itamar
MEDICAL

Watch-PAT
Summary of Evidence

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The Science of Peripheral Arterial Tone:

ABSTRACT: We report a novel approach to the determination of sleep apnea based on measuring the peripheral circulatory responses in a primary condition of disordered breathing. The apparatus is a finger plethysmograph coupled to a constant volume, variable pressure, pneumatic system. The plethysmograph's tip (measurement site) is composed of two parallel opposing longitudinal half thimbles, which is attached to a contiguous annular cuff. Each compartment consists of an internal membrane surrounded by an outer rigid wall. These provide a uniform pressure field and 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 cuff extends the effective boundary of the pressure field beyond the measuring site.

In 42 patients with Obstructive Sleep Apnea Syndrome (OSAS) profound, transient vasoconstriction and tachycardia usually of a periodic nature, were clearly seen with each apneic event, possibly related to transient arousal. Good agreement was found between standard total apnea-hypopnea scoring, 129.5 ± 22.4 (Mean $\pm$ SEM), and transient vasoconstriction and tachycardia events, 121.2 ± 19.4 (R=.92, p<.0001).

We conclude that the finger tip exemplifies the scope of peripheral vascular responsiveness due to its high density of alpha sympathetic innervation, and its high degree of blood flow rate ability. Given that elevated peripheral resistance and tightly linked transient heart rate elevation is a consistent part of the hemodynamic response to arousal and OSAS, we believe that pulsatile finger blood flow patterns can be clearly diagnostic of OSAS and other sleep-disordered breathing conditions.

ABSTRACT: This is the first article published describing the PAT probe and the intricate technology that is involved in measuring Peripheral Arterial Tonometry (PAT). The article describes how the PAT probe increases sensitivity by unloading arterial wall tension; it improves accuracy of measurement by restricting the actual measurement to arterial volume changes; and prevents venous pooling.

ABSTRACT: In this Letter to the Editor, Lavie et al, introduce the readers to a new plethysmographic technique to measure peripheral arterial tone (PAT). They report that REM sleep in humans is associated with considerable peripheral vasoconstriction. The apparatus that they use is essentially a plethysmograph that, unlike models available, is able to envelop the finger up to and beyond its tip with a uniform pressure field. In their study of 26 cohorts, it was found that REM sleep was associated with considerable attenuation of the PAT signal.

Dvir I, Adler Y, Freimark D, Lavie P. Evidence for fractal correlation properties in the variations of peripheral arterial tone during REM sleep. *American Journal of Physiology 2002; 283(1):H434-H439.*

ABSTRACT: Previous studies utilizing detrended fluctuation analysis (DFA) of heart rate variability during sleep revealed a higher fractal exponent during rapid eye movement (REM) sleep than non-REM sleep. The aim of this study was to determine whether the same difference exists in the variations of peripheral arterial tone (PAT). Finger pulse wave measured by a novel plethysmographic technique was monitored during sleep in 12 chronic heart failure patients, 8 heavy snorers, and 12 healthy volunteers. For each subject, at least two 15-min time series were constructed from the interpulse intervals and from pulse wave amplitudes during REM and non-REM sleep. Fractal scaling exponents of both types of time series were significantly higher for REM than non-REM sleep in all groups. In each of the groups and in both sleep stages, the fractal scaling exponents based on pulse wave amplitude were significantly higher than those based on pulse rate variability. A repeat of the analysis for short-, intermediate-, and long-term intervals revealed that the fractallike exponents were evident only in the short- and intermediate-term intervals. Because PAT is a surrogate of sympathetic activation, our results indicate that variations in sympathetic activation during REM sleep have a fractallike behavior.

O'Donnell CP, Allan L, Atkinson P, Schwartz AR. The effect of upper airway obstruction and arousal on Peripheral Arterial Tonometry in Obstructive Sleep Apnea. *Am J Respir Crit Care Med 2002; 166(7):965-71.*

ABSTRACT: We evaluated the effects of airflow limitation and arousal on digital vascular tone in 10 patients with obstructive sleep apnea (OSA) using the recently developed, noninvasive technique of peripheral arterial tonometry (PAT). Subjects were maintained at a therapeutic level of continuous positive airway pressure, and nasal pressure was acutely dropped for three to five breaths during non rapid eye movement sleep over 1.3 cmH2O, leading to increasing airway obstruction and decreasing levels of inspiratory airflow. In the absence of a detectable electro-encephalographic (EEG) arousal, severe reductions of inspiratory airflow to below 200 ml/second caused significant decreases in PAT amplitude (1.000 _ 0.007 to 0.869 _ 0.007 arbitrary units; p 0.001), whereas mild airflow limitation (_ 200 ml/second) had no effect (1.000_0.009 to 1.011_0.007 arbitrary units). The presence of an EEG arousal accentuated the response to airflow obstruction, such that the PAT amplitude decreased more (p _ 0.001) in the presence of arousal (1.000 _ 0.007 to 0.767 _ 0.010 arbitrary units) than in the absence of arousal (1.000 _ 0.007 to 0.923 _ 0.007 arbitrary units). We conclude that airflow obstruction in patients with OSA causes an acute digital vasoconstriction that is accentuated in the presence of an EEG arousal.

Pillar G, Bar A, Shlitner A, Schnall RP, Sheffy J, Lavie P. Autonomic Arousal Index (AAI): An Automated Detection based on Peripheral Arterial Tonometry. SLEEP 2002; 25(5):543-549.

ABSTRACT: Summary: Arousals from sleep are associated with increased sympathetic activation and are therefore associated with peripheral vasoconstriction. We hypothesized that digital vasoconstrictions as measured by peripheral arterial tonometery (PAT), combined with an increase in pulse rate, would accurately reflect arousals from sleep, and can provide an autonomic arousal index (AAI). Based on a previously studied group of 40 sleep apnea patients simultaneously recorded by both polysomnography (PSG) and PAT systems, an automated algorithm using the PAT signal (and pulse rate derived from it) was developed for detection of arousals from sleep. This was further validated in a separate group of 96 subjects (85 patients referred with suspected obstructive sleep apnea and 11 healthy volunteers mean age 46.2±14.4 years, BMI 28.5±5.4 kg/m2). All underwent a whole night PSG with simultaneous PAT recording. The PSG recordings were blindly manually analyzed for arousals based on American Academy of Sleep Medicine (AASM) criteria, while PAT was scored automatically. There was a significant correlation between PSG and PAT arousals (R=0.82, p<0.0001) with a good agreement across a wide range of values, with a ROC curve having an area under the curve (AUC) of 0.88. We conclude that automated analysis of the peripheral arterial tonometry signal can detect EEG arousals from sleep, in a relatively quick and reproducible fashion.

