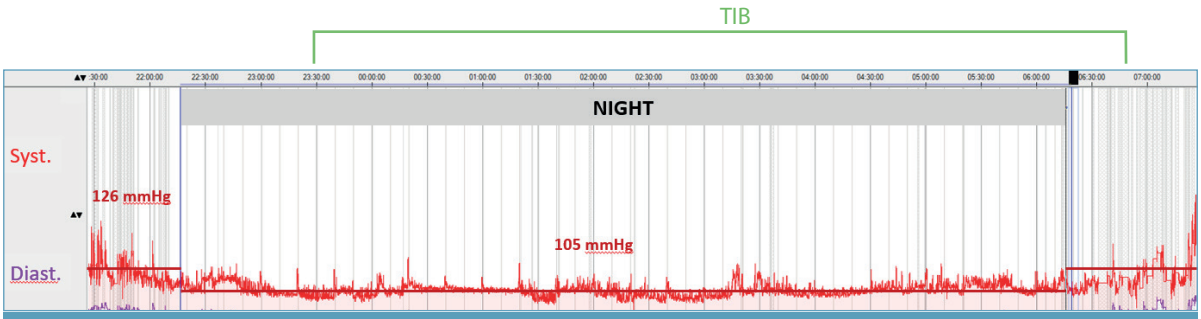
With the help of the sleep/wake analysis (8), BP values can be assigned to periods of sleep or wake and can be considered for analysis.



BP (Systol/ Diastol) during sleep, 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.

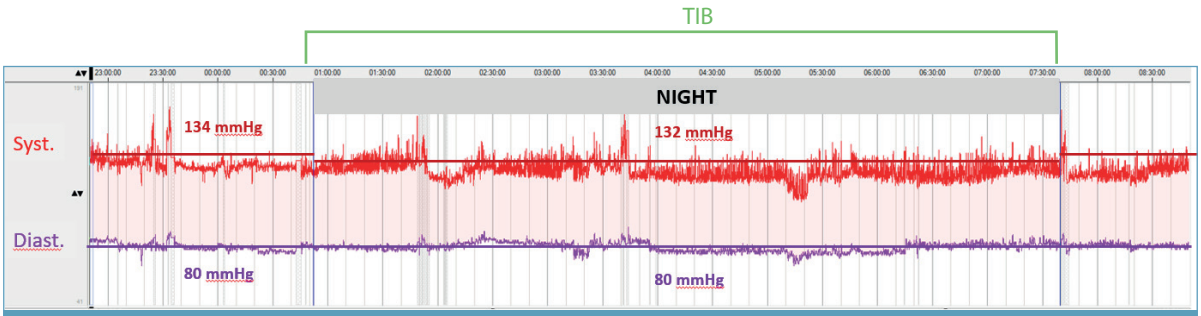
The circadian rhythm of BP has a high relevance from a clinical point of view. Normally, BP drops during sleep by 10 to 20% (Dipper). A smaller drop (Non-Dipper) or even an increase (inverted Dipper) leads to a higher cardiovascular risk. Consequently, in this patient group, a more frequent occurrence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

Dipper



Drop of BP during night for a Dipper (SBP -16.7%, DBP -12.5%)

Non-Dipper



Nocturnal BP behavior for a Non-Dipper (SBP -1.5%, DBP +/- 0%)

The day/night drop of BP can be shown visually (above) and statistically (see the section "Blood Pressure Report" on page 20).

Dipper Classification

Normal Dipper	A nocturnal BP drop of 10% to 20% from daytime level
Non-Dipper	A nocturnal drop of < 10% from daytime level
Inverted Dipper	An increase of BP level at night
Extreme Dipper	A nocturnal 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.

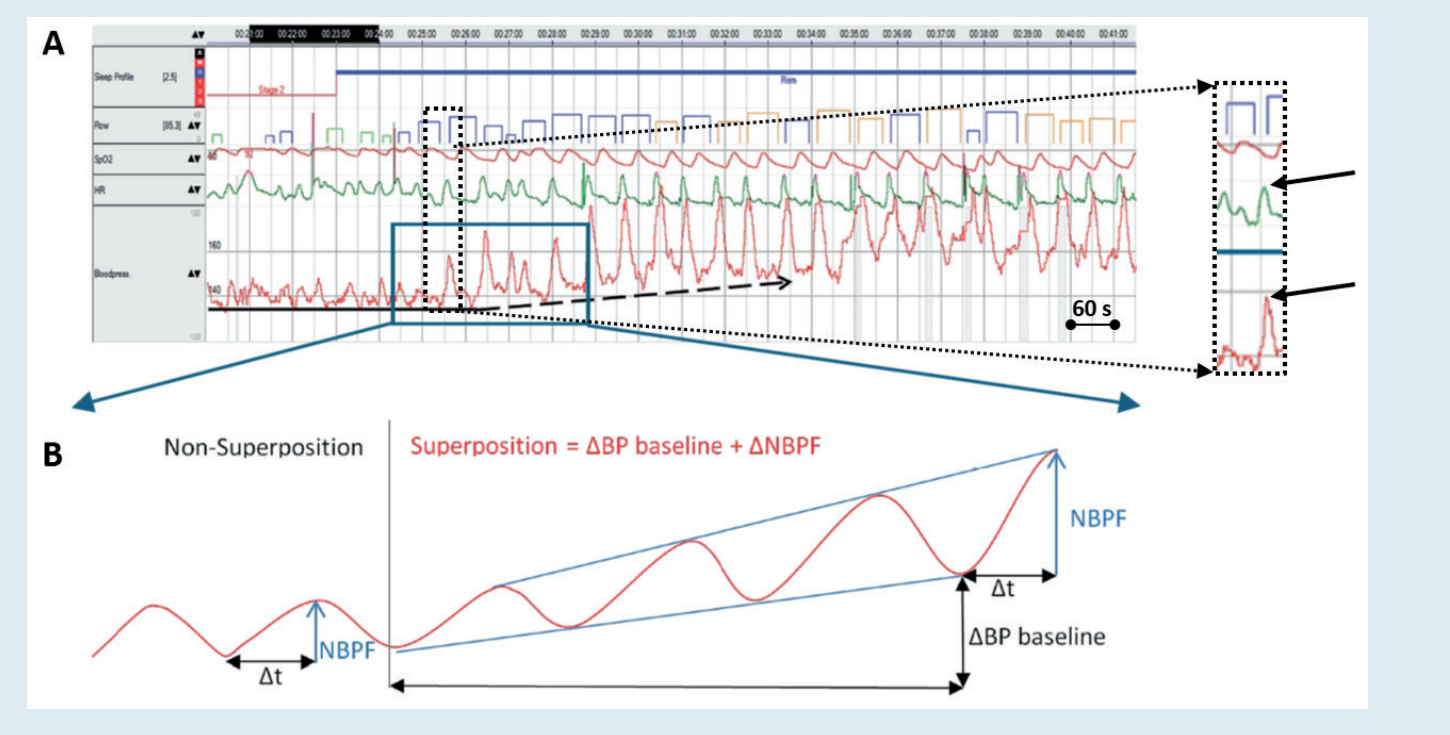
Obviously, respiratory disturbances of sleep such as apnea, hypopnea, snoring, but also periodic leg movements (PLM) provoke a not consciously perceived arousal reactions, each time causing a co-activation of sympathetic and parasympathetic nervous system and short-term systolic blood pressure increases of approximately 27 mmHg and 20 sec duration (= nocturnal BP fluctuations, NBPFs).

The obstructive sleep apnoea 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 behavior 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.

