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TECHNICAL REVIEW

Peripheral arterial tonometry—PAT technology

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SUMMARY

PAT Technology is a plethysmographic based measurement method which facilitates the accurate recording of the pulsatile volume changes of the arteries of peripheral vascular beds at the distal end of the fingers over sustained periods of time.

It represents a departure from previously available plethysmographic methods, in so far as it applies a uniform pressure field which completely envelopes the measured part of a digit, including its distal-most tip.

Applying near diastolic blood pressure levels of pressure within the PAT probe optimizes the dynamic range of the signal, prevents confounding veno-arteriolar reflex vasoconstriction at the measurement site, reduces respiratory and movement artifacts and thus facilitates accurate long term measurement.

The vascular bed of the distal phalanx of the finger is a major site of sympathetic nervous system mediated vasoconstrictor activity, and the PAT response to sympathetic changes provides a platform for accurate and robust measurement in a number of sleep and sleep related clinical areas, foremost as a patient friendly and extensively validated home sleep testing device.

Overview and rationale of PAT technology

PAT technology is a plethysmographic measurement method specifically designed to optimize arterial compliance, and prevent induced venous blood pooling distal to the measurement site and the consequent reflex vasoconstrictor changes that would affect the measurement.

The motivation for the development of PAT technology stemmed from the inability of prior plethysmographic methods to optimize arterial compliance by enclosing the tip of the finger within an applied pressure field of sufficient magnitude [1], without expelling the finger [2], and without causing distal venous blood pooling [3,4].

Since the vascular bed of the distal phalanx of the finger is a major site of sympathetic nervous system mediated vasoconstrictor activity [5], and the PAT response to sympathetic outflow such as that following apnea related arousal, has been shown to be attenuated in a dose dependent manner by the alpha adrenergic antagonist phentolamine [6], PAT measurements can be used to track changes in the sympathetic nervous system non-invasively, continuously, and accurately.

Principles of PAT technology

Measuring the PAT signal involves applying a uniform pressure field which covers the mid and distal phalanges of the finger, including its distal-most extremity in its entirety. The level of applied pressure is preferably at a slightly sub-diastolic blood pressure value, and is designed to optimally counterbalance arterial wall tension which otherwise reduces the dynamic range of the recorded pulse signal by restricting arterial wall motion [4], while avoiding arterial collapse at any stage of the pulse cycle.

Enclosing all of the measured tissue within the sub-diastolic uniform pressure field prevents venous distention, and thus avoids potential induction of veno-arteriolar reflex local vasoconstriction and other problems [3,4], while optimizing the signal dynamic range [1], and ensuring tissue perfusion.

The veno-arteriolar reflex or response, is postulated to act as an edema protecting mechanism [3,4]. The magnitude of this effect is considerable, induced venous pressure levels of 25 mm Hg have been reported to induce a 50% reduction in blood flow in forearm subcutaneous tissue [3] and a 35% reduction in blood flow during venous stasis of 40 mmHg in the cutaneous tissues of the hand [4].

The ability of PAT technology to prevent venous blood pooling at all levels of applied counter pressure without being forced off the

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finger is due to a specific design feature of the probe, which effectively results in the pressurized probe being clamped to the finger [7].

Fig. 1 illustrates the benefits of applying a near diastolic pressure field which covers the entire measurement site.

Comparing the interceptions between the hatched areas and black curves in panels A and B in Fig. 1 [8], shows how the dynamic range of arterial volume changes can be maximized.

This shows that the same span of pulse pressure, (denoted by the width of the hatched areas), can give rise to greatly differing volume changes in the arteries. When higher external pressure is applied surrounding the arteries, this reduces the transmural pressure (i.e., internal arterial pressure minus external pressure), which increases the pulse signal (A - no external pressure, B – near diastolic external pressure). This occurs because of the curvilinear pattern of the volume versus pressure curve of the arterial network.

An unfortunate consequence of applying pressure sufficient to unload arterial wall tension in the previously available segmental cuff like devices is that it causes blood to be trapped in, and distend the veins distal to the site of pressure application. As depicted in panel B, the result of leaving the distal end of the finger unexposed to counterpressure is to cause venous distention distal to the cuff, which is known to induce local veno-arteriolar reflex vasoconstriction [3,4].

The transition from the black (upper) curve, and it's associated pulse amplitude, to the red (lower) curve and its associated relatively attenuated pulse amplitude in panel B of Fig. 1, schematically illustrates how varying degrees of vasoconstriction can affect the pulsatile volume change of an artery, even when the same difference in blood pressure prevails within that artery, and the same external pressure is applied.

If the vasoconstriction due to distal venous distention can be prevented, then the combined benefits of applying both sufficient levels of counter pressure, and preventing distal venous pooling, will allow the pulse amplitude to reach its greatest value. This is illustrated in panel C of Fig. 1.

The situation depicted in the red curve in panel B of Fig. 1 represents the case of pre-existing segmental cuffs and circumferential tubes, which were unable to cover the fingertip with an equal level of pressure to that applied around the finger, and were thus subject to distal venous blood pooling.

It is to be noted that those previous plethysmographic devices which were designed to envelope the fingertip, such as venous occlusion plethysmography collection cuffs, were intended to operate at very low pressures, and tended to be pushed off the finger when pressurized, even at low levels [1].

The PAT measurement technology was thus developed with the express purpose of providing the combination of both a counter pressure sufficient to optimize signal dynamic range, and a pressure field capable of preventing venous pooling anywhere within the distal phalanges of the finger, without generating a force vector tending to push the finger out of the plethysmograph.

By enabling the pressure field to completely enclose the distal extremity without expelling the finger from the probe, PAT technology can thus be characterized by its ability to.