Penzel T, Kesper K, Pinnow I, Becker HF, Vogelmeier C. Peripheral arterial tonometry, oximetry and actigraphy for ambulatory recording of sleep apnea. *Physiol Meas. 2004; 25(4):1025-1036.*

Abstract. Autonomous nervous functions change with sleep stages and show characteristic changes associated with sleep disorders. Therefore, continuous monitoring of autonomous nervous functions during sleep can be used for diagnostic purposes. Recently, the peripheral arterial tonometry (PAT) has been introduced to determine peripheral arterial vascular tone on the finger being determined by sympathetic activity. We investigate a new ambulatory recording system which uses PAT, oximetry and actigraphy (Watch-PAT) in order to detect sleep apnea and arousal. The Watch-PAT is battery operated and attached to the wrist and has two finger sensors. Twenty-one patients with suspected sleep apnea were recorded with cardiorespiratory polysomnography and the new system in parallel. Seventeen recordings could be evaluated. The correlation for the apnea/hypopnea index derived from the sleep laboratory and the respiratory disturbance index derived from the Watch-PAT was $r = 0.89$ ($p < 0.01$) and between arousals and the respiratory disturbance index was $r = 0.77$ ($p < 0.01$). The correlation for the total sleep time compared between the two systems was $r = 0.15$ (n.s.). The Watch-PAT detects apneas and hypopneas with a reasonable reliability and it is very sensitive to arousals. The number of Watch-PAT events lies between the sum of apneas plus hypopneas and arousals. Arousals are not unique to apnea events and therefore the specifity of the Watch-PAT is limited. In conclusion, the Watch-PAT is well suited to perform therapy control studies in patients suffering from sleep apnea and being treated.

Zou D, Grote L, Eder ND, Peker Y, Hedenr J. Obstructive Apneic Events Induce Alpha-receptor Mediated Digital Vasoconstriction. *SLEEP 2004; 27(3):485-489.*

Study Objective: To characterize the role of alpha-receptors in autonomic control of digital skin blood flow change in response to obstructive apnea-hypopnea events.
Design: Experimental intervention study.
Setting: Sleep laboratory in a university hospital.
Patients: Eight male patients with severe obstructive sleep apnea (OSA).
Interventions: Patients received four cumulative dosage steps of phentolamine (0.066, 0.2, 2 and 5[n=3] μg/min/100ml forearm tissue) via brachial artery infusion during nonrapid eye movement sleep (stage 1 and 2).
Measurements and Results: The pulse amplitude determined with peripheral arterial tonometry (PAT) was periodically attenuated during the immediate post apnea-hypopnea period coinciding with arousal. PAT ratio (smallest pulse amplitude post apnea divided by largest pulse amplitude during apnea), was determined as a measure of digital vasoconstriction. We found that, compared with baseline, PAT ratio dose-dependently increased during phentolamine (0.2, 2 and 5 μg) infusion by 11.2±1.7%, 24.4±2.1% and 30.9±4.1%, respectively (P<0.001). Systemic blood pressure and heart rate were largely unaffected by the pharmacological intervention.
Conclusion: OSA related alteration of the pulse amplitude includes a constriction of digital skin vasculature that to a large extent is mediated via sympathoadrenergic α-receptors.

Herscovici S, Peer A, Papyan S, Lavie p. Detecting REM sleep from the finger: automatic REM sleep algorithm based on Peripheral Arterial Tone (PAT) and actigraphy. *Physiol Meas 2007; 28(2): 129-140.*

ABSTRACT: Scoring of REM sleep based on polysomnographic recordings is a laborious and time-consuming process. The growing number of ambulatory devices designed for cost-effective home-based diagnostic sleep recordings necessitates the development of a reliable automatic REM sleep detection algorithm that is not based on the traditional electroencephalographic, electrooccolographic and electromyographic recordings trio. This paper presents an automatic

REM detection algorithm based on the peripheral arterial tone (PAT) signal and actigraphy which are recorded with an ambulatory wrist-worn device (Watch-PAT100). The PAT signal is a measure of the pulsatile volume changes at the finger tip reflecting sympathetic tone variations. The algorithm was developed using a training set of 30 patients recorded simultaneously with polysomnography and Watch-PAT100. Sleep records were divided into 5 min intervals and two time series were constructed from the PAT amplitudes and PAT-derived inter-pulse periods in each interval. A prediction function based on 16 features extracted from the above time series that determines the likelihood of detecting a REM epoch was developed. The coefficients of the prediction function were determined using a genetic algorithm (GA) optimizing process tuned to maximize a price function depending on the sensitivity, specificity and agreement of the algorithm in comparison with the gold standard of polysomnographic manual scoring. Based on a separate validation set of 30 patients overall sensitivity, specificity and agreement of the automatic algorithm to identify standard 30 s epochs of REM sleep were 78%, 92%, 89%, respectively. Deploying this REM detection algorithm in a wrist worn device could be very useful for unattended ambulatory sleep monitoring. The innovative method of optimization using a genetic algorithm has been proven to yield robust results in the validation set.

Ofek E, Pratt, H A questionnaire for quantifying subjective significance of names: Physiological validation with PAT. Physiol Behav. **2008 Jun 9;94(3):368-73**

Abstract: A questionnaire was developed in order to assess the subjective significance of names. Autonomic activation by the names was measured physiologically - by the PAT (peripheral arterial tonus) signal, and correlated with affective significance as revealed by the questionnaire. The final version of the questionnaire included 22 dichotomous and 24 rating questions. Subjective significance to the participant of first names was defined as subjective significance of persons in the participant's life that bear the name. Three reliable factors affecting questionnaire scores were found: (1) general subjective significance (26 items); (2) recency of contact (8 items); and (3) negative impact (12 items). These 3 factors accounted for 98% of the variance in questionnaire scores, and correlated in the expected direction with autonomic response measures. This questionnaire can serve psychological and social studies of relationships and personality.

