nox medical

DeepRESP

INSTRUCTIONS FOR USE

English

DeepRESP Instructions for Use

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DeepRESP – version 1.0
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Intended Use

DeepRESP is a cloud-based artificial intelligence-enabled software application used for analysis (automatic scoring), retrieval, and summarization of data recorded with monitoring devices used to categorize sleep-related events that help aid in the diagnosis of sleep-related disorders. The data is then transferred to another software for manual scoring, display, and reporting.

Indications for Use

DeepRESP is an aid in the diagnosis of various sleep disorders where subjects are often evaluated during the initiation or follow-up of treatment of various sleep disorders. The recordings to be analyzed by DeepRESP can be performed in a hospital, patient home, or an ambulatory setting. It is indicated for use with adults (22 years and above) in a clinical environment by or on the order of a medical professional.

DeepRESP is intended to mark sleep study signals to aid in the identification of events and annotation of traces; automatically calculate measures obtained from recorded signals (e.g., magnitude, time, frequency, and statistical measures of marked events); and infer sleep staging with arousals with EEG and in the absence of EEG. All output is subject to verification by a medical professional.

Patient population

The patient group includes adults (22 years and above).

Intended Users

The end users of DeepRESP are medical professionals who have received training in the areas of hospital/clinical procedures, or sleep disorder investigation.

Information for Safety

- DeepRESP is intended to be used as an additional source of information for diagnostic or treatment purposes. Medical professionals remain responsible for reviewing the device output and for the diagnosis or treatment decision.
- Medical professionals are responsible for checking the suitability of the data intended to be processed by the device. Any corrupted data, distorted data or signals lost may result in incorrect device outputs.
- For operational support, in case of user errors, cybersecurity events or other type of events, please contact support@noxmedical.com

Warnings and Cautions for Use

- **Warning:** The output of DeepRESP is not the only source of data to make a diagnosis. Medical professionals remain responsible for reviewing the device output and for the diagnosis or treatment decision.
- **Warning:** DeepRESP does not classify the scored apneas and hypopneas as central or obstructive, this should be done by a medical professional when reviewing or interpreting the sleep recording.
- **Caution:** U.S. federal law restricts this device to sale by, or on the order of, a physician.

DeepRESP Description

DeepRESP is a cloud-based software as a medical device (SaMD), designed to perform analysis of sleep study recordings, with and without EEG signals, providing data for the assessment and diagnosis of sleep-related disorders. Its algorithmic framework provides the derivation of sleep staging including arousals, scoring of respiratory events and key parameters such as the Apnea-Hypopnea Index (AHI).

DeepRESP is hosted on a serverless stack. It consists of:

- A web Application Programming Interface (API) intended to interface with a third-party client application, allowing medical professionals to access DeepRESP's analytical capabilities.
- Predefined sequences called Protocols that run data analyses, including artificial intelligence and rule-based models for the scoring of sleep studies, and a parameter calculation service.
- A Result storage using an object storage service to temporarily store outputs from the DeepRESP Protocols.

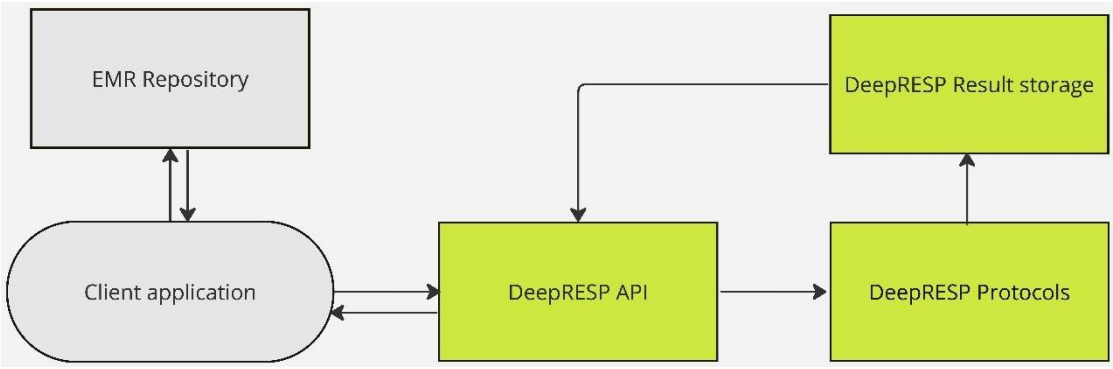


Figure 1 - DeepRESP dataflow

DeepRESP operates without a graphical user interface (GUI). The client application assumes the responsibility to provide the user interface to the end-user, manage sleep study and protocol selection, present the DeepRESP results to the end user and manage any exceptions encountered by DeepRESP (i.e., during accessing the sleep study or analyzing the study). The client application can call specific protocols but cannot customize any protocols or create its own protocols.

Signals and Parameters

The following Table 1 presents the input and output parameters of DeepRESP, for sleep studies with EEG signals (PSG studies) and without EEG signals (HSAT studies) in .ndf and .protobuf format uploaded by the user:

Table 1 - Input and output parameters for DeepRESP

Study type	Physiological input signals	Output parameters
PSG	EEG signals EOG signals Chin EMG signals	Sleep stages: Wake, REM, N1, N2 and N3
	Abdomen and Thorax RIP Nasal Pressure Desaturation Events Arousal Events	Respiratory events: hypopneas
	Abdomen and Thorax RIP Nasal Pressure	Respiratory events: apneas
	SpO2	Respiratory events: oxygen desaturations
	EEG signals EOG signals Chin EMG signals	Arousals events
	Respiratory events, sleep stages and arousal events	Parameters such as AHI.
HSAT	Abdomen and Thorax RIP	Sleep states: Wake, REM, NREM
	Abdomen and Thorax RIP Nasal Pressure Desaturation Events Arousal Events	Respiratory events: hypopneas
	Abdomen and Thorax RIP Nasal Pressure	Respiratory events: apneas
	SpO2	Respiratory events: oxygen desaturations
	Abdomen and Thorax RIP	Arousals events
	Respiratory events, sleep states and arousal events	Parameters such as AHI.

To provide the outputs, DeepRESP features a suite of automated protocols to analyze sleep data. The protocols orchestrate analyses according to a predefined sequence. To run a protocol, DeepRESP receives study data and a specification of which protocol to run. It then runs the corresponding protocol which will launch the corresponding analysis. The following provides the analysis ouputs in more detail according to the type of study uploaded:

1. **For PSG studies:**
    - PSG Preprocessing Protocol

- Position Detection: Identifies patient positions (upright, prone, supine, left and right positions).
- Analysis Period Finder: Determines the likely period the patient attempted to sleep.
- Desaturation Detector: Identifies significant drops in blood oxygen saturation.
- Nox Respiratory Analysis: Detects various respiratory events, including apneas and hypopneas.
- PSG Sleep Staging: Categorizes sleep into distinct stages from EEG signals (Wake, REM, N1, N2 and N3)
- PSG Arousal Detection: Identifies arousal events.

    - PSG Postprocessing Protocol

- Parameter Engine: Computes sleep parameters such as AHI.
- Sleep Apnea Endotypes: Predicts the underlying causes of sleep apnea.
- Sleep Apnea Burden: Calculates the hypoxic and ventilatory impacts of sleep apnea.

2. **For HSAT studies:**
    - HSAT Preprocessing Protocol

- Position Detection: Identifies patient positions (upright, prone, supine, left and right positions).
- Analysis Period Finder: Determines the likely period the patient attempted to sleep.
- Desaturation Detector: Identifies significant drops in blood oxygen saturation.
- Nox BodySleep: Estimates sleep states (Wake, REM, NREM) and detects arousal events from respiratory signals.
- Nox Respiratory Analysis: Detects various respiratory events, including apneas and hypopneas.

    - HSAT Postprocessing Protocol
- Parameter Engine: Computes sleep parameters such as AHI.
- Sleep Apnea Endotypes: Predicts the underlying causes of sleep apnea.
- Sleep Apnea Burden: Calculates the hypoxic and ventilatory impacts of sleep apnea.

After a protocol is done, DeepRESP returns a structured human readable payload with all calculated parameters and provides a link (i.e., URL) to object artifacts such as scoring and new signals in the client application which incorporates and presents them to the end user for review.

Development

This device contains artificial intelligence/