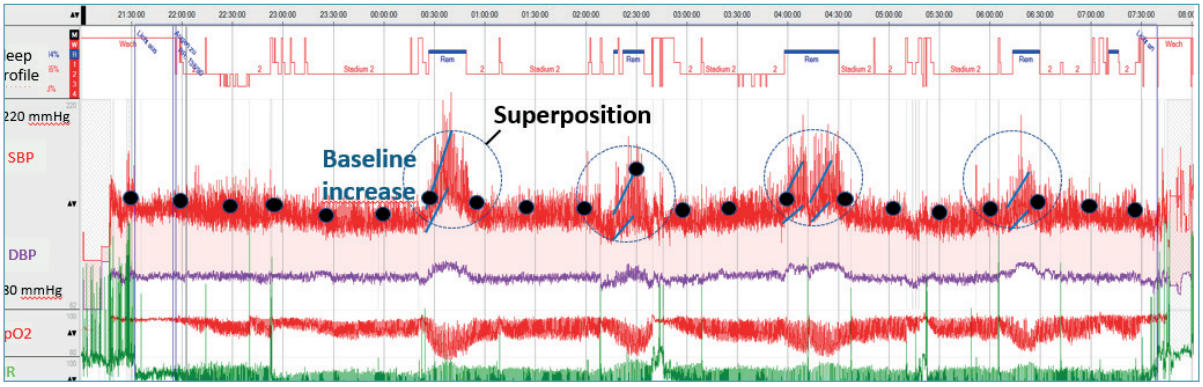
In the study of Gehring et al., night-time SBP was investigated beat-to-beat using the PTT method (10).

97 patients with the diagnosis of OSAS (AHI ≥ 30) were included in the study. A polysomnography (SOMNOscreen™ plus) of night sleep was performed and physiological data were analyzed 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 and showed phenomena of continuous increases of the SBP baseline. Such periods of SBP baseline elevations ≥ 10 mmHg were called “Superposition”. Periods of „Superposition“ were analyzed in comparison to periods of „Non-Superposition“.



(A) Sequence of obstructive apneas (blue) during NON-REM and REM transition (signal track Flow; BLUE = Apnea, GREEN = hypopnea, YELLOW = Mixed apnea) . At the end of an apnea, there is a transient increase of HR (green) and SBP (red); shown 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).



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

In all patients, periods of obstructive apnea were accompanied with NBPFs. That BP transiently increased at the end of each apneic period. Forty-eight patients showed the phenomenon of superposition. A total of 84 periods of superpositions were detected in this group. They occured 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 areas 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.

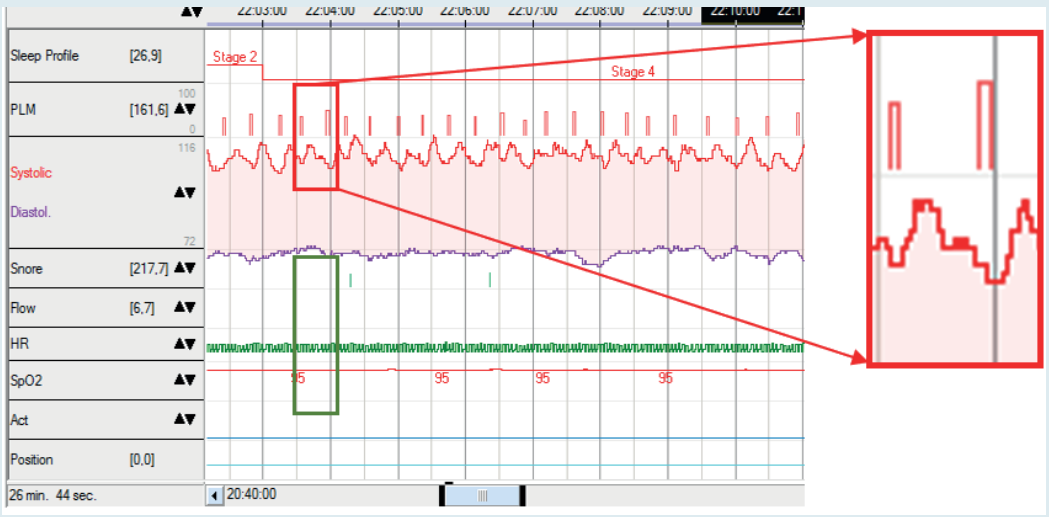
This study demonstrates a new phenomenon, namely the superposition of nocturnal BP fluctuations (NBPF), leading to extremely high BP peaks. Only with a continuous BP measurement based on PTT, can one see these superposition periods. These BP elevations reflect sympathetic activation and might be important 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 aponoe-indicated BP increases in order to reduce the cardiovascular risk to the patient.

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 in 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 (11). The RLS can lead to sleep disorders and is associated with cardiovascular diseases including hypertension.

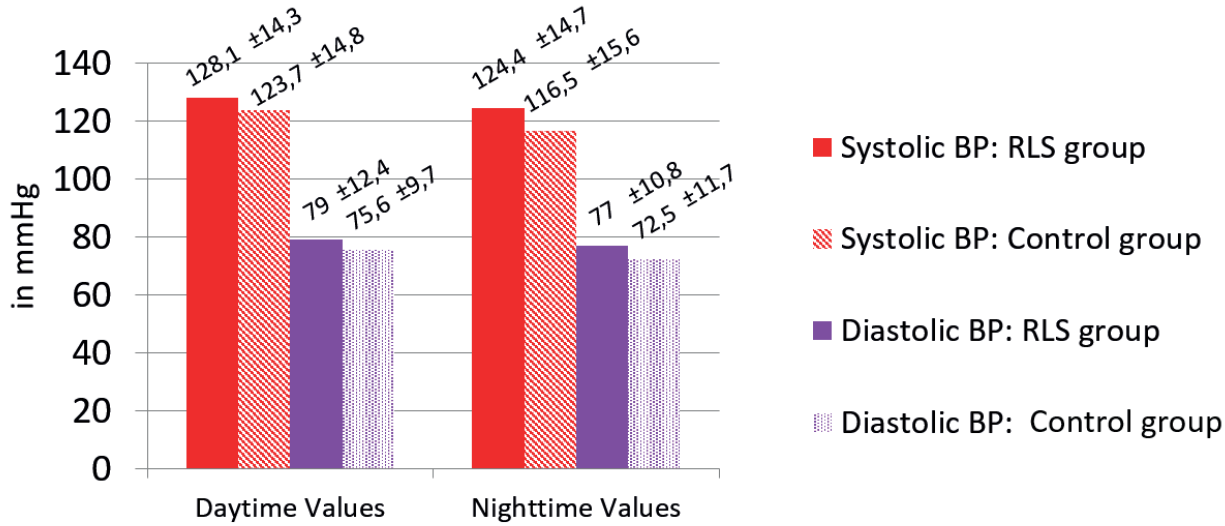
To test the hypothesis that nocturnal BP is higher in patients with RLS than in subjects without sleep disorders, patients (30 RLS patients, 27 controls) were polysomnographically



Example measurement of a patient. Periodic leg movements (highlighted in red) 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.

examined (SOMNOscreen™ plus) including beat-to-beat measurement by the PTT method (11). 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 behavior was found in the RLS group.

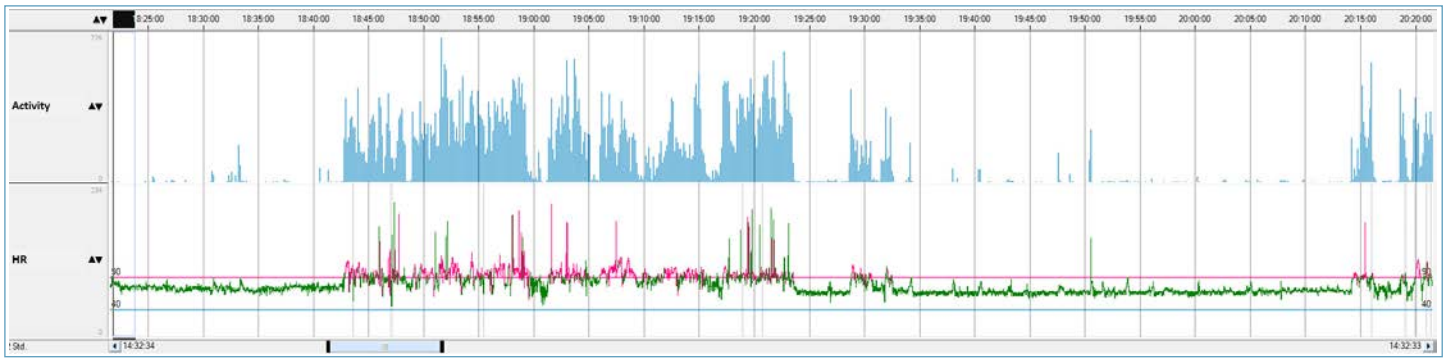


Values of BP in patients with RLS and controls (adapted from (11)).

