



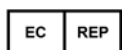


Introduction to SleepImage®

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This document is only available in an electronic format, as a PDF document, on www.sleepimage.com. This document is updated periodically, identified by a sequential revision number. The contents of this document refer to the SleepImage System, a prescription Software as a Medical Device (SaMD), which is identified by the following:

	Manufacturer	MyCardio LLC, dba SleepImage 3003 E 3 rd Ave., Suite 201 Denver, CO 80206, USA support@sleepimage.com www.sleepimage.com
	Instructions for Use Version Number	Please read Instructions for Use carefully and periodically as it is updated from time to time. The current version (D-6.00285 – Rev. 11) was issued on December 1, 2020 – Previous editions are not applicable, as all users always use a current version of the cloud-based SleepImage System. Printed copy will be provided within 7 calendar days if requested at no additional cost. Please contact support@sleepimage.com
	Prescription Use Only	FDA-cleared K182618 : Federal law restricts sales of this device as “by or on the order of a licensed healthcare practitioner”. The FDA Unique Device Identifier (UDI) is *+B315sleepimage.com0.*
	CE Mark	The CE mark is a declaration that the SleepImage System is in compliance with the EU Medical Device Directive.



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Introduction

The SleepImage® System is in compliance with the EU Medical Device Directive and U.S. Food and Drug Administration (FDA) cleared Software as a medical Device (SaMD) that establishes Sleep Quality.¹ The technology is based on Cardiopulmonary Coupling (CPC). The SleepImage algorithms analyze data, typically collected during sleep, derived from electrocardiogram (ECG) or photoplethysmogram (PPG) sensors to establish sleep quality, measure sleep duration and to detect sleep fragmentation, periodicity and Cyclic Variation of Heart Rate (CVHR). The SleepImage System optionally analyzes SpO₂ data to measure oxygen desaturation and to calculate the SleepImage Apnea Hypopnea Index (sAHI) that is FDA-cleared to aid clinical diagnosis of Sleep Disordered Breathing (SDB) in children and adults. The SleepImage System optionally graphs accelerometer data, that can display snoring and body position from actigraphy if these signals are recorded on the torso.

The SleepImage System is patented, cloud-based and Health Insurance Portability and Accountability Act (HIPAA) compliant. It is intended for use by, or on the order of, a Healthcare Professional to aid in the evaluation of sleep disorders and for diagnosis and management of sleep disordered breathing in children and adults.

The SleepImage System is cleared 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 for use, it is available in the English language only and is intended for general educational purposes. It is not intended to be Instructions for Use of the SleepImage System, for that 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.

Understanding the SleepImage Benefits

Good sleep quality is crucial for good health. One of the key benefits of using the SleepImage system in clinical practice is that, unlike most clinical sleep measurements, it is not restricted to measure sleep disordered breathing. SleepImage is a comprehensive measure of sleep health, presented through easy to understand biomarkers, that are presented with expected thresholds and color-coded results for each biomarker. The SleepImage FDA-clearance states that “SleepImage establishes Sleep Quality.” The Sleep Quality Index (SQI) is a summary biomarker of sleep health, cleared as a unit of measure, presented on a scale of 0 – 100. The SQI has demonstrated a direct relationship with health outcomes in clinical studies.^{2,6-12}

SleepImage is a tool that can enhance clinical practice across all medical specialties. Sleep is an important modulator of various functional mechanisms in the body and prior to the onset of any chronic disease, symptoms are present, and prior to symptoms there are reflections of changes in the autonomic nervous system (ANS) regulation that are not obvious. SleepImage is based on measuring biomarkers regulated by the ANS, heart rate variability (HRV) and respiration during sleep, when there are minimum environmental stimuli that can affect the ANS as happens during wake. The sleep period, on average, represents one third of a person’s life and getting sufficient good quality sleep at the right times is vital for good health and well-being as during sleep muscles and tissues are rebuilt, neuroendocrine function is regulated, information collected during the waking hours are reorganized and consolidated for learning and memory, and the immune system is strengthened.

These benefits of sleep can only happen when sleep is dominated by parasympathetic activity. The SleepImage output clearly distinguishes between parasympathetic and sympathetic dominance as ‘Stable’ and ‘Unstable’ sleep reflecting sleep health. That is why SleepImage brings value beyond the ability to diagnose sleep disordered breathing.

The SleepImage System Features and Benefits are summarized as follows:

		SleepImage	PSG	HSAT
Patient Populations	Asymptomatic	✓		
	Symptomatic	✓	✓	✓
	Children	✓	✓	
	Adults	✓	✓	✓
Types of Testing	Sleep Disorder Evaluation ¹	✓		
	Sleep Disorder Screening	✓		
	OSA Diagnosis in Children	✓	✓	
	OSA Diagnosis in Adults	✓	✓	✓
	Treatment Tracking ²	✓		
Test Output	Sleep Quality	✓	✓	
	Sleep Duration	✓	✓	
	NREM & REM Sleep	✓	✓	
	Phenotype OSA vs. CSA ³	✓	✓	

¹ To evaluate clinical symptoms of Insomnia or Sleep Apnea

² To track if treatment is improving objective sleep parameters

³ OSA = Obstructive Sleep Apnea; CSA = Central

For the purpose of diagnosing sleep disordered breathing, 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.”

https://www.accessdata.fda.gov/cdrh_docs/pdf18/K182618.pdf

Understanding the SleepImage Science

The SleepImage Cardiopulmonary Coupling (CPC) analysis is based on continuously and evenly sampled data from electrocardiogram (ECG) or photoplethysmogram (PPG) sensors to generate reports of sleep quality, sleep duration and sleep pathologies to aid in the evaluation of sleep disorders, where it may inform or drive clinical management.

The SleepImage System provides clinical users with access to the raw data collected for manual interpretation of the study output. The data collected contains information on heart (pulse) rate, heart (pulse) rate variability (HRV/PRV) as a measure of autonomic drive, as well as tidal volume fluctuations in respiration, called Electrocardiogram Derived Respiration (EDR) and Plethysmograph Derived Respiration (PDR) respectively. CPC is the coupling of HRV (PRV) and EDR (PDR) (Figure 1).

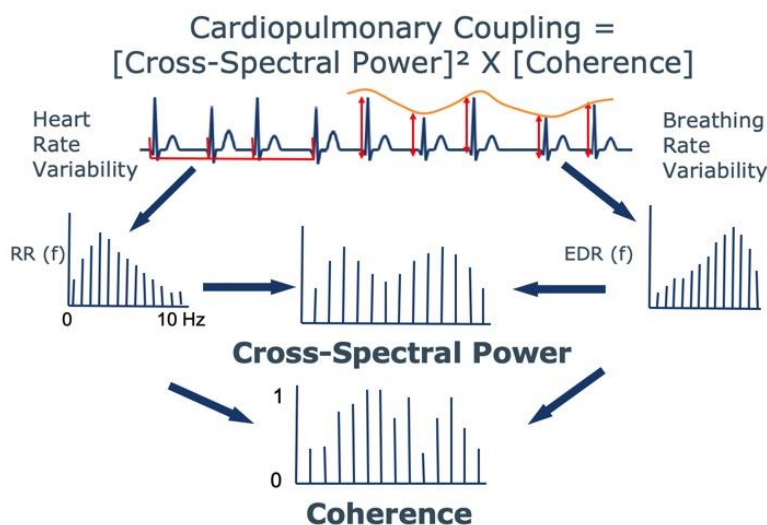


Figure 1. Cardiopulmonary Coupling.

Cardiopulmonary Coupling (CPC) analysis is based on patented algorithms developed and validated by sleep researchers, using continuous, evenly sampled, normal sinus rhythm ECG- or PLETH (Plethysmogram from a PPG sensor) signal as the only input requirement.

The validation of CPC utilized clinical Polysomnography (PSG) as the standard upon which it was compared. Simultaneous SleepImage and PSG recordings were performed, data presenting periods of sleep identified by both systems were compared for validation and published. Please refer to [Publications Reference List](#) which can be found on the last few pages of this document.