Ma'ayan Bresler, Koby Sheffy, Giora Pillar, Meir Preiszler, Sarah Herscovici Differentiating between light and deep sleep stages using an Ambulatory Device Based on Peripheral Arterial Tonometry. Physiol Meas. 2008; 29(5): 571-584.

The objective of this study is to develop and assess an automatic algorithm based on the peripheral arterial tone (PAT) signal to differentiate between light and deep sleep stages. The PAT signal is a measure of the pulsatile arterial volume changes at the finger tip reflecting sympathetic tone variations and is recorded by an ambulatory unattended device, the Watch-PAT100, which has been shown to be capable of detecting wake, NREM and REM sleep. An algorithm to differentiate light from deep sleep was developed using a training set of 49 patients and was validated using a separate set of 44 patients. In both patient sets, Watch-PAT100 data were recorded simultaneously with polysomnography during a full night sleep study. The algorithm is based on 14 features extracted from two time series of PAT amplitudes and inter-pulse periods (IPP). Those features were then further processed to yield a

prediction function that determines the likelihood of detecting a deep sleep stage epoch during NREM sleep periods. Overall sensitivity, specificity and agreement of the automatic algorithm to identify standard 30 s epochs of light and deep sleep stages were 66%, 89%, 82% and 65%, 87%, 80% for the training and validation sets, respectively. Together with the already existing algorithms for REM and wake detection we propose a close to full stage detection method based solely on the PAT and actigraphy signals. The automatic sleep stages detection algorithm could be very useful for unattended ambulatory sleep monitoring assessing sleep stages when EEG recordings are not available.

White DP. Monitoring peripheral arterial tone (PAT) to diagnose sleep apnea in the home. J Clin Sleep Med. 2008 Feb 15;4(1):73

In this editorial, Professor David White, Chief Medical Officer for Respironics, takes on the findings of the Clinical Guidelines for the Use of Unattended Portable Monitors in the Diagnosis of Obstructive Sleep Apnea in Adult Patients, published by the Portable Monitoring Task Force (Nancy Collop et al) and refutes a number of claims held against the Watch-PAT. These include the inability to manual score, the failure rate of 0% in his own study.

Validation Studies:

Freimark D, Adler Y, Sheffy J, Schechter D, Schwammenthal E, Motro M, Lavie P. Oscillations in peripheral arterial tone in CHF patients: A new marker for Cheyne-Stokes breathing. *Cardiology 2002; 98(1-2):21-4.*

ABSTRACT: Cheyne-Stokes breathing (CSB), which is a prevalent finding in congestive heart failure (CHF) patients, has been shown to be of prognostic value. The oscillations in
respiration were shown to be associated with oscillations in sympathetic nerve activation. We tested the hypothesis that the peripheral arterial tone (PAT) as measured by a novel finger plethysmograph's can be used to detect CSB. Using a novel technique to measure the PAT, we monitored 10 patients with advanced CHF simultaneously with conventional polysomnographic recordings for either 1 or 2 nights. Records were scored for CSB during 3-min periods based on either respiratory effort and nasal-buccal airflow or on the PAT signal alone. The PAT sensitivity and specificity for the detection of periods containing CSB were 91 and 91% for the entire recording, 90.7 and 92.9% for non-REM sleep, 90.7 and 70% for REM sleep, and 73 and 97.3% for awake periods, respectively. PAT is a reliable marker of CSB in CHF patients. The novel finger plethysmograph can be used for screening and monitoring CSB.

Bar A, Pillar G, Dvir I, Sheffy J, Schnall RP, Lavie P. Evaluation of a Portable Device Based on Peripheral Arterial Tone for Unattended Home Sleep Studies. *Chest 2003; 123(3): 695-703.*

Diagnosis of obstructive sleep apnea syndrome (OSAS) by ambulatory systems is a growing practice in view of the large number of patients awaiting correct diagnosis. The Watch PAT100 (WP100) [Itamar Medical; Caesarea, Israel] is a portable device based on the peripheral arterial tone (PAT) signal, and is designed for unattended home sleep studies.

Objectives: To evaluate the efficacy, reliability, and reproducibility of the WP100 device for the diagnosis of OSAS as compared to in-laboratory, standard polysomnographic-based manual scoring.

Design and methods: One hundred two subjects (78 men; 69 patients with OSAS and 33 normal volunteers; mean _ SD age, 41.4 _ 15.2 years; body mass index, 26.8 _ 5.5) underwent in laboratory full polysomnography simultaneously with WP100 recording. Fourteen subjects also underwent two additional unattended home sleep studies with the WP100 alone. The polysomnography recordings were blindly scored for apnea/hypopnea according to the American Academy of Sleep Medicine criteria (1999), and the polysomnography respiratory disturbance index (RDI) [PSG-RDI] was calculated. The WP100 data were analyzed automatically for the PAT RDI (PRDI) by a proprietary algorithm that was previously developed on an independent group of subjects.

Results: Across a wide range of RDI levels, the PRDI was highly correlated with the PSG-RDI (r _ 0.88, p < 0.0001), with an area under the receiver operating characteristic curve of 0.82 and 0.87 for thresholds of 10 events per hour and 20 events per hour, respectively. The PRDI scores were also highly reproducible, showing high correlation between home and in-laboratory sleep studies (r _ 0.89, p < 0.001).

Conclusion*:* The WP100 may offer an accurate, robust, and reliable ambulatory method for the detection of OSAS, with minimal patient discomfort.

Objective: To assess the accuracy of a wrist-worn device (Watch_PAT100) to diagnose obstructive sleep apnea (OSA).

Methods: Thirty adult subjects with and without suspected OSA simultaneously had a standard in-laboratory polysomnogram (PSG) and wore the Watch_PAT100 during a full-night recording. PSG sleep and respiratory events were scored according to standard criteria.
Watch_PAT data were analyzed with an automated computerized algorithm which calculated the frequency of respiratory events per hour of actigraphy measured sleep using a combination of peripheral arterial tonometry (PAT) signal attenuation, desaturation on pulse oximetry, and changes in heart rate. This yielded a PAT apnea hypopnea index (AHI).