This study showed that patients with RLS have significant higher BP values during the night and a Non-Dipping behavior could be observed int this patient group. Patients with RLS require a close observation with regard to cardiovascular risk factors, i.e. 24h ambulatory blood pressure measurement (ABPM).

5.2 Long-term ECG (up to 24h)

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. Utilising the integrated acceleration sensor, motoric activity can be compared to the heart rate. With this - activity related rhythm disturbances can be detected and diagnosed.



Increase of the motoric activity (Act) with simultaneous increase 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 (an additional cost option).

Screenshot of the Schiller Darwin2 software interface.

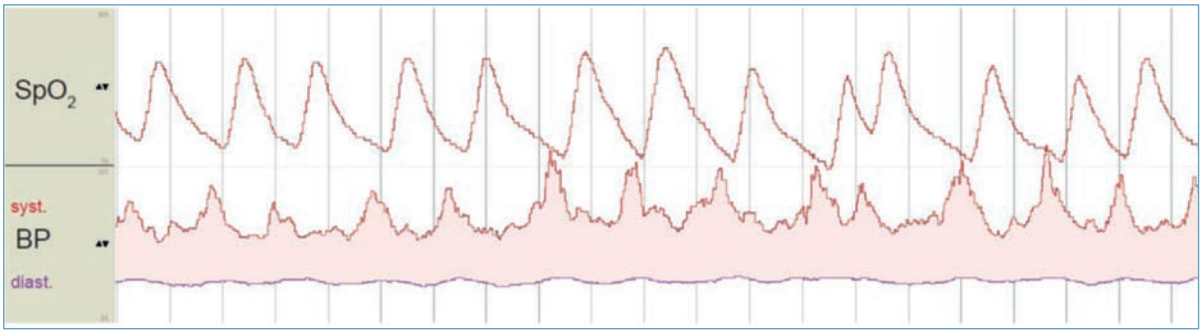
5.3 Extended Diagnosis

Oximetry

Utilising 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) (13). 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.



Comparison of the oxygen saturation (above) and the 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 the measurement, users also have the option to create, export and print out a comprehensive report. In the detailed 24h BP report the following information is included:

Blood pressure Day/Night

Total report

	∅ Min.	Aver.	∅ Max.	SD	> Limit
Syst. [mmHg]	90	**118**	**179**	12,9	4,8 %
Diast. [mmHg]	65	**85**	110	8,2	41,5 %
HR [bpm]	47	92	153	23,7	57,4 %
MAP [mmHg]	75	**96**	132	9,5	17,6 %
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**	**179**	9,6	6,5 %
Diast. [mmHg]	68	**91**	110	4,2	51,8 %
HR [bpm]	58	101	153	18,8	81,1 %
MAP [mmHg]	79	**103**	132	5,7	20,1 %
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**	92	3,9	18 %
HR [bpm]	47	60	85	5,0	3,8 %
MAP [mmHg]	75	**85**	100	4,2	12 %
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

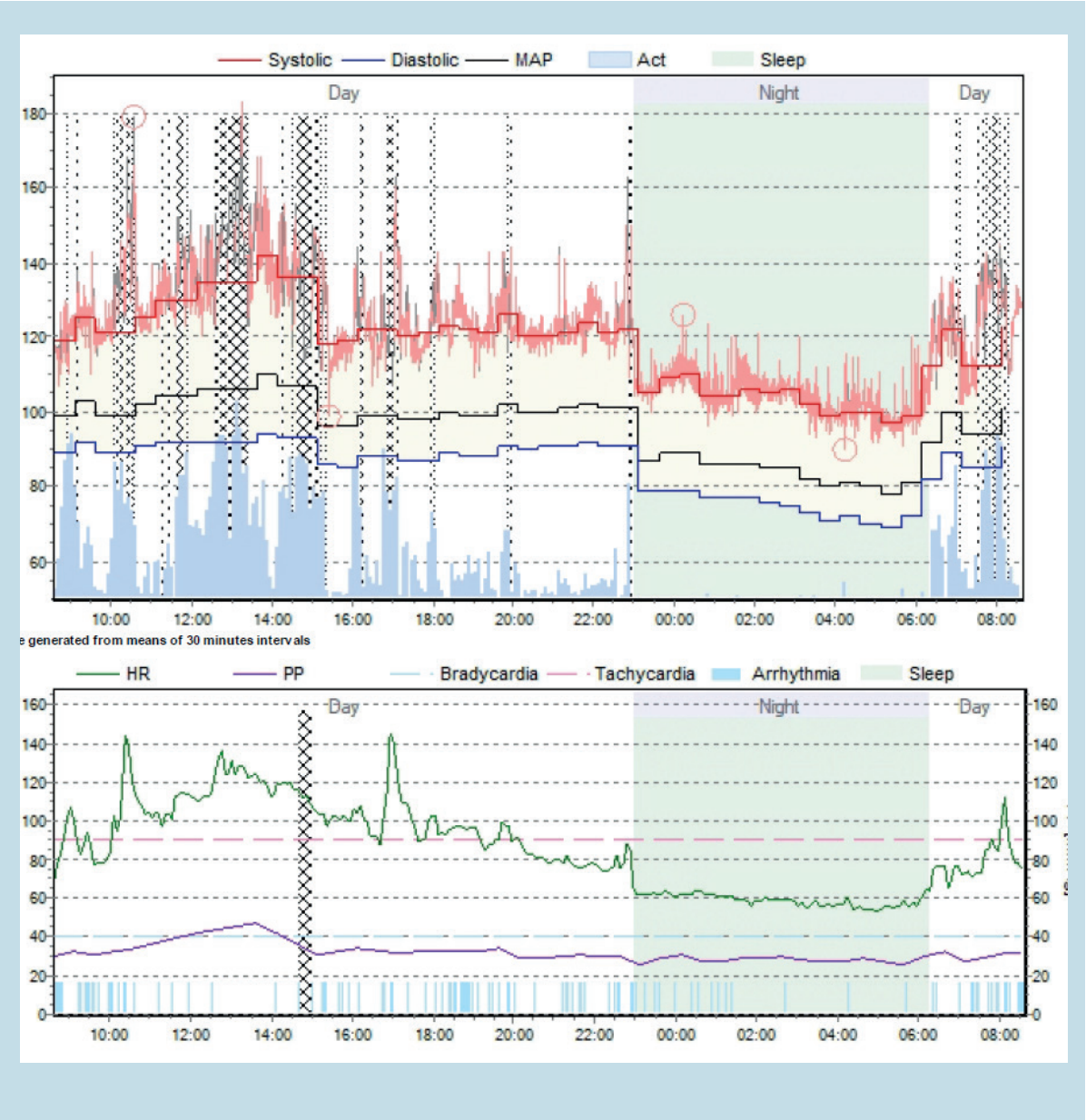
Classification according to the mean blood pressure during day.

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" shows the percentage of recording time, in which a parameter exceeds a defined limit (this is set as a default to the ESH/ESC guidelines but can also be set by the user).

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

The dipping behavior as well as classification of BP levels according to the applied parameters and can be seen be easily seen at a glance.



A graphical overview from the entire recording is also displayed. The upper part of the figure shows the systolic and diastolic BP, the mean arterial pressure (MAP) and the activity (Act). In the lower part the patients heart rate (HR) and pulse pressure (PP) are presented. Arrhythmias are indicated and the sleep time (TIB) is highlighted as a light green panel behind the graph.

Conventional BP recording

No. BP-Values: 89538 (82% TRI)

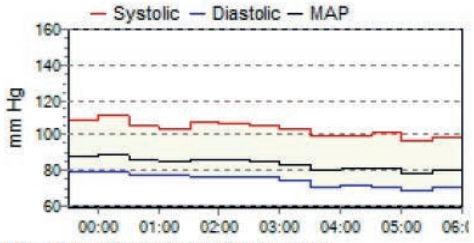
Time	Ø BP [mm Hg]	BP [mm Hg]	Ø HR [bpm]	HR [bpm]	Ø Activity [mg]	Desat.
18:00:00	127 / 89	128 / 88 (W)	102	104	138	-
18:15:00	123 / 89	122 / 89 (W)	94	96	21	-
18:30:00	123 / 89	A (W)	96	102	38	-
18:45:00	126 / 91	121 / 92 (W)	98	96	46	-
19:00:00	119 / 86	125 / 88 (W)	97	97	64	-
19:15:00	120 / 88	119 / 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)
13.12.2016 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	-
Ø Day (6-22 o'clock)	124 / 90	125 / 90	98	97	113	
Ø Night (22-6 o'clock)	106 / 77	106 / 79	63	61	9	
Ø 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 SpO2 analysis, if patient asleep
(W/S): Sleep/Wake state at the given time index
Green rows: Intervals the patient spent predominantly in sleep

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 user-defined) and desaturations (only during sleep). Desaturation events are detected when blood oxygen saturation is decreased >4%. Sleep is once again highlighted in green.

