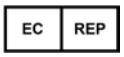
SleepImage

Introduction to SleepImage

Introduction to SleepImage is a clinician's guide that is available only in an electronic PDF format on www.sleepimage.com. It is updated periodically, identified by a release date and a sequential revision number. The contents of this document refer to the SleepImage System, a prescription Software as a Medical Device (SaMD), identified as follows:

	**Manufacturer**	MyCardio LLC 3200 E Cherry Creek South Drive, Suite 540, Denver, CO 80209, USA support@sleepimage.com www.sleepimage.com
	**Instructions for Use**	Please read the SleepImage® System Instructions for Use carefully and periodically as it is updated from time to time. Current Version: D-6.00285 Rev. 48 Issued on October 2, 2026 An electronic version of the current SleepImage® System Instructions for Use is available at www.sleepimage.com. Printed copy will be provided upon request within 7 calendar days at no additional cost. Please contact support@sleepimage.com.
	**Medical Device**	This product is a Medical Device.
	**Prescription Use Only**	FDA-cleared K182618 U.S. Federal law restricts sales of this device as "by or on the order of a licensed healthcare practitioner".
	**Unique Device Identifier**	The FDA Unique Device Identifier (UDI) is *+B315SLEEPIMAGESYSTEM0/$2.29/Q0Y*
	**CE Mark**	The CE mark is a declaration that the SleepImage System complies with the EU Medical Device Regulation (EU MDR 2017/745).



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Patent Marking

SleepImage (MyCardio LLC) is a provider of medical systems and services intended to establish sleep quality, evaluate sleep disorders and aid in diagnosis and management of sleep disorder breathing.

The technology in SleepImage systems and services is covered by patents owned and/or licensed in the United States and/or in other countries. This marking is intended to serve as notice under 35 U.S.C. § 287(a).

The following patents apply to SleepImage systems and services, including but not limited to the SleepImage System:

U.S. Patent Number(s): 7,324,845; 7,734,334; 8,401,626; 8,403,848; 12,144,592; 12,257,067. Other patent(s) pending.

Australian Patent Number(s): 2006269263, 2019345287. Other patent(s) pending.

Canadian Patent Number(s): 2566193; 2619617. Other patent(s) pending.

Chinese Patent Number(s): ZL 201980049494.3, ZL 201980071633.2, ZL 202080079952.0. Other patent(s) pending.

European Patent Number(s): 1765156, 1906817, 3809957. Validated in France, Germany, Italy, Spain, United Kingdom. Other patent(s) pending.

Japanese Patent Number(s): 5005539; 5005687; 7253047; 7455815, 7799604. Other patent(s) pending.

Other Patents Pending:
WO2019246234A1; WO2020061014A1; WO2021055943A1; WO2007008706A1; WO2005115230A1

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The SleepImage® System is in compliance with the EU Medical Device Regulation (MDR) 2017/745 (CE 2862) and is United States (US) Food and Drug Administration (FDA) cleared Software as a Medical Device (SaMD), K182618. The SleepImage System analyzes simultaneous recordings of heart rate, oxygen saturation and actigraphy from a photoplethysmography (PPG) sensor for sleep and respiratory analysis. The following signals (channels) are continuously sampled during sleep and analyzed with the proprietary algorithm cardiopulmonary coupling (CPC), not using Artificial Intelligence (AI): (1) changes in peripheral arterial tone (pat; a measurement of pulsatile volume changes reflecting changes in sympathetic tone and hemodynamics), (2) heart (pulse) rate (HR/PR), (3) heart (pulse) rate variability (HRV/PRV), (4) blood oxygenation (oximetry, SpO_2), (5) changes in breathing (respiration, tidal volume variability; TVV) and (6) movement (actigraphy). All channels of raw data are presented for the purpose of visualizing concurrent physiology and to review the autoscored respiratory events with ability for manual scoring/analysis as determined appropriate by the clinical user. The signal quality of the recorded raw physiological data is documented and presented with the color-coded "Signal Quality" line.

The SleepImage System is FDA-cleared to aid clinical diagnosis and management of Sleep Disordered Breathing (SDB) in children, adolescents, and adults. The output from the SleepImage System is based on cardiopulmonary coupling (CPC) analysis to calculate various sleep related output metrics. The output metrics include sleep stages: Stable Non-Rapid Eye Movement (sNREM), Unstable NREM (uNREM) and REM sleep), sleep onset (SO), sleep conclusion (SC), sleep duration (SD), total sleep time (TST), wake after sleep onset (WASO) and a proprietary sleep quality index (SQI). The sleep disordered breathing (SDB) related output metrics include 3% and 4% desaturation events, including a total SleepImage Apnea Hypopnea Index (sAHI), an obstructive AHI (sAHIobstructive), a central AHI (sAHIcentral), hypoxic burden (HB), a Respiratory Disturbance Index (sRDI), an Oxygen Desaturation Index (ODI), and the Sleep Apnea Indicator (SAI) that is derived from Cyclic Variation in Heart Rate (CVHR) and does not include changes in blood oxygenation.

The SleepImage System is a patented, Health Insurance Portability and Accountability Act (HIPAA) compliant cloud-based system. It is intended for use by, or on the order of a Healthcare Professional to establish sleep quality, and to aid in the evaluation of sleep disorders to inform or drive clinical management, as well as to aid in diagnosis and management of SDB. The SleepImage System is FDA-cleared/MDR-CE-marked for use with children aged 2 and older, adolescents and adults. The validation of the SleepImage System utilized clinical Polysomnography (PSG) as the standard upon which it was compared. Data presenting periods of sleep identified by both systems were compared for validation and published. Please refer to the List of Publications which can be found on the last few pages of this document.

The SleepImage System is cleared (registered) for use in various countries around the world. This document is intended to be relevant for clinical users in all countries where the SleepImage System is cleared or registered for use and is intended for general educational purposes. For information on how to use the SleepImage System, please refer to SleepImage System Instructions for Use. For information on where the SleepImage System is available and contact information for SleepImage representatives in different countries, please contact support@sleepimage.com.

For the purpose of diagnosing SDB, the US FDA-clearance for SleepImage states the following: *"Clinical evaluation has confirmed that the SleepImage System auto-scoring algorithms calculating the SleepImage Apnea*

Hypopnea Index (sAHI) generate comparable output to human manual scoring of an Apnea Hypopnea Index (AHI) from Polysomnography (PSG) studies, using American Academy of Sleep Medicine (AASM) scoring guidelines for children and adult patients."

The Sleeping Brain & Body

Good sleep quality is crucial for good physical and mental health. One of the key benefits of using the SleepImage System in clinical practice is that unlike most clinical home sleep measurements systems, it is not restricted to evaluate only SDB but includes evaluation of sleep states, sleep stages and a proprietary sleep quality index (SQI). SleepImage is a comprehensive measure of physiology during sleep, based on collecting and analyzing signals controlled by the autonomic nervous system (ANS), reflecting changes in hemodynamics and breathing (Bartsch et al., 2012; Chiang et al., 2024; Chiang, Lee-Iannotti, et al., 2026; Penzel et al., 2016; Thomas, 2016; Thomas et al., 2014).

Sleep is controlled in the midbrain that sends sleep signals to both the surface of the brain and to peripheral organs allowing sleep to be measured through (1) changes in the Central Nervous System (CNS), using changes in brainwaves measured with electroencephalographic (EEG) signals to estimate sleep states and stages by utilizing Polysomnography (PSG) and/or (2) changes in the Autonomic Nervous System (ANS) output by recording changes in heart rate and breathing that change with sleep depth, which allows for estimation of sleep states and sleep stages (Figure 1).



I. Hypothalamus

Ventrolateral preoptic nucleus (VLPO) the wakefulness-sleep switch (flip-flop model) and body temperature. Suprachiasmatic nuclei (SCN) regulate melatonin and circadian rhythms.

II. Midbrain & Pons

Pedunculopontine tegmentum (PPT) contributes to the EEG activity of REM sleep, periaqueductal grey (PAG) regulates timing of REM and responses in the cardiovascular system.

III. Thalamus

Directly or indirectly receives inputs from and modulates output to ANS and is one of the subcortical structures/locations highly involved in synchronization of slow-waves during sleep (SWS) recorded using EEG-equipment for sleep staging.

IV. Brainstem

The Reticular Activating System (RAS) projecting to intralaminar nuclei of thalamus, which projects diffusely to the cerebral cortex has a fundamental role in regulating arousals and sleep-wake transitions.

Figure 1. Changes in brain- and peripheral activity during sleep.

Autonomic neural control in sleep regulation refers to how the ANS – which governs involuntary bodily functions like heart rate (HR), heart rate variability (HRV) and breathing which significantly impacts sleep cycles by adjusting physiological activity coherent to different sleep states and stages, thereby contributing to the overall quality and stability of sleep (Figure 2). The ANS is regulated in totally different ways during wakefulness, lighter sleep stages, deep sleep- and dream-sleep (Somers et al., 1993). The lowest activity of the sympathetic nervous system (SNS) is observed during deep sleep and is associated with predominant activity of the parasympathetic nervous system (PNS). During dream sleep increased activity is observed in the sympathetic branch. Recording changes in the ANS through changes in cardio-reparatory function (HR/HRV and breathing) during sleep allows for sleep state and staging, providing sleep disorder diagnostic information (Bartsch et al., 2012; Penzel et al., 2016).

The ANS includes two branches, the sympathetic- and parasympathetic branch, that "*work antagonistically, synergistically and independently to gather information from sensory organs and coordinate responses to internal and external demands*".

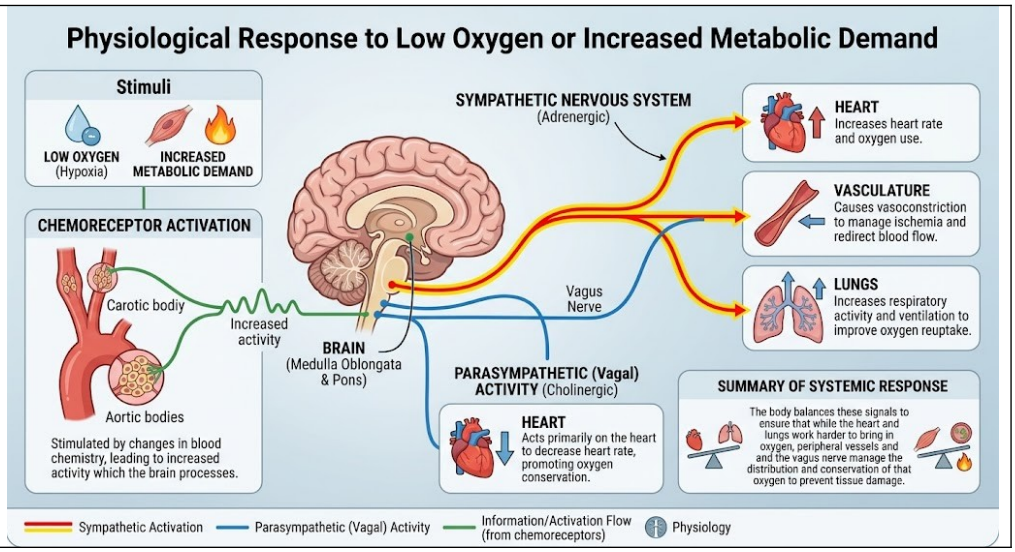


Figure 2. The sympathetic- and parasympathetic branches of the autonomic nervous system.

The interplay between sleep and cardiovascular activity has been investigated using non-invasive methods including HRV with time-domain and/or frequency-domain analysis to identify ANS modulations in sleep (Penzel et al., 2016). Recording HR/HRV and changes in breathing is simpler to record when compared to EEG, EOG and EMG due to larger signal amplitude and much better signal to noise ratio, requiring less sophisticated amplifiers and simpler sensors. Consequently, and based on knowledge of the underlying physiology of the ANS, recording HR/HRV became highlighted as a candidate to record and compute data for studying sleep and diagnosing sleep disorders that could serve as a simple surrogate method to sleep recordings from the skull with EEG, EOG and EMG (Penzel et al., 2016).

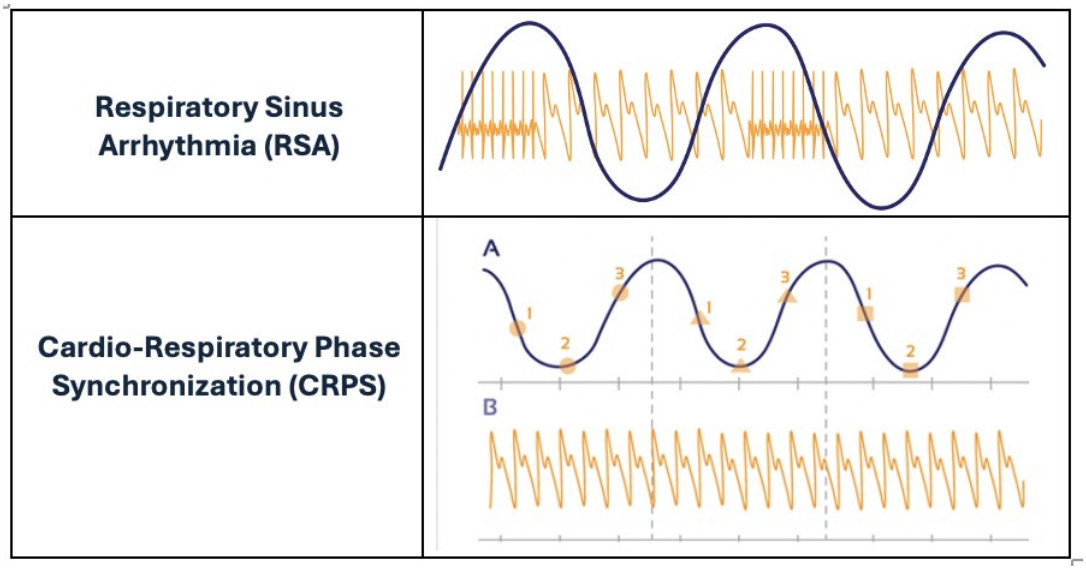


Figure 3. The relationship between changes in heart rate and breathing during respiratory sinus arrhythmia (RSA) and cardio-respiratory phase synchronization (CRPS).

Regulation in breathing and heartbeats changes from wake to light sleep, to deep sleep and dream sleep, as these bio-signals are intimately coupled but very different during wake and the different sleep states and stages. The best studied mechanisms of this cardiopulmonary coupling are: 1) respiratory sinus arrhythmia (RSA) that describes the respiratory-gated fluctuation of heart rate: during inspiration heart rate increases and during expiration it decreases and 2) Cardio-Respiratory Phase Synchronization (CRPS) can occur without RSA. During CRPS heartbeats occur more often during some phases of the respiratory cycle, e.g., at the beginning of inspiration, at the end of inspiration and in middle of inspirations. CRPS is most prominent during deep sleep (Figure 3) (Bartsch et al., 2012).