Both HRV/PRV and respiration are strongly modulated by autonomic sleep regulating mechanisms (sympathovagal balance). The CPC-software utilizes mathematical and frequency analysis to calculate synchronization between HRV/PRV and respiration to provide visualization of sleep states and sleep pathologies. The Sleep Spectrogram demonstrates that there are clear boundaries with sleep-stage transition from parasympathetic dominance (Stable sleep or High Frequency Coupling (HFC)) to sympathetic dominance (Unstable sleep or Low Frequency Coupling (LFC) and then Rapid Eye Movement (REM) sleep and wake). The spectrogram provides a clear view of sleep health during the sleep period and is useful for sleep disorder evaluation. SleepImage is a helpful tool to diagnose sleep disorders and to monitor therapy success for any disease or condition that affects sleep, by demonstrating a relative increase in stable sleep and relative decrease in unstable sleep. (Figure 2)

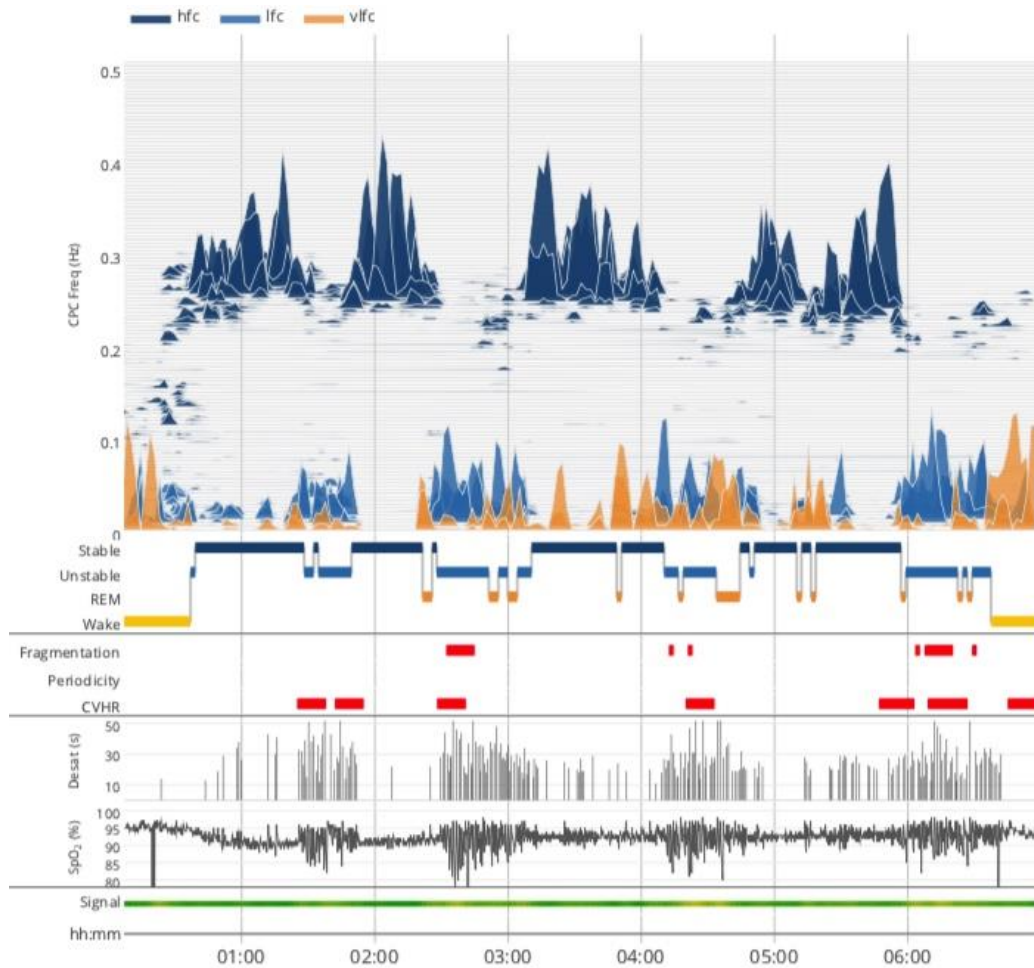


Figure 2. The sleep spectrogram reveals that NREM sleep has a distinct bimodal-type structure marked by distinct alternating and abruptly varying periods of strong high and low frequency cardiopulmonary coupling (HFC and LFC, respectively). These CPC states are separated widely in signal space with no overlap – that is, the boundaries are clean.

The medical literature historically divided sleep into Non-Rapid-Eye-Movement (NREM) sleep 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 a 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. How the biologic role of NREM sleep is associated with delta power is 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 of PSG on interpretation of EEG morphology, CPC utilizes the physiological changes that occur with sleep via the Autonomic Nervous System (ANS) through the “lower” brain centers and networks (including thalamus, hypothalamus, and hippocampus). It integrates information from brain electrical activity, respiration and autonomic drives, capturing the essence of sleep, making traditional “sleep staging” comparison a misnomer. The CPC-method is based on synchronization of HRV and respiratory cycles and is independent of absolute EEG amplitudes. The degree of this synchronization dramatically changes with sleep stages, offering sleep-stage identification as Stable and Unstable NREM-sleep and REM-Sleep.¹³ This synchronization/coupling is most prominent in healthy children. Starting in adolescence, the coupling reduces but remains relatively stable across subjects through adulthood, suggesting that sleep regulation has a significantly stronger effect on cardiopulmonary coupling than aging. Cardiopulmonary coupling thus provides a more meaningful method to correctly evaluate sleep in elderly adults that is not

constrained by the dependence of slow wave sleep that shows to deteriorate with age when measured through EEG from the cortex.³⁻⁵

While PSG requires interpretation of observations (manual or automated) from EEG morphology to determine stages of NREM sleep, SleepImage displays autonomic nervous system regulation that has this distinct bi-modal structure demonstrating that sleep only has two distinct types, driven by sympathetic or parasympathetic dominance. This concept is supported by various biological system behavior like being either awake or asleep and when sleeping, being either in non-rapid eye movement (NREM) sleep or in rapid eye movement (REM) sleep.

Therefore, rather than the conventional graded classification of NREM stage 1, 2 and 3 that is based on interpretation of EEG morphology, SleepImage represents NREM sleep based on ANS morphology (sympathovagal balance). The software-generated output is fully automated and directly reports distinct alternating and abruptly varying periods of strong high and low frequency cardiopulmonary coupling as Stable sleep (High Frequency Coupling, HFC) and Unstable sleep (Low Frequency Coupling, LFC).

When comparing Stable NREM-sleep using SleepImage 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 the correlation between Stable sleep (HFC) and Delta Waves (deep sleep).²⁻⁵ In this state, desirable sleep features dominate, including high vagal tone/sinus arrhythmia, blood pressure dipping, high slow wave power, and stable breathing. 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) and lower delta power. 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 the eyes. The EEG physiology of REM sleep and Wake is closely linked from the standpoint of PSG 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.

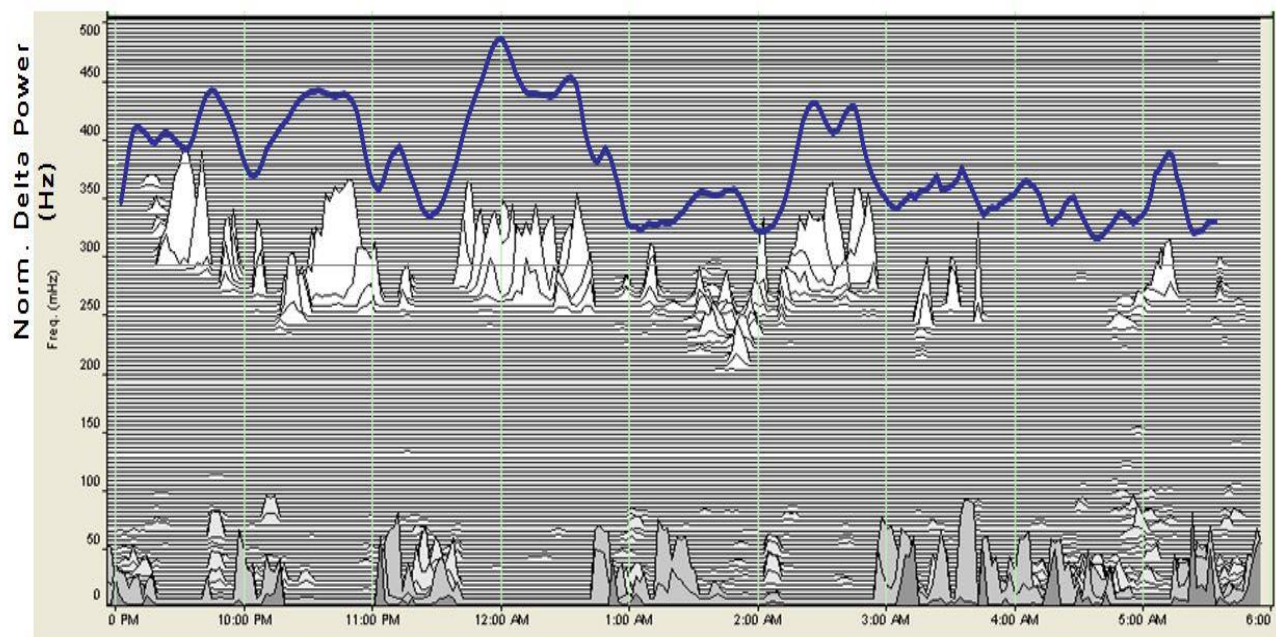


Figure 3. The figure above reveals the relationship between HFC and normalized delta power (blue line) during simultaneous data collection using CPC and PSG as discussed in the paper "Relationship between delta power and the electrocardiogram-derived CPC Spectrogram: possible implications for assessing the effectiveness of sleep". Dr. Robert Joseph Thomas et al. Sleep Med.2014 Jan; 15(1); 125-131.

During the validation of the SleepImage technology, output comparison to tens of thousands of PSG studies 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- or PLETH-derived Cardiopulmonary Coupling high-frequency power (Figure 3, blue line), further supporting a link between cortical EEG electrical activity and brainstem-related cardiorespiratory functions. ²⁻⁵

While SleepImage and PSG analyze and present biological activity during sleep from different directions (Autonomic Nervous System regulation vs. Cortical Brain Wave regulation, respectively), they both reflect sleep. Sleep regulation is complex, and mainly regulated by two parallel mechanisms, homeostatic regulation and circadian regulation, controlled by light, circadian clock, suprachiasmatic nucleus (SCN), thalamic structures, adenosine accumulation and neurohumoral control, respectively. The two methods (CPC and PSG) do therefore not vary as much as it may seem at first, as demonstrated in Figure 4.