Nocturnal Blood Pressure Fluctuations (NBPF)

	Number (Index)	Time
Inc. (Index)	**68 (9,4)**	
Maximum Increase (mmHg)	34	01:01:01
Average Increase (mmHg)	16	
Max. Systolic (mmHg)	**126**	**00:12:19**
Min. Systolic (mm Hg)	90	04:13:54
Average Systolic (mmHg)	105	
Artefact (min)	5 (1,1%)	

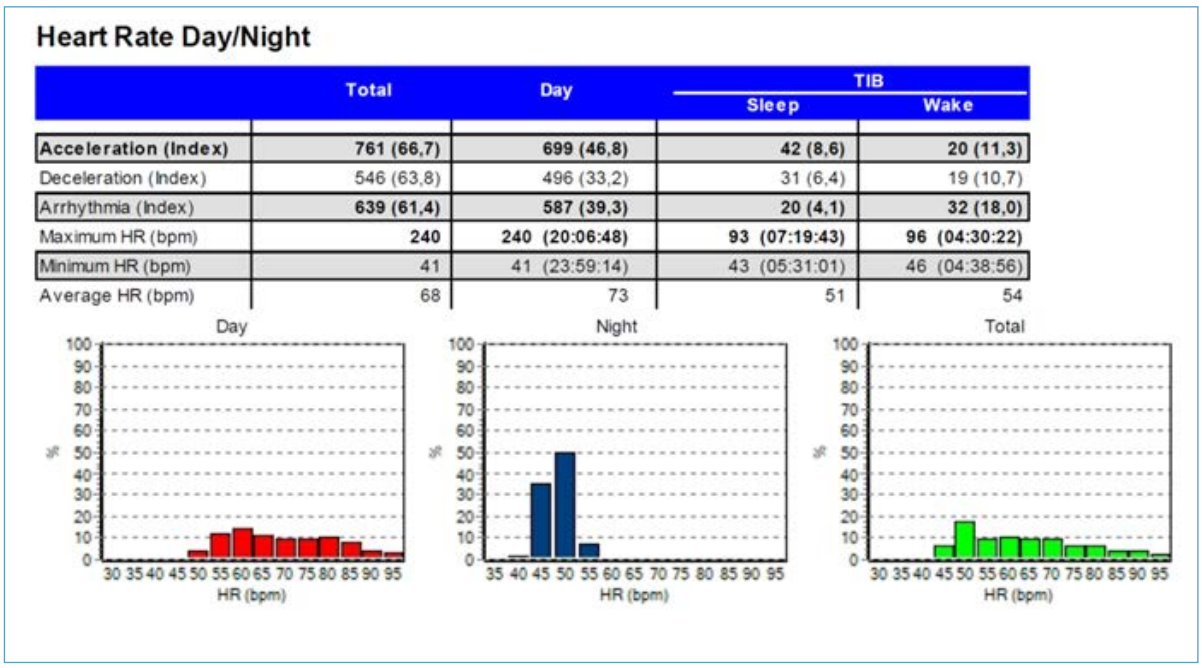


Def. NBPF: Continuous blood pressure increase higher than 12 mmHg within 3 – 30 seconds. Min and Max computed as mean value from 8 values.

The NBPF™ (Nocturnal Blood Pressure Fluctuations) are shown as an indicator for cardiac stress. 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 its recommended that a patient with a high number of NBPBs should undergo further cardiorespiratory screening.

6.2 Heart Rate Report

With the Heart Rate Report function in the software, the users will find an 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.

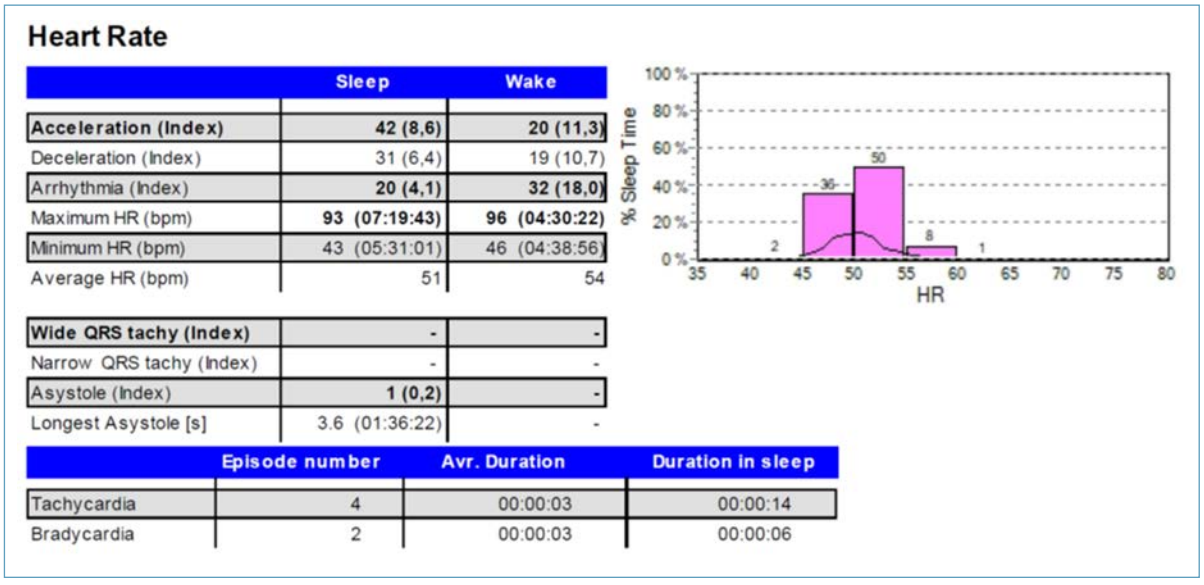


Heart Rate Day/Night

	Total	Day	TIB Sleep	TIB Wake
Acceleration (Index)	**761 (66,7)**	**699 (46,8)**	**42 (8,6)**	**20 (11,3)**
Deceleration (Index)	546 (63,8)	496 (33,2)	31 (6,4)	19 (10,7)
Arrhythmia (Index)	**639 (61,4)**	**587 (39,3)**	**20 (4,1)**	**32 (18,0)**
Maximum HR (bpm)	**240**	**240 (20:06:48)**	**93 (07:19:43)**	**96 (04:30:22)**
Minimum HR (bpm)	41	41 (23:59:14)	43 (05:31:01)	46 (04:38:56)
Average HR (bpm)	68	73	51	54

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

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 sympatho-vagale balance thereof. These analyses can be displayed with the HRV Report/Stress Report or as a Poincaré-Plot (not shown).



Heart Rate

	Sleep	Wake
Acceleration (Index)	**42 (8,6)**	**20 (11,3)**
Deceleration (Index)	31 (6,4)	19 (10,7)
Arrhythmia (Index)	**20 (4,1)**	**32 (18,0)**
Maximum HR (bpm)	**93 (07:19:43)**	**96 (04:30:22)**
Minimum HR (bpm)	43 (05:31:01)	46 (04:38:56)
Average HR (bpm)	51	54
Wide QRS tachy (Index)	-	-
Narrow QRS tachy (Index)	-	-
Asystole (Index)	**1 (0,2)**	-
Longest Asystole [s]	3.6 (01:36:22)	-

	Episode number	Avr. Duration	Duration in sleep
Tachycardia	4	00:00:03	00:00:14
Bradycardia	2	00:00:03	00:00:06

6.3 O_2 Report

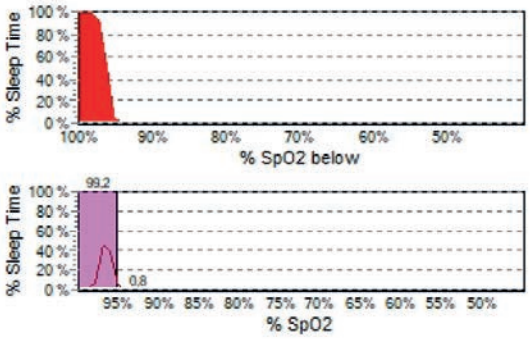
With the report function, users get an overview of the SpO2 analysis which provides detailed information about the respiratory status of the patient during the night.