Results: Mean age was 47.0 ^ 14.8 years, mean body mass index 31.0 ^ 7.6 kg/m2, mean PSG AHI 23 ^ 23.9 events per hour, and mean PAT AHI 23 ^ 15.9 events per hour. There was a significant correlation between PAT AHI and AHI by PSG (r ¼ 0:87, P , 0:001). To assess sensitivity and specificity of Watch_PAT, we constructed receiver operator characteristic curves using a variety of AHI threshold values (10, 15, 20, and 30 events per hour). Optimal combinations of sensitivity and specificity for the various thresholds were 82.6/71.4, 93.3/73.3, 90.9/84.2, and 83.3/91.7, respectively.

Conclusions: The Watch_PAT is a device that can detect OSA with reasonable accuracy. Thus, the Watch_PAT may be a useful method to diagnose OSA.

Objectives and background: Arousals from sleep are associated with increased sympathetic activation and therefore with peripheral vasoconstriction. Sleep fragmentation in the form of multiple arousals is associated with daytime somnolence and cognitive impairment; however, manual scoring of arousal is time consuming and problematic due to relatively high inter-scorer variability. We have recently shown that automated analysis of in-lab recorded peripheral arterial tone (PAT) signal and the pulse rate derived from it can accurately assess arousals from sleep as defined by the American Academy of Sleep Medicine (AASM). In the current study we sought to extend these findings to the Watch_PAT100 (WP100), an ambulatory device measuring PAT, oximetry and actigraphy.

Methods: Sixty-eight subjects (61 patients referred to the sleep lab with suspected obstructive sleep apnea and seven healthy volunteers, mean age 46.3 ^ 14.2 years) underwent a whole night polysomnography (PSG) with simultaneous recording of PAT signal by the ambulatory WP100 device. The PSG recordings were blindly manually analyzed for arousals based on AASM criteria, while PAT was scored automatically based on the algorithm developed previously.

Results: There was a significant correlation between AASM arousals derived from the PSG and PAT autonomic arousals derived from the WP100 (R ¼ 0:87, P , 0:001), with a good agreement across a wide range of values. The sensitivity and specificity of PAT in detecting patients with at least 20 arousals per hour of sleep were 0.80 and 0.79, respectively, with an receiver operating characteristic curve having an area under the curve of 0.87.

Conclusions: We conclude that automatic analysis of peripheral arterial tonometry signal derived from the ambulatory device Watch_PAT100 can accurately identify arousals from sleep in a simple and time saving fashion.

Hedner J, Pillar G, Pittman DS, Zou D, Grote L, White D. A Novel adaptive wrist actigraphy algorithm for Sleep-Wake assessment in sleep apnea patients. *SLEEP 2004; 27(8):1560-1566.*

Study Objectives: Current actigraphic algorithms are relatively less accurate in detecting sleep and wake in sleep apnea patients than in people without sleep apnea. In the current study, we attempted to validate a novel automatic algorithm, which was developed for actigraphic studies in normal subjects and patients with obstructive sleep apnea by comparing it on an epoch-by-epoch basis to standard polysomnography.
Design: Prospective cohort study.
Setting: Multicenter, university hospital, sleep laboratories.
Participants: A total of 228 subjects from 3 different sleep centers (Skara, Boston, Haifa) participated.
Intervention and Measurements: Simultaneous recording of polysomnography and Watch_PAT100, an ambulatory device that contains a built-in actigraph. The automatic sleep/wake algorithm is based on both the quantification of motion (magnitude and duration) and the various periodic movement patterns, such as those occurring in patients with moderate to severe obstructive sleep apnea.
Results: The overall sensitivity and specificity to identify sleep was 89% and 69%, respectively. The agreement ranged from 86% in the normal subjects to 86%, 84%, and 80% in the patients with mild, moderate, and severe obstructive sleep apnea, respectively. There was a tight agreement between actigraphy and polysomnography in determining sleep efficiency (78.4 ± 9.9 vs 78.8 ± 13.4%), total sleep time (690 ± 152 vs 690 ± 154 epochs), and sleep latency (56.8 ± 31.4 vs 43.3 ± 45.4 epochs). While for most individuals the difference between the polysomnography and actigraphy was relatively small, for some there was a substantial disagreement.
Conclusions: We conclude that this actigraphy algorithm provides a reasonably accurate estimation of sleep and wakefulness in normal subjects and patients with obstructive sleep apnea on an epoch-by-epoch basis. This simple method for assessment of total sleep time may provide a useful tool for the accurate quantification of obstructive sleep apnea in the home environment.

Pittman DS, Ayas NT, MacDonald MM, Malhotra A, Fogel RB, White D. Using a Wrist-Worm Device Based on Peripheral Arterial Tonometry to Diagnose Obstructive Sleep Apnea: In-Laboratory and Ambulatory Validation. *SLEEP 2004; 27(5):923-933.*

Study Objectives: To assess the accuracy of a wrist-worn device (Watch_PAT 100) to diagnose obstructive sleep apnea in the home. Design: Participants completed 2 overnight diagnostic studies with the test device: 1 night in the laboratory with concurrent polysomnography and 1 night in the home with only the Watch_PAT. The order of the laboratory and home study nights was random. The frequency of respiratory events on the PSG was quantified using indexes based on 2 definitions of hypopnea: the respiratory disturbance index (RDI) using American Academy of Sleep Medicine Task Force criteria for clinical research, also referred to as the Chicago criteria (RDI.C), and the Medicare guidelines (RDI.M). The Watch_PAT RDI (PAT RDI) and oxygen desaturation index (PAT ODI) were then evaluated against the polysomnography RDI.C and RDI.M, respectively, for both Watch_PAT diagnostic nights, yielding INLAB and HOME-LAB comparisons.
Setting: Sleep laboratory affiliated with a tertiary-care academic medical center.
Patients: 30 patients referred with suspected OSA.
Interventions: N/A.
Measurements and Results: The polysomnography and PAT measures were compared using the mean [2 SD] of the differences and the intraclass correlation coefficient (ICC). The receiver-operator characteristic curve was used to assess optimum sensitivity and specificity and calculate likelihood ratios. For the IN-LAB comparison, there was high concordance between RDI.C and PAT RDI (ICC = 0.88, mean difference 2.5 [18.9] events per hour); RDI.M and PAT ODI (ICC = 0.95, mean difference 1.4 [12.9] events per hour; and sleep time (ICC = 0.70, mean difference 7.0 [93.1] minutes) between the test device and PSG. For the HOME-LAB comparison, there was good concordance between RDI.C and PAT RDI (ICC = 0.72, mean difference 1.4 [30.1] events per hour) and RDI.M and PAT ODI (ICC = 0.80, mean difference 1.6 [26.4] events per hour) for the test device and PSG. Home studies were performed with no technical failures.
Conclusions: In a population of patients suspected of having obstructive sleep apnea, the Watch_PAT can quantify an ODI that compares very well with Medicare criteria for defining respiratory events and an RDI that compares favorably with Chicago criteria for defining respiratory events. The device can be used with a low failure rate for single use in the lab and home for self-administered testing.

Subject Objective: To assess the accuracy of a portable monitoring device based on peripheral arterial tonometry to diagnose obstructive sleep apnea (OSA). To propose a new standard for limited-channel device validation using synchronized polysomnography (PSG) home recordings and a population-based cohort.
Design: Single-night, unattended PSG and Watch_PAT 100 (WP_100).
Setting: Home environment.
Participants: Ninety-eight subjects (55 men; age, 60 ± 7 year; body mass index, 28 ± 4 kg/m2) consecutively recruited from the Skaraborg Hypertension and Diabetes Project.
Measurements and Results: The WP_100 records peripheral arterial tone, heart rate, oxygen saturation and actigraphy for automatic analysis of respiratory disturbance index (RDI), apnea-hypopnea index (AHI), oxygen desaturation index (ODI), and sleep-wake state. The accuracy of WP_100 in RDI, AHI, ODI, and sleep-wake detection was assessed by comparison with data from simultaneous PSG recordings. The mean PSG-AHI in this population was 25.5 ± 22.9 events per hour. The WP_100 RDI, AHI, and ODI correlated closely (0.88, 0.90, and 0.92; $p < .0001$, respectively) with the corresponding indexes obtained by PSG. The areas under the curve for the receiver-operator characteristic curves for WP_100 AHI and RDI were 0.93 and 0.90 for the PSG-AHI and RDI thresholds 10 and 20 ($p < .0001$, respectively). The agreement of the sleep-wake assessment based on 30-second bins between the 2 systems was $82 \pm 7\%$.
Conclusions: The WP_100 was reasonably accurate for unattended home diagnosis of OSA in a population sample not preselected for OSA symptoms. The current design, including simultaneous home PSG recordings in population-based cohorts, is proposed as a reasonable validation standard for assessment of simplified recording tools for OSA diagnosis.

Objective: Our goal was to validate the WatchPAT in the diagnosis of obstructive sleep apnea.
Study Design: We conducted a prospective, blinded, nonrandomized clinical trial.
Methods: Patients with suspected obstructive sleep apnea scheduled for an overnight level I Polysomnogram were offered enrollment in a study to compare the WatchPAT (Itamar Ltd, Israel) device with polysomnography. Patients wore the Watch-PAT device simultaneously while undergoing polysomnography during evaluation in the sleep lab.
Results: Thirty-seven patients participated in the study. They had a mean age of 50.1 years (range, 31_73 years) and mean body mass index of 34.6 kg/m2 (range, 21.2_46.8 kg/m2). There was high correlation between the Polysomnogram and WatchPAT apnea-hypopnea index (r _ 0.9288; 95% confidence interval _0.8579_0.9650, P _ 0.0001). The lowest oxygen saturation also showed high correlation (r _ 0.989; 95% confidence interval .9773_0.9947, P _ 0.0001). The overall Polysomnogram and WatchPAT sleep times revealed a correlation of r _ 0.5815 (P_ 0.005).
Conclusion: The WatchPAT showed a high correlation with the polysomnogram in apnea-hypopnea index, lowest oxygen saturation, and sleep time.
Significance: It's use as a reliable tool in the diagnosis of Obstructive Sleep Apnea.

Outcome Studies:

Pittman S.D, Pillar G, Berry RB, Malhotra A, MacDonald MM, White DP. **Follow-Up Assessment of CPAP Efficacy in Patients with Obstructive Sleep Apnea using an Ambulatory Device Based on Peripheral Arterial Tonometry.** *Sleep and Breathing 2006; 10(3):123-131.*

ABSTRACT: This study aimed to assess the accuracy of a wrist-worn device based on peripheral arterial tonometry (Watch_PAT 100) to detect residual episodes of respiratory disturbance during continuous positive airway pressure (CPAP) therapy. Concurrent polysomnography was used as the reference standard to identify sleep disordered breathing (SDB) events. The study was conducted in three sleep laboratories affiliated with tertiary care academic medical centers. Seventy patients using CPAP to treat obstructive sleep apnea for at least 3 months, following an in-laboratory titration to determine the optimal therapeutic positive airway pressure, participated in this study. Symptoms indicating suboptimal therapy were not required for participation, but self-reported adherence to CPAP therapy was necessary for inclusion. Interventions are not applicable in this study.

The accuracy of the PAT derived respiratory disturbance index (PAT RDI scored by automated algorithm) to detect residual SDB on CPAP was assessed against polysomnography (PSG) using Bland−Altman analysis, receiver−operator characteristic (ROC) curves, and likelihood ratios for increasing (LR+) and decreasing (LR−) the probability of moderate−severe SDB in the study population. Respiratory events on the PSG were quantified using standard criteria for research investigations ("Chicago criteria") to yield a PSG RDI.C. Based on the PSG results, 19% of the participants had moderate−severe SDB (PSG RDI.C>15 events per hour) on their prescribed pressure. For PAT RDI >15 events per hour, the area under the ROC curve was 0.95 (SE 0.03, $p<0.0001$, 95% CI 0.89 to 1.00), the LR+ was 8.04 (95% CI 3.64−17.7), and the LR− was 0.17 (95% CI 0.05−0.62). The mean difference between the PAT RDI and PSG RDI.C was three (2SD 14.5) events per hour. Therefore, residual moderate−severe SDB on CPAP was not uncommon in a multicenter population self-reporting adherence to CPAP therapy to treat obstructive sleep apnea. The Watch_PAT device accurately identified participants with moderate−severe SDB while using CPAP in the attended setting of a sleep laboratory.

Townsend D, Sharma A, Brauer E, Scattarelli D, McEiver J, Eiken T, Freiberg M. **Assessing Efficacy, Outcomes , and Cost Savings for Patients with Obstructive Sleep Apnea Using Two Diagnostic and Treatment Strategies.** *Sleep Diagnosis and Therapy. 2007; 1(7):1-8.*

Objectives*:* Interest in portable monitoring (PM) to asses obstructive sleep apnea (OSA) has grown in recent years spurred by new technologies. Peripheral Arterial Tonometery (PAT) is one such technology, which records episodic changes in peripheral arterial tone due to bursts of sympathetic nervous system activation in response to respiratory events. PM devices have been compared to PSG but have not been used to assess clinical decision-making, patient outcomes or cost savings.

Methods: 303 consecutive new patients were screened and 103 met strict inclusion and exclusion criteria. Individuals were randomly assigned to PSG (n=53) or PAT (n=50) testing. Positive airway pressure (PAP) therapy was provided for some patients based on predetermined OSA severity criteria. Outcomes at 8-week and 6-month follow-up included hours of PAP use, measures of overall functioning and cost.

Results: At both 8-week and 6-month follow-up, both groups demonstrated significant improvements in most variables assessed however attrition rates were high. At 8-weeks, hours of PAP use were higher for participants in the PSG group (PSG 5.1, PAT 4.0 hours), however at 6-months this difference was not significant (PSG 5.5, PAT 5.4 hours). PAT group demonstrated higher ESS at 8-week but not 6-months. Cost of assessment using PAT was significantly less than PSG.

Conclusions: Using PAT to assess OSA can be a clinically and financially effective approach when used for select patients by a sleep specialist. Patient adherence to PAP and quality of life measures improved in both groups and were similar at 6-month FU. Cost savings are significant when using PM

Itzhaki S, Dorchin H, Clark GT, Lavie l, Lavie P, Pillar G. The Effects of One Year Treatment with a Herbst Mandibular Advancement Splint on Sleep Apnea, Oxidative Stress and Endothelial Function. *CHEST 2007; 131:740-749.*

Background: Obstructive sleep apnea (OSA) is associated with endothelial dysfunction. In the current study, we assessed the effect of long-term modified Herbst mandibular advancement splint (MAS) treatment on OSA, oxidative stress markers, and on endothelial function (EF). *Methods:* A total of 16 subjects participated (11 men and 5 women; mean [_ SD] age, 54.0 _ 8.3 years; mean body mass index, 28.0 _ 3.1 kg/m2), 12 of whom completed the 1-year evaluation. Apnea severity, levels of oxidative stress markers, and EF were assessed after 3 months and 1 year of receiving treatment. For comparison, 6 untreated patients underwent two evaluations 9 months apart, and 10 non-OSA individuals were assessed once as a reference group. The results are presented as the mean _ SD.

Results: The mean apnea-hypopnea index (AHI) decreased significantly from 29.7 _ 18.5 events/h before treatment to 17.7 _ 11.1 events/h after 3 months of treatment and 19.6 _ 11.5 events/h after 1 year of treatment ($p < 0.005$ for both). The mean Epworth sleepiness scale score decreased significantly from 12.4 _ 6.0 before treatment to 10.2 _ 6.6 after 3 months of treatment and 7.8 _ 3.8 after 1 year of treatment ($p < 0.001$ for both). The mean EF improved significantly from 1.77 _ 0.4 before treatment to 2.1 _ 0.4 after 3 months of treatment ($p < 0.05$) and 2.0 _ 0.3 after 1 year of treatment (p _ 0.055), which were similar to the values of the reference group. Thiobarbituric acid-reactive substance (TBARS) levels decreased from 18.8 _ 6.2 nmol malondialdehyde (MDA)/mL before treatment to 15.8 _ 3.9 MDA/mL after 3 months of treatment (p _ 0.09) and 15.5 _ 3.2 nmol MDA/mL after 1 year of treatment $p < 0.05$). There was a correlation between the improvement in AHI and in EF or TBARS levels (r _ .55; p _ 0.05). The untreated control group remained unchanged.

Conclusions: The Herbst MAS may be a moderately effective long-term treatment for patients with OSA. EF improved to levels that were not significantly different than reference levels, even though apneic events were not completely eliminated. We think that these data are encouraging and that they justify the performance of larger randomized controlled studies.

Richard B. Berry, Gilbert Hill, Linda Thompson, Valorea McLaurin, Malcom Randall. Portable Monitoring and Auto-Titration versus Polysomnography for the Diagnosis and Treatment of Sleep Apnea. SLEEP, Vol 31, No. 10, 2008.

Study Objectives: Compare a clinical pathway using portable monitoring (PM) for diagnosis and unattended auto-titrating positive airway pressure (APAP) to select an effective continuous positive airway pressure (CPAP) with another pathway using polysomnography (PSG) for diagnosis and treatment of Obstructive Sleep Apnea (OSA).

Design: Randomized parallel group

Setting: Veterans Administration Medical Center

Patients: 106 patients with daytime sleepiness and a high likelihood of having OSA

Measurements and Results: The AHI in the PM-APAP group was 29.2 ± 2.3/hour and in the PSG group was 36.8 ± 4.8/hour (p = NS). Patients with an AHI > 5 were offered CPAP treatment. Those accepting treatment (PM-APAP 45, PSG 43) were begun on CPAP using identical devices at similar mean pressures (11.2 ± 0.4 versus 10.9 ± 0.5 cm H2O). At a clinic visit 6 weeks after starting CPAP, 40 patients in the PM-APAP group (78.4% of those with OSA and 88.8% started on CPAP) and 39 in the PSG arm (81% of those with OSA and 90.6% of those started on CPAP) were using CPAP treatment (p=NS). The mean nightly adherence (PM-APAP: 5.20 ± 0.3 versus PSG 5.25 ± 0.4 hours/night), decrease in Epworth sleepiness scale ($- 6.5 \pm 0.7$ versus -6.97 ± 0.73), improvement in the global Functional Outcome of Sleep Questionnaire score (3.1 ± 0.05 versus 3.31 ± 0.52), and CPAP satisfaction did not differ between the groups.

Conclusions: A clinical pathway utilizing PM and APAP titration resulted in similar CPAP adherence and clinical outcomes as one using PSG.

General Topics on the Watch-PAT:

Respiratory Disturbances:

Margel D, White D, Pillar G. long-Term intermittent exposure to high ambient CO2 causes respiratory disturbances during sleep in submariners. *Chest 2003; 124(5):1716-1723.*

During most of the cruise, submarines are detached from their environment. Therefore, O2 levels are relatively low (19 kPa, 144 mm Hg) and CO2 levels are high (1 kPa, 7.6 mm Hg). There are, however, periods during ventilation of the submarine in which CO2 levels drop and O2 levels increase. The objective of this study was to determine whether these unique gas changes might result in sleep-disordered breathing in submariners.

Methods and materials: The sleep of eight healthy soldiers was assessed three times: (1) control night, in submarine docking; (2) at the beginning of the cruise (reflecting acute exposure to gas changes); and (3) at the end of the cruise (chronic exposure to gas changes). Each night was divided to three parts because of different CO2 levels (secondary to ventilation of the submarine). Sleep and breathing were measured using the portable Watch PAT100 device (Itamar Medical, Ltd; Caesarea, Israel) to detect breathing abnormalities during sleep.

Results: Sleep and breathing data were categorized according to four CO2 conditions: acute moderate (inhaled CO2 levels of 2.3 to 5 mm Hg during first 1 to 2 nights of the cruise); acute high (inhaled CO2 levels of 5 to 9.2 mm Hg during the first 1 to 2 nights of the cruise); chronic moderate (inhaled CO2 levels of 2.3 to 5 mm Hg during nights 9 to 10 of the cruise); and chronic high (inhaled CO2 levels of 5 to 9.2 mm Hg during nights 9 to 10 of the cruise). Respiratory disturbance index (RDI) was significantly higher in the chronic moderate CO2 condition than the chronic high condition (18.9/h vs 8/h, $p < 0.005$). RDI did not correlate with CO2 levels during the first nights of the cruise (R _ _ 0.2, not significant), but significantly negatively correlated with it during the last nights of the cruise (R _ _ 0.56, $p < 0.05$).

Conclusions: We conclude that during an 11-day cruise, submariners adapt to high CO2 levels, as evidenced by the significant dependence of RDI on CO2 during the final but not initial days of the cruise. This adaptation resulted in a significant increase in RDI when CO2 levels declined during the later nights of the cruise.

Pediatrics:

Objectives To assess the interactions between nocturnal hypoglycemia and sleep in children with type 1 diabetes mellitus (DM).

Study design Children with DM (n = 15) and 15 matched control children underwent full night polysomnographic recordings. Blood glucose levels were measured in the diabetic children by means of the MiniMed Continuous Glucose Monitoring System. Six of the diabetic children were also studied by peripheral arterial tonometry (an indirect indicator of sympathetic responses).

Results Five children with DM (33%) had profound nocturnal hypoglycemia, which was associated with increased sleep efficiency, increased slow wave sleep, and increased Δ power in spectral analysis of the electroencephalogram. Hypoglycemic episodes were not associated with sympathetic activation. Rapid decline in glucose levels (>25 mg/dL/hour) but not the absolute degree of hypoglycemia were associated with awakenings from sleep.

Conclusions We conclude that sleep may inhibit sympathetic and arousal response to hypoglycemia. Rapid changes in glucose levels, independent of absolute glucose levels, may result in awakening from sleep. Continuous measurement of glucose levels during sleep may add important features in the treatment of children with DM.

Study Objectives: Peripheral arterial tonometry (PAT) is a sensitive measure of moment-to-moment changes in sympathetic activity and reliably identifies arousals in adult subjects. We investigated whether PAT events during sleep are associated with visually recognizable electroencephalographic arousals in healthy children and in children with sleep-disordered breathing.

Design: Prospective cohort.

Setting: Pediatric Sleep Research Laboratory.

Participants: Twenty children with obstructive sleep apnea syndrome, 20 children with mild sleep-disordered breathing, and 20 control children with a mean age of 7.6 ± 2.6 years (range: 5.7-16.5 years); 53% of children were boys.

Interventions and Measurements: Polysomnographic evaluation in the sleep laboratory with concomitant recording of PAT. PAT events were defined as attenuations from immediately preceding baseline of 20% to 50% (PAT20) and > 50% (PAT50) for at least 5 seconds and the indexes calculated per hour of sleep time that included good-quality PAT signals. Total PAT index (the sum of PAT20 index and PAT50 index) was also calculated.

Results: Total PAT index correlated with total arousal index and spontaneous arousal index ($r = 0.55$, $P < .0001$, $r = 0.64$, $P < .001$, respectively), especially in the group with obstructive sleep apnea syndrome ($r = 0.71$, $P < .0001$). The sensitivity and specificity of PAT for identifying electroencephalographic arousals were 95% and 35%, respectively. The PAT device identified pathologic arousals indexes (ε 16 per hour) (area under the curve 0.79, $P = .002$). Thirty-five percent of respiratory events (eg, obstructive apnea or hypopnea) were associated with a visual electroencephalographic arousal, compared to 92% being associated with PAT attenuation events.

Conclusions: Arousals in sleeping children are associated with increased sympathetic discharge, as evidenced by attenuations in PAT signal. However, a significant proportion of PAT attenuations were not accompanied by visual electroencephalographic arousals. Thus, the importance of these autonomic arousals has yet to be explored in association with morbidities related to sleep-disordered breathing and, therefore, PAT technology cannot be recommended as an alternative tool for measuring arousals in children. Nevertheless, these data further support the contention that adult criteria for the measurement for arousals may not be adequate in children.

Endothelial Function

Itzhaki S et al. Endothelial Dysfunction in Obstructive Sleep Apnea Measured by Peripheral Arterial Tone Response in the Finger to Reactive Hyperemia. *SLEEP 2005; 28(5):594-600.*

Study Objective: The aim of this study was to investigate endothelial functioning in sleep apnea patients using a novel plethysmographic device that monitors peripheral arterial tone response in the finger to reactive hyperemia induced by forearm ischemia.
Participants: Forty-six sleep apnea patients, 74.0% men, mean age 46.8 ± 9.3 years, and 17 control subjects without sleep apnea, 64.7% men, mean age 47.1 ± 6.7 years.
Setting: Eight-bed Technion Sleep Medicine Center in Haifa, Israel.
Design: Endothelial functioning assessed by the reactive hyperemia peripheral arterial tone index was measured twice, before sleep and after waking from sleep monitored by polysomnography in the laboratory. The reactive hyperemia peripheral arterial tone index was calculated as the average amplitude of the peripheral arterial tone signal after the cuff deflation
divided by the average amplitude before the cuff inflation.
Results: Morning index of endothelial functioning was significantly lower in patients with moderate to severe sleep apnea (apnea-hypopnea index ≥ 30) than in patients with mild sleep apnea ($30 <$ apnea-hypopnea index ≤ 10) and in the control group without sleep apnea (apnea-hypopnea index <10). The morning index was significantly inversely correlated with apnea-hypopnea index. Patients with a history of hypertension or cardiovascular disease had significantly lower morning and evening indexes of endothelial functioning than patients without such a history. Multivariate analysis revealed that apnea-hypopnea index and sleep efficiency were significant predictors of the morning index.
Conclusion: Measurements of the response of the peripheral arterial tone in the finger to reactive hyperemia can be used as a substitute for the brachial artery ultrasound technique to measure endothelial functioning in patients with sleep apnea.

Yinon D, Levenstein L, Suraya S, Beloosesky R, Zmora O, Malhotra A, Pillar G. Pre- eclampsia toxemia is associated with sleep disordered breathing and endothelial dysfunction. *European Respiratory Journal 2006; 27(2):328-333.*

ABSTRACT: Pre-eclamptic toxaemia (PET) may be associated with both endothelial dysfunction (ED) and sleep-disordered breathing (SDB). It was hypothesised that females with PET would demonstrate both SDB and ED, and that a correlation between these two would suggest a potential causative association. A total of 17 females with PET and 25 matched females with uncomplicated pregnancy were studied. They underwent a nocturnal ambulatory sleep study (using Watch_PAT100) and noninvasive evaluation of endothelial function utilising the reactive hyperaemia test (using Endo_PAT 2000). A higher ratio of post- to pre-occlusion pulse-wave amplitude (endothelial function index (EFI)) indicated better endothelial function. Females with PET had a significantly higher respiratory disturbance index (RDI) and lower EFI than controls (18.4¡8.4 versus 8.3¡1.3?h-1, and 1.5¡0.1 versus 1.8¡0.1, respectively). Blood pressure significantly correlated with RDI and with EFI. EFI tended to correlate with RDI. In conclusion, these results suggest that both sleep-disordered breathing and endothelial dysfunction are more likely to occur in females with pre-eclamptic toxaemia than in females with uncomplicated pregnancies. The current authors speculate that respiratory disturbances contribute to the functional abnormality of the blood vessels seen in females with pre-eclamptic toxaemia, although causality cannot be determined based on this study.

General Reviews

Minal R. Patel, BA, Thomas H. Alexander, MD, MHS, Terence M. Davidson, MD Home sleep testing. Otolaryngology 2007; 18:33-51.

ABSTRACT: Sleep disordered breathing, also known as obstructive sleep apnea (OSA), is a highly prevalent disease occurring with a variety of life threatening comorbidities. For years, polysomnography has been considered the gold standard in diagnosis, consequently resulting in high costs and difficulty for head and neck surgeons to participate in the practice of sleep medicine. The development of multichannel home sleep testing by a variety of manufacturers offers a cost-effective and highly reliable method of screening for and diagnosing OSA. To complete the head and neck surgery sleep medicine practice, surgeons should provide sleep consultations and comprehensive diagnostic services out of their offices utilizing multichannel home sleep testing. Minal et al reviews a number of ambulatory devices including the Embletta, Apnea Link and the Watch-PAT100.

Madani M, Frank M, Lloyd R, Madani F. Polysomnography versus Home Sleep Study: Overview and Clinical Application. *Atlas of the oral and maxillofacial surgery clinics of North America 2007; 15(2):101-109*

The cost, complexity, availability, and limitations of PSG have led to the development of simpler diagnostic techniques in the field of sleep-disordered breathing. Growing insight from clinicians indicates that diagnosing OSA may affect prognosis of hypertension, stroke, and other cardiovascular-related disorders. If there were a convenient way to diagnose and treat OSA at early onset, treatment could be expedited to avoid serious co-morbidities associated with sleep apnea. In this study, the Watch-PAT100 was evaluated simultaneously against a standard in-laboratory PSG for detecting OSA with reasonable sensitivity and specificity as measured by AHI and RDI. It is not our belief that the wrist-worn PAT will replace standard PSG completely. Rather, it is our hope that the WatchPAT-100 will be seen as an accurate and affordable alternative for patients so that they may enjoy the benefits associated with a proactive approach to managing their sleep disorders.

Women Issues

Lior Lowenstein, Kimberly Kenton, Linda Brubaker, Giora Pillar,Nidhi Undevia, Elizabeth R. Mueller, Mary Pat FitzGerald. The relationship between obstructive sleep apnea, nocturia, and daytime overactive bladder syndrome in women. Am J Obstet Gynecol 2008; 198(5): 598.e1-5.

OBJECTIVE: The purpose of this study was to corroborate the association between obstructive sleep apnea (OSA) and nocturia in a clinical sample of urogynecologic patients and to explore whether night-time urine concentration predicts the presence of OSA. STUDY DESIGN: Patients with nocturia and control subjects underwent a home sleep study, completed validated nocturia questionnaires, and provided evening and morning urine specimens that were analyzed for osmolarity. RESULTS: Twenty-one patients with nocturia (16 of whom also had daytime overactive bladder [OAB] symptoms) and 10 control subjects were studied. OSA was present in 17 of 21 women (81%) with nocturia: 13 women (81%) with OAB, 4 women (80%) with nocturia/no OAB, and 4 control subjects (40%; P < .001). The percentage of rapid eye movement sleep time was correlated inversely with nocturic frequency (rho = -.51; P < .004). The presence of diluted nighttime urine in a patient with nocturia was 88% sensitive for the presence of OSA. CONCLUSION: We should consider a diagnosis of OSA in all patients with nocturia, even those patients with daytime OAB.

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- Watch-PAT is FDA cleared, CE certified and CSA certified.

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