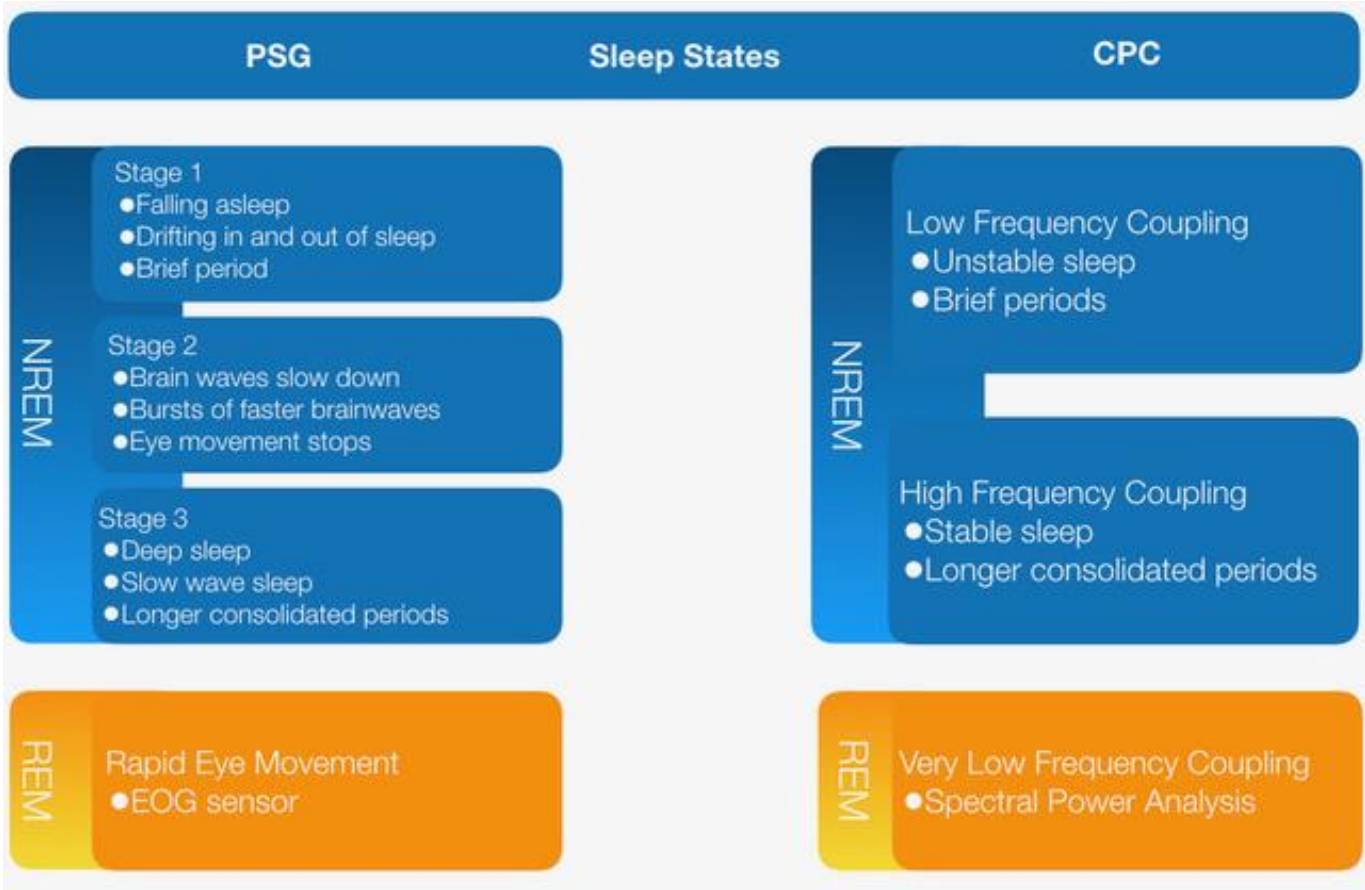


Figure 4. The relationship between conventional sleep scoring system and the Cardiopulmonary Coupling (CPC) scoring system.

Both SleepImage and PSG methods are quite capable instruments to assess sleep, with some important differences. The Sleep Spectrogram and the software generated biomarkers of sleep quality, sleep pathology as well as sleep duration, efficiency and latency, provide a practical approach to assess sleep as a vital sign of health. The SleepImage method 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. The simple interface offers the potential to treat sleep disorders as other chronic diseases, by repeated testing in patients’ natural sleep environment over multiple nights and multiple time points to optimize disease management. ^{6,14-16}

Further description and information on the technology of Cardiopulmonary Coupling is described in a medical textbook on sleep medicine, Principles and Practice of Sleep Medicine, (Kryger – Roth – Dement) Sixth Edition, Chapter 166. Cardiopulmonary Coupling Sleep Spectrogram. ²

SleepImage Output Parameters

Stable sleep (High-frequency coupling; 0.1-0.5Hz) is a biomarker of stable NREM sleep, which is characterized by stable breathing, high vagal tone, a non-cyclic alternating pattern (n-CAP) on the electroencephalogram (EEG), high relative 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 network health, metabolic etc.), such that spending periods in this state enables recovery and restoration processes.^{2,3}

Unstable sleep (Low-frequency coupling; 0.01-0.1Hz) is a biomarker of unstable NREM, with exactly opposite features when compared to stable sleep: low-frequency tidal volume fluctuations, cyclic variation in heart rate, a cyclic alternating pattern (CAP), electroencephalogram (EEG) low relative delta power, non-dipping of blood pressure and variable arousal thresholds. This state may be considered “ineffective” NREM sleep. Ineffective sleep fails to accomplish the desirable functions of healthy sleep. A subset of low-frequency coupling is termed Elevated Low-Frequency Coupling (e-LFC) and has two subsets; an indicator of Periodicity (elevated low frequency coupling narrow band; e-LFC_{NB}) and Fragmentation (elevated low frequency coupling broad band (e-LFC_{BB})).

Sleep-fragmenting stimuli increases unstable sleep (low-frequency coupling), and sleep-consolidating stimuli increases stable sleep (high-frequency coupling) as a percentage of sleep, thereby allowing dynamic tracking of sleep physiology and pathology in health and disease.^{2,3,17}

Fragmentation (elevated low frequency coupling broad-band e-LFC_{BB}) is a subset of low-frequency coupling during NREM sleep which is an indicator of sleep pathology (e.g. pain) or airway disordered breathing patterns like Obstructive Sleep Apnea (OSA) and Upper Airway Resistance Syndrome (UARS).^{2,17-20}

Periodicity (elevated low frequency coupling narrow-band e-LFC_{NB}) is a subset of low-frequency coupling, consisting of periodic-type breathing patterns that may occur during NREM and/or REM and indicates sustained periods of Central Sleep Apnea (CSA) and periodic breathing, or "physiologic" periodicity due to Periodic Leg Movements (PLM's).^{9,17,19}

Sleep Quality Index (SQI) is a summary index of the CPC biomarkers of sleep quality, sleep stability, fragmentation and periodicity, and 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. 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 for the patient or other lay persons, while at the same time being a comprehensive measure of sleep health based on clinical validation.^{6,16,18-20}

Sleep Apnea Indicator (SAI) provides a measure of SDB and is based on detecting oscillations in cardiac intervals associated with prolonged cycles of sleep apnea, based on Cyclic Variation of Heart Rate (CVHR) during unstable breathing (tidal volume fluctuations 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 the SleepImage output. When SAI is presented with the SQI, as well as the biomarkers of Fragmentation and Periodicity, it is possible to use the SAI to not only help detect apneas, but also to differentiate between obstructive and central sleep apnea.¹⁸⁻²¹

The SAI is always displayed in the SleepImage Report, irrespective of whether SpO₂ is recorded or not. CVHR can be detected during stable 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.

The SAI can be compared categorically to the AHI from PSG-studies, although 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. Despite that, classification of SDB utilizing CPC-analysis is based on the same premise as the AHI, the common biomarker used to quantify severity of SDB, as Mild, Moderate and Severe based on the American Academy of Sleep Medicine (AASM) guidelines. Table 1 summarizes a comparison of SAI / CVHR values to AHI from Polysomnography (PSG) studies at each of the severity thresholds for mild, moderate and severe sleep apnea in children and adults. Both SAI and CVHR are useful metrics to inform and guide clinical management of sleep disorders and when used with SQI, values tracked over time have clinical utility to guide timing of SDB interventions, guide therapy and track disease management in both children and adults.

Table 1. 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%

Sleep Apnea is associated with significantly increased risk of cardiovascular morbidity and mortality. In patients with cardiac autonomic dysfunction, that presents as decreased heart rate variability (HRV) that ultimately can lead to a fixed heart rate due to progressive dysfunction of the cardiac sympathetic nervous system. In this subgroup of sleep apnea patients, the Sleep Apnea Indicator 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 are useful biomarkers to aid in the diagnosis of Sleep Disordered Breathing in this patient population. In patients with chronic Atrial Fibrillation, complex patterns cannot be identified and the chaos of the autonomic nervous system results in less meaningful CPC output, thus warranting caution in interpretation.