A table and a graphical overview contain detailed information about the respiratory status of the patient during the night.

Oxygen desaturation index (ODI): number of desaturations of more than 4% per hour sleep.

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%)	



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 the information about BP during sleep. This allows conclusions to be drawn about nocturnal BP behavior and to determine dipping/non-dipping patients.

Non-reactive, cuffless and non-invasive:
- high patient comfort: no sleep disturbance due to an uncomfortable cuff inflation.
- no distortion of nocturnal BP values caused by cuff based arousal reactions.

Arrhythmias:
Many 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 cuased by changes to the body position are 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 physiologically and psychogenically caused hypertension

Internal sleep/wake-analysis (8):
Individual sleep phases can be defined and corresponding BP values are evaluated. Dipping/Non-Dipping behavior can be determined more reliably.

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 behavior during day and night.
- The dipping behavior of the BP can be more reliably determined because the real sleep time is determined.
- The SOMNOtouch™ NIBP can be used to diagnose white-coat hypertension, masked hypertension or orthostatic hypotension, and for therapy monitoring.

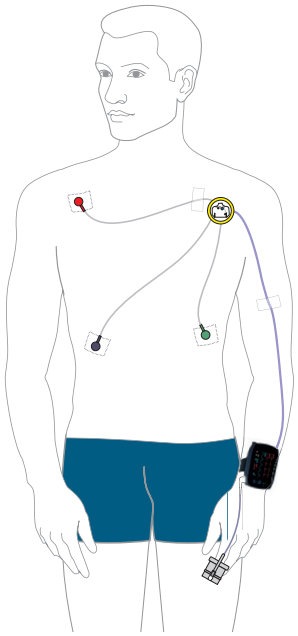
Comparison of cuff-based vs. PTT Method		
Measurement method	discontinuous	Beat-to-Beat
No. of measurements/ 24 h	80	86.400
Movement artefacts	15 %	15 %
Disturbance of sleep	18 %	-
Arrhythmia	7 %	-
Remaining BP values	48	73.440
Body position effect	high +/- 15 mmHg	low +/- 6 mmHg

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

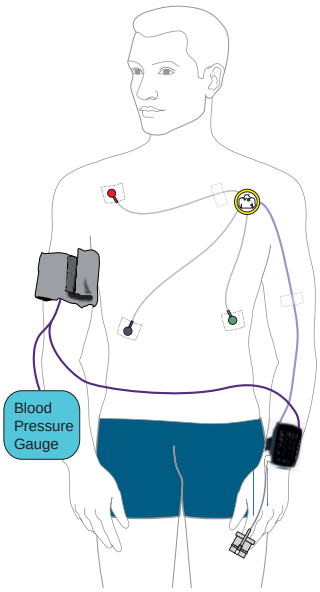


1. Apply SOMNOtouch™ NIBP on the non-dominant wrist
2. Clean the area of the skin where the electrodes will be placed. Connect the disposable ECG electrodes to the electrode cables. Connect the sensor to one of the free AUX connections.
3. Adhere the electrodes as close as possible to the collarbone (the bony area of the skin is ideal).
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

IMPORTANCE OF CALIBRATION

For calibration of the PTT device a single manual BP measurement during the current measurement is required. To do this, apply the cuff of an external BP monitor on to the opposite arm to the one with the SOMNOtouch™ NIBP.

Requirements for the patient during the calibration process:



1. Patient is at rest for 5-10 min before the measurement
2. Sit straight, relaxed and do not cross legs
3. Do not talk and do not move
4. Put arms on a table: Cuff should be at heart level
5. Choose the right cuff size
6. Ensure the correct application of the cuff

Calibration is imperative for a PTT based BP measurement.

8.2 Troubleshooting

You can solve many problems with the SOMNOtouch™ NIBP yourself. The following list shows the most common errors and suggestions to fix the problem.

Problem	Possible cause	Solution
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 correct fingerclip size
A recording cannot be transferred	Hard disk is full	Archive all recordings and then delete them from the hard disk
		Has Windows logged off the network drive? Check in Windows explorer if there is a red X next 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 are 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.
	Height of patient is not entered correctly	Check values
	Systolic od diastolic BP not entered correctly in the FW or SW	Check values

Problem	Possible cause	Solution
	BP was calibrated in anarea with artefacts	Relocate calibration area
One channel was not recorded	Montage was not correctly programmed	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, activate a default printer
Error 002 on the display	An internal memory error	Device must be returned for repair

If you need further support, you are welcome to contact our support team.

Our service is free of charge and can be accessed 24/7.

☎ **+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 ± 6.1mmHg 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
Haberl et al. (in preparation)	n = 30	24 hours contralateral arm	RR (cuff)	SBP: r = 0.89 (n = 921) DBP: r = 0.7 (n = 921)	1.4 mmHg; +18/-15 mmHg
Hulpke-Wette et al. (2018, poster)	n = 27 (100 planned) Age: 5-18	24 hours contralateral arm	RR (cuff) (Manschette)	SBP: r = 0,8 DBP: r = 0,7 (n = 228)	2,2 mmHg; +22/-17 mmHg 4,8 mmHg; +22/-12 mmHg
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
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	

9.1 Validation of the SOMNOtouch™ NIBP according to ESH 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 (14).

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 as required by the ESH-IP (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 1).

Table 1 Validation results (adapted from Bilo et al.):

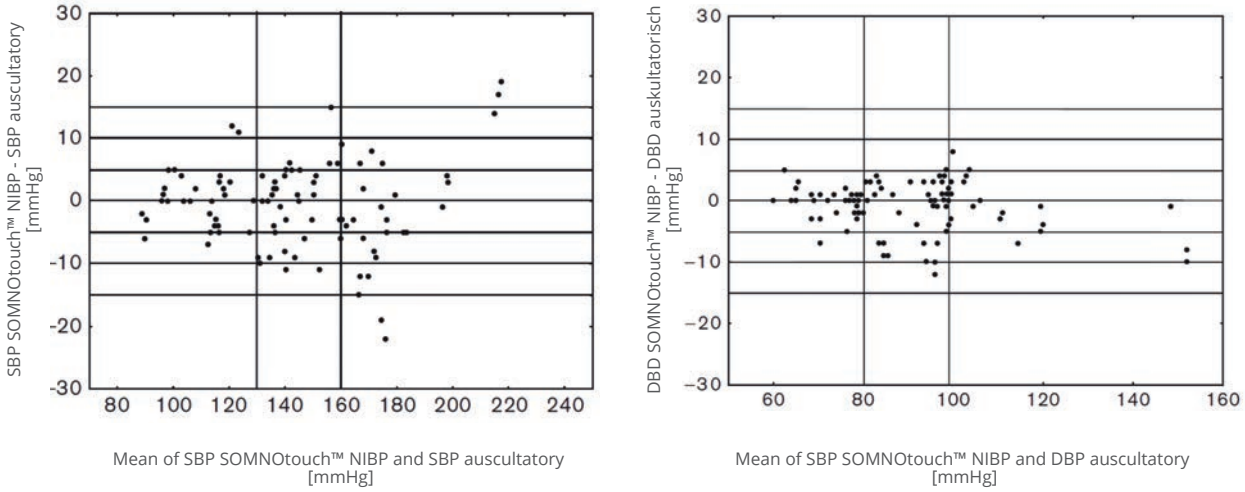
Requirement	≤ 5 mmHg	≤ 10 mmHg	≤ 15 mmHg	2/3 ≤ 5 mmHg**	0/3 ≤ 5 mHg***	Result
required	73 oder 65*	87 oder 81*	96 oder 93*	≤ 24	≤ 3	
SBP - achieved	75	90	96	28	2	PASS
DBP - achieved	90	99	99	31	1	PASS

* 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 absulte 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 below, left). For DBP, a strong correlation of 0.976 with a device-observer disagreement of 0.33 +/- 3.4 mmHg was detected (see figure below, right).