(a) substantially prevents venous pooling in the digit,

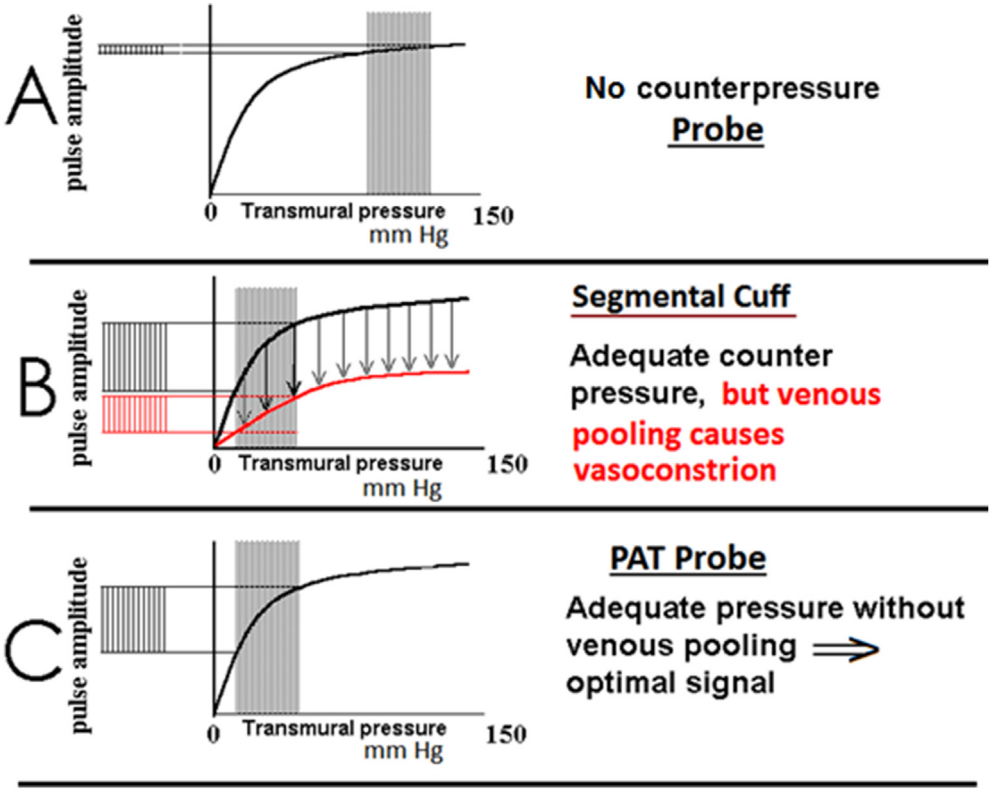

Fig. 1. Opposing effects of vascular unloading and venous pooling (adapted from 8). A) Without applied counter pressure, pulse signal has a low dynamic range and low amplitude. B) External counter pressure can increase arterial wall motion due to a leftward shift along the pressure volume curve. External counter pressure can also induce venous pooling related vasoconstriction distal to the site of the pressure application (see arrows & red curve), leading to indeterminate and possibly unstable signal amplitude over time. C) The effect of preventing distal venous pooling whilst applying significant counter-pressure in the PAT probe facilitates a stable signal with optimal dynamic range.

(b) substantially prevents uncontrolled venous backflow in the measured areas, and,
(c) substantially unload the arterial wall tension, but not occlude the arteries in the digit at any part of the pulse cycle.

These design features facilitate accurate and sustainable measurement of changes in the digital arterial tone.

Specific design feature of the PAT probe

The PAT probe is a composition of two basic elements: (a) a passive sensing element that can be any type of plethysmographic method such as a photoelectric plethysmograph (PPG) or volumetric plethysmography and (b) an active conditioning element that applies substantial pressure to the finger including its terminal most extremity, with no tendency to expel the digit.

In its most general form, the PAT probe can be described as a socket like pressure compartment which is surrounded by a deformable tubular membrane, and comprises means for preventing axial movement of the membrane when pressurized, so as to avoid expelling a finger placed within the probe.

Functionally, it can be considered as a split thimble, with a contiguous cuff, which is capable of generating a clamping effect to the finger, including its tip [7].

This is depicted in Fig. 2, which shows; (a) a pneumo-optical sensing PAT probe, and (b) a pneumatic sensing probe, which make up the two types of PAT probes in current use.

The optical sensing based probe **(A),** utilizes a transmission mode, PPG, to detect optical density changes of the measured finger pulse volume changes. This type of probe generates its own self-contained pressure field, by virtue of an arrangement of inner and outer membranes [9]. The pressure applied within the probe is independent of the volume of the finger, based on use of the outer pre-tensioned elastic membrane, and governed by Laplace's law.

The pneumatic sensing based probe **(B),** utilizes volumetric plethysmography to detect pulsatile finger volume changes, measured as pressure changes within a closed chamber by Boyle's Law (Pressure $\times$ Volume = Constant). An external pressure reservoir and control system provides the desired level of pressure field within the probe.

In both cases, the sensing region is located towards the distal finger region, and a proximal region of pressure application serves as a buffer region. Collectively, both regions act as anti-venous pooling regions [10].

This special design represents a departure from previously available plethysmographs, since the device is capable of being pressurized without being forced off the finger due to its ability to actively clamp firmly to the finger, and can thus engender its important physiological benefits.

This is in contrast to segmental cuffs and circumferential tubes [1], which neither covers the finger tip nor impart their full pressure near their boundaries. As mentioned, leaving the distal end of the finger unexposed to counter-pressure causes venous distention distal to the cuff which may induce local reflex veno-arteriolar vasoconstriction, which could mask the response to sympathetic activation, and cause the fingertip to become cold, cyanotic, and uncomfortable over time [3,4,7].