Apnea Hypopnea Index (sAHI) is an automated measure of Apnea/Hypopnea events, comparable to the American Academy of Sleep Medicine (AASM) scoring guidelines of the Apnea Hypopnea Index (AHI) for both adults and children. When oxygen data (SpO₂) is recorded, SleepImage analyzes the SpO₂ data to generate desaturation events, display an SpO₂ graph and automatically calculate SleepImage Apnea Hypopnea Index (sAHI) by combining CPC-analysis and hypoxic events that are detected through the SpO₂ signal where a qualifying event is characterized by a minimum of ten (10) seconds in duration for both 3% and 4% oxygen desaturation.^{22,23} The sAHI is FDA-cleared to aid diagnosis of Sleep Disordered Breathing (SDB) in both children and adults and follows AASM categorization (mild, moderate, severe) as summarized in table 2. This analysis was based on 3% desaturations.

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

The sAHI, like the Apnea Hypopnea Index (AHI), reports the number of paused breathing events during the sleep period. Events are displayed based on both 3% and 4% desaturations and reported as “Total”, “Obstructive” and “Central” events in line with American Academy of Sleep Medicine (AASM) guidelines for event scoring. When reviewing the sAHI scores, it is recommended to consider SDB events concurrent with CPC sleep states (sAHI_{STABLE}, sAHI_{UNSTABLE}, and sAHI_{REM}) to evaluate and determine disease 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 sAHI for diagnosis.^{6,9,17, 18}

Both SAI and sAHI are meaningful indices to evaluate sleep apnea in children and adults. The SAI, based on CVHR events during unstable sleep, has a scale of 0 – 100. The sAHI is an event counter of paused breathing events per hour of sleep, the same as AHI derived from in-laboratory PSG-studies.

The performance of the SleepImage Apnea Hypopnea Index (sAHI) was validated by comparing the fully automated software generated sAHI to manually derived AHI from in-laboratory PSG-studies currently considered as the “reference standard” collected in prospective clinical trials that included both children and adults. Additionally, the sAHI was compared to REI using adult data 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 2.

The comparison of sAHI to AHI is based on published guidelines from the American Academy of Sleep Medicine (AASM), Obstructive Sleep Apnea Devices for Out-Of-Center (OOC) Testing: Technology Evaluation.²⁴ 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. Additionally, guidelines from the American Academy of Pediatrics (AAP),²⁵ calling for information to be available for physicians to familiarize themselves with sensitivities, specificities and predictive values when outcome of a test is compared to polysomnography to evaluate the test for use in clinical diagnosis are included. Finally, as tonsillectomy is the primary intervention for pediatric obstructive sleep apnea (POSA), clinical guidelines from the American Academy of Otolaryngology – Head and Neck Surgery Foundation have been incorporated (Table 3).²⁶

In children, AHI from a total of 1,334 PSG-studies were compared to the software generated sAHI. 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).

In adults, a total of 839 studies were analyzed from PSG (n=189) and from HSAT (n=572) where 12% had no sleep apnea (n=102), 30% had mild sleep apnea (n=251), 37% moderate sleep apnea (n=313) and 21% severe sleep apnea (n=173).

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) in adults and children. The results are summarized in table 3. The difference between Likelihood Ratios and Predictive Values, can be explained as follows:

Likelihood Ratios (LR) are used to assess the value of performing a diagnostic test and is performed to determine whether a test result usefully changes the probability that a disease state exists. AASM guideline defines acceptable results as sensitivity of at least 82.5% and LR+ of at least 5 at an in-lab AHI of at least 5, demonstrating a 95% post-test probability of the disease based on 80% pre-test probability of the disease.²⁴

Predictive Values (PV) reflect the diagnostic power of the test and depend 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. Neither AASM or AAP require an overall agreement to be reported, although, in practical terms, is what is most commonly used to determine test accuracy and is therefore reported. AAP does not have a guideline for what values are sufficient to generate passing results to diagnose a disease.²⁵

The SleepImage Apnea Hypopnea Index (sAHI) is intended to aid healthcare professionals in diagnosis and management of Sleep Disordered Breathing (SDB) in children, adolescents and adults, including differential diagnosis of obstructive and central sleep apnea. The benefit of using the SleepImage System with an AHI output is that it provides both an event count (AHI) to help quantify Sleep Disordered Breathing (SDB), while also categorizing paused breathing events in context of the SleepImage Spectrogram. It presents an overview of the sleep period, the SleepImage biomarkers that measure sleep stability, sleep quality, as well as Fragmentation and Periodicity.

Table 3. Results of 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	280 ¹
	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				

While sleep disordered breathing patterns are commonly quantified using AHI, the SleepImage biomarkers are still useful for identification and management of SDB when oxygen saturation is not recorded. Using SQI and SAI together with Fragmentation (e-LFC_{BB}) and Periodicity (e-LFC_{NB}) it is possible to identify the presence of sleep disordered breathing and categorize between obstructive and central sleep apnea.^{9,17,19} In certain countries, an sAHI is required to qualify for treatment of SDB. When this is the case, SleepImage recommends that a diagnosis of SDB is confirmed with a SleepImage test that records oxygen saturation to generate a report that includes sAHI, that is reported as ‘total’; ‘obstructive’ and ‘central’ events.

Optional Output Parameters include snoring and/or body position when recorded with an accelerometer of compatible devices worn on the torso. Neither body position nor snoring are included in the SleepImage output of Sleep Quality, Sleep Duration, Sleep Apnea or Sleep Pathologies. These output parameters are displayed on the report when available.

SleepImage in Sleep (Disorder) Management

SleepImage is simple to use and low-cost, it offers the opportunity to track changes in sleep over time, as part of sleep health management as well as to aid diagnosis and management of sleep disorders. Before prescribing a study using a PPG sensor (also known as pulse oximeters), ensure that the sensor size fits the patient properly. When using the Nonin 3150 BLE that has a fingertip sensor, discuss with patients that these sensors cannot be used with artificial nails or nail polish, as it may prevent proper function. SleepImage recommends that healthcare professionals familiarize themselves with the most appropriate collection method and sensor type for each patient.

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. While SQI values are comparable between individuals, the greatest value is to track sleep quality for each individual over time.

Night-to-night variability in sleep is recognized and this variance should be expected to increase between nights with increased sleep disorders (sleep pathology) or the presence of comorbidity. Differences should also be expected over time due to environmental conditions, lifestyle changes or other factors that can cause night-to-night variability in sleep that can affect the recording. It is well documented in peer-reviewed clinical publications 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%.²⁷⁻²⁹ 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 time points to capture the dynamics of sleep physiology and pathology is important. 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.³⁰

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 between ECG and PPG sensors. It is normal to expect $\pm 10\%$ differences between the sensor types that can be greater for certain patients. For clinical use, it is recommended to consistently use the same sensor type in the patient's natural sleep environment.²⁹

Expected Values - Sleep Quality and Sleep Pathology

Expected Values	Adults	Children
Sleep Quality Index (SQI)	>55	>70
Sleep Apnea Indicator (SAI) Mild / Moderate / Severe threshold markers	$\geq 5 / \geq 15 / \geq 30$	$\geq 1 / \geq 5 / \geq 10$
Apnea Hypopnea Index (sAHI) Mild / Moderate / Severe threshold markers	$\geq 5 / \geq 15 / \geq 30$	$\geq 1 / \geq 5 / \geq 10$
Elevated Low Frequency Coupling, Broad Band (e-LFC _{BB})	<15	<8
Elevated Low Frequency Coupling, Narrow Band (e-LFC _{NB})	≤ 2	0

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.

Children

Clinical guidelines regarding diagnosis of sleep disordered breathing (SDB) in children, emphasize that attempts to specify severity of SDB and make treatment decisions solely on the basis of the Respiratory Event Index (REI) or Apnea Hypopnea Index (AHI) and minimum oxygen saturation may lead to misclassification.^{22,31,32}

The most common form, obstructive sleep disordered breathing (oSDB), characterized by abnormal respiratory and ventilation patterns during sleep, is a highly prevalent condition in children with disease severity ranging from primary habitual snoring (6-25%) to obstructive sleep apnea (OSA), diagnosed when apnea-hypopnea index (AHI) ≥ 1.0 on nocturnal polysomnography (PSG). Tonsillar-hypertrophy and obesity are the most common risk factors for OSA in children and tonsillectomy is recommended as first-in-line therapy for children with tonsillar-hypertrophy and OSA.³³

The considerable variability in symptom presentation in children makes OSA difficult to diagnose, demanding increased awareness of SDB in children among clinicians. Excessive daytime sleepiness is not a frequently reported symptom in children, and sleep fragmentation and disrupted sleep architecture often presents as hyperactivity, difficulties concentrating, attention-behavioral- and mood-problems, enuresis, persistent mouth breathing with dry mouth and morning headaches.^{32,34,35}

To further complicate disease management of OSA in children, spontaneous polysomnographic improvements are well known and documented (46%)^{36,37} as well as residual disease following surgery with less than a third of children with OSA achieving complete resolution with surgery.^{38,39} Additionally, surgery may potentially cause both serious short-term surgical complications and in the long-term significantly increased delayed respiratory, allergic and infectious sequelae.⁴⁰⁻⁴³ Although several screening questionnaires have been developed to identify children with OSA, they have not proven accurate, 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.⁴⁴⁻⁴⁷

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 prior to surgery, as questionnaires alone do not provide a good diagnostic prediction of OSA in children.^{25,32} These academic guidelines to establish objective evidence of OSA prior to surgical decisions are though frequently bypassed.⁴⁸ This may be caused by 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.^{26,43}

When test output is used to aid diagnosis or management of SDB in children, consideration should be given to clinical guidelines:

- 1) Clinicians need to determine if the test result is inconclusive for diagnosis before determining the need for another test and assess the risk of an adverse treatment outcome because of inappropriate management.
- 2) The role for individualized decisions based on needs of the child and its caregiver(s).