The SOMNOtouch™ NIBP fulfills 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.



Scatter plots comparing SOMNOtouch™ NIBP and auscultatory measurements of systolic (left) and diastolic (right) BP values (adapted from Bilo et al.).

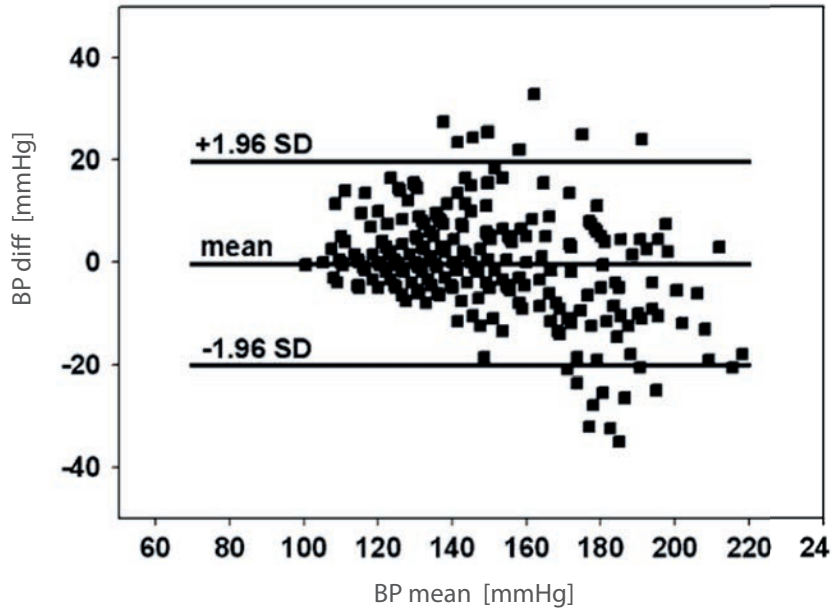
9.2 Comparison of the PTT Method against **CUFF-BASED Method: during ERGOMETRY**

Continuous blood pressure measurement by using the pulse transit time: comparison to a cuff-based method.

Gesche, H., et al. (2011), 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 2,5W/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.

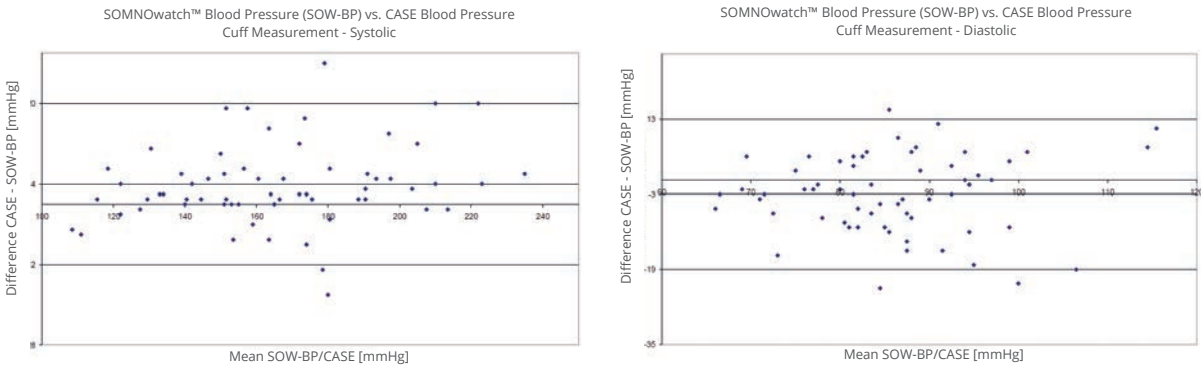


Bland-Altman Plot PTT vs. RR.
93.5% of pairs of values are inside the "limits of agreement". The outliers are based on artefacts which occur due to movement during intensified excercise.

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 (15).

A standard exercise test was performed with 21 subjects (age 54 years +/- 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.



Bland-Altman plots for SBP (left) and DBP (right).

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

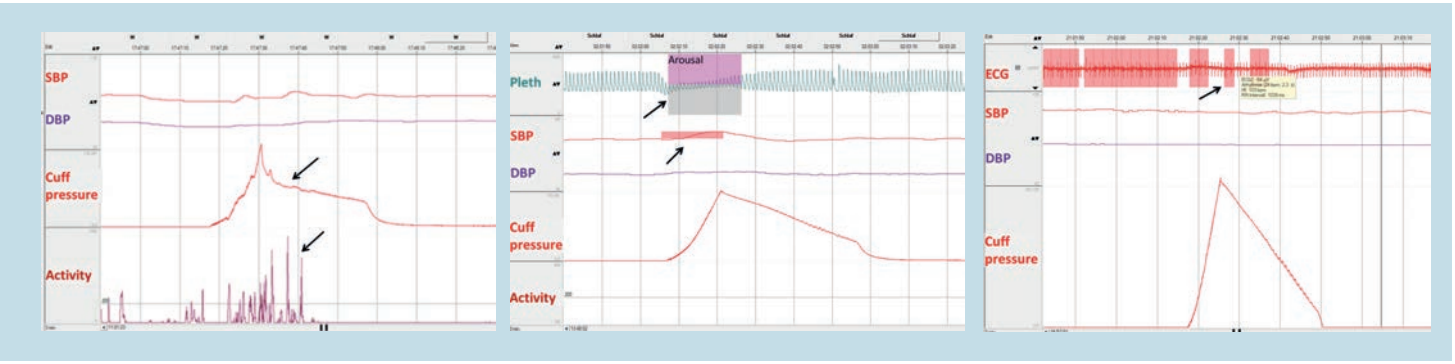
Continuous and non-invasive blood pressure measurement based on pulse transit time: Comparison to oscillometric 24 h ambulatory blood pressure measurement.
Haberl, R., et al., in preparation.

Ambulatory blood pressure monitoring (ABPM) with cuff is considered the gold-standard for diagnosis of hypertension and assessment of cardiovascular risk.

This study aimed to investigate the reliability of the PTT method compared to oscillometric ABPM (12).

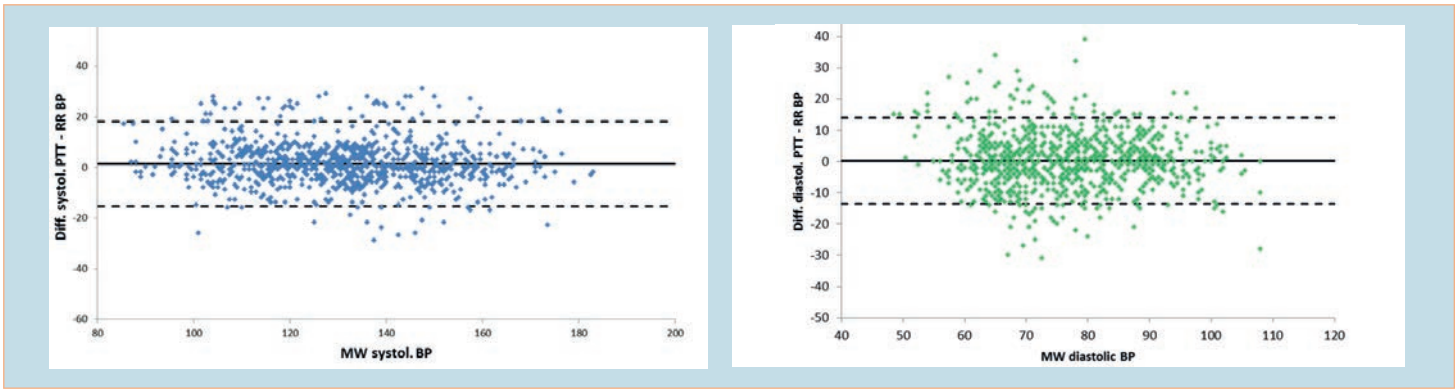
SBP and DBP were measured in 30 adults (9 women, mean age 65.5 +/- 9.3 years) using an oscillometric ABPM device at intervals of 15 min (6-22 h) and 30 min (22-6 h). Simultaneously, BP was recorded beat-to-beat based on PTT (SOMNOtouch™ NIBP) on the contralateral arm. In addition to BP, a 3-channel ECG, motoric activity, finger plethymogram, oxygen saturation and cuff pressure were recorded by the SOMNOtouch™ NIBP.