Isobaric, volume displacement PAT probe design

A unique feature of the self-contained PAT finger pneumo-optic probe is its ability to generate its own pressure field at a fixed level of pressure irrespective of the size of the finger [9]. The pressure field is created by the insertion of a finger into the probe as depicted in Fig. 3A and Fig. 3B [9].

When the finger is inserted into the probe, air is shifted from the inner compartment of the probe to its outer compartment, causing the pre-tensioned outer membrane to be pushed off the wall of the inner shell and to thus apply pressure to the air within the probe. The elastic properties of the balloon-like outer membrane are such that over a wide range of volumes it creates a constant pressure, as shown in C [9].

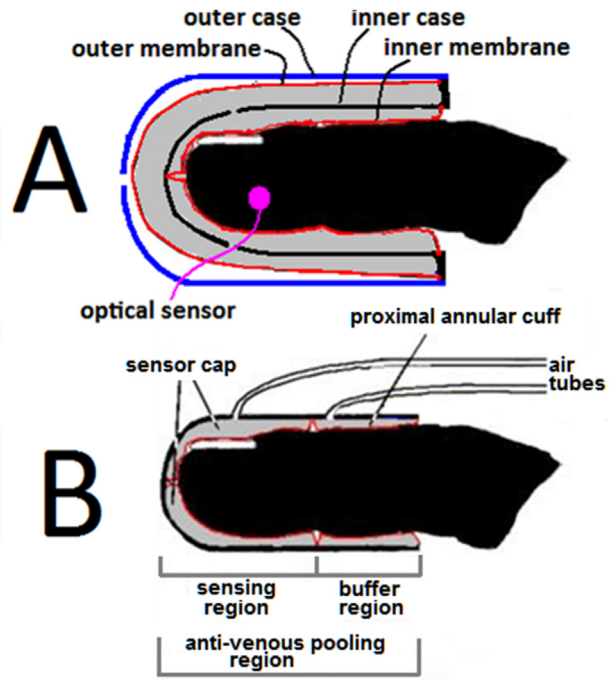

Fig. 2. Schematic view of types of A) Pneumo-optical Probe, and B) Pneumatic Probe. *The two types of PAT probes, A-opto-pneumatic, B – pneumatic* [10] *share the common attributes of a* sub-diastolic uniform pressure field which impart a two-point locking action preventing axial and longitudinal motion of the finger. Subdiastolic pressure is applied to prevent venous pooling, engorgement, and stasis, to inhibit retrograde venous shock wave propagation and partially unload arterial wall tension. The annular region extends the effective boundary of the pressure field beyond the measuring site [7,9,10].

Functional effects of PAT technology

When blood in the venous system begins to pool in the finger, which can happen due to lowering the hand below heart level or by partially blocking venous outflow with a circumferential pressure cuff, the intravenous pressure increases and this can result in substantial changes in the pulse wave signals measured by an optical sensor (PPG) which is not covered by the PAT pressure field. These changes may be due to the veno-arteriolar vasoconstrictor reflex.

This is shown in Fig. 4A, which shows that when a PAT probe and a simple PPG sensor were attached to two adjacent fingers of the same hand and venous pressure was raised by intermittently inflating and deflating a forearm blood pressure cuff to 40 mmHg. It was clear that the PAT probe derived signal was unaffected, whereas the finger the PPG without a PAT probe showed very strong reductions in the size of the signal due to the elicited venous-arterial vasoconstrictor reflex. When proximal venous occluding pressure was removed, the signal from the finger without the PAT probe increased back to its normal size. These changes related to venous pooling were highly reproducible [8].

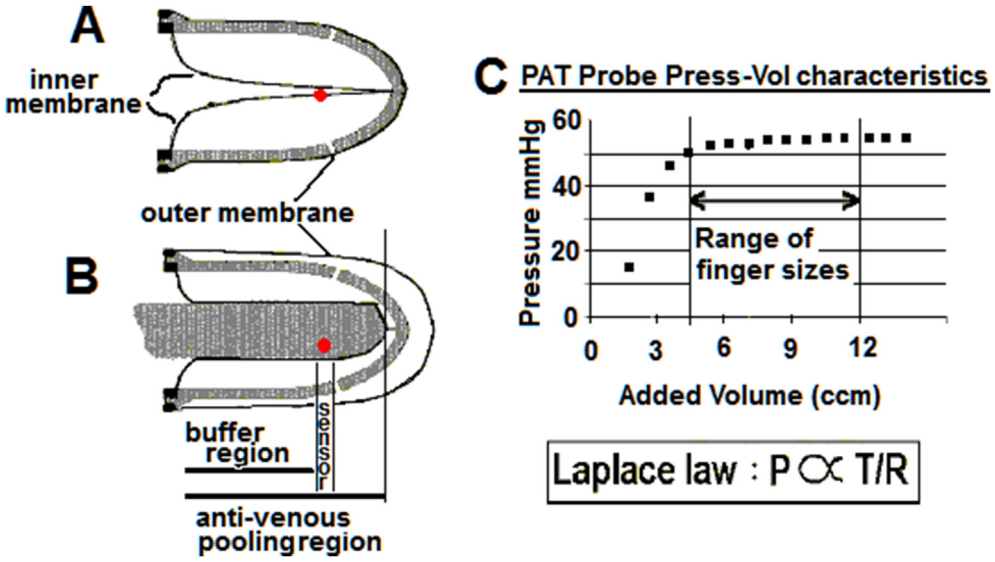

Fig. 3. Functional attributes of the self-contained PAT probe. A. The WatchPAT probe contains an inner and an outer membrane on either side of a rigid plastic thimble. With approximately 10 mL of air situated between them. The outer membrane is fitted to the external wall of the plastic thimble in a pretensioned state. B. When the finger is inserted into the probe, a proportionate amount of air is shifted from the inner compartment of the probe to its outer compartment, causing the pretensioned outer membrane to be pushed off the wall of the inner shell and to thus apply pressure to the air within the probe. Insertion tabs for aiding in the insertion of the finger and an external probe cover are not shown. C. The pressure vs added finger volume graph of the PAT finger probe. Above an added value of approximately 7 mL, the applied pressure remains constant. This constant pressure at variable volume behaviour is characteristic of elastic balloons [9].