Diagnosis of SDB requires both clinical and objective sleep data and diagnosis of SDB in children is defined as AHI > 1/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. Because of age related airway growth, children in particular stand to benefit from objective and clinical symptom evaluation over a time period. The fact that 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.⁴⁹

SleepImage is FDA-cleared for diagnosis of OSA in children based on the sAHI. The system displays sleep biomarkers of sleep duration, sleep quality, Fragmentation and Periodicity. The SleepImage test is low-cost, it is simple to use and not intrusive for the child. This offers the potential to measure multiple nights of sleep to capture the dynamics of SDB in children, which may be a more appropriate method than making a therapy decision from presentation of symptoms and objective measure at one specific point in time. The SleepImage biomarkers include:^{6,9,18-23}

1. Sleep quality (captured by the Sleep Quality Index – SQI)
2. Cyclic variation of heart rate (captured by Sleep Apnea Indicator – SAI)
3. Fragmentation, indicative of arousals (captured by eLFC_{BB})
4. Periodicity, indicative of periodic breathing/central sleep apnea (captured by e-LFC_{NB})
5. Time spent below an oxygen saturation of 90% and 88%
6. State of sleep (REM vs. NREM stable/unstable)
7. Sleep latency, and sleep duration.

The 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.⁵⁰ It is furthermore important to implement therapy-tracking post intervention for objective evaluation with longitudinal care to improve clinical management. If left untreated the disease may adversely affect the child's neurocognitive, behavioral, cardiovascular and cardiometabolic health over time.^{21,35,37}

Adults

The same approach for sleep management in adults is important as 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 around 85% of the patient population or more than 936 million people⁵¹ are estimated to have the disease. Long-term compliance on therapy is considered generally low and is problematic as effectiveness of therapy is greatly dependent on consistent use. The lack of compliance to therapy 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 CPAP-therapy on sleep quality (SQI). 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.^{4,16,52,53}

Only with this kind of repeated objective testing, will the opportunity for more comprehensive phenotypic profiling in both clinical management of sleep disorders as well as in design and conduction of research studies be fully utilized. Sleep disorder management needs to become comparable to how other chronic conditions like diabetes or hypertension are managed.^{6,16} 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 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 a 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:

- 1) Stable sleep tracks slow wave power and results of repeated testing could provide new insights into night-to-night sleep homeostatic mechanism.^{2,3,15}
- 2) Substantial overlap in symptom presentation of insomnia and OSA is documented. This advances a need for a new perspective for methods capturing both insomnia and OSA before making diagnostic decisions and initiation of therapy. Offering access to objective, medically validated tests for patients with sleep complaints who currently are considered ineligible for PSG or HSAT testing could fill a void in clinical management of sleep disorders.^{15,20,54}
- 3) sAHI detects and categorizes sleep apnea as obstructive and central events.²² The CPC-biomarkers of Periodicity (e-LFC_{NB}) and Fragmentation (e-LFC_{BB}) further aid clinical evaluation to distinguish between Obstructive and Central events. These two methods offer improvements in disease evaluation and tracking of therapy efficacy, including detection of persistence or emergence of loop gain features, all from recording of a signal from a single sensor and automated analysis. In general, periodic breathing and hypocapnic central apnea are NREM-dominant and do not occur in REM-sleep (exception, a patient with congestive heart failure who can demonstrate periodic breathing during wake) and are features of idiopathic central sleep apnea, opiate-induced sleep apnea and high-altitude periodic breathing.^{55,56} In patients with mixed sleep apnea events, treated with continuous positive airway pressure, therapy can induce or amplify respiratory instability and the loop gain has found to be higher in patients in whom central apneas persist on therapy than in patients with short cycle periodic breathing or treatment-emergent central sleep apnea.^{9,17,18,57-59}
- 4) SAI documents autonomic reaction to altered breathing and oxygen desaturations and has a good correlation with AHI.¹⁸⁻²¹ The SAI (CVHR) should be used in context of other SleepImage biomarkers and as a parameter to track over time.
- 5) The possibility to record sleep for more than one night in the patient's natural sleep environment should offer 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 (insomnia, sleep apnea etc.) could have a meaningful and measurable positive impact on both disease management and public health.

Understanding the SleepImage Spectrogram

SleepImage graphically displays the coupling of heart (pulse) rate variability (HRV/PRV) and respiration activity (EDR/PDR) 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/EDR or PRV/PDR) are in phase (coupled), peaks are generated on the graph to form a visual representation of the frequencies collected during the recording.

Full View Spectrogram

The full view Spectrogram displays the peaks and oscillation pattern of HFC, LFC and vLFC for the time series. The vertical axis uses frequency range 0.004Hz to 0.5Hz and time in hours on the horizontal axis.

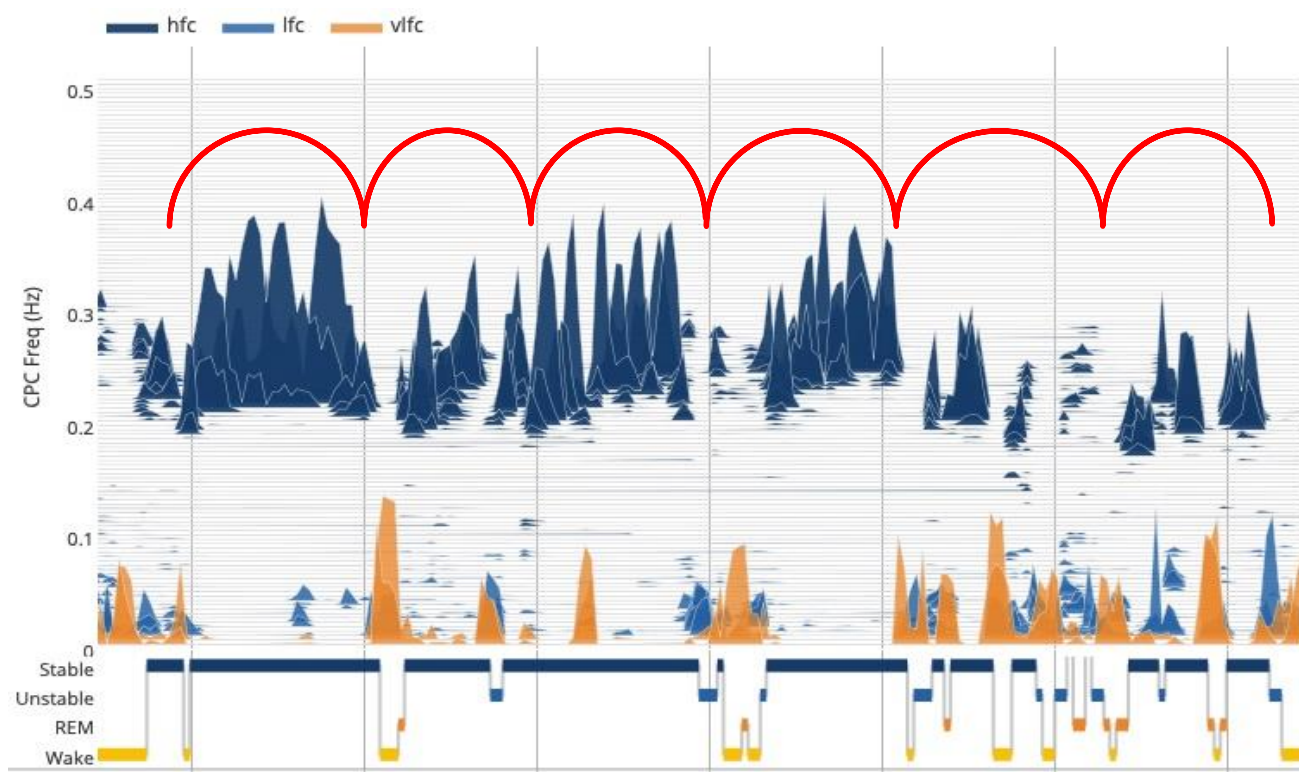


Figure 5. Oscillations between stable and unstable sleep are expected to modulate in 30-90-minute cycles that range from 4-8 Cycles in an adult 8-hour healthy night's sleep and correspond to the alternating periods of NREM and REM sleep. When sleep is disrupted (sleep apnea, insomnia, stress, pain and a variety of other factors), the healthy sleep rhythm is disrupted.

HFC peak amplitude is in relation to the 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 rate activity. A lack of coupling between these two input data streams will result in zero value and no peak generation.

Stable Sleep or High Frequency Coupling - HFC

Stable sleep (High frequency coupling) is displayed on the Spectrogram as dark blue peaks in the frequency range of 0.1 - 0.5Hz. Most Stable sleep occurs during part of NREM stage-2 and all of NREM stage-3, especially with the EEG morphology called

noncyclic alternating pattern (n-CAP) and delta waves. Stable sleep is a biomarker of integrated stable NREM sleep and is associated with periods of stable breathing, high vagal tone, generally a non-cyclic alternating pattern on the electroencephalogram, high relative delta power, physiologic blood pressure dipping, and stable arousal threshold.

Unstable Sleep or Low Frequency Coupling - LFC

Unstable (Low frequency coupling) is displayed on the Spectrogram as light blue peaks in the frequency range of 0.01 - 0.1Hz. Unstable sleep is a biomarker of integrated unstable NREM sleep, with opposite features to Stable sleep and occurs during NREM stage-1 and part of NREM stage-2 sleep. Unstable sleep is associated with EEG activities called cyclic alternating pattern (CAP), periods of fluctuating breathing patterns (tidal volume fluctuations), cyclic variations in heart rate (CVHR), blood pressure non-dipping and variable arousal thresholds. Fragmented REM sleep has low-frequency coupling characteristics.

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 course of the sleep period, spontaneous shifts occur between stable and unstable sleep. Oscillations between stable and unstable sleep are expected to modulate in 30-90 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 5). 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 normal rhythm and is associated with stable NREM sleep (HFC).

3D View Spectrogram

The SleepImage Spectrogram can be displayed in an interactive three-dimensional view by rotating the image for a more detailed observation of the low frequency range. Using the 3D view helps to interpret and differentiate between Sleep-Disordered Breathing (SDB) phenotypes (Obstructive vs. Central Sleep Apnea).

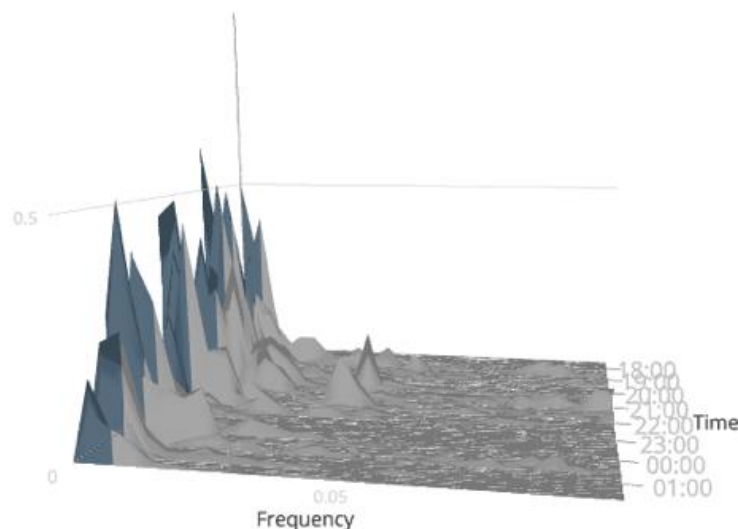
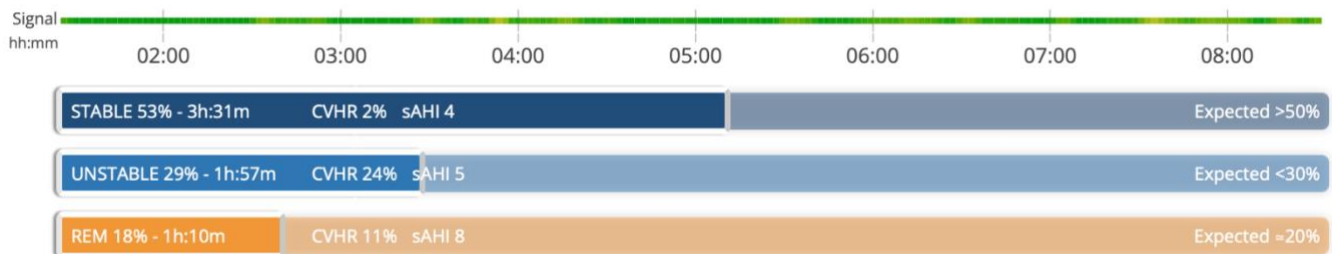
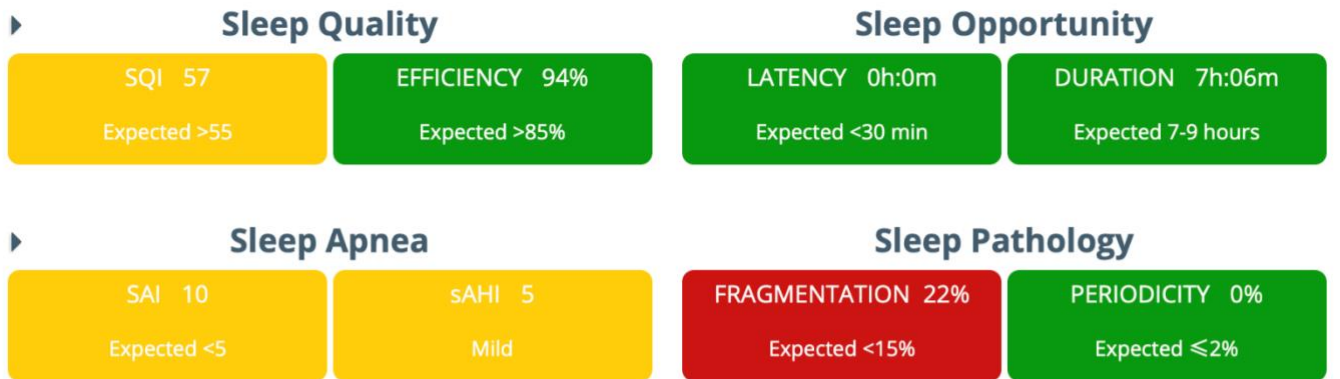


Figure 6. The 3D Spectrogram shows distribution of the peaks in the LFC frequency range. The three axes show 1) time in hours, 2) the LFC frequency range 0.004Hz-0.1Hz and 3) CPC.

The SleepImage Report & Graphics

The SleepImage Report



TST	6h:38m
WASO	0h:23m
WAKE TRANSITIONS	#9
SNORE	N/A
BODY POSITION	N/A

SpO ₂ <90%	0m:46s - 0%
SpO ₂ <88%	0m:07s - 0%
SpO ₂ <80%	0h:0m - 0%
MIN-MAX-MEAN SpO ₂	87% - 97% - 94%

	Desaturations	
	3%	4%
SAHI _{TOTAL}	5	2
SAHI _{OBSTRUCTIVE}	5	2
SAHI _{CENTRAL}	0	0
ODI	4	2

	Min Max Mean		
	Min	Max	Mean
APNEA DURATION (sec)	14	36	24
HEART RATE (BPM)	38	94	50

Automated Summary Output

Test Summary:

Patient: 50 year old Male

Average Signal Quality is **95 %**.
Sleep Quality is **above** 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 **Mild**.
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 should be evaluated for artifacts and arrhythmias.
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. Sleep Efficiency is the ratio of Total Sleep Time divided by Sleep Opportunity and should be >85%.
3. **Evaluate Sleep Opportunity** which is defined by time in bed allocated to sleep, including Sleep Onset Latency (SOL) and Sleep Duration (SD). SD includes Total Sleep Time (TST), Wake After Sleep Onset (WASO) and the time after the last sleep period until recording is stopped. Expected SL is generally defined as <30min. SD is defined by age groups. Although Insomnia cannot be diagnosed from a single night of sleep, SL and Sleep Efficiency (SE) 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 recoding.
4. **Evaluate Sleep Apnea.** The SleepImage Apnea Hypopnea Index (sAHI) (when SpO₂ is recorded) and/or Sleep Apnea Indicator (SAI) indicate the presence of sleep apnea. The sAHI is cleared to aid diagnosis of Sleep Disordered Breathing and is categorized as 'Mild'; 'Moderate' and 'Severe' with values for Children for each category ≥1, ≥5 and ≥10 respectively and for Adults values for each category are ≥5, ≥15 and ≥30 respectively. SAI can indicate SDB with good agreement against sAHI values despite being a different method to detect and quantify sleep apnea and has the same threshold values as sAHI for children and adults, respectively.
5. **Review Sleep Pathology.** The Sleep Pathology biomarkers are Fragmentation (e-LFC_{BB}) indicating sleep fragmentation, arousals and obstructive apneas, and Periodicity (e-LFC_{NB}) indicating central apneas.
6. **Review Sleep Stability.** Stable Sleep is the most important indicator of restorative sleep that has good agreement with Slow Wave (Delta) Sleep in PSG recordings and is expected to be >50% in adults and >65% in children.
7. **Review Transitions, Snore and Body Position.** Sleep Stability is affected by transitions to Wake that should be evaluated to enhance clinical investigation. Snore and Body Position (when recorded) may indicate Positional Sleep Apnea, as snore is generally most prevalent when sleeping on the back (Supine).
8. **Review CVHR.** Evaluating CVHR events in relation to sleep stability may help clinical evaluation of apnea severity beyond the prevalence that is reported by the sAHI. CVHR during Stable Sleep is excluded from calculations of the Sleep Apnea Indicator (SAI), but it may indicate events typically scored as mild hypopnea events in PSG studies and can be caused by leg movements. Review CVHR during REM sleep to differentiate REM sleep apnea.
9. **Apnea Hypopnea Index (sAHI).** Observe the sleep stages (Stable-, Unstable- and REM sleep) to evaluate where sAHI is dominant and observe relationship with CVHR. sAHI is displayed based on 3% and 4% desaturations and separated to obstructive and central events in the sAHI Summary Table. Observe the relationship of SQI and sAHI (SAI) to 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).
10. **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 SpO₂ during the sleep period.
11. **Summary,** the SleepImage Report automatically summarizes the key metrics from CPC analysis to aid the Clinician in summarizing the Clinical Evaluation and recommendations for further testing, further evaluation (referral of patient to another clinician) or therapy.
12. **Clinicians Notes.** Allows treating clinicians to document signs and symptoms of sleep disorders, patient's medications and medical history and to document sleep disorder diagnosis.

Clinician Notes

Add Clinician Notes :

Metric

US Customary

Height :

ft

in

Weight :

lbs

BMI :

Medicare :

Yes

No

Clear

Epworth Sleepiness Scale :

Sleep Complaints :
Select all that apply

Excessive Daytime Sleepiness

Irregular (Paused Breathing During Sleep)

Snoring

Bruxism / Teeth Grinding

Morning Headaches

Waking Up Gasping Or Choking

Difficulty Falling Or Maintaining Sleep

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

G47.31 Primary Central Sleep Apnea

G47.32 High Altitude Periodic Breathing

G47.9 Sleep Disorder, Unspecified

G47.10 Hypersomnia, Unspecified

F51.01 Primary Insomnia

R06.3 Periodic Breathing

R06.83 Snoring

Other Fatigue

Other

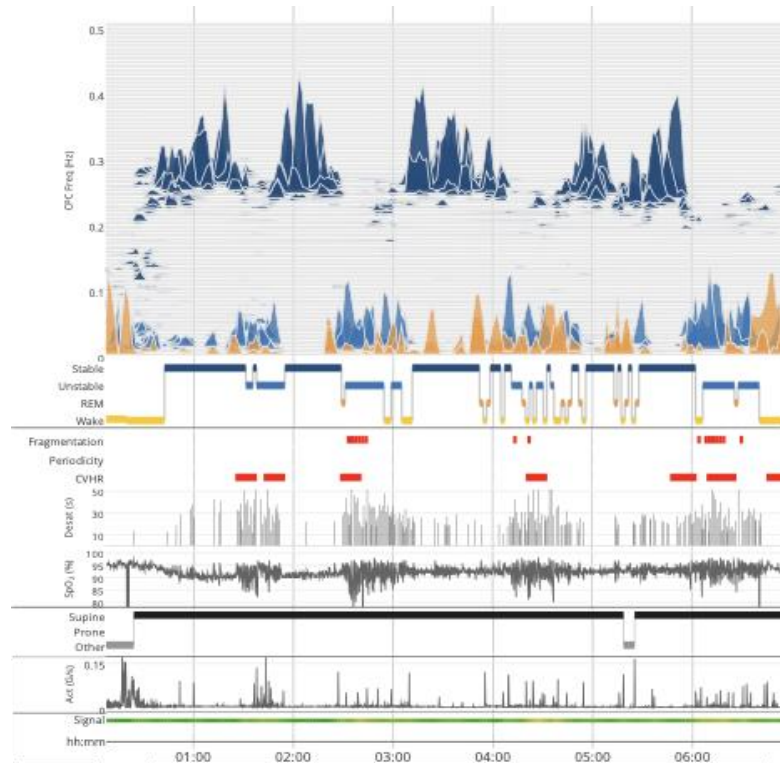
Impressions and Recommendations

Character Count: 0 / 1040

Publish

21

Reviewing SleepImage Graphics for Associations & Patterns

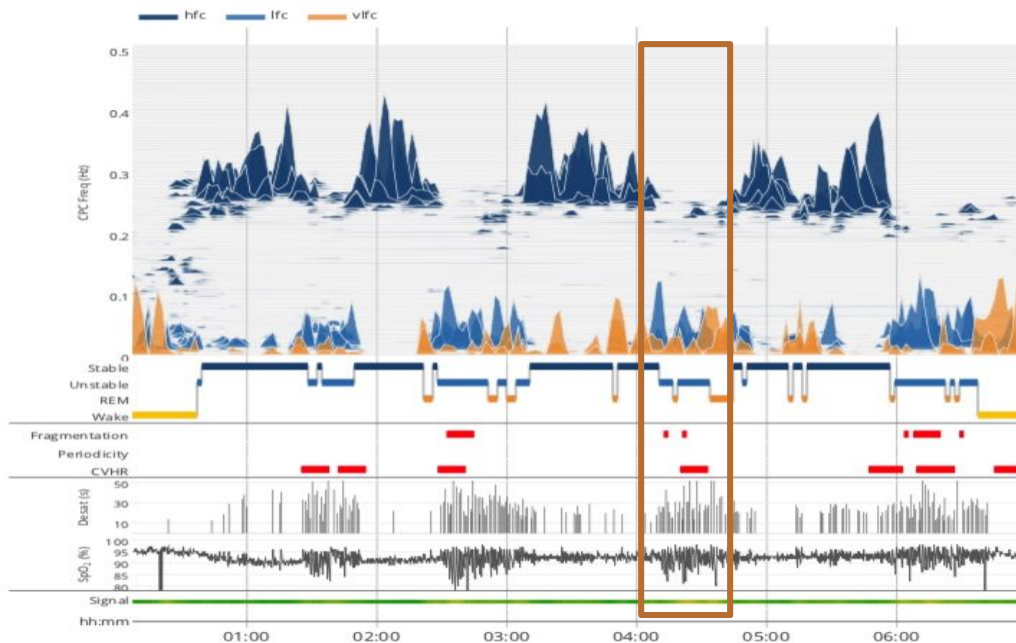


ASSOCIATIONS

1. **Spectrogram:** Review for HFC (stable sleep), LFC (unstable sleep) and vLFC (wake and REM sleep) distribution during the recording period in association with body position, movement, snoring (when recorded), CVHR (cyclic variation of heart rate, presented as SAI (Sleep Apnea Indicator) and sAHI is (when recorded) on the report).
2. **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.
3. **Sleep Disordered Breathing:** Look for presence of fragmentation and periodicity. Fragmentation indicates events that may be caused by obstructive apnea or pain and are termed e-LFC_{BB}. Periodicity indicates metronomic activity that may be caused by central apnea or periodic breathing and are termed e-LFC_{NB}.
4. **CVHR:** Evaluate CVHR in association with the Spectrogram, body position, snoring, movement and oxygen saturation. CVHR is a marker of changes in heart rate happening during and at the cessation of an apnea event.
5. **Snore and Body Position:** Evaluate snore (when recorded) in association with sleep stability, body position (when recorded), CVHR and oxygen saturation (when recorded). Snore in Supine position may indicate Positional Sleep Apnea. and examine the snore trace for a crescendo pattern indicating upper airway resistance (the report displays snore count and duration).
6. **Desaturation and SpO₂** (when recorded): Review desaturation events and correlate in association with stable, unstable and REM sleep, look for concurrent CVHR and correlation with body position and snoring (when recorded). Areas of SpO₂ signal loss are often demonstrated by a large and sudden drop in SpO₂.
7. **Actigraphy** (when recorded): Associate level of Actigraphy with concurrent events, assess any patterns across the recording period and examine the actigraphy graph - see next page.
8. **Signal Quality:** Evaluate the quality of the signal during the recording period. Red may indicate signal loss and therefore the CPC algorithm is not able to produce accurate data during these periods. If long periods of signal loss are present it is recommended to repeat the sleep study.
9. **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.
10. **Toggle HFC, LFC and vLFC peaks** (Clinician Users): The hfc, lfc, vlfc 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.

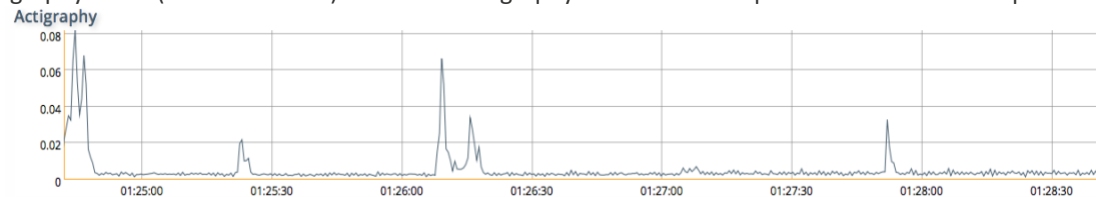
Patterns

After analyzing Associations, an overview of Patterns within the raw data traces below the Spectrogram should be considered. By reviewing the Spectrogram from Left (Start) to Right (End) and examining the traces that coincide with the timeline of the recording, concurrent events can be observed in increments or 10 sec., 30 sec., 1 min., 2 min. and 4 min.

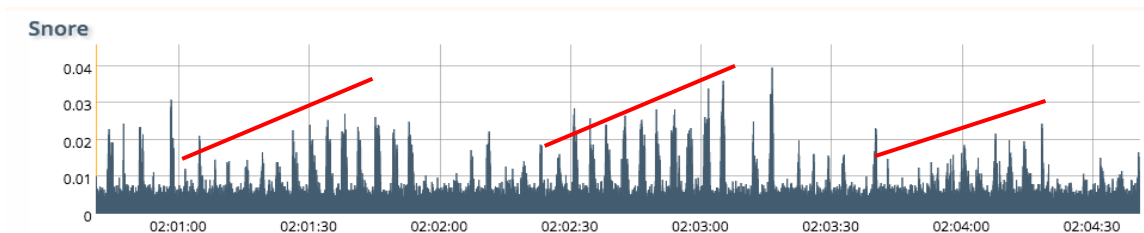


P A T T E R N S

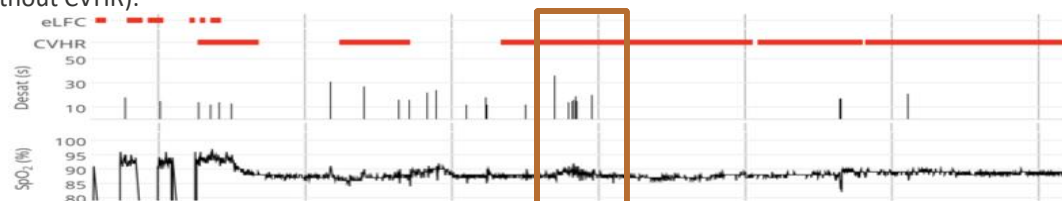
1. Actigraphy Trace (when recorded): Increased actigraphy associated with periods of unstable sleep



2. Snore Trace (when recorded): Snoring with crescendo pattern during periods of unstable sleep



3. SpO₂ Trace: Oxygen saturation of areas <90% during periods of e-LFC_{BB} (with and without CVHR) and e-LFC_{NB} (with and without CVHR).



Distinguishing Sleep Disordered Breathing Types

Sleep Disordered Breathing (SDB) comprises a wide spectrum of sleep-related breathing abnormalities. There are two major categories of SDB:

1. **Obstructive Sleep Apnea (OSA)** is the most common one and is related to increased upper airway resistance and includes snoring, upper airway resistance syndrome (UARS) and obstructive sleep apnea (OSA). Patients who suffer from OSA periodically struggle to breathe and are unable to inhale effectively because of a collapsed airway.
2. **Central Sleep Apnea (CSA)** happens when the brain temporarily stops 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 called idiopathic central sleep apnea. A condition, Cheyne-Stokes respiration, subtype of CSA presents similarly on the CPC-Spectrogram.

An exceptional feature of SleepImage analysis is its capacity to easily distinguish between SDB types. Each SDB type has a visually discernable Spectrogram pattern that makes identification simple and intuitive. The CPC algorithms identify Obstructive Sleep Apnea pathology both as obstructive events ($sAHI_{obstructive}$) and as fragmentation, presented as increased elevated LFC 'broad band' ($e-LFC_{BB}$). Periodic-type breathing pattern (i.e. Central Sleep Apnea) is identified both as central events ($sAHI_{central}$) and by elevated LFC 'narrow band' ($e-LFC_{NB}$). This two-pronged method helps clinicians make a better-informed evaluation to aid diagnosis or management of sleep apnea. A combination of both obstructive and central events in an alternating pattern of elevated LFC broad and narrow bands can be identified in patients with sleep apnea.

To aid the clinician in identifying individuals with SDB when oxygen saturation is not recorded, the SleepImage system offers the Sleep Apnea Indicator (SAI) that is automatically calculated from known changes in heart rate that occur during apneas, called Cyclic Variation of Heart Rate (CVHR). A simple way to explain CVHR is that it consists of bradycardia during apnea followed by a relative tachycardia when breathing resumes. Although SAI is a different measure with a different unit of measure when compared to $sAHI$, it is possible to use the same numeric values in both metrics to evaluate the presence of sleep apnea. Mild, Moderate and Severe Sleep Apnea values are ≥ 5 / ≥ 15 / ≥ 30 (adults) and ≥ 1 / ≥ 5 / ≥ 10 (children) respectively.

3D Spectrogram - Obstructive Sleep Apnea

OSA causes sleep fragmentation. The presence of a broad band of peaks indicates that the upper airway is the primary pathophysiological contributor to the patient's Sleep-Disordered Breathing. $e-LFC_{BB}$ is presented by broad gray peaks on the 3D Spectrogram.

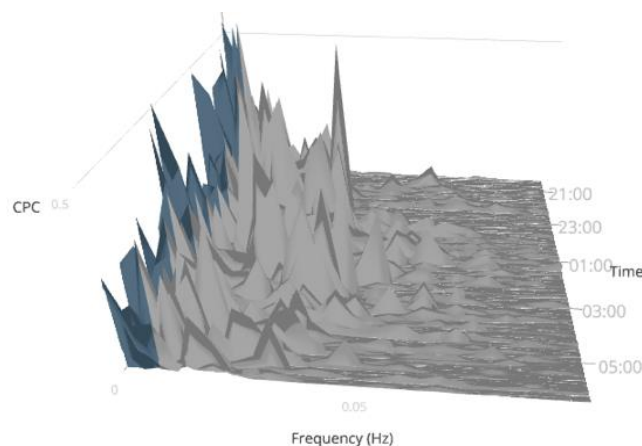


Figure 7. The 3D View Spectrogram - Obstructive Sleep Apnea shows a "broad" distribution of the peaks called Elevated Low Frequency Coupling broad-band ($e-LFC_{BB}$).

3D Spectrogram - Central Sleep Apnea

Central Sleep Apnea or periodic breathing is represented by narrow red colored peaks as $e\text{-LFC}_{NB}$ on the 3D Spectrogram view and identifies patterns of breathing or movement having a “narrow band” LFC profile.

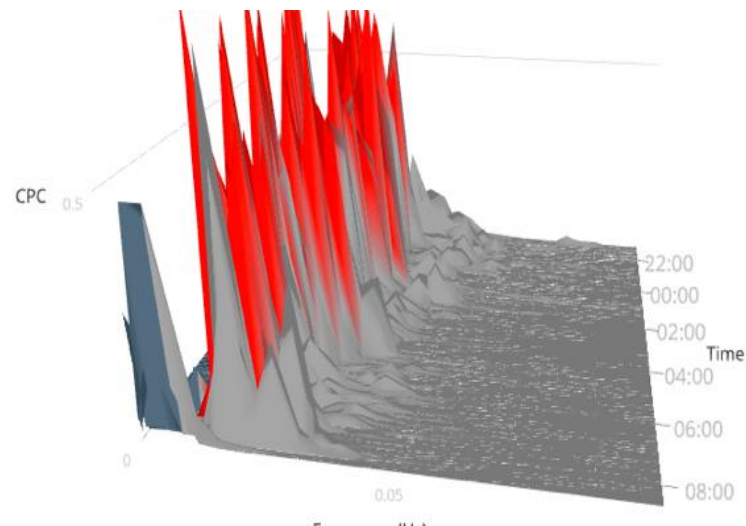


Figure 8. 3D Spectrogram - Central Sleep Apnea is presented as a line of narrow peaks. The system colors these peaks red to make it easier for users to identify the periodicity.

3D Spectrogram - Mixed Sleep Apnea

A combination of both obstructive and central components showing narrow band $e\text{-LFC}$ ($e\text{-LFC}_{NB}$) and broad band $e\text{-LFC}$ ($e\text{-LFC}_{BB}$).

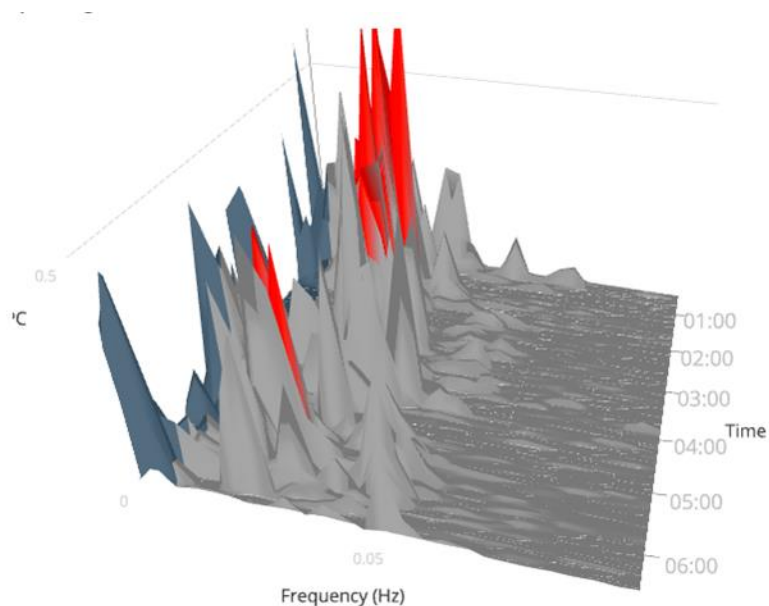


Figure 9. 3D Spectrogram – Mixed Sleep Apnea is a combination of both obstructive and central components.

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Glossary

AAP: American Academy of Pediatrics

AASM: American Academy of Sleep Medicine

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

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

PDR: Plethysmograph Derived Respiration

PRV: Pulse Rate Variability

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

REM: Rapid Eye Movement

SA: Sleep Apnea

SAI: Sleep Apnea Indicator. Displays “one number” for apnea events through the recording period by automatically detecting known changes that occur in the cardiovascular system during periods of sleep disordered breathing.

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

SpO₂: Oxygen Saturation

SQL: 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](#))