The PTT method and oscillometric ABPM revealed a moderate agreement in direct comparison (SBP: r = 0.77 and DBP: r = 0.53; n = 1293). The limits of agreement in Bland-Altman plot were +28 and -25 mmHg, with a mean difference of 1.6 mmHg for SBP (DBP: +30 and -26 mmHg; mean difference of 1.9 mmHg). However, it was found that 29% of all measurements were affected by the following cuff related artefacts: motoric activity (18%), arrhythmia (5%) and arousal reactions during sleep (6%, corresponding to 18% of all nocturnal BP measurements). Examples for cuff-related artefacts are shown below:



Original data showing PTT based SBP, PTT based DBP, plethysmogram (Pleth), cuff pressure, activity and ECG. Example traces indicating an artefact during cuff pumping caused by motoric activity of the patient (left), arousal reaction (middle) and arrhythmia (right). The arrows highlight artefact sources during cuff measurement.

After exclusion of values affected by artefacts, the agreement between both methods considerably increased (SBP: r = 0.89; DBP: r = 0.7; n = 921). The limits of agreement in Bland-Altman plot for SBP were +18 and -15 mmHg with a mean difference of 1.4 mmHg (DBP: +14 and –13 mmHg; mean difference of 0.3 mmHg, see figure below).



Bland-Altman plot of SBP (left) and DBP (right) values.

The present study aimed to collect clinical performance data for the SOMNOtouch™ NIBP in order to demonstrate its long-term measurement qualification over a time period of up to 24 hours in comparison to a conventional cuff-based ABPM.

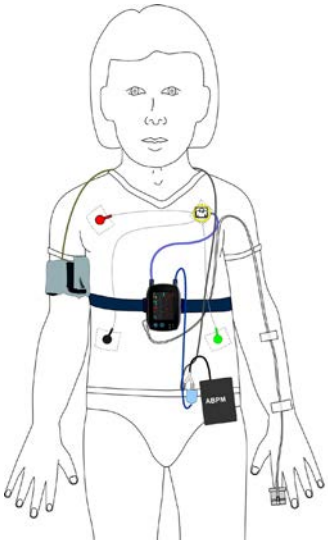
PTT based SBP and DBP is comparable to BP values obtained with the oscillometric ABPM method after removal of cuff-based artefacts such as motoric activity, arrhythmia and arousals. Overall, this study demonstrates that the PTT method is a reliable and favorable method for BP measurement over 24 hours.

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.

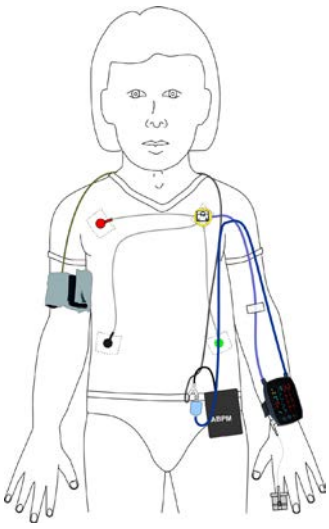
Previous studies in adults have shown a good agreement between conventional ABPM and the PTT method for determination of BP.

In this study (currently recruiting patients), both methods are compared over 24 hours in children (100 planned, 5-18 years) (17).

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:



5-12 years: application at thorax via belt.

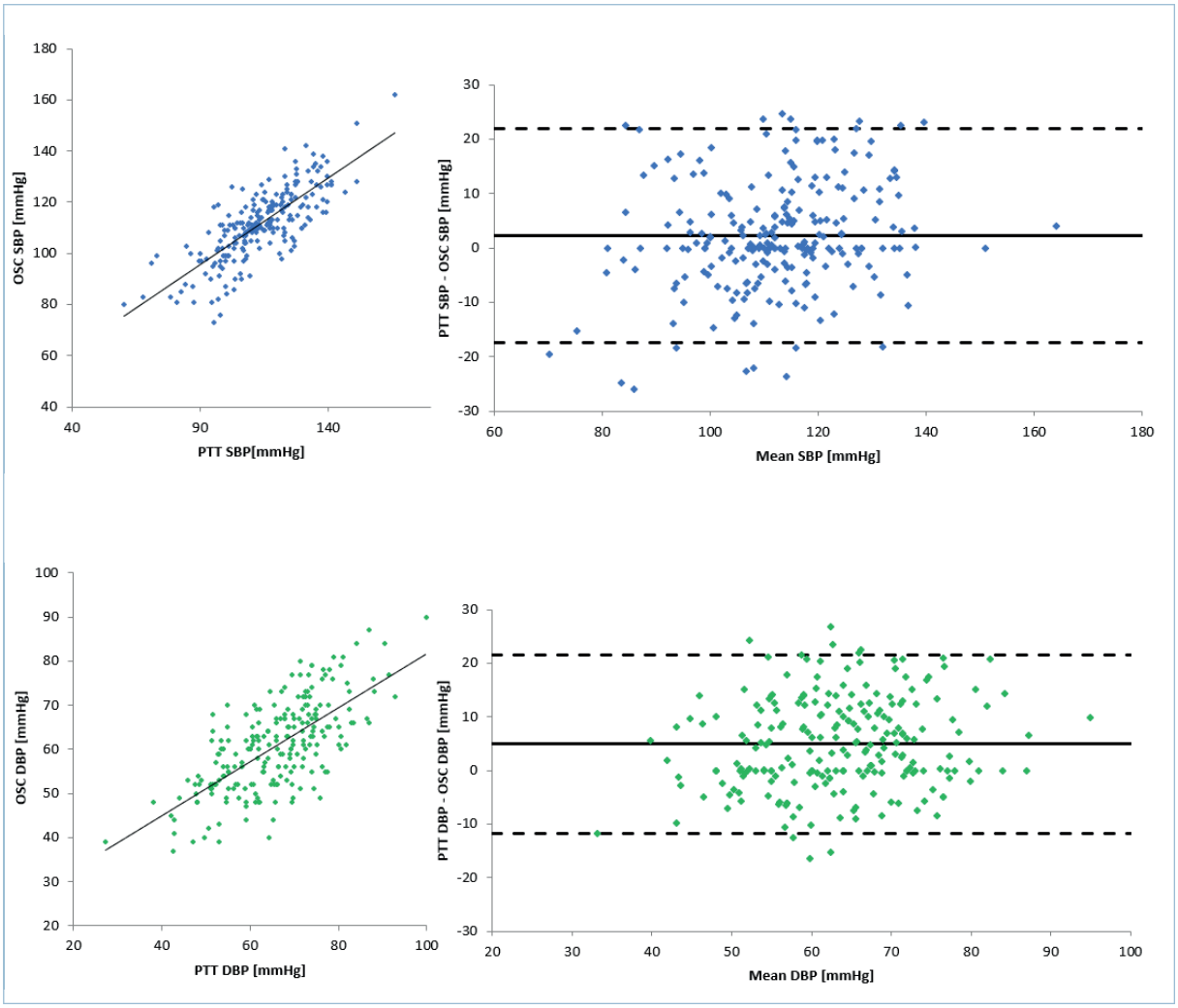


13-18 years: application at wrist.

SBP and DBP are determined over 24 hours using an ABPM device at intervals of 2/h during daytime (6-22 h) and 1/h during night-time (22-6 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 below).



Scatter plots and Bland-Altman plots of SBP (blue) and DBP (green) values.