Sleep Architecture, Sleep States and Sleep Stages

Significant progress has been made to better understand sleep and sleep mechanisms since the release of the "*Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects*" in 1968 (Allan Rechtschaffen, 1968). In the past, most studies have been focused on the link between electrophysiological events of the central nervous system (CNS) during sleep electroencephalography (EEG), while dynamic shifts in autonomic neural control through the ANS during sleep and ANS-dynamics can be recorded and interpreted in a similar way to derive sleep states and sleep stages as the EEG-waves are utilized to derive sleep stages of non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. Until more recently ANS-based sleep staging has, to a certain degree, been overlooked (Bakker et al., 2021; Bartsch et al., 2012; Chen et al., 2022; Cysarz et al., 2004; Penzel et al., 2016; Thomas et al., 2005; Tsai et al., 2022).

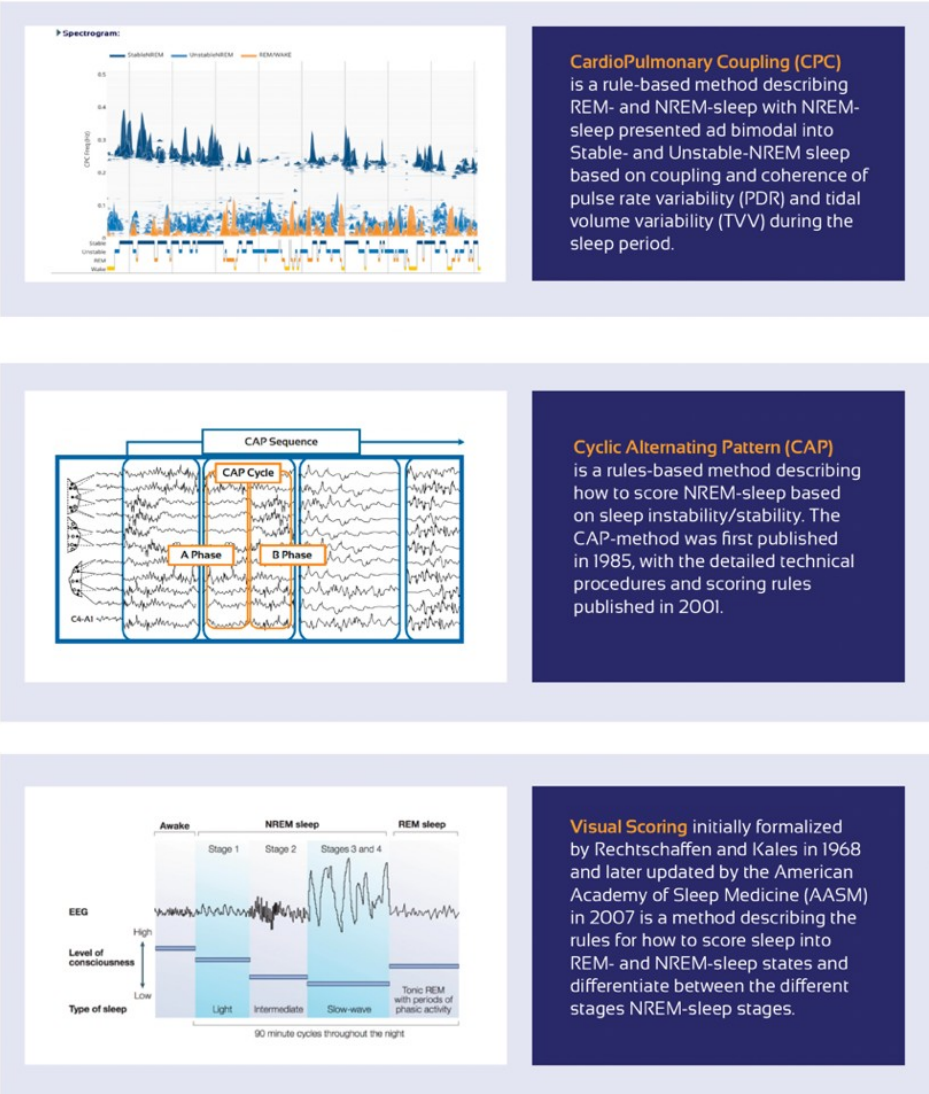


Figure 4. Comparison of methods to classify sleep states and sleep stages, (1) cardiopulmonary coupling (CPC), (2) cyclic alternating pattern (CAP) and (3) scoring of the brain's electrical activity (EEG).

Sleep architecture and classification of sleep into sleep states and sleep stages is used to investigate the duration, quality of sleep, and the structure of the sleep cycles during the night. The most common method to classify sleep states and sleep stages is based on identifying changes in brainwaves recorded with an electroencephalogram (EEG) during a polysomnography (PSG) sleep study. PSG is a multi-sensor recording system of various physiological signals including EEG, electrooculogram (EOG) and electromyogram (EMG), airflow, arterial oxygen saturation (SpO_2), and respiration during sleep.

Sleep staging in the PSG-system is based on cyclic alternation of two major and distinct neurophysiological states: (1) Rapid Eye Movement (REM) sleep, where EEG desynchrony is the dominant feature and there is a sympathetic dominance in the ANS and (2) Non-REM (NREM) sleep that is further differentiated into NREM-stage-1, NREM-stage-2 and NREM-stage-3. EEG synchrony grows with increasing sleep depth and parasympathetic influence is dominant during NREM-stage-3 sleep during when slow wave sleep (SWS) is high. NREM-stage-3 is a restorative sleep state that is known to facilitate cognitive function and memory consolidation and is associated with endocrine secretion and adaptive immune response. The alternating

pattern of NREM and REM sleep constitutes the sleep cycle, and its recurrence during the night determines the classical stepwise sleep profile (macrostructure). There are two methods described and published on how to approach sleep-stage classification from EEG which are presented in Figure 4 above.

Visual Scoring initially formalized by Rechtschaffen and Kales in 1968 (A. Rechtschaffen, 1968), and later updated by the American Academy of Sleep Medicine (AASM) in 2007 (Iber & Medicine, 2007); it is a method describing rules for scoring sleep into REM- and NREM-sleep states and to differentiate between the different stages of NREM-sleep.

Cyclic Alternating Pattern (CAP) is also a rules-based method describing how to score NREM-sleep based on sleep instability/stability. The CAP-method was first published in 1985 (Terzano et al., 1985), with the detailed technical procedures and scoring rules published in 2001 (Terzano et al., 2001). The presence or absence of CAP provides useful insights into sleep stability. The CAP cycle is defined as a sequence of two alternating stereotyped EEG patterns, (phase A and phase B) each lasting more than 2 seconds and less than 60 seconds. CAP is the EEG defined marker of sleep instability i.e., unstable sleep and which is enhanced when sleep is disturbed ty internal or external factors (Parrino et al., 2012; Parrino et al., 2026).

Cortical sleep staging is based on convention rather than its clinical relevance over ANS sleep staging and more recent experimental and clinical evidence suggests a noteworthy activation of different biological systems where the key role is played by the ANS (Tobaldini et al., 2013). Increasing body of evidence is surfacing that the ANS, long recognized to modulate cognition during wake, can impact memory processing during sleep in patients with mild cognitive impairment (MPI) (Whitehurst et al., 2022) who are more vulnerable to sleep related parasympathetic dysfunction (Kong et al., 2021) and that increased sympathetic activity during sleep increases risk of metabolic disease (Magnusdottir, Thomas, et al., 2021; Nevels et al., 2023) demonstrating that ANS sleep staging has, in research, shown to correspond to functional outcomes.

Cardiopulmonary Coupling (CPC)

In 2005 Thomas et al., published a method developed to evaluate sleep states and sleep stages based on cardiopulmonary coupling (CPC), analyzing heart (HRV) or pulse (PRV) rate variability (e.g., RR interval time series) as well as fluctuations in R-wave amplitude induced by respiration to detect changes in breathing (TVV, tidal volume variability); bio-signals which are highly influenced by the ANS (sympathetic and parasympathetic influence) and is the core of the SleepImage System (Thomas et al., 2005). For CPC- sleep state and stage evaluations the method calculates the cross spectral power and coherence of the RR-time series and corresponding TVV-time series which are calculated for consecutive windows to analyze coherence and cross-spectral power which is used to obtain the ratio of coherent cross power in the low frequency band (LFC, 0.01-0.1 Hz) to that in the high-frequency band (HFC, 0.1-0.4 Hz). When evaluating the synchronization between the two signals, there are two key factors to observe: (1) Coupling: The oscillations in the signals at given frequency (amplitude relationship), and (2) Coherence: the synchronization of the signals at given frequency (phase relationship).

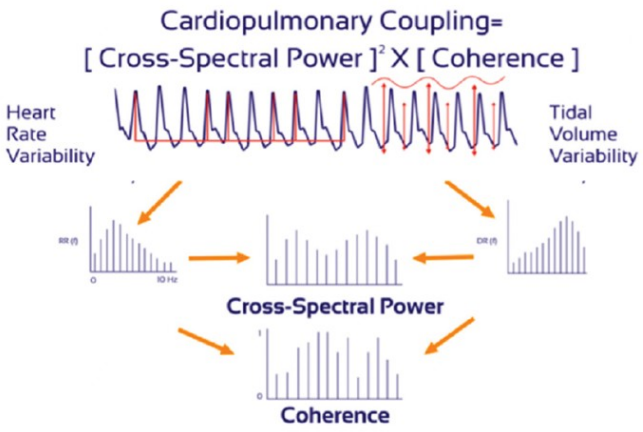


Figure 5. Cardiopulmonary Coupling (CPC).

The SleepImage System algorithm can be computed from any source with quality recordings of HRV/PRV and TVV, including a photoplethysmography (PLETH) signal that meet the defined data acquisition characteristics. Once a sleep study has been recorded and uploaded, the PRV is calculated, ectopic beats and outliers identified, filtered, and removed and normal sinus (N-N) intervals are extracted, TVV is obtained by using R-S wave amplitudes and variations in the QRS complexes area and baseline changes and Fast Fourier Transform is applied (Figure 6) (Thomas et al., 2005).

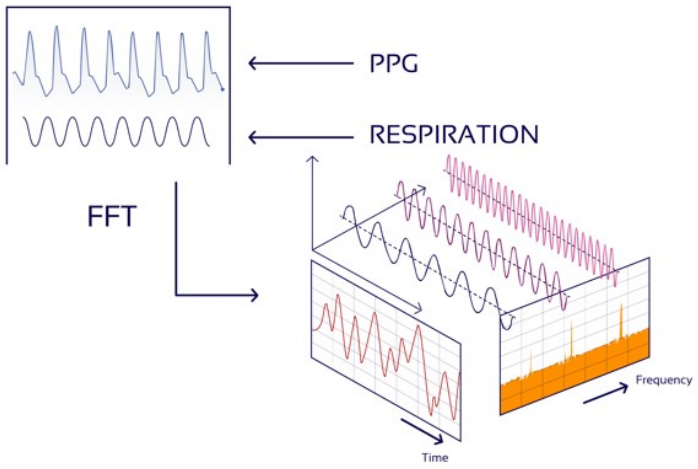


Figure 6. Fast Fourier Transform (FFT)

The degree of CPC coupling/coherence dramatically changes with the sleep states and stages, offering the capability to evaluate sleep and report on sleep duration, sleep onset (SO), sleep conclusion (SC), total sleep time (TST), wake after sleep onset (WASO) and differentiate between sleep states and sleep depth (Thomas et al., 2005; Thomas et al., 2014; Wood et al., 2020). This synchronization (coupling/coherence) is most prominent in healthy children as expected, as sleep depth/delta waves and non-CAP are most prominent in healthy children. In healthy individuals, CPC-synchronization shows a low intraindividual variability from night-to-night. Starting in early adolescence, the synchronization gradually reduces but remains relatively stable across subjects into early adulthood when it starts to gradually decline with age (Hilmisson et al., 2026; Hilmisson et

al., 2025b) as do the EEG-produced delta-waves and sleep instability on CAP-increases (Ohayon et al., 2004). Inter-individual variation (standard deviation) of sleep parameters needs to be kept in mind when evaluating sleep stability/instability that is explained by both the individual sleep trait and the individual health status.

Bimodality of Sleep

Data from in-laboratory polysomnography studies was analyzed to develop the CPC-method where Thomas et al., described their findings of a bi-modal structure of NREM-sleep as two sleep stages, displaying distinct alternating and abruptly varying periods of strong High Frequency Cardiopulmonary coupling (HFC, 0.1-0.5Hz) as Stable NREM-sleep and Low Frequency Cardiopulmonary coupling (LFC, 0.001-0.1 Hz) as Unstable NREM-sleep (Thomas et al., 2005). This is seen in the Sleep Spectrogram that demonstrates clear boundaries with sleep-stage transition from parasympathetic dominance (Stable NREM-sleep) to sympathetic dominance (Unstable NREM-sleep) and REM-sleep and Wake (very low frequency coupling (vLFC), <0.001Hz) (Haitham S. Al Ashry et al., 2021; Bartsch et al., 2012; Thomas, 2016; Thomas et al., 2005; Thomas et al., 2014; Wood et al., 2020). The concept is supported by various biological system behaviors, like being either awake or asleep and when sleeping, being either in NREM- sleep (stable or unstable) or in REM- sleep (phasic- or tonic).

Stable NREM sleep (HFC)

Stable NREM sleep relates to a global condition of stability when all the subsystems that control and influence the sleep mechanisms are balanced. Stable NREM-sleep is characterized by stable breathing and stable oxygenation, high vagal tone, non-cyclic alternating pattern (n-CAP) on EEG, continuous occurrence of slow oscillations, high delta power, blood pressure dipping and stable arousal threshold. This state may be considered as "*effective*" NREM sleep. Effective sleep enables the desirable functions of sleep across multiple dimensions (e.g., neuronal networks, cardiovascular, metabolic, immune etc.), such that spending periods in this state enable recovery and restorative processes.

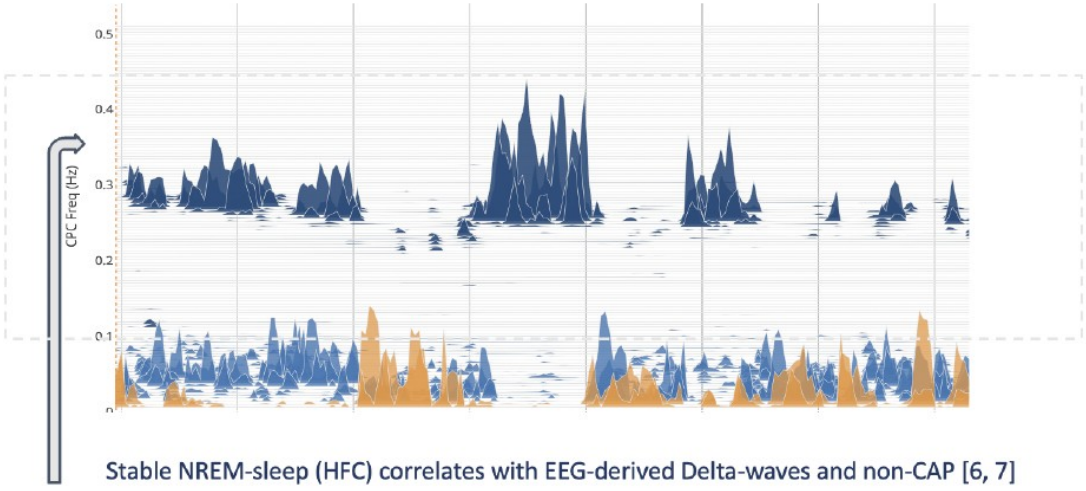


Figure 7. The sleep spectrogram reveals that NREM sleep has a distinct bimodal-type structure marked by distinct alternating and abruptly varying periods of strong high and low frequency cardiopulmonary coupling (HFC and LFC, respectively). These CPC states are separated widely in signal space with no overlap – that is, the boundaries are clean.

Unstable NREM sleep (LFC)

Unstable NREM sleep is a marker of sleep instability. Unstable NREM-sleep has opposite features when compared to Stable NREM-sleep, with tidal volume variability (TVV), cyclic variation in heart rate (CVHR), CAP on EEG, low relative delta power, non-dipping of blood-pressure and unstable arousal thresholds. This state may be considered as "*ineffective*" NREM sleep. Ineffective sleep fails to accomplish the desirable functions of healthy sleep. As Unstable NREM-sleep is a highly sensitive but non-specific index, it cannot reveal the nature of perturbation, only the existence. A certain amount of Unstable NREM-sleep should be expected as this is a state that includes transitions from other sleep stages, however, excessive duration of Unstable NREM-sleep certainly indicates that one or more factors are interfering with the process of sleep consolidation and quantifies the magnitude and thus may prohibit sleep to perform its task of health promotion and maintenance.

The CPC-based sleep state classification in the SleepImage System is not limited to the finding of a single event (e.g., isolated arousal), as it identifies patterns of Stable vs. Unstable NREM-sleep. The SleepImage System translates a physiological state that involves autonomic function, cerebral activities, and behavioral features into sleep architecture/sleep stages. In other words, what happens physiologically at "*upper levels*" (brain/CNS) is reflected at "*lower levels*" (ANS) and vice versa (Figure 7).

Unlike EEG-based manual scoring, CPC-sleep staging is performed in the frequency domain vs the time domain analysis of EEG. Thus, CPC offers a fully automated analysis that only needs a qualified healthcare provider to review the recorded channels for signal quality, recording time, sleep state and stage outputs including sleep onset, sleep offset, wake after sleep onset and total sleep time. The respiratory-event scoring can however be modified, when needed, to determine the type, pattern, severity and features of respiratory events and the automatically scored events can be removed, edited and/or added as/if needed.

Sleep State Classification, Cardiopulmonary Coupling & Polysomnography

The medical literature historically divided sleep into NREM- and REM-sleep, with NREM-sleep having four stages, that later were reduced to three stages (by combining Stage 3 and 4). Stage 3 represents "*deep sleep*" or "*slow wave sleep*" a stage where the brain almost exclusively produces slow delta waves. Stage 1 is usually a short period, a transition stage between wake and sleep. Stage 2 is defined as a state when cortical brain waves slow down and eye movements stop, but still with an occasional burst of faster brain waves, sleep spindles and K-complexes. How the biologic role of NREM sleep is associated with delta power is still unclear. Restricting such periods produces adverse consequences, similar to those of total sleep deprivation, including sleepiness and metabolic dysregulation. Delta power as a proportion of total EEG power is highest during the initial cycles of NREM sleep and gradually decreases across the biological night and shows rebound effects after a period of sleep deprivation.

It is important to note that CPC does not rely on the same data input streams as PSG. Rather than the primary dependence and interpretation of EEG morphology through the "*upper*" brain centers as PSG, CPC utilizes the physiological changes that occur with sleep via changes in the ANS signaled through the "*lower*" brain centers and networks (including thalamus, hypothalamus, hippocampus and brain stem), all brain centers that are highly involved in sleep regulation (Figure 1). The CPC-method integrates information from brain activity on ANS and changes that occur in respiration and cardiac output (changes in hemodynamics) to capture the ebb and flow of sleep, making traditional "*sleep staging*" comparisons a misnomer. The CPC-method is based on evaluating the strength of coherence/coupling of HRV and respiration and is independent of absolute EEG

amplitudes. The degree of CPC dramatically changes with sleep states and stages, offering identification of sleep states and sleep stages (Bartsch et al., 2012; Thomas et al., 2014; Wood et al., 2020). This coupling/coherence is most prominent in healthy children, then in early adolescence it starts to decline with a continuum of gradual decline throughout the lifespan (Figure 7) (Hilmisson et al., 2025a; Hilmisson et al., 2025b).

While PSG requires interpretation of observations (manual or automated) from EEG morphology to determine stages of NREM-sleep (stage 1, 2 and 3) and REM-sleep, SleepImage automatically displays sleep stages based on analyzing ANS-regulation of the cardiovascular- and respiratory systems during sleep.

When comparing Stable NREM sleep to traditional sleep staging from PSG, Stable NREM sleep is equivalent to part of Stage 2 and all of Stage 3 NREM sleep derived from PSG. Research has demonstrated correlation between Stable sleep (HFC) and Delta Waves (deep sleep) (Bartsch et al., 2012; Thomas, 2016; Thomas et al., 2014). In this state, desirable sleep features dominate, including high vagal tone/sinus arrhythmia, high delta power, non-cycling alternating pattern (CAP), continuous occurrence of slow oscillations (SO), blood pressure dipping, stable breathing/oxygenation/ventilation and scant arousals. Unstable sleep (LFC) equates to the part of NREM sleep that is unstable, meaning all of Stage 1 and part of Stage 2 NREM sleep. In this stage, generally less desirable features dominate, such as cyclic variation in heart rate, absence of blood pressure dipping, tidal volume fluctuations (with sleep apnea of a degree exceeding clinical thresholds), lower delta power and CAP. REM sleep and Wake are detected and separated through SleepImage's spectral power analysis (Very Low Frequency Coupling; vLFC). During REM-sleep the person is near motionless or in state of "*skeletal muscular paralysis*" where the primary mechanical motion is in the eyes. The EEG physiology of REM sleep and Wake is closely linked from the standpoint of EEG, with the electrooculography (EOG) as the main tool for distinguishing between the two states. SleepImage defines REM sleep into Stable and Unstable REM sleep based on frequency analysis of how the dominant sleep state has been classified as vLFC, where fragmented REM sleep is often accompanied by elevated Low Frequency Coupling (Figure 7), (Wood et al., 2020).

During the validation of the SleepImage System's technology, output comparison to tens of thousands of PSG sleep recordings were performed and a high level of correlation with PSG sleep power mapping has been confirmed. The ebb and flow of slow wave power is the accepted marker of sleep drive in humans and in non-human species. Delta power measured from surface EEG correlates with ECG- and PPG-derived Cardiopulmonary Coupling high-frequency power (Figure 8, blue line), further supporting a link between cortical EEG electrical activity and brainstem-related cardiorespiratory functions (Bartsch et al., 2012; Thomas et al., 2014).

Figure 8. The figure above reveals the relationship between HFC (white peaks) and normalized delta power (blue line) during simultaneous data collection using CPC and PSG as discussed in the paper "Relationship between delta power and the electrocardiogram-derived CPC Spectrogram: possible implications for assessing the effectiveness of sleep" (Thomas et al., 2014).

Restorative sleep depends on sleep duration, sleep depth and sleep continuity, as well as the capacity of the brain to create periods of sustained sleep stability (Stable NREM-sleep, NREM-3). Stability is not confined to EEG activity only but reverberates upon the ongoing EEG- and ANS-activity, which are mutually entrained and allow for utilizing the oscillations in PRV and TVV for estimation of sleep stages.

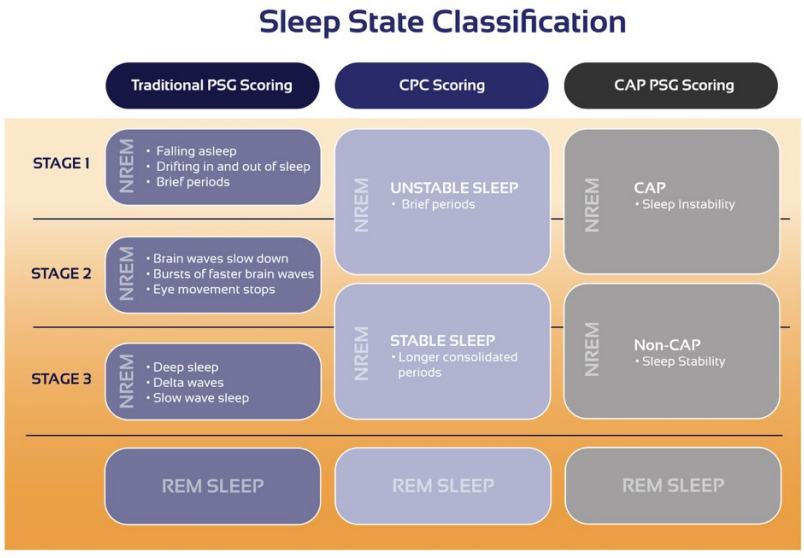


Figure 9. The relationship between conventional EEG-sleep scoring system (PSG/CAP) and the Cardiopulmonary Coupling (CPC).

PSG primarily depends on EEG morphology, whereas CPC utilizes the physiological changes that are triggered by subcortical brain centers and signaled through the ANS. The CPC-method integrates information from "*Upper-levels or brain activity*" through ANS-signaling on "*Lower-levels or cardiovascular and respiratory*",

respiration (changes in breathing, TVV) and the cardiovascular system (changes in hemodynamics, PRV) to capture the ebb and flow of sleep. Observing the coherence/coupling between the cardiovascular- and respiratory systems during sleep when there are minimum environmental stimuli that can affect the ANS as happens during wake, allows for measures of sleep and sleep staging (Bartsch et al., 2012; de Chazal & Sadr, 2016; Thomas, 2016; Thomas et al., 2014). The two methods (CPC and PSG) are quite capable instruments to evaluate sleep, though with some important differences, and do therefore not vary as much as it may seem at first, as is demonstrated in Figure 9.

CPC-based sleep staging follows CAP-scoring closely (kappa >0.75). Unstable sleep (LFC) is associated with CAP and Stable sleep (HFC) is associated with non-CAP (Parrino et al., 2012; Thomas et al., 2005). Despite the reliability of CPC-based CAP detection, a tighter correlation between the two methods would not be expected as the time scales are different. To be scored as CAP, phasic EEG-activity should occur within 60 seconds (Parrino et al., 2012) when CPC-scoring is based on analyzing the signals for windows of 2.1-minutes (Thomas et al., 2005). Both CAP and Unstable NREM-sleep (LFC) increase when sleep is disturbed by internal or external factors. CAP and Unstable NREM-sleep reflect subjective sleep quality, with higher CAP and Unstable NREM-sleep objectively relating to health outcomes, demonstrated as poorer sleep quality (lower SQI) as measured by CPC using the SleepImage System:

(1) Blood pressure dipping occurs only during periods of Stable NREM-sleep (Wood et al., 2020), which is consistent with the demonstration that non-CAP is the EEG correlate of blood pressure dipping (Iellamo et al., 2004).

(2) Increasing Stable NREM-sleep improves blood pressure control (Magnusdottir et al., 2020), increases adiponectin levels (Magnusdottir, Thomas, et al., 2021), is associated with less step width variability and falls (Marino et al., 2026) and better pregnancy outcomes (Ni et al., 2025).

(3) Unstable NREM-sleep is associated with hypertension and stroke (Thomas et al., 2009) and decreases with successful therapy (Cho & Kim, 2017; Choi et al., 2015; Lee et al., 2014; Lee et al., 2016).

(4) Unstable NREM-sleep and CAP is increased in patients with obstructive sleep apnea (OSA), and Stable NREM-sleep is reduced in patients with fibromyalgia syndrome (Thomas et al., 2010).

(5) Unstable NREM-sleep and CAP are increased in depression (Farina et al., 2003; Yang et al., 2011), and in insomnia (Terzano et al., 2003; Thomas et al., 2018).

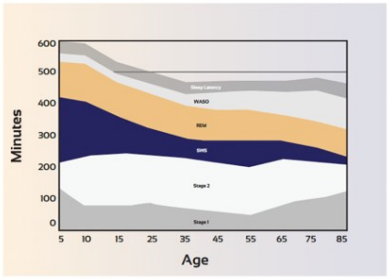
(6) Unstable NREM-sleep and CAP, negatively affect cognition and behavior in children (Magnusdottir, Hilmisson, et al., 2021; Magnusdottir et al., 2022; Parrino et al., 2012; Yuanjie, Yunxiao, Thomas, Tangyufen, et al., 2025) .

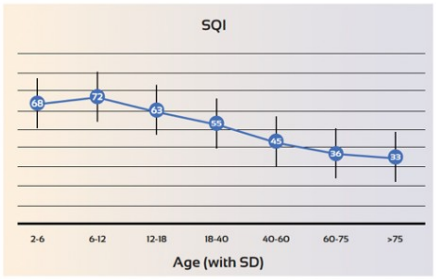
(7) Children with higher Stable NREM-sleep have better cardiovascular- and metabolic-health (Hilmisson, Lange, & Magnusdottir, 2019; Magnusdottir et al., 2022) and memory recall (Yuanjie, Yunxiao, Thomas, Yufen, et al., 2025).

Changes in Sleep Architecture Over the Lifetime

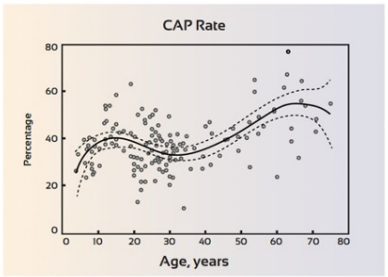
Sleep reflects the physiological changes that accompany the different periods (ages) of the lifespan. In particular, slow wave sleep (SWS) dominates during the younger decades in contrast to lighter NREM sleep states which increase with the aging process (Ohayon et al., 2004). As well as conventional measures, EEG NREM/REM and CAP/non-CAP, CPC-calculated parameters undergo dynamic changes across the lifespan. Age-related values of NREM/REM-sleep stages, CAP/non-CAP and CPC-calculated parameters of sleep stability/instability have been measured and defined to establish the physiological ranges of sleep quality for different ages (Figure 10).

Age related trends for stage-1, stage-2, slow wave (SWS), rapid eye movement (REM) sleep and sleep latency (left) and trends in the sleep quality index (SQI) (right) across the lifespan.





Age-related modifications of CAP-rate (left) and Unstable sleep (right) across the lifespan.



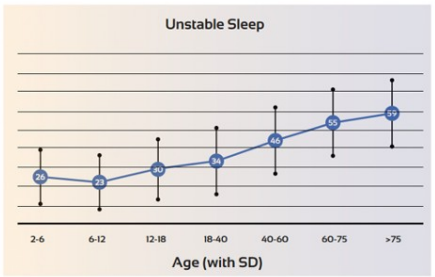


Figure 10. Age related trends in sleep stages evaluated from Rechtschaffen & Kale scoring, trends in sleep quality (SQI) across the lifespan, and cyclic alternating pattern scoring (CAP) compared to scoring utilizing cardiopulmonary coupling across the lifespan.

Everyone sleeps and sleep is an important modulator of various biological functions. SleepImage is a tool that can enhance clinical practice across all medical specialties. Prior to the onset of a chronic disease, symptoms may be present, and prior to symptoms there are reflections of changes in ANS regulation that are not obvious but can be measured. The sleep period, on average, represents one third of a person's life and getting sufficient good quality sleep at the right circadian times is vital for good health and wellbeing. During sleep, muscles and tissues are rebuilt, neuroendocrine- and metabolic functions are regulated, information collected during the waking hours are reorganized and consolidated for learning and memory consolidation, and the immune system is strengthened (Rasch & Born, 2013; Schmidt, 2014). These benefits of sleep can only happen when sleep is dominated by parasympathetic activity (the restful part of the sleep period facilitating good quality sleep). The SleepImage output clearly distinguishes between parasympathetic and sympathetic dominance and presents the output as 'Stable' and 'Unstable' NREM-sleep reflecting sleep health. That is why SleepImage brings clinical value and relevance for health maintenance and chronic disease management beyond the focus on diagnosis of SDB.

During the past two decades, multiple papers have been published that have utilized the CPC-method to evaluate sleep stages as well as sleep disorders which have demonstrated that the 2 distinct (bimodal) regimes demonstrate a closer relationship with visual cyclic alternating pattern (CAP) and non-cyclic alternating pattern (non-CAP) states (Parrino et al., 2026; Terzano et al., 1985; Terzano et al., 2001) than with standard sleep stages from PSG (Thomas et al., 2005). Regardless of different definitions of the duration of scoring windows (CPC 2.1-min vs. PSG 30/2 sec), tight temporal relationship between slow wave power, both within and outside conventional SWS periods, and high frequency cardiopulmonary coupling (HFC), a biomarker of "stable" NREM-sleep is observed (Thomas et al., 2014). Alterations in cardiac autonomic drives (HRV and breathing) during sleep may not be a product of sleep derived from EEG but rather from the ANS as changes in HRV are ahead of SWS-activity with a time lag of 1-5 minutes (Rothenberger et al., 2015) and stable-NREM sleep calculated from CPC appears on average 4.27 minutes ahead of SWS-activity (Thomas et al., 2014), reflecting the role of the ANS to regulate wake and sleep.

In adults, the SleepImage method has been utilized in research to quantify sleep quality/stability and sex-specific changes with aging (Hilmisson et al., 2026; Tam et al., 2024) in different occupational and patient populations (Chen et al., 2018; Chien et al., 2013; Christian et al., 2021; Hou et al., 2024; Hu et al., 2024; Liu et al., 2024; Marino et al., 2026; Mirabal et al., 2026; Pawar R., 2022; Seo et al., 2020; Thomas et al., 2010; Wang et al., 2023); how changes in sleep stability affects cardiovascular and cardiometabolic markers (Alhassan et al., 2026; Magnusdottir et al., 2020; Magnusdottir, Thomas, et al., 2021; Pogach et al., 2012; Sivam et al., 2021), and the relationship with brain health (Marino et al., 2026; Tang et al., 2024; Thomas, 2021; Zhang et al., 2021). The method has also been used in research to evaluate sleep stability and insomnia severity (Thomas et al., 2018; Yang et al., 2011); changes in insomnia severity over multiple nights (Schramm et al., 2013); changes with treatment (Wu et al., 2021); the relationship to cognitive deterioration in insomnia patients (Ran et al., 2024; Zhang et al., 2021); in comorbid insomnia and obstructive sleep apnea (COMISA) (Hilmisson, Sveinsdottir, et al., 2019) and Idiopathic Hypersomnia (Pawar R., 2022). Changes in sleep stability/sleep quality have been documented to evaluate response to treatment with cognitive behavioral therapy (Schramm et al., 2016; Sylvia et al., 2014); tai chi in patients with chronic heart failure and depression (Ma et al., 2018; Yeh et al., 2008), to medications (Schramm et al., 2014; Sun et al., 2019; Wu et al., 2020) and catheter ablation in atrial fibrillation (Kim et al., 2020). Changes in sleep quality/stability have also been evaluated in patients with obstructive sleep apnea (OSA) treated with mandibular advancement device therapy (Lee et al., 2014), with CPAP therapy (Cho & Kim, 2017; Lee et al., 2016; Ni, Lei, Tang, Liang, Hilmisson, et al., 2024) and surgery (Choi et al., 2015) and to estimate residual disease when treated for OSA (Chopra et al., 2026; Simmons et al., 2025).

In children, the SleepImage technology has been reported to be able to detect undiagnosed OSA in cohort of population-based children (Chiang, Canapari, et al., 2026; Ingolfsdottir et al., 2026). When utilized to evaluate trends in a large cohort of children and adolescents, sleep quality/stability was found to decrease during late childhood and adolescence and during adolescence in boys who have lower sleep stability/sleep quality and sleep efficiency than girls, a trend that continues through the lifespan (Figure 11), reflecting similar findings that have been documented in PSG studies (Hilmisson et al., 2025b; Ohayon et al., 2004). Sleep quality/stability varies based on severity of sleep disordered breathing (SDB) (Seo et al., 2021) and improves after successful adenotonsillectomy surgery (eAT) (Lee et al., 2012). Children who have mild OSA and high sleep quality (SQI) have better cardiovascular and cardiometabolic health (Hilmisson, Lange, & Magnusdottir, 2019). This group also has better attention, executive function and quality of life at baseline (Magnusdottir, Hilmisson, et al., 2021), are more likely to have spontaneous resolution of their disease at follow-up after watchful waiting and

are less likely to benefit from eAT (Magnusdottir et al., 2022). Good sleep quality in childhood also facilitates memory and learning (Yuanjie, Yunxiao, Thomas, Tangyufen, et al., 2025).

Figure 11. Trends in the sleep quality index (SQI) and the apnea hypopnea index (AHI over the lifespan.

Sleep Apnea Detection with the SleepImage System

The SleepImage® System analyzes photoplethysmography (PPG) sensor data. PPG is a non-invasive optical technique that detects blood flow and other cardiovascular information through changes in light absorption in the arterial bed of the finger (a.k.a. peripheral arterial tone (pat)). PPG is used to measure: (1) Plethysmography-waveform (PLETH) that corresponds to blood volume variations/fluctuations in the cardiovascular system and (2) SpO_2 (Figure 12).

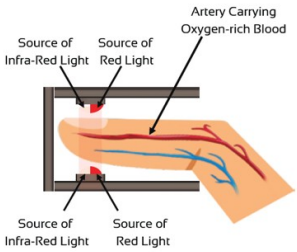


Figure 12. Photoplethysmography (PPG) sensor including the light source (LED) and the light receiver (PD), transmission mode.

The PLETH-waveform embeds information on sympathetic activation and respiratory-induced pulse wave modulation reflecting: (1) Blood flow/blood pressure changes affected by changes in breathing (work of breath-to-breath) and intrathoracic pressure, (2) Respiration and (3) Heart rate and heart rate variability as shown in Figure 13.

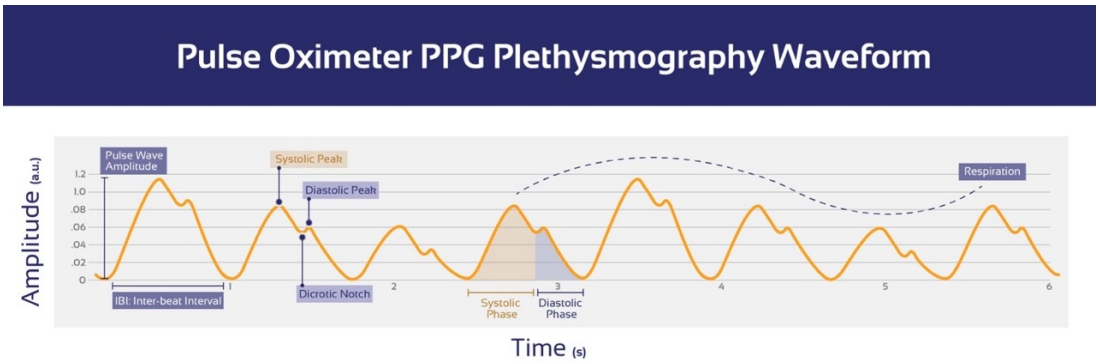


Figure 13. The amplitude of the cardiac component of the PLETH-waveform modulates due to respiratory-related changes in intrathoracic pressure.

The CPC algorithms utilize the PLETH-wave for sleep analysis and combined with SpO_2 information the SleepImage System calculates and automatically reports the SleepImage Apnea Hypopnea Index (sAHI), the SleepImage Respiratory Disturbance Index (sRDI) and hypoxic burden (HB). The output is presented through easy-to-understand biomarkers that are displayed with expected normative thresholds and color-coded results for each biomarker. The SleepImage Apnea Hypopnea Index (sAHI) has been clinically validated and FDA-cleared for children (2+), adolescents and adults for diagnosis and management of Sleep Disordered Breathing (SDB) (H. S. Al Ashry, H. Hilmisson, Y. Ni, R. J. Thomas, et al., 2021; Hilmisson et al., 2020b; Lu et al., 2023).

Evaluation of Sleep Breathing Events During Sleep

Awareness among both the general population and clinicians has increased in the past decade, which has introduced unprecedented influx of undiagnosed patients and increased demands for sleep testing. The American Academy of Sleep Medicine (AASM) practice guidelines for scoring of sleep and associated events defines two methods to evaluate respiration, (1) an airflow channel and an effort channel, that introduces inherent limitations to sleep testing with operational complexity, reduced patient tolerability and elevated technical failure rates (Sabil et al., 2020), or alternatively (2) peripheral arterial tone (pat[1]as a surrogate for "airflow/effort") that offer the possibility to expand diagnostic capacity (Chiang et al., 2024). These alternative

[1] Measurement of pulsatile volume changes reflecting changes in sympathetic tone.

methods are also commonly defined in insurance reimbursement policies for Home Sleep Apnea Testing (HSAT).

Airflow measurement is a conventional physiological parameter in SDB monitoring where airway occlusion directly manifests as alterations in ventilatory flow. Quantitative airflow metrics have served as a fundamental signal for SDB evaluation for decades, enabling respiratory event classification. The airflow channel is commonly recorded using a nasal pressure transducer (measuring changes in pressure of nasal airflow) or an oronasal thermal flow sensor (measuring differences in temperature during inhalation and exhalation). The limitation is that these sensors can be uncomfortable and not well tolerated by patients and are prone to displacement during the night. The effort channel is commonly recorded using respiratory inductance plethysmography (RIP) belts measuring movement of the chest and/or abdominal wall during breathing to evaluate lung volume changes, presented as a derived digital signal that represents a breathing curve. As RIP belts are a surrogate way to measure airflow, the signal fidelity is susceptible to degradation from belt displacement, folding or positional shifts during sleep (Chiang, Lee-Iannotti, et al., 2026). The peripheral arterial tone method utilizes a photoplethysmography (PPG) sensor to record the PLETH-wave to evaluate changes in breathing during sleep and represents a non-invasive optical technique that measures blood volume fluctuations in microvascular tissue beds (Ryals et al., 2023). Respiratory activities manifest within the PPG signal through characteristic modulations of pulse wave amplitude (PWA), signal intensity and pulse rate variations. During inspiration, a drop in intrathoracic pressure diminishes stroke volume and reduces vascular perfusion in cutaneous vascular beds. These hemodynamic changes manifest as decreases in PWA and PPG signal intensity, accompanied by compensatory increases in heart rate. Expiration results in the opposite, increasing in PWA and PPG signal intensity while decreasing heart rate.

A review article in the Journal of Clinical Sleep Medicine, published in May 2026 summarizes respiratory analysis techniques as falling into three domains: airflow dynamics, respiratory effort mechanics (including respiratory-induced pulse wave modulation from the PPG), and sympathetic activation patterns (including cardiopulmonary coupling) (Chiang, Lee-Iannotti, et al., 2026). PPG, as an optical measurement modality is susceptible to poor contact, skin pigmentation, skin thickness, hair, tattoo, nail polish and motion artifact that can affect signal quality.

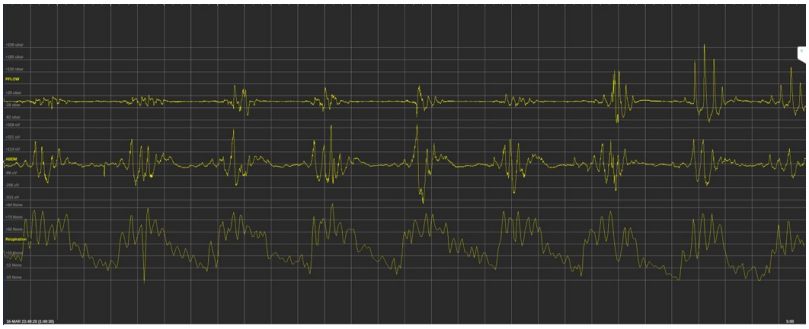


Figure 14. Respiratory Analysis (Airflow, RIP belt, PPG).

Comparing these three commonly used channels to evaluate respiration (airflow, respiratory inductance plethysmography belts (RIP), and respiratory-induced pulse wave modulation from the PPG), is best visualized from a sleep study using PSG that has all three sensors to evaluate respiration. Figures 14 & 15 demonstrate how these three methods compare in the respective raw signals and how each method provides clinical

information that can be used for the same intended use, to evaluate respiratory events that can be manually reviewed and scored to define respiratory events.

Figure 15. Breathing signal from a thorax belt (top line) and derived breathing signal from PLETH (bottom line) from a patient with obstructive sleep apnea (a) and central sleep apnea (b).

The SleepImage System calculates respiratory events during sleep, starting with CPC-analysis:

(1) Evaluates sleep, by calculating sleep duration, sleep onset (SO), sleep conclusion (SC), total sleep time (TST) and wake after sleep onset (WASO).

(2) Identify potential sleep pathologies evidenced by activity in a subset of the low-frequency band, called elevated low-frequency (e-LFC) which has been correlated with sleep apnea (Magnusdottir & Hilmisson, 2018; Thomas et al., 2007; Thomas et al., 2005).

Fragmentation (elevated low frequency broadband, e-LFCBB) has high sensitivity but low specificity and is increased in patients with pain, in patients with obstructive sleep apnea (OSA), insomnia and sleep movement disorders. The sleep fragmentation caused by OSA presents "*broad band peaks*" on the 3-D spectrogram when the primary pathophysiologic contributor is obstruction in the upper airway. During OSA breathing effort continues, but the upper airway is mechanically obstructed, resulting in interruptions of airflow (Haitham S. Al Ashry et al., 2021; Thomas et al., 2005; Thomas et al., 2018).

Periodicity (elevated low-frequency narrow-band, e-LFCNB) identifies periodic-type breathing, Cheyne Stokes breathing and heart-rate patterns that may occur during NREM and/or REM-sleep indicating sustained periods of Central Sleep Apnea (CSA) and periodic breathing like high-loop gain, or "physiologic" periodicity due to Periodic Leg Movements (PLM's) when drop in SpO_2 is not observed. During central events there is a periodic lack of neural drive to breathe during sleep (Thomas et al., 2007; Thomas et al., 2017).

Sleep fragmentation and abnormal amount of Unstable NREM-sleep reduces the restorative properties of sleep. In sleep apnea, respiration can be resolved by the central nervous system (CNS) without involving a

cortical arousal, but when cortical arousal is triggered, the ANS is enhanced with changes in heart rate and breathing causing sleep fragmentation.

(3) The TVV and SpO_2 information from the PLETH-wave are then combined with the CPC-sleep analysis, to calculate the SleepImage Apnea Hypopnea Index (sAHI) using American Academy of Sleep Medicine (AASM) scoring guidelines.

At the onset of apnea, the amplitude of the PLETH wave decreases, and the amplitude of the dicrotic notch increases. Apneas are usually accompanied by a decrease in heart rate and blood pressure, and a drop in oxygen saturation (SpO_2). At the end of the apneic event, there is sympathetic activation with vasoconstriction and temporal decrease in the amplitude of the PLETH-wave, accompanied by a sudden increase in heart rate, and an increase of SpO_2 (Figure 16).

Figure 16. Changes in the plethysmography-wave during sleep apnea. Schnall et. al., Sleep Medicine Reviews 2022 (Schnall et al., 2022).

One of the key features of the SleepImage spectrogram is a differentiation of non-overlapping sleep states during the sleep period (Figure 7) which provides a clear visual of stable NREM-sleep (high-frequency coupling, HFC) and unstable-NREM sleep (low-frequency coupling, LFC). REM and wake have similarities (very low-frequency coupling, vLFC) but can be differentiated by incorporating movement signals. The CPC calculations of sleep, used with the SpO_2 measurements to detect desaturation events, collectively create output parameters for diagnosis and management of sleep disordered breathing (obstructive and central sleep apnea) that can be manually scored in addition to the autoscoring output. For diagnosis of SDB the SleepImage Apnea Hypopnea Index (sAHI) has a strong agreement with AHI calculated from PSG (H. S. Al Ashry, H. Hilmisson, Y. Ni, & R. J. Thomas, 2021; H. S. Al Ashry, H. Hilmisson, Y. Ni, R. J. Thomas, et al., 2021; Lu et al., 2023) and the method also differentiates between obstructive and central sleep apnea (Magnusdottir & Hilmisson, 2018; Thomas, 2007).

Validation of the sAHI

The performance of the sAHI was validated by comparing the software generated sAHI to manually derived AHI from in-laboratory PSG-sleep studies, currently considered as the “reference standard”. The data were collected in prospective clinical trials that included both children and adults. Additionally, in adults the sAHI was

compared to respiratory event index (REI) from prospective clinical trials collected with Home Sleep Apnea Tests (HSAT). All comparisons are based on disease severity categorization of sleep apnea based on definition by the American Academy of Sleep Medicine (AASM), Table 1. The comparison of sAHI to AHI was further based on published guidelines from the American Academy of Sleep Medicine (AASM), Obstructive Sleep Apnea Devices for Out-Of-Center (OOC) Testing: Technology Evaluation (Collop et al., 2011). This guidance was prepared to "help clinicians decide which out-of-center (OOC) testing devices are appropriate for diagnosing obstructive sleep apnea (OSA)" and is based on emphasizing Sensitivity and Positive Likelihood Ratio. Guidelines from the American Academy of Pediatricians (AAP) (Marcus et al., 2012), calls for information on sensitivities, specificities and predictive values to be available for physicians to familiarize themselves with, before use in clinical evaluation and diagnosis of pediatric obstructive sleep apnea (POSA).

Table 1. Results comparing automated sAHI (CPC) and manually scored AHI (PSG) output.

sAHI vs AHI		Mild	Moderate	Severe
Agreement	Adults	96.3%	90.5%	98.9%
	CI95%	[.936, .990]	[.863, .947]	[.975, 1.000]
	Children	89.1%	95.2%	98.1%
	CI95%	[.875, .908]	[.941, .964]	[.974, .989]
Sensitivity	Adults	98.7%	92.6%	95.1%
	CI95%	[.970, 1.000]	[.869, .983]	[.835, .994]
	Children	90.7%	89.3%	91.3%
	CI95%	[.887, .927]	[.852, .934]	[.855, .971]
Specificity	Adults	84.8%	88.9%	100%
	CI95%	[.726, .971]	[.830, .948]	[.975, 1.000]
	Children	86.7%	96.3%	98.6%
	CI95%	[.834, .895]	[.951, .974]	[.978, .992]
Positive Likelihood Ratio	Adults	6.52	8.33	2801
	Children	6.81	24.37	66.71
Negative Likelihood Ratio	Adults	0.015	0.083	0.060
	Children	0.107	0.111	0.088
Positive Predictive Values	Adults	96.9%	86.2%	100%
	Children	91.5%	82.4%	83.2%
Negative Predictive Values	Adults	93.3%	94.1%	98.7%
	Children	85.5%	97.9%	99.4%
1 Division by zero. PLR estimated using substitution formula				

- Children (n=1,334) in the cohort; 39% of the children had no disease (n=518), 45% had mild sleep apnea (n=601), 9% moderate sleep apnea (n=123) and 7% had severe sleep apnea (n=92).
- Adults (n=761) in the cohort; 11% had no sleep apnea (n=84), 29% had mild sleep apnea (n=219), 39% moderate sleep apnea (n=295) and 21% severe sleep apnea (n=163).

Performance testing, comparing the two indices sAHI (CPC-output) and AHI (PSG-output), demonstrated strong correlation as well as significant agreement in both defining events/hour and to identify SDB categories (no-disease, mild sleep apnea, moderate sleep apnea, severe sleep apnea). The results are summarized in Table 1.

The difference between Likelihood Ratios and Predictive Values, can be explained as follows (Collop et al., 2011; Marcus et al., 2012):

Likelihood Ratios (LR) are used to assess the value of performing a diagnostic test and are performed to determine whether a test result usefully changes the probability that a disease state exists. AASM guidelines define acceptable results as sensitivity of at least 82.5% and LR+ of at least 5 at an in-lab AHI of 5, demonstrating a 95% post-test probability of the disease based on 80% pre-test probability of the disease.

Predictive Values (PV) reflect the diagnostic power of the test and depends on sensitivity, specificity, and disease prevalence, as well as the reporting probability of the patient being positive/negative based on a positive/negative test result. AAP does not have a guideline for what values are sufficient to generate passing results to diagnose a disease.

The sAHI, sRDI and SAI are indices intended to aid clinical evaluation, diagnosis, and management of sleep apnea in children, adolescents, and adults. The sAHI is a counter of paused breathing events during sleep using the same scale and reporting metrics as AHI derived from in-laboratory PSG studies and is reported on the same scale as the AHI from PSG studies. The sRDI adds autonomic arousal detection to the sAHI. The SAI is based on cardiovascular reaction to paused breathing (CVHR) during unstable sleep with a scale of 0 – 100. The SAI is based on different scaling-rules than sAHI/sRDI, and they are not expected to have the same numerical output.

Sleep Apnea is associated with significantly increased risk of cardiovascular- and cardiometabolic morbidity and mortality. In patients with cardiac autonomic dysfunction, that presents as decreased heart rate variability (HRV) and ultimately can lead to a fixed heart rate due to progressive dysfunction of the cardiac sympathetic nervous system. In this subgroup of patients, the SAI is an ineffective tool to detect apneas, as they do not exhibit the oscillatory heart rate dynamics, but the CPC e-LFC biomarkers (Fragmentation and Periodicity) and the sAHI/sRDI are useful biomarkers to aid in the diagnosis of SDB in this patient population. In patients with chronic Atrial Fibrillation (AF), the algorithm is degraded as complex patterns cannot be identified and the chaos of the ANS results in less meaningful CPC output, thus warranting caution in interpretation.

The SleepImage method is an accurate method for sleep apnea diagnosis, and it is particularly useful to track sleep health over time to identify relative changes in sleep quality, and in individuals with sleep disorders, for disease management, whether it is for insomnia or sleep disordered breathing, obstructive sleep apnea (OSA) and central sleep apnea (CSA). The simple interface offers the potential to implement personalized approach into sleep medicine by treating sleep disorders as other chronic diseases, (Collins & Varmus, 2015; Mazzotti et al., 2018; Pack, 2016; Penzel, 2021) with repeated testing in the patients' natural sleeping environment in their home, over multiple nights and multiple time points to optimize disease management and patients' health (de Chazal et al., 2020; Parrino et al., 2022; Penzel et al., 2025).

Further description of Cardiopulmonary Coupling can be found in the sleep medicine textbook, Principles and Practice of Sleep Medicine, (Kryger – Roth – Dement) Seventh Edition, Chapter 202. Cardiopulmonary Coupling.

SleepImage in Sleep and Sleep Disorder Management

The SleepImage System is a simple to use and low-cost method that offers the opportunity of multi-night testing to evaluate night-to-night variability during the process of evaluating sleep complaints, and to track changes in sleep over time, as part of sleep health management. Before prescribing a study using a PPG sensor (also known as pulse oximeters), ensure that the sensor size fits the patient properly and if needed secure the sensor to prevent removal of the sensor during the sleep recording.

The Sleep Quality Index (SQI) is a summary index of the SleepImage output, indicating sleep health in individuals of all ages. Healthy aging is accompanied by a reduction in HRV and respiratory variability, causing an expected gradual reduction of SQI values to be a normal part of healthy aging (Hilmisson et al., 2026; Hilmisson et al., 2025b). While SQI values are comparable between individuals of similar age, the greatest value of the SQI is to track sleep quality for each individual over time.

Night-to-night variability in sleep is recognized (Ding et al., 2025) and this variance should be expected to increase in patients with sleep disorders (sleep pathology) and/or the presence of comorbidity. Differences should also be expected over time due to environmental conditions, lifestyle changes and behavior, or other factors that can affect sleep and cause night-to-night variability in sleep. It is well documented in the peer-reviewed clinical literature that sleep apnea severity can vary considerably from night to night as has been reported in SDB-patients undergoing PSG-studies on consecutive nights or one month apart, where changes in AHI were observed to be in the range of 18%-65%. (Punjabi et al., 2020; Thomas et al., 2020; White et al., 2015). When sleep disorders are suspected, it is important to treat them as other chronic conditions that can present different levels of symptoms over time. Measuring sleep in patients' normal sleep environment over multiple nights and on multiple occasions to capture the dynamics of sleep physiology and pathology is important (Mazzotti et al., 2018; Pack, 2016; Penzel, 2021). Capturing and mitigating the night-to-night variability respects the chronic nature of sleep disorders that should improve the diagnostic process, the management of the disease and patient outcomes (Levendowski et al., 2009).

None of the values for the SleepImage biomarkers should be considered absolute threshold values; they are expected to be generally similar when using the same sensor type. Although there are no signal specific contraindications, certain conditions such as cardiovascular disease and arterial stiffness can reflect signal specific differences that can cause variability where it is normal to expect ±10% differences that can be greater for certain patients based on disease conditions. For clinical use, it is recommended to consistently use the same sensor type.

Sleep and Sleep Disorder Management in Children

Prevalence of sleep disorders in children are high, and prevalence of sleep disordered breathing (SDB) has likely been increasing over the last 10 – 20 years (Magnusdottir & Hill, 2024). At the same time, sleep is rarely addressed during routine pediatric visits (Honaker & Meltzer, 2016). During the preschool years (3-5 years of age) lymphoid tissue growth peaks, increasing the likelihood of symptoms of SDB developing (Dayyat et al., 2009). Clinical guidelines regarding diagnosis of SDB in children, emphasize that attempts to specify severity of SDB and make treatment decisions solely based on the Respiratory Event Index (REI) or Apnea Hypopnea Index (AHI) and minimum oxygen saturation may lead to misclassification as children often present with changes in sleep architecture and fragmented sleep. Multi-night testing will assist clinicians to evaluate SDB in children (Lloyd et al., 2019; Paruthi, 2021).

There is considerable variability in symptom presentation in children with OSA. This makes OSA difficult to diagnose and demands increased awareness of SDB in children among clinicians. Excessive daytime sleepiness is not a frequently reported symptom in children with OSA, who often present with hyperactivity, difficulty concentrating, attention- behavioral- and mood-problems, enuresis, persistent mouth breathing with dry mouth and morning headaches (Lloyd et al., 2019).

The most common form of SDB in children is obstructive sleep apnea (OSA), characterized by abnormal respiratory and ventilation patterns during sleep. OSA is a highly prevalent condition in children, with disease severity ranging from primary habitual snoring (6%-25%) to obstructive sleep apnea (OSA), diagnosed when the apnea-hypopnea index (AHI) ≥1.0 on nocturnal PSG (Marcus et al., 2012). Tonsillar-hypertrophy and obesity are the most common risk factors for OSA in children and adenotonsillectomy (AT) is recommended as first-in-line therapy for children with tonsillar-hypertrophy and OSA (Patel et al., 2014). The prevalence of pediatric obesity has been increasing worldwide over the past five decades (1975-2016) with the global age-standardized prevalence of obesity in children and adolescents aged 5–19 years increasing from 0.7% to 5.6% in girls and 0.9% to 7.8% in boys (Abarca-Gomez, 2017). This global epidemic of pediatric obesity is likely to have contributed to increase in prevalence of pediatric OSA as obesity is associated with higher prevalence of OSA in children (Ingolfsdottir et al., 2026) and may occur in up to 60% of obese children (Narang & Mathew, 2012). This is seen in the more recent literature as the prevalence of OSA was estimated in a systematic review in 2008 as 1-4% when a systematic review from 2023 estimates prevalence of OSA in young children as 12-20% (Magnusdottir & Hill, 2024).

Clinical studies have demonstrated limited success of the adenotonsillectomy surgical intervention to treat pediatric OSA, indicating the potential benefit for regular sleep testing in children during the years of rapid growth and development to evaluate the need for and optimal timing of an intervention to treat pediatric OSA (Kang & Hsu, 2023).

Majority of children that undergo AT are diagnosed based on subjective evaluation/complaints and without any objective confirmation. A study including healthy children suspected of OSA included PSG evaluation before the AT surgery based on parent's concern and preference for their child to have objective evaluation of their sleep before surgery, found that only about 45% of the children had OSA and might benefit from surgery (Abraham et al., 2021). Performing a surgery on a child without a need may cause both unnecessary distress for the child and affect their future health prospects as well as incurring unnecessary cost for both parents and payers. To further complicate disease management of OSA in children, spontaneous polysomnographic improvements are well known and documented (46%) (Bhattacharjee et al., 2010; Marcus et al., 2013) as well as residual disease following surgery with less than a third of children with OSA achieving complete resolution with surgery (Mitchell & Kelly, 2007; Suri et al., 2015). Additionally, surgery may potentially cause both serious short-term surgical complications and in the long-term significantly increase delayed respiratory, allergic, and infectious sequelae (Byars et al., 2018; Cote et al., 2014; Goldman et al., 2013).

Studies looking at sleep management in pediatric care have observed a mismatch between prevalence of parents reported symptoms of sleep problems, including snoring, SDB and insomnia and documented diagnoses by the physician. In a study screening for snoring in primary care, only 38% of the children that screened positive for snoring were referred for further evaluation (Erichsen et al., 2012). Although several screening questionnaires have been developed to identify children with OSA, they have not proven accurate and are rarely used (Honaker & Meltzer, 2016). Parent/caregiver reports of symptoms correlate poorly with PSG findings, and subjective clinical evaluation of tonsillar size is not a reliable indicator of need for surgery or surgical success (Borgstrom et al., 2013; Chervin et al., 2007; Pierce & Brietzke, 2019; Villa et al., 2015).

Because of age related airway growth, children in particular stand to benefit from repeated objective and clinical symptom evaluation over time. This symptom variability of OSA in children as well as the complexity of

the disease, mandates a careful data-driven clinical decision-making process prior to therapy, including surgery (Machado Junior & Crespo, 2020). It is furthermore important to implement therapy-tracking post intervention for objective evaluation with longitudinal care to improve clinical management as residual disease is common after AT-surgery in children. If left untreated, the disease may adversely affect the child's neurocognitive, behavioral, cardiovascular, and cardiometabolic health over time and their health prospects (Reynaud et al., 2018; Song et al., 2016).

Both the American Academy of Pediatrics (AAP) and the American Academy of Sleep Medicine (AASM) recommend a PSG-study to objectively assess and diagnose OSA in children prior to surgery, as questionnaires alone do not provide a good diagnostic prediction of OSA in children (Incerti Parenti et al., 2021). These academic guidelines to establish objective evidence of OSA prior to surgical decisions are though frequently bypassed (Friedman et al., 2013). This may be caused by the limited access to pediatric sleep laboratories, high cost of testing with increased parent out-of-pocket expenses, or reported inconvenience for both the child and their caregivers (Mitchell & Kelly, 2007) and alternatives are needed (Garde et al., 2022; Landry et al., 2024).

Diagnosis of SDB requires clinical, subjective- and objective sleep data. OSA in children is defined as AHI > 1.0/per hour of sleep. However, the AHI must be considered in the context of the child's health, symptoms, and daytime functional impairment to most accurately assess SDB significance, severity, and impact. The fact that the majority of treatment-related changes in outcomes of OSA in children are not causally attributable to polysomnographic resolution or changes in severity calls for additional sleep metrics that can be tracked over time (Isaiah et al., 2019).

Sleep testing small children should take into consideration the strength of their cardiac and respiratory systems that may not result in a demonstrated positive diagnosis from a single night of testing, using the AHI as the diagnostic output. It is therefore important to monitor other parameters, such as arousals from PSG and fragmentation from CPC as indicators of a masked disease based on the AHI, warranting a careful review of the raw data to evaluate the need for manual over-scoring of the automated output. It should also be taken into consideration that children tend to move more during sleep than adults which may cause movement artifacts that need to be removed for output accuracy and as children have strong tendency to want to remove sensors (often subconsciously) during sleep. Therefore, it is important to secure the sensor on small children for optimization of the recording. When evaluating the output, it is important to evaluate the quality of the signal from each recording to remove areas of poor signal quality that can artificially identify areas as apneas where they may have applied pressure on the sensor if the child sleeps on the sensor and when there are areas of movements, causing an artifact identified as an apneic event. A primary value with SleepImage is that there is only one sensor applied to the child, thus minimizing the situations explained here to mitigate the risk of a failed study; beyond that a single sensor with no wires is also less likely to disturb the child's sleep than a multi-sensor setup, such as with a PSG sleep test.

SleepImage is FDA-cleared for diagnosis of OSA in children based on the sAHI, it is low-cost, simple to use and not intrusive for the child. This offers the potential to measure multiple nights of sleep in the child's natural sleeping environment to capture the dynamics of SDB, which may be a more appropriate method than making a therapy decision from presentation of subjective symptoms, clinical evaluation, and objective measure at one specific point in time.

Sleep and Sleep Disorder Management in Adults

The same approach for sleep management in adults is important, and PSG and HSAT generally do not offer the opportunity for repeated testing prior to disease diagnosis or to track efficacy of therapy. Currently the ratio of undiagnosed SDB is estimated to be over 80% of the patient population or more than 936 million people (Benjafield et al., 2019) are estimated to have the disease. Long-term compliance on positive airway pressure (PAP) therapy is considered generally low and problematic, as effectiveness of therapy is greatly dependent on consistent use. The lack of compliance may be caused by patients' own subjective evaluation of not finding the benefit from therapy to outweigh the burden of the therapy or be caused by negative effects of PAP-therapy on sleep quality (Magnusdottir et al., 2020; Magnusdottir, 2021). Sleep quality evaluation at baseline as well as repeated testing for therapy efficacy is therefore highly desirable for both patients and their clinicians to improve clinical management of sleep disorders (Magnusdottir et al., 2020; Magnusdottir, 2021; Patil et al., 2019; Sawyer et al., 2011).

Only with this kind of repeated objective testing, enabling dynamic longitudinal tracking and the opportunity for more comprehensive phenotypic profiling in both clinical management of sleep disorders as well as in design and conduct of research studies, will the value of sleep testing children be fully recognized. Sleep disorder management needs to be practiced comparably to how other chronic conditions like diabetes or hypertension are managed (Collins & Varmus, 2015; Mazzotti et al., 2018; Pack, 2016; Penzel, 2021). A change in clinical protocols to this extent could have a meaningful and measurable positive impact on patient outcomes and on quality of research to provide insight into sleep, beyond focusing only on the presence of sleep apnea in both health and disease. Improvements in management of sleep disorders will only be achievable with access to accurate and actionable clinical sleep tests that are evidence based, simple, low-cost, scalable, and can be self-administered in the patients' own natural sleep environment.

The SleepImage system offers an FDA-cleared, fully automated and rigorously validated output, that is simple to use both for patients and clinicians for unique insight into sleep health and sleep regulation (FDA, 2020):

(1) Stable sleep tracks slow wave power and results of repeated testing which could provide new insights into night-to-night sleep homeostatic mechanism (Ding et al., 2025; Thomas, 2016; Thomas et al., 2014; Thomas, 2018).

(2) Substantial overlap in symptom presentation of insomnia and OSA is documented. This advances the need for methods that capture data and provide output that can be used for clinical evaluation of both insomnia and OSA before making diagnostic decisions and initiation of therapy. Validated sleep tests for patients with sleep complaints who currently are considered ineligible for PSG or HSAT testing fill a void in clinical management of sleep disorders (Hilmisson, Sveinsdottir, et al., 2019; Krakow et al., 2019; Thomas, 2018).

(3) The possibility to record sleep for more than one night in the patient's natural sleep environment should offer an opportunity for improved clinical management of sleep disorders. Change in clinical protocols to objectively test all patients with sleep complaints for more than one night before any therapy is initiated could have a meaningful and measurable positive impact on patient's health and quality of life, disease management and public health (Collins & Varmus, 2015; Pack, 2016; Penzel, 2021).

SleepImage Output Parameters

Stable sleep (High-frequency coupling; 0.1-0.5Hz)

A biomarker of Stable NREM-sleep which occurs during part of NREM stage 2 and all NREM stage 3 sleep, correlating with EEG morphology called noncyclic alternating pattern (n-CAP), continuous occurrence of slow oscillations (SO), and delta waves on the electroencephalogram (EEG). Stable sleep is a biomarker of integrated stable NREM sleep and is associated with periods of stable breathing and oxygenation, high vagal tone, blood pressure dipping, and stable arousal threshold. This state may be considered as “effective” NREM sleep. Effective NREM sleep enables the desirable functions of sleep, across multiple dimensions (e.g., neuronal network health, metabolic, immune etc.), such that spending periods in this state enables recovery and restoration processes (Magnusdottir et al., 2020; Magnusdottir, 2021; Thomas, 2016; Thomas et al., 2014; Wood et al., 2020).

Unstable sleep (Low-frequency coupling; 0.01-0.1Hz)

A biomarker of Unstable NREM-sleep, with exactly opposite features when compared to stable sleep: low-frequency and tidal volume fluctuations, cyclic variation in heart rate, CAP on the EEG-trace, low relative delta power, non-dipping of blood pressure and variable arousal thresholds. This state may be considered “ineffective” NREM sleep. Ineffective NREM sleep fails to accomplish the desirable functions of healthy sleep. A subset of low-frequency coupling is termed Elevated Low-Frequency Coupling (e-LFC) that has two subsets; an indicator of Periodicity (elevated low frequency narrow band; e-LFC_{NB}) and Fragmentation (elevated low frequency coupling broad band (e-LFC_{BB}) (Magnusdottir et al., 2020; Magnusdottir, 2021; Thomas, 2016; Thomas et al., 2014; Thomas, 2007; Wood et al., 2020).

Fragmentation (elevated low frequency coupling broad-band e-LFC ßß)

A subset of low-frequency coupling during NREM-sleep which is an indicator of sleep pathology (e.g., pain, insomnia, anxiety) or disordered breathing patterns like Obstructive Sleep Apnea (OSA) and Upper Airway Resistance Syndrome (UARS) (Hilmisson, Lange, & Duntley, 2019; Hilmisson, Sveinsdottir, et al., 2019; Lee et al., 2012; Magnusdottir & Hilmisson, 2018; Seo et al., 2021; Thomas, 2016; Thomas et al., 2005; Thomas et al., 2009)

Periodicity (elevated low frequency coupling narrow-band e-LFC NB)

A subset of low-frequency coupling, consisting of periodic-type breathing, Cheyne Stokes breathing and heart-rate patterns that may occur during NREM and/or REM-sleep indicating sustained periods of Central Sleep Apnea (CSA) and periodic breathing, or "physiologic" periodicity due to Periodic Leg Movements (PLM’s) when drop in SpO_2 is not observed. (Hilmisson, 2019; Hilmisson, Lange, & Duntley, 2019; Thomas et al., 2017; Thomas, 2007)

Sleep Quality Index (SQI)

A summary index of the CPC biomarkers of sleep quality, sleep stability, fragmentation, and periodicity, which provides a meaningful unit of measure of sleep health. The SQI is displayed on a scale of 0-100 with expected values for both children and adults (Hilmisson et al., 2026; Hilmisson et al., 2025b). The SQI is useful to track sleep health over time, whether to identify the need for further clinical investigation or to track therapy. The SQI is easily communicated and relatable to the patient or other lay persons, while at the same time being a comprehensive measure of sleep health based on clinical validation. (Hilmisson et al., 2020a; Hilmisson, Sveinsdottir, et al., 2019; Magnusdottir et al., 2020; Magnusdottir, 2021; Maijer, 2019; Marino et al., 2026; Yuanjie, Yunxiao, Thomas, Yufen, et al., 2025)

Apnea Hypopnea Index (AHI)

An automated measure of Apnea/Hypopnea events that is FDA-cleared to aid diagnosis of Sleep Disordered Breathing (SDB) in both children and adults following AASM categorization (mild, moderate, severe) as summarized in Table 2. The SleepImage Apnea Hypopnea Index (sAHI) represents the total number of apneas (paused breathing) and hypopneas (periods of shallow breathing) that occur on average per hour of sleep during the sleep recording. The sAHI is calculated from respiratory-induced pulse wave modulation as a result of changes in thorax pressure affecting hemodynamics during apneas combined with SpO_2 analysis and sleep evaluation and arousal detection from the CPC-analysis. Qualified events are displayed based on: (1) both 3% and 4% oxygen desaturation (2) as "Total", "Obstructive" and "Central" events, (3) the sAHI, like the Apnea Hypopnea Index (AHI), reports the number of paused breathing events during the sleep period calculated according to the rules set by the American Academy of Sleep Medicine (AASM) guidelines for event scoring. (H. S. Al Ashry, H. Hilmisson, Y. Ni, & R. J. Thomas, 2021; Hilmisson et al., 2020b; Lu et al., 2023) The severity indicator (normal, mild, moderate, or severe) that appears on the SleepImage report is based on AASM's disease severity categorization of sleep apnea. Diagnosis of sleep apnea is based on the evaluation of patient's medical history, clinical complaints and the sleep study results combined. The severity of OSA has historically been quantified by utilizing the AHI that is a frequency rate measure and disregards the depth and duration of the respiratory event, as well as related changes such as oxygen desaturations. Also, the AHI has not been found to be strongly correlated with symptoms and other physiologically driven measures of OSA severity, and other indices may help improve evaluation of SDB and the accuracy of diagnosis and therapy (Azarbarzin et al., 2019).

Table 2: Categorization of Sleep Apnea by American Academy of Sleep Medicine (AASM) for adults and children (events/hr.)

	No Sleep Apnea	Mild Sleep Apnea	Moderate Sleep Apnea	Severe Sleep Apnea
Adults	AHI/REI < 5.0	AHI/REI 5.0 to < 15.0	AHI/REI 15.0 to < 30.0	AHI/REI 30.0
Children	AHI < 1.0	AHI 1.0 to < 5.0	AHI 5.0 to < 10.0	AHI 10.0

Hypoxic Burden (HB)

HB is defined as the total area under respiratory-event related oxygen desaturation curve derived from a pre-event baseline oxygen desaturation and is reported as sum of all areas divided by total sleep time where the resulting metric is reported with a unit of measure of percentage minutes per hour of sleep (%min/hour). The measure was developed to better quantify the frequency, depth and duration of respiratory event-related desaturation and has demonstrated significant association with several adverse health outcomes. (Azarbarzin et al., 2019; Martinez-Garcia et al., 2023; Ni, Lei, Tang, Liang, & Thomas, 2024)

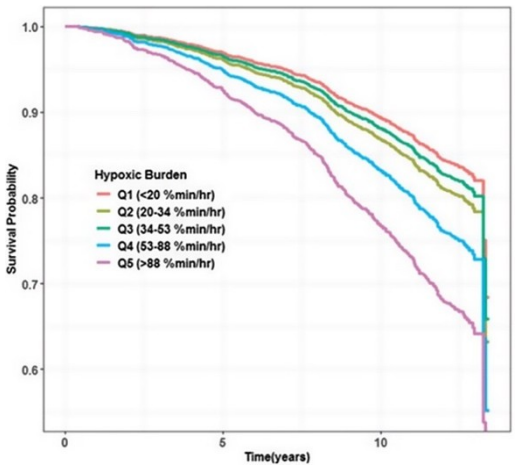


Figure 17. Hypoxic burden quintiles defined based on adjusted survival curves for cardiovascular mortality across categories of the hypoxic burden (Azarbarzin et al., 2019)

The Respiratory Disturbance Index (RDI)

RDI is intended to aid in the characterization of respiratory events during sleep in addition to sAHI. While the sAHI includes events that meet the definitions of apneas and/or hypopneas for diagnosis of OSA, AHI does not include arousals that do not meet the criteria for desaturations. The sRDI includes apnea- and hypopnea events and in addition arousals that are not related to desaturations but may disrupt sleep and cause sleep fragmentation and may therefore provide information for more comprehensive evaluation of respiratory disturbances during sleep. During a PSG-study, the RDI, unlike AHI, also accounts for EEG-arousals from sleep that do not meet the definitions of apneas or hypopneas. As the SleepImage system is not based on recording EEG brainwaves but rather cardiovascular and respiratory parameters, where presence of respiratory effort related arousals (RERAs) is detected from changes in the autonomic nervous system (ANS) reflecting changes in the sympathetic tone based on changes in heart rate acceleration (HRa) and Fragmentation (eLFC BB) without the requirement of a co-occurring oxygen desaturation of 3% or more. The sRDI, when put into the context of patient symptoms for SDB, may thus provide the clinician with additional relevant information to aid clinical evaluation of SDB and to track treatment benefits. It is important to understand that the sRDI detects changes in sympathetic tone (autonomic arousal), which should be treated as a non-invasive surrogate measure for EEG-arousal associated with non-desaturating hypopneas and RERA's scored during a PSG-study.

Sleep Apnea Indicator (SAI)

SAI is based on detecting cardiac reaction associated with prolonged cycles of oxygen desaturation based on Cyclic Variation of Heart Rate (CVHR) during unstable breathing (tidal volume variability in breathing). During each apnea event, blood oxygen decreases and is accompanied by a physiological reaction of bradycardia and, when breathing resumes, a relative tachycardia; hypoxemia is thus reflected in this cardiac response and in the SleepImage output as SAI. (Hilmisson, Lange, & Duntley, 2019; Magnusdottir & Hilmisson, 2018) CVHR can be detected during Stable NREM-sleep that often may reflect events that are typically scored as mild hypopneas but may also be triggered by other pathologies such as periodic limb movements (PLMS) or restless leg syndrome (RLS). For clinical evaluation, it is important to consider both SAI that is likely to reflect apnea events that disturb sleep to lower the SQI, and CVHR that is likely to reflect milder apneas and hypopneas that may or may not disturb sleep to lower the SQI.

Although SAI is categorically comparable to the AHI from PSG-studies, it is based on different physiological signals and the unit of measure to quantify sleep apnea is different. SAI can be perceived as a severity biomarker for CPC-derived parameters of SDB, while the AHI is literally a prevalence measure counting events per hour of sleep. Classification of SDB utilizing the SAI is based on the same premise as the AHI, the common biomarker used to quantify severity of SDB, as Mild, Moderate and Severe. Table 3 summarizes a comparison of SAI to AHI from Polysomnography (PSG) studies at each of the severity thresholds for mild, moderate, and severe sleep apnea in children and adults.

Table 3. Results of comparing automated SleepImage Apnea Indicator (SAI/CVHR) and manually scored AHI (PSG) output.

SAI/CVHR vs AHI			Mild	Moderate	Severe
Agreement	Adults	SAI	79%	79%	87%
		CVHR	83%	81%	89%
	Children	SAI	88%	87%	96%
		CVHR	88%	85%	94%

When reviewing the sAHI and sRDI scores, it is recommended to consider SDB events concurrent with CPC sleep states ($sAHI_{STABLE}$, $sAHI_{UNSTABLE}$, and $sAHI_{REM}$) when evaluating and determining disease category and severity. It is furthermore recommended to take into consideration the pathology biomarkers of Fragmentation (associated with obstruction) and Periodicity (associated with periodic breathing) when interpreting the study output for diagnosis.

Expected Values - Sleep Quality and Sleep Pathology

Table 4. Expected values for CPC biomarkers are not absolute thresholds and need to be considered in context of patients' sleep complaints, comorbidity and patient history

Expected Values	Adults	Children
Sleep Quality Index (SQI)	>55	>70
Sleep Apnea Indicator (SAI) Mild / Moderate / Severe threshold markers	≥5 / ≥15 / ≥30	≥1 / ≥5 / ≥10
Apnea Hypopnea Index (sAHI) Mild / Moderate / Severe threshold markers	≥5 / ≥15 / ≥30	≥1 / ≥5 / ≥10
Respiratory Disturbance Index (sRDI) Mild / Moderate / Severe threshold markers	≥5 / ≥15 / ≥30	≥1 / ≥5 / ≥10
Elevated Low Frequency Coupling, Broad Band (e-LFCBB)	<15	<8
Elevated Low Frequency Coupling, Narrow Band (e-LFCNB)	≤2	0

Understanding the SleepImage Spectrogram

SleepImage graphically displays the coupling of heart (pulse) rate variability (HRV) and tidal volume variability (TVV) in the Sleep Spectrogram. On the front-view Spectrogram, time (hh:mm) is displayed on the horizontal axis, and frequency (Hz) is on the vertical axis. When both data streams (HRV & TVV) are in phase (coupled/synchronized), peaks are generated on the graph to form a visual representation of the frequencies collected during the recording.

Full View Spectrogram

The full view of the Spectrogram (Figure 18) displays the peaks and oscillation pattern of HFC ($NREM_{Stable}$), LFC ($NREM_{Unstable}$) and vLFC (REM/WAKE) for the time series. The vertical axis uses frequency range 0.004Hz to 0.5Hz and time in hours on the horizontal axis.

HFC peak amplitude is in relation to the strength, and amount, of coupling or synchronization between the curves generated by the coupling activity. Greater coupling results in higher amplitude peaks. Low amplitude peaks result from less overlap between the curves generated by heart (pulse) rate variability and respiratory activity. A lack of coupling between these two input data streams will result in zero value and no peak generation.

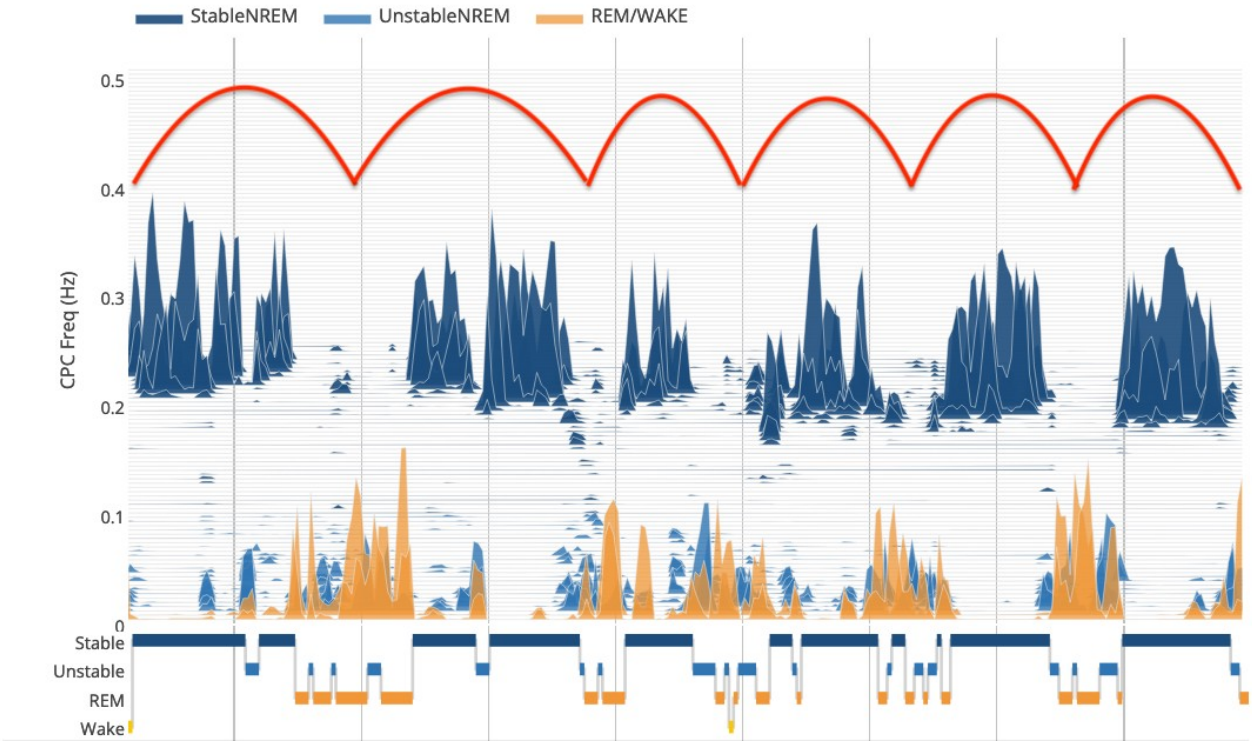


Figure 18. Oscillations between stable and unstable sleep are expected to modulate in 30-90-minute cycles that range from 4-8 Cycles in an adult 8-hour healthy night's sleep and correspond to the alternating periods of NREM and REM sleep. When sleep is disrupted (sleep apnea, insomnia, stress, pain and a variety of other factors), the healthy sleep rhythm is disrupted.

Stable Sleep or High Frequency Coupling - HFC

Stable NREM sleep (high frequency coupling) is displayed on the Spectrogram as dark blue peaks in the frequency range of 0.1 - 0.5Hz.

Unstable Sleep or Low Frequency Coupling - LFC

Unstable NREM sleep (low frequency coupling) is displayed on the Spectrogram as light blue peaks in the frequency range of 0.01 - 0.1Hz.

Wake & REM sleep or Very Low Frequency Coupling - vLFC

Very low frequency coupling (vLFC) is displayed on the Spectrogram as orange peaks in the frequency range of 0.004 - 0.01Hz and represent REM sleep & wake.

During the sleep period, spontaneous shifts occur between stable and unstable sleep. Oscillations between stable and unstable sleep are expected to modulate in 60–90-minute cycles ranging from 4-8 cycles for an adult's 8-hour healthy sleep and correspond to the alternating periods of NREM and REM sleep (Figure 18). Disease states negatively impact this pattern. Healthy, stable sleep is dominated by high vagal tone, and results in characteristic heart rate variability where the heart rate slows down and speeds up in synchrony with regular respiration. This is a normal rhythm and is associated with stable NREM sleep (HFC).

Distinguishing Between Sleep Disordered Breathing Types

Sleep Disordered Breathing (SDB) comprises a wide spectrum of sleep-related breathing abnormalities, from snoring to severe sleep apnea. There are two major categories of SDB:

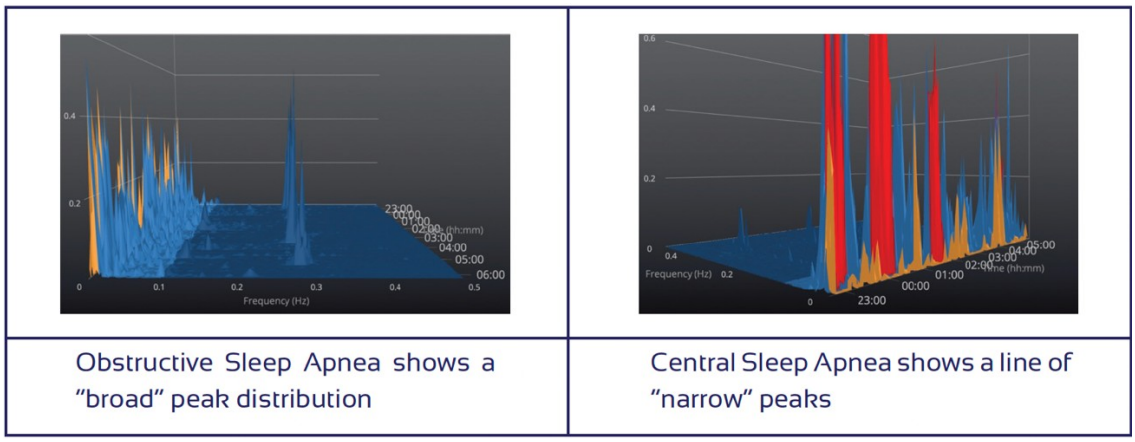


Figure 19. Spectral analysis of fragmented sleep ("broad" peak distribution) on the left and central event ("narrow" peaks) on the right.

Obstructive Sleep Apnea (OSA) - 3D Spectrogram

OSA, the most common type of sleep apnea which is related to increased upper airway resistance and/or closure of the airway during sleep causing oxygen levels to drop and fragments sleep causing arousals (RERAs) and/or awakenings. The presence of a broad band of peaks indicates that the upper airway is the primary pathophysiological contributor to the patient's sleep apnea. The e-LFC BB is presented by broad light blue peaks on the 3D Spectrogram (Figure 19 on the left).

Central Sleep Apnea (CSA) - 3D Spectrogram

CSA is caused by the brain temporarily not sending signals to the muscles that control breathing. This condition often occurs in people who have certain medical problems and when not associated with another disease, it is referred to as idiopathic central sleep apnea. A condition, Cheyne-Stokes respiration, subtype of CSA presents similarly on the SleepImage Spectrogram. CNS or periodic breathing is represented by narrow red colored peaks as e-LFC NB on the 3D Spectrogram view and identifies patterns of breathing or movement having a

“narrow band” LFC profile as a visual identifier in addition to the sAHI quantifying central events (Figure 19 on the right).

The SleepImage Report & Graphics

The SleepImage Report

Sleep Quality

SQI 39	EFFICIENCY 95%
Expected > 55	Expected > 85%

Sleep Opportunity

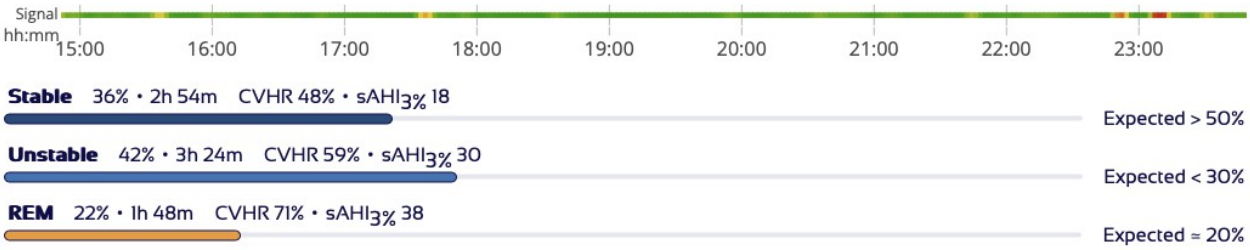
LATENCY 0h 14m	DURATION 8h 36m
Expected < 30 min	Expected 7-9 hours

Sleep Apnea

$sAHI_{4\%}$ 14.9	$sAHI_{3\%}$ 27.4
Mild	Moderate

Sleep Pathology

FRAGMENTATION 15% ($eLFC_{BB}$)	PERIODICITY 0% ($eLFC_{NB}$)
Expected < 15%	Expected ≤ 2%



Report Start	02:51 PM
Report End	11:49 PM
Time in Bed (TIB)	8h 57m
Sleep Onset	3:06 PM
Sleep Conclusion	11:42 PM
Total Sleep Time (TST)	8h 08m
WASO	0h 25m
Unknown	0h 10m
Wake Transitions	7
SAI	41%

	Min	Max	Mean
sAHI Event Duration (sec)	10	50	18
Heart Rate (BPM)	51	107	70

	Desaturations 3%	Desaturations 4%
$sAHI_{TOTAL}$	27.4	14.9
$sAHI_{OBSTRUCTIVE}$	27.4	14.9
$sAHI_{CENTRAL}$	0.0	0.0
sRDI	29.2	29.2
ODI	36.7	19.9

SpO_2 <90%	0h 29m - 5%
SpO_2 <88%	0h 06m - 1%
SpO_2 <80%	0h 0m - 0%
Min-Max-Mean SpO_2	80% - 98% - 92%
Hypoxic Burden	52.4 (%min/hr)

Test Summary:

Patient: 54 year old Male

Average Signal Quality is **94** %.
Sleep Quality is **below** expected value.
Sleep Efficiency is **above** expected value.
Sleep Duration is **within** expected value.

Sleep Apnea Indicator is **above** expected value.
Apnea Hypopnea Index is **Moderate** .
Sleep Fragmentation is **above** expected value.
Periodicity is **below** expected value.

Reviewing SleepImage Report Output

1. Check Signal Quality. Only predominantly green signal quality should be considered for clinical decision-making. Yellow and Red signal quality should be evaluated for signal abnormalities (signal noise) or signal loss.
2. Evaluate Sleep Quality. SQI indicates sleep health, with expected values as SQI >55 (adults) or >70 (children). SQI is a summary of sleep stability, fragmentation, and periodicity on a scale from 0 – 100.
3. Sleep Efficiency is the ratio of Total Sleep Time divided by Sleep Opportunity and should be >85%.
4. Evaluate Sleep Opportunity which is defined by time in bed (TIB) allocated to sleep, including Sleep Onset Latency (SOL) and Sleep Duration (SD). SD includes Total Sleep Time (TST) & Wake After Sleep Onset (WASO). Expected SL is generally defined as <30min. SD is defined by age groups. Although Insomnia cannot be diagnosed from a single night of sleep and needs to be combined with subjective evaluation, including daytime symptoms, SL and Sleep Efficiency (SE), these are the most commonly used metrics to evaluate symptoms of Insomnia. For accurate SE during the sleep period, exclude the wake period after the last sleep period by recalculating the sleep recording.
5. Sleep Apnea Evaluation.
    a. The SleepImage Apnea Hypopnea Index (sAHI) presents obstructive and central events based on 3% and 4% desaturations in the sAHI Summary Table along with the SleepImage Respiratory Disturbance Index (sRDI) that adds RERAs to the sAHI based on autonomic arousals, and the Oxygen Desaturation Index (ODI).
    b. The sAHI is intended to aid in diagnosing sleep apnea (SA) and characterization of respiratory events during sleep. The indices are categorized as 'Mild'; 'Moderate' and 'Severe' for children and adults with the following threshold values: Children ≥1, ≥5 and ≥10 and Adults ≥5, ≥15 and ≥30, respectively.
    c. Observe the sleep stages (Stable-, Unstable- and REM sleep) to evaluate where sAHI is dominant.
    d. Observe sleep pathology biomarkers: Fragmentation indicating obstructive respiratory events, autonomic arousals and sleep fragmentation, and Periodicity indicating central apneas.
    e. Evaluate CVHR events in relation to sleep stability which may help clinical evaluation of apnea severity beyond the prevalence that is reported by the sAHI and/or sRDI. CVHR during Stable Sleep may indicate events typically scored as mild hypopnea events in PSG sleep studies, or caused by periodic leg movements.
    f. Review Oxygen Summary. The percentage of oxygen saturation <90%, <88%, <80% are indicators of hypoxemia severity during sleep, in addition to the Min, Max, and Mean SpO_2 during the sleep period.
    g. Review Hypoxic Burden. Hypoxic burden is an indicator of drops in oxygen levels during the night. It is measured as % minutes per hour of sleep.
    h. Evaluate how severely sleep apnea is affecting sleep quality, the maximum, minimum and mean duration of apnea events and how the events affect heart rate (BPM).
6. Review Sleep Stability. Stable Sleep is the most important indicator of restorative sleep with good agreement with Slow Wave Sleep from PSG-sleep recordings, expected to be >50% in adults and >65% in children.
7. Review Transitions. Sleep Stability is affected by transitions to Wake and should be evaluated.

8. Summary. The SleepImage Report automatically summarizes the key metrics from the SleepImage analysis to aid the Clinician in summarizing the Clinical Evaluation and recommendations for further testing and evaluation (referral of patient to another clinician) or therapy.
9. Clinician Notes. Allows treating clinicians to document signs and symptoms of sleep disorders, patient medications, and medical history to document sleep disorder diagnosis. As additional information is gathered from multi-night testing, the Clinician can edit the Notes to reflect changes, commonly used to document treatment tracking.

Clinician Notes

Add Clinician Notes :

Metric US Customary

Height : Weight : BMI : ----------

Medicare : Yes No Clear

Epworth Sleepiness Scale :

Sleep Complaints :
Select all that apply

- Excessive Daytime Sleepiness
- Snoring
- Morning Headaches
- Difficulty Falling Or Maintaining Sleep
- Irregular (Paused Breathing During Sleep
- Bruxism / Teeth Grinding
- Waking Up Gasping Or Choking

Medical History

Character Count: 0 / 1040

Medications Used :

1.
2.
3.

Add More

Treatment Device Used :

1.
2.
3.

Add More

Diagnosis :
Select all that apply

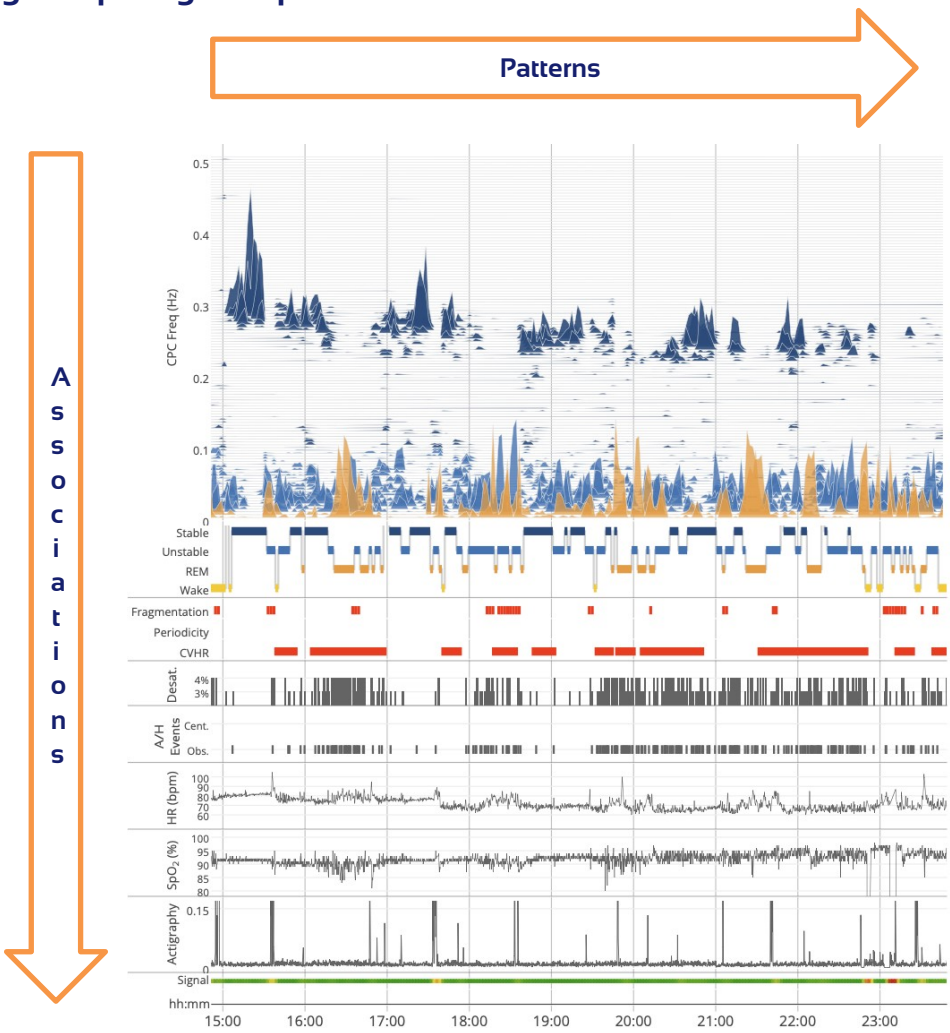
- G47.33 Obstructive Sleep Apnea
- G47.32 High Altitude Periodic Breathing
- G47.10 Hypersomnia, Unspecified
- R06.3 Periodic Breathing
- R53.83 Other Fatigue
- G47.31 Primary Central Sleep Apnea
- G47.9 Sleep Disorder, Unspecified
- F51.01 Primary Insomnia
- R06.83 Snoring
- Other

Impressions and Recommendations

Character Count: 0 / 1040

Publish

Reviewing SleepImage Graphics for Associations & Patterns



1. Signal Quality: Evaluate the signal quality during the recording period. Red may indicate signal loss, and therefore the SleepImage algorithms may not produce clinically relevant data during these periods. If long periods of signal loss are present, it is recommended to repeat the sleep study.
2. Spectrogram: Review for HFC (stable sleep), LFC (unstable sleep) and vLFC (REM sleep and wake) distribution during the recording period, CVHR (cyclic variation of heart rate, during unstable sleep presented as SAI) and sAHI/sRDI.
3. Hypnogram: Observe the frequency of transitions between Stable Sleep, Unstable Sleep, REM Sleep and Wake. A high number of transitions indicate more fragmented sleep. Healthy sleep is indicated by higher prevalence of Stable Sleep during the first third of the sleep period, with increased REM sleep towards the last third of the sleep period.
4. Sleep Disordered Breathing (sAHI, sRDI): While evaluating SDB, also consider fragmentation and periodicity. Fragmentation indicates events that may be caused by obstructive apnea and are termed e-LFC_{BB}. Periodicity indicates metronomic activity that may be caused by central apnea or periodic breathing and is termed e-LFC_{NB}.
5. Desaturation and SpO_2: Review desaturation events and correlate in association with stable, unstable and REM sleep and look for concurrent CVHR. Areas of SpO_2 signal loss are often demonstrated by a large and sudden drop in SpO_2.
6. Actigraphy: Associate level of Actigraphy with concurrent events, assess any patterns across the recording period.

7. Adjust the study period (Clinician Users): Drag the green and red markers on the orange line above the spectrogram to the desired beginning and end of the study and click the Recalculate button.
8. Examine the raw data traces in the interactive graph that coincide with the timeline of the recording; concurrent events can be observed in increments of 10 sec., 30 sec., 1 min., 2 min. and 4 min.
9. Toggle $Stable_{NREM}$, $Unstable_{NREM}$ and REM/Wake peaks (Clinician Users): The $Stable_{NREM}$, $Unstable_{NREM}$, REM/WAKE buttons above the spectrogram can turn stable, unstable and REM/Wake peaks on and off to isolate coupling types for analysis of each sleep state.

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Glossary

AAP: American Academy of Pediatrics

AASM: American Academy of Sleep Medicine

ANS: Autonomic Nervous System

CAP: Cyclic Alternating Pattern

CPAP: Continuous Positive Airway Pressure

CPC: Cardiopulmonary Coupling - the synchronization of heart (pulse) rate variability and breathing activity

CSA: Central Sleep Apnea

CVHR: Cyclic Variation of Heart Rate. Heart rate pattern that happens during and at cessation of apnea events.

DSAT: Desaturation Events

e-LFC_{BB}: Elevated Low Frequency Coupling, Broad Band - an indicator of sleep fragmentation (e.g. pain) or airway disordered breathing patterns (e.g. Obstructive Sleep Apnea, Upper Airway Resistance. (see Understanding the SleepImage Spectrogram)

e-LFC_{NB}: Elevated Low Frequency Coupling, Narrow Band - an indicator of periodic-type breathing patterns e.g. Central Sleep Apnea (see Understanding the SleepImage Spectrogram)

ECG (EKG): Electrocardiogram - recording the electrical activity of the heart over a period of time

EDR: Electrocardiogram Derived Respiration

EEG: Electroencephalogram - recording electrical activity of the brain along the scalp

HB: Hypoxic Burden

HFC: High Frequency Coupling – an indicator of stable sleep (see Understanding the SleepImage Spectrogram)

HRV: Heart Rate Variability

LFC: Low Frequency Coupling – an indicator of unstable sleep (see Understanding the SleepImage Spectrogram)

N-CAP: Non-Cyclic Alternating Pattern

NREM: Non-Rapid Eye Movement

OSA: Obstructive Sleep Apnea

PLETH: Plethysmography

PPG: Photoplethysmography

PDR: Plethysmograph Derived Respiration

PRV: Pulse Rate Variability

PSG: Polysomnography – an in-laboratory sleep study where each 30 sec window (epoch) is manually scored.

PSN: Parasympathetic Nervous System

PWA: Pulse Wave Amplitude

REM: Rapid Eye Movement

SA: Sleep Apnea

SAI: Sleep Apnea Indicator

sAHI: SleepImage Apnea Hypopnea Index

SaMD: Software as a Medical Device

SDB: Sleep Disordered Breathing - refers to a wide range of sleep-related breathing abnormalities

SpO_2: Oxygen Saturation

SNS: Sympathetic Nervous System

sRDI: SleepImage Respiratory Disturbance Index

SQI: Sleep Quality Index. Presents “one number” encompassing overall sleep health based on CPC metrics.

Spectrogram: Visual representation of the spectrum of the frequencies of Cardiopulmonary Coupling.

UARS: Upper Airway Resistance Syndrome

vLFC: Very Low Frequency Coupling – Wake/REM Sleep (see more in Understanding the SleepImage Spectrogram)

Cardiopulmonary Coupling Publications

Medical Textbooks

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Relationship: Cardiopulmonary Coupling (CPC) & Polysomnography (PSG)

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Sleep Disordered Breathing (SDB)

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(2) L'Houtellier et.al., The Relationship Between Marital Status and OSA in Black/African Americans https://academic.oup.com/sleep/article/48/Supplement_1/A283/8135944

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