The PAT probe also shows its ability to protect the arterial pulse-wave signal from artifacts when looking at the effects of loaded breathing on the signal. This is depicted in Fig. 4B, which shows the effects on the pulse wave signal when a person is breathing intermittently against a substantial resistance, as happens during obstructive sleep apnea events. During such episodes, large intrathoracic pressure swings develop which impinge on the large veins in the chest. These venous pressure swings can be reflected back to the finger vasculature. During normal breathing this may occur though to a much lesser extent. The PAT probe is able to eliminate most of the venous interference during loaded and normal breathing, while a simple PPG sensor is not.

Another important effect of the PAT pressure field is its ability to protect the measured signal from motion artifacts, as shown in Fig. 4C. This effect is demonstrated when comparing signals from a PAT pressure field covered probe and a simple PPG sensor attached to an adjacent finger. It is clear that the finger with the simple PPG probe showed very strong motion related artifacts that obscured the measured signal while the PAT signal was essentially unaffected.

PAT measurement modalities

PAT probes are based on either directly measured volume changes, termed volumetric plethysmography which is based on pressure changes within a closed, fixed volume measurement system (PAT pneumatic probe), or on a PPG signal using a transmission mode optical plethysmograph coupled to the skin, and located within a finger mounted PAT probe which provides a self-contained pressure field (PAT pneumo-optic probe). The latter method is used in a specially developed ambulatory home sleep testing system.

As can be seen in Fig. 5, PAT pneumo-optic probe sensing closely corresponds to PAT pneumatic probe sensing. In this case, both signals were simultaneously derived from the two types of PAT probes, during a 15 min recording, with a 5 min period of arterial occlusion in the middle (reactive hyperemia test).

Clinical applications of PAT technology

Since its development in the late 1990s, PAT technology has been applied in a number of clinical areas.

The main focus has been in the areas of sleep disordered breathing (SDB), in which a series of ambulatory "WatchPAT®" systems have been developed for Home Sleep Testing (HST), and in the area of non-invasive endothelial function testing in which the "Endo PAT®" system has been developed for the assessment of cardiovascular risk.

Cardiac disorders and risk are strongly related to sleep in general and SDB in particular, and endothelial function has been shown to be adversely affected in sleep disordered breathing conditions [11–15]. The development of these two PAT technology based devices may offer an interesting window of research to this important association in a variety of clinical conditions [11].

Additional areas of research have included the use of PAT in mental stress testing [16–18] and exercise stress testing [10,19] but these have not been developed to a widespread research interest and clinical use and are therefore not included in the focus of this review.

PAT technology in sleep disordered breathing conditions

A hallmark of sleep disordered breathing conditions is the occurrence of sleep arousals. These arousals elicit generalized autonomic activation, which among other physiological changes, includes sympathetic nervous system mediated peripheral vasoconstriction and pulse rate elevation, both of which can be clearly detected by PAT.

Fig. 6 shows the concordance between the peak amplitude of EEG spectrum and the nadir in the amplitude of PAT detected vasoconstrictory events. The nadir of the PAT signal envelope (on top), coincides with the peaks of simultaneously measured alpha activity analyzed by Fast Fourier Transformation and displayed as a function of time based on a sliding window of 4 s EEG segments with 75% overlap. The raw EEG signal is shown at the bottom. All

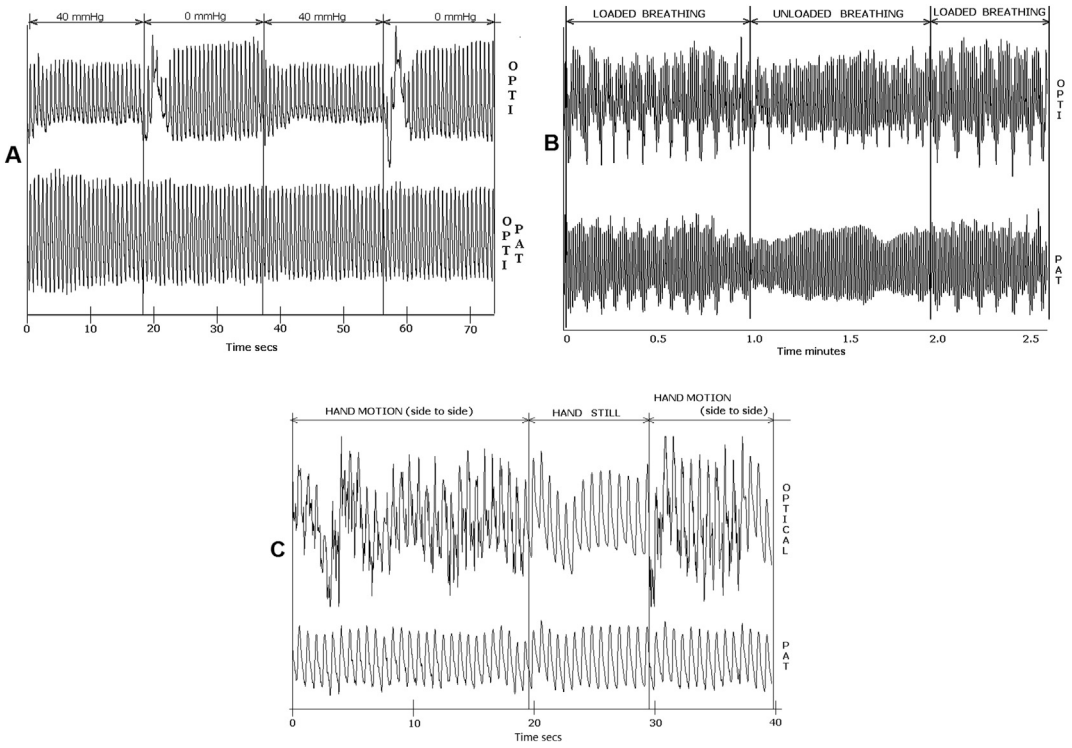

Fig. 4. A. Time-course of pulse wave amplitude in adjacent fingers within different pressure fields when a proximal cuff on the upper arm is alternately inflated to a pressure of 40 mmHg and then deflated to 0 mmHg. Inflating the cuff to 40 mmHg induces venous distention in the tissues distal to the cuff. Upper trace – pulse signal from finger within minimal external counter pressure environment. Lower trace – pulse signal from a finger within near diastolic pressure field is applied over the entire surface of the two distal most phalanges (using a PAT probe). In the absence of the pressure field, periods of induced venous distention are associated with substantial attenuation of the pulse signal, in sharp contrast simultaneous recording from the finger within the pressure field is essentially unaffected by the induced venous distention [8]. B. Effects of loaded breathing on the finger pulse with (below), or without (above) the covering of the sensor by a PAT pressure field. C. Effects of hand motion on the finger pulse with (below), or without (above) the covering of the sensor by a PAT pressure field.

PAT attenuation events during light or deep sleep were associated with bursts of alpha activity that coincided with the vasoconstrictory phase [20].

The cardiovascular correlates of arousals during sleep also reveal a striking concordance between PAT amplitude attenuations and surges in blood pressure at the termination of apneic events, and increased heart rate can be seen in Fig. 7 [21].

The first publication to describe PAT signal based detection of sleep disordered breathing was published in 1999, and found that in 42 patients with Obstructive Sleep Apnea Syndrome (OSAS) transient vasoconstriction and tachycardia, both measured with PAT, were seen at the onset of arousals generated when breathing resumed after apneic events. Based on an automated algorithm, a high correlation coefficient of total apnea-hypopnea events was found between PSG and PAT ($r = 0.92$, $P < .0001$) [7].

In a mechanistic study, the PAT response to apneic event was shown to be directly related to induced airflow obstruction which was elicited by dropping the applied level of positive airway pressure in patients with OSA [22].

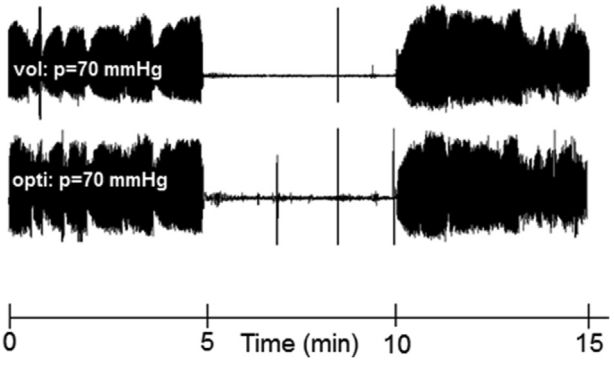

Fig. 5. Simultaneous recordings of PAT volumetric and photoplethysmographic signals from the same tissue bed, over 15 min. Both signals recorded within the same PAT probe on the same finger. Note a 5 min period of arterial occlusion between 5 and 10 min.

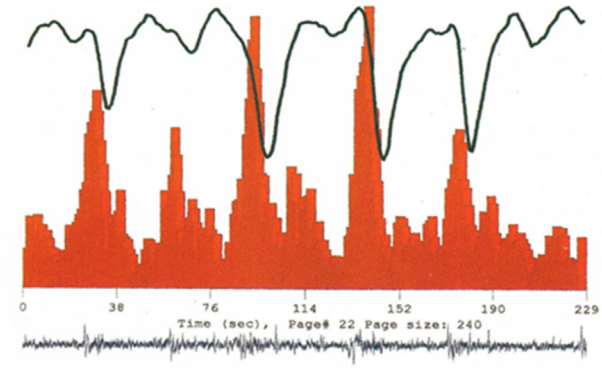

Fig. 6. The relationship between PAT detected vasoconstrictory events and simultaneously measured alpha EEG activity (8–11Hz) analyzed by Fast Fourier Transformation and displayed as a function of time based on a sliding window of 4 s EEG segments with 75% overlap. Without exception, all PAT attenuation events, during light or deep sleep, were associated with bursts of alpha activity that coincided with the vasoconstrictory phase [20].

Principles of WatchPAT automated algorithms for the detection of SDB events

The WatchPAT automated algorithms provide two SDB indices – pAHI which is an estimate of Apnea/Hypopnea Index and pRDI which is an estimate of Respiratory Disturbances Index which additionally counts RERA (Respiratory Effort Related Arousal) events. The algorithm is based on combinations and inter-relationships of PAT amplitude, PAT derived pulse rate, oxygen de-saturations (desats) and re-saturations (resats) and has been tuned to detect the SDB events and calculate the related respiratory indexes for a pre-selection of a 3% or 4% oxygen desaturations approach. The basic structure of the algorithm is summarized in the schematic block diagram in Fig. 8.

The algorithm first marks periods of sleep from the sleep wake algorithm (block 1) based on input from the WatchPAT actigraphy system. All following calculations are then applied to the sleep periods only. The selection of whether 3% or 4% desaturation approach for SDB events scoring is provided from the Graphic User Interface (GUI) by the operator and adjusts filters and coefficients (block 3). A PAT amplitude and rate based likelihood function is generated (blocks 4,5,6,7) which if within a very high level range (block 8) is coupled with significant desaturations (3% or 4%) to provide n PAT AHI event (blocks 8, 9, 11). An estimated Apnea Hypopnea index (pAHI) is then returned to the GUI. A very high likelihood function (block 8) also generates a PAT RERA event (block 12) and so does a moderate likelihood function when coupled with a minor resaturation of less than 2% (block 10). A RERA event or a PAT AHI event are both considered a PAT RDI event (block 13). An estimated Respiratory Disturbances index (pRDI) is then returned to the GUI.

Numerous validation studies have shown a high correlation between WatchPAT and PSG with high sensitivity, and specificity to diagnosing SDB [9,23–35].

A comprehensive meta-analysis of 14 validation studies with simultaneous WatchPAT and PSG recording, including over 900 patients, reported an overall high correlation of RDI and AHI, between PAT and PSG of r = 0.879 [95% CI, 0.849–0.904]; P < .001) and r = 0.893 (0.857–0.920; P < .001) respectively; and a combined overall correlation for RDI and AHI of r = 0.889 [95%CI, 0.862–0.911; P < .001]. ODI had a correlation of r = 0.942 (0.894–0.969; P < .001) [36]. The authors concluded that *"Respiratory indexes calculated using PAT-based portable devices positively correlated with those calculated from the scoring of PSG. Strengthened by the blinded design of most of the included studies, this technology represents a viable alternative to PSG for confirmation of clinically suspected sleep apnea."* [36].

Potential limitations of PAT technology for detecting SDB could have occurred in conditions which may potentially affect the regularity of the PAT signal.

A case in point is atrial fibrillation (AF), which is the most common cardiac tachyarrhythmia. It has been estimated that between 49% and 62% of AF patients have some degree of OSA [42]. Tanaka et al. assessed WatchPAT in 776 AF patients, and found that 774 (99.7%) were successfully tested by the WatchPAT system [37]. This is consistent with the findings of Tauman et al. who assessed the ability of the WatchPAT to detect SDB relative to PSG in 101 AF patients, and found a significant correlation between WatchPAT and PSG derived AHI values (r = 0.80, p < .0001), irrespective of the use of anti-arrhythmic therapy [38]. These authors concluded that:

> *"WatchPAT can detect sleep apnea events in patients with AF. AF should not be an exclusion criterion for using the device"* [38].

The application of PAT technology in other common conditions such as hypertension and diabetes mellitus may also potentially adversely affect WatchPAT accuracy.

In a meta-analysis of PSG based validation studies of WatchPAT [36], hypertensive patients were included in all 14 included studies, and in the validation study of Zou et al. [29], 21 of 98 subjects were hypertensive. In both cases no particular deficiency in Watch PAT accuracy was noted in the hypertensive patients.

While we are not aware of a PSG based validation study of WatchPAT in a specifically diabetic population, a study by Shinoda et al. found an AHI ≥5/hour to be present in 80.5% of 200 patients with type 2 diabetes (64.5% men; aged 60.1 ± 13.6 years) [39], which might suggest that type 2 diabetes did not impair the ability of WatchPAT to detect autonomic changes in this population given such a high reported disease prevalence.

Aging does not appear to adversely impact PAT technology's ability to accurately assess OSA, as reported by Onder et al. [33], who compared 56 patients aged 20–35 to 29 patients aged 50–65 years, undergoing simultaneous WatchPAT and in lab PSG studies. They found that the overall AHI correlation between WatchPAT and PSG in younger and older groups were similarly high, at r = 0.92 and r = 0.94, (p < .001) respectively [33].

An interesting study by Zhang et al. [40], which examined the effects of applying a manual editing protocol to WatchPAT automated algorithms in a validation group of 160 patients with suspected SDB (77 males, 93 females), however found that *"younger patients had better concordances for the automated and manual algorithm than older patients."* In this study, the older age group (n = 26) was aged 65 or older.

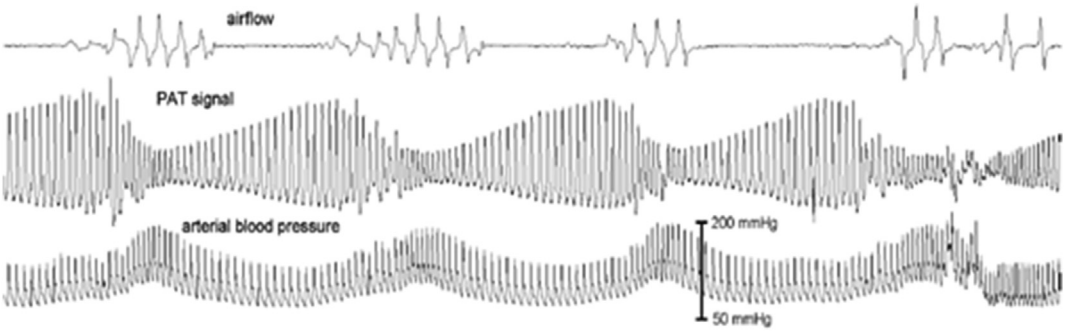

Fig. 7. Direct comparison with blood pressure and the PAT signal reflects the concomitant cardiovascular changes in blood pressure, peripheral resistance and heart rate related to the evoked autonomic response to arousal [21].

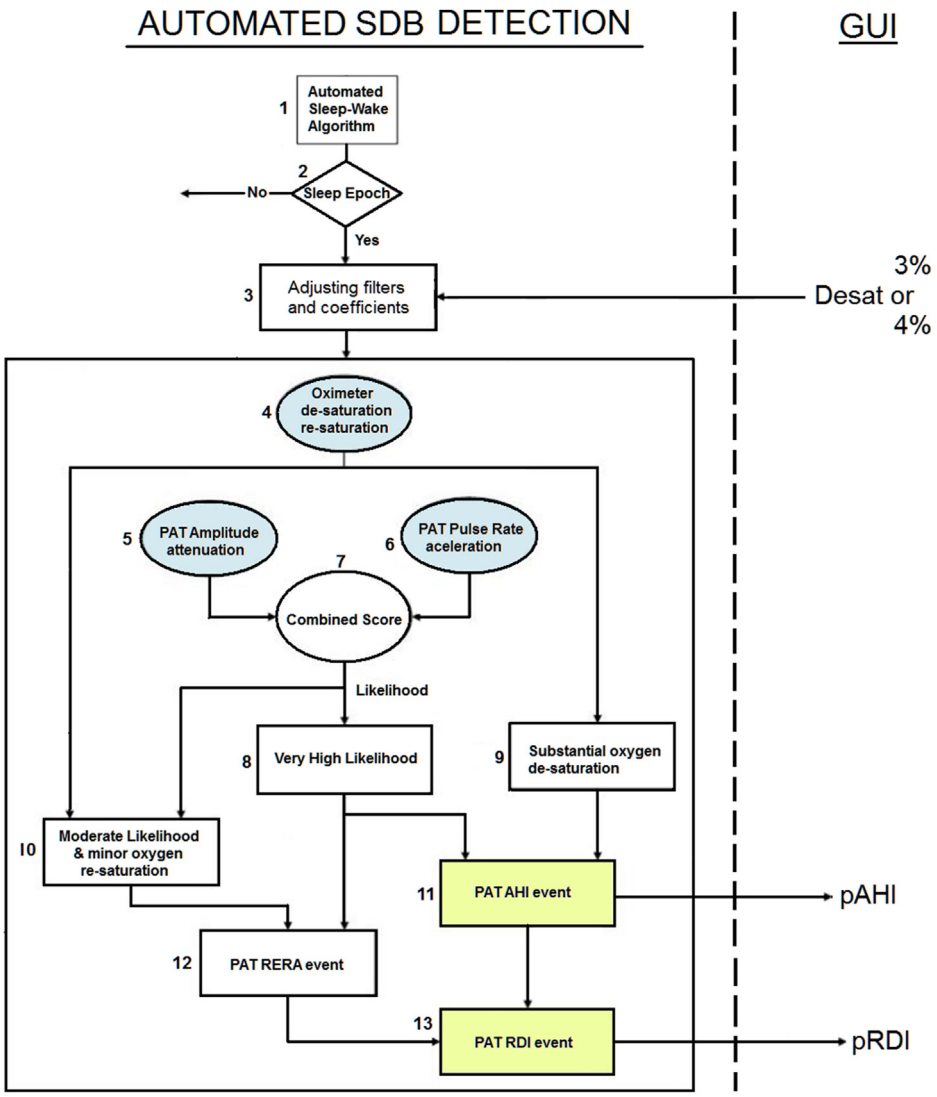

Fig. 8. A schematic block diagram of the automated WatchPAT algorithm (left to the dashed line) and the data exchange with the Graphic user interface (GUI- right to the dashed line).

These authors further examined the effect of gender on WatchPAT accuracy, which has been scantily reported in the literature.

> *"Strikingly, we found that the performance of the automated algorithm was similar between women and men, yet the manual editing process improved the concordance more in women than in men."*

A simultaneous comparison of Watch PAT and PSG by O'Brien et al. in 31 pregnant women, reported that "*the Watch-PAT* 200 has *excellent sensitivity, specificity, and positive and negative predictive values for identification of pregnant women with SDB (defined as AHI* $\geq$ *5 events/hour)*" [41].

Considered in the light of the consistently high correlations between WatchPAT and PSG reported in numerous validation studies which tended to be male predominated [36], this suggests that gender does not appear to affect the SDB diagnostic performance of WatchPAT.

PAT technology in detecting central sleep apnea and Cheyne-Stokes breathing

Cheyne-Stokes breathing (CSB) is a central respiratory disorder occurring mainly during sleep. It is characterized by periodic cessation or decrement of respiratory activity resulting in a repetitive crescendo decrescendo respiratory pattern and is associated with periodic changes in sympathetic activity. CSB is common among Congestive Heart Failure patients where it is considered to be an ominous prognostic marker. The PAT signal was shown to accurately identify CSB by virtue of a characteristic crescendo decrescendo pattern in the PAT signal over time [42].

A method using amplitude normalized PAT systolic upstroke signals, which reflects the changing level of intrathoracic pressure during a series of breathing cycles which directly affects the pressure of arterial blood and the PAT signal, coupled with respiratory movement analysis utilized by WatchPAT was shown to enable effective differentiation between Central and Obstructive Sleep Apnea [43].

Fig. 9 shows comparative montages of pulse upstroke signals normalized for amplitude and synchronized at the foot of the pulse. It can be seen that while pulses during central apnea exhibit very little variability in the upstroke pattern, the opposite is observed during obstructive events [43].

PAT technology in REM stage, and sleep staging

REM (rapid eye movement) sleep stage is characterized by rapid eye movements, muscles tone decrease and is associated with elevated sympathetic activity. It can be detected by identifying specific "sympathetic signatures" in the PAT signal, such as reported by Lavie et al., in 2000. These authors reported that in addition to the phasic changes in PAT signal amplitude characteristic of arousals, a different facet of the PAT signal during sleep was that REM stage sleep is characterized by tonic reductions in PAT amplitude of extended duration [44].

Using sophisticated signal processing procedures applied to PAT signal time series of pulse wave amplitude and interpulse periods (IPP) Herscovici et al. reported a 16 variables based prediction function, in both temporal and frequency domains, that can be used to identify REM epochs in the WatchPAT [45].

In addition to distinguishing between REM and non-REM sleep stages, that group used the same approach to further stage non REM sleep into light and deep sleep stages [46]. Together with the algorithms for REM and wake detection, this provides a close to full stage detection method based solely on the PAT and actigraphy signals.

A multi-center validation study vs. PSG, reported that overall agreement in detecting light/deep and REM sleep were 88.6% ± 5.9% and 88.7% ± 5.5%, respectively [32].

PAT technology in endothelial function testing

As mentioned, endothelial function has been shown to be adversely affected in sleep disordered breathing conditions [11–15]. Endothelial dysfunction can be assessed with the Endo PAT, using the PAT signal in a flow mediated dilation (FMD) procedure, in which an induced reactive hyperemia response to a standardized period of arterial occlusion elicits an increased level of sheer stress acting on the arterial walls. Such sheer stress is known to mediate the release of nitric oxide (NO), an established Endothelium-derived relaxing factor, (EDRF), which causes local vasodilatation and has been shown to play a central role in the Endo PAT response following reactive hyperemia [47].

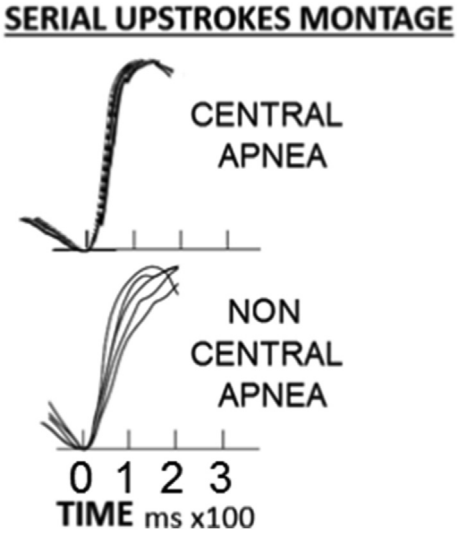

Fig. 9. Comparative montages of pulse upstroke signals normalized for amplitude and synchronized at the foot of the pulse in representative examples of central (above), and non central apnea (below) [38].

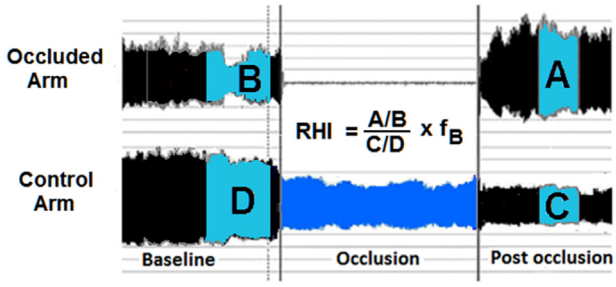

Fig. 10. This illustrates how the un-occluded contralateral control arm PAT signal ratio C/D is used to correct the corresponding occluded arm ratio, A/B, which is also subject to the same pan-systemic factors affecting peripheral vascular tone. Baseline, occlusion and post occlusion periods are all 5 min. A logarithmic baseline amplitude correction factor is applied to compensate for the observed ceiling effect of baseline PAT amplitude. Note the attenuation of the un-occluded side signal.

Endo PAT utilizes two PAT pneumatic probes and is designed to cancel out systemic autonomic effects, based on parallel measurement on contralateral arms. One side only is subjected to an endothelial stimulatory hyperemic provocation, while the other side serves as a control for sympathetic or other non-endothelial related systemic changes.

As shown in Fig. 10, Endo PAT provides a Reactive Hyperemia Index (RHI), a measure of the dilatory response. RHI is calculated as the ratio of the PAT signal amplitude before and after release of the occluding cuff, (A/B), normalized to the corresponding ratio of simultaneously recorded signal amplitudes from the control side (C/D). This value is further corrected to compensate for the known ceiling effect of the initial PAT signal amplitude (B), by applying a predetermined baseline correction factor which varies according to the occluded side baseline amplitude.

Summary

PAT technology represents a departure from previously available plethysmographic methods that measure digital pulse wave amplitude, either optically or volumetrically, as it incorporates an active conditioning element that is capable of applying a predetermined uniform near diastolic pressure field which completely envelopes the measured part of a digit, including its distal-most tip and is especially designed to effectively clamp itself to the finger without being forced off it.

It thereby improves the dynamic range of the signal, reduces respiratory and movement artefacts and prevents locally induced vasomotor reflexes from adversely confounding the measured signal.

This method provides a platform for an accurate and robust measurement in a number of clinical, physiological and pathophysiological areas.

Practice points

- PAT technology is based on a special probe design which;
  a) facilitates optimal signal gain by applying a uniform, sub-diastolic pressure field to unload vascular wall tension, and
  b) prevents venous blood pooling in the entire distal finger to preclude veno-arteriolar reflex vasomotor changes.
  c) is less affected by motion and breathing artefacts.
  d) supports pneumatic or pneumo-optical design.
- PAT technology reflects sympathetic tone by measuring arterial pulse wave amplitude and pulse interval variations, and together with pulse oximetry and actigraphy, detects and categorizes sleep disordered breathing and sleep stages.
- PAT technology implemented as Endo PAT is used to detect endothelial function changes by testing vasoreactive changes on opposing occluded and control arms.

Research Agenda

- The Watch PAT can detect obstructive and central sleep apnea.

It needs to be investigated as to how far sympathetic tone activation predicts cardiovascular outcomes.

- How far can additional parameters derived by PAT technology help to phenotype patients with obstructive sleep apnea.
- The Endo PAT has shown that it can predict late adverse cardiovascular events. This needs to be further investigated in sleep apnea patients.

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Conflicts of interest

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