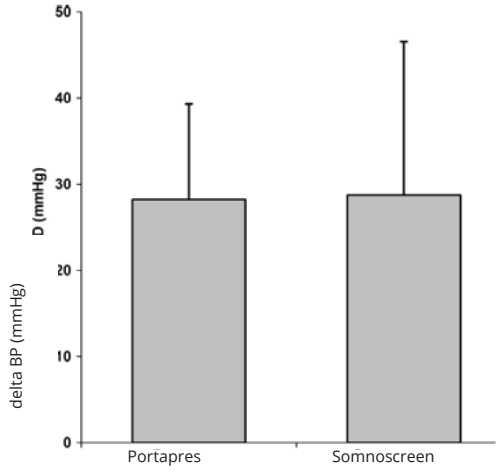
Our preliminary results imply that PTT and ABPM-based BP values are closely correlated in children during a 24-hour measurement if invalid recordings were excluded. Despite the generally high activity of children, the PTT method provides considerably more BP values than the cuff-based method.

9.4 Comparison of the PTT Method against **PENAZ-Method**

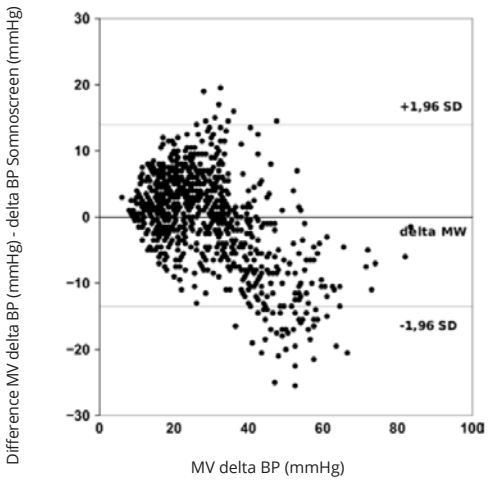
Measurement of apnea related blood pressure changes using pulse transit time and Penaz principle (translated from German).
Hennig A, et al. (2012), Atemwegs- und Lungenerkrankungen, 38(11): p. 447–454.

A causative relationship between arterial hypertension and obstructive sleep apnoea (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, we validated the PTT method against the Portapres System from the company FMS (18). Eleven patients with diagnosis of sleep apnoea were polysomnographically investigated. The SBP was recorded for 8 hours using the PTT method and the Penaz method.

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



Mean values of apnoe-induced BP increases.



Bland-Altman plot of apnoea-induced BP increases.

It could be shown that apnoea/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.

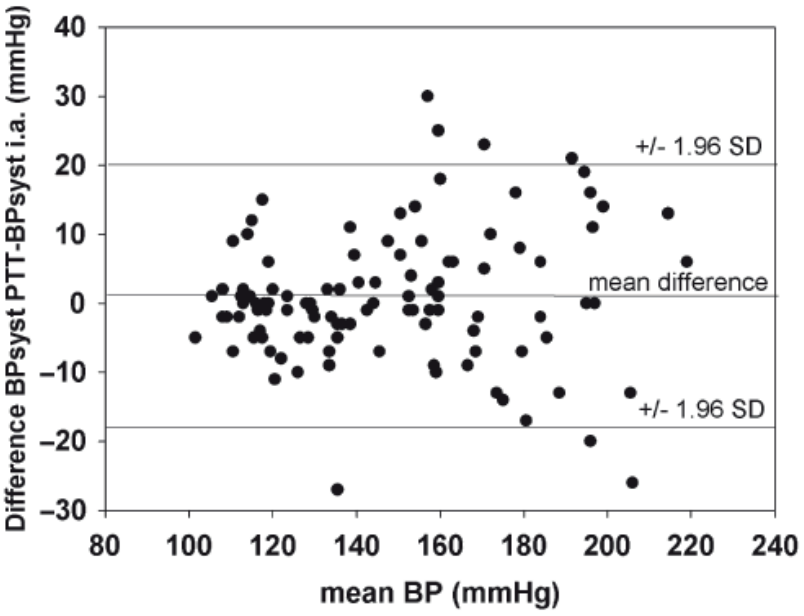
9.5 Comparison of the PTT Method against INVASIVE Blood Pressure Recording: DOBUTAMINE

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 (19).

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 blood pressure 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.



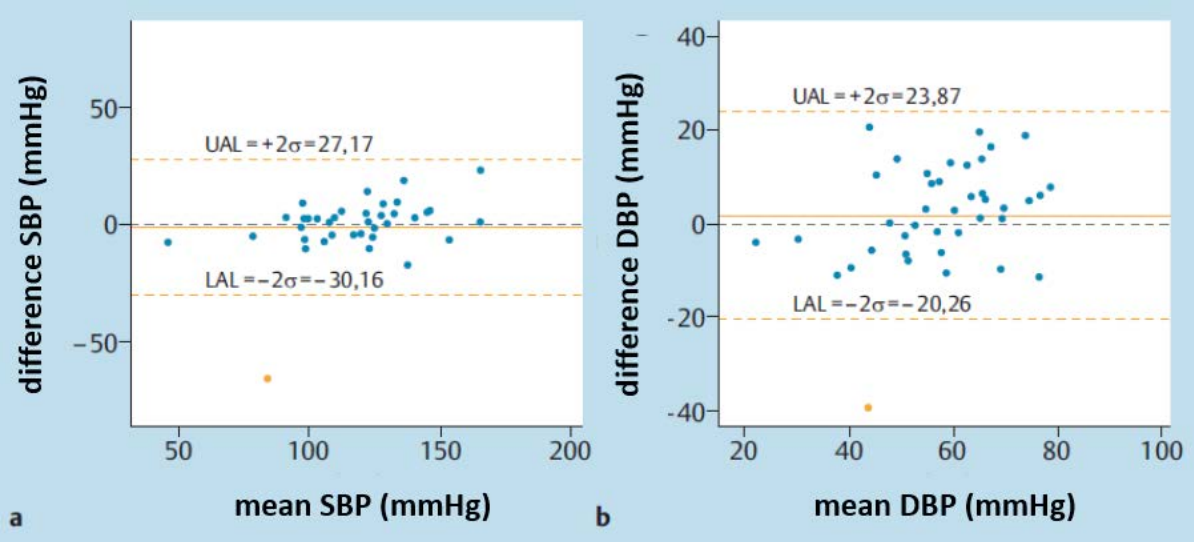
Bland-Altmann plot of SBP of all patients (n = 107).

9.6 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) (20). 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 arrhythmia 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).

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 analyzable data compared to the gold standards.



Bland-Altman plot of SBP and DBP values in whole group (adapted from Bartsch et al.).

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:

- SBD and DBD
- ECG
- SpO_2
- Finger pulse waveform (plethysmogram)
- Motoric activity
- Body position
- Patient marker

Specifications:

- High resolution, color touch display, resolution 320 x 240 pixels
- Size and weight: 74 x 55 x 16 mm, 58 g (incl. battery)
- Li-Ion-battery (rechargeable)
- Up to 24 hours recording duration
- Charging and data file transfer via a docking station
- Data transfer via bluetooth, wireless data transfer in realtime to tablet PC or smartphone
- 12 Bit signal resolution
- Individually adjustable recording rate from 1/60s to 512/s
- Internal data storage, 512 MB capacity

11. LIST OF ABBREVIATIONS

Act	-	Motoric activity
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
OSAS	-	Obstructive Sleep Apnea Syndrome
PP	-	Pulse Pressure
PTT	-	Pulse Transit Time
PWV	-	Pulse Wave Velocity
RLS	-	Restless Legs Syndrome
SBP	-	Systolic Blood Pressure
SOT	-	SOMNOtouch™
SVB	-	Sympatho-vagale Balance
TIB	-	Time in Bed

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13. PUBLISHER

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SOMNOmedics designs, manufactures & distributes diagnostic devices that streamline your workflow by providing, innovative, clever, mobile and easy to use solutions that give a deeper insight into your patients health. Coming from the sleep medicine field we see ourselves as specialists for polysomnography and polygraphy screenings.

Additional to that, our experience from the last 20 years allowed us to tap into the fields of cardiology and neurology. Today we provide sophisticated solutions for long-term diagnostic EEG, long-term ECG or innovative continuous, ambulatory blood pressure measurement without a cuff.

We are a global company with dealers and customers in more than 40 countries worldwide. In Italy and the US, SOMNOmedics is directly represented through subsidiaries and keeps offices in China, India, USA and the Middle East.

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SOMNOmedics GmbH
Am Sonnenstuhl 63
D - 97236 Randersacker

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

www.somnomedics.eu
info@somnomedics.eu

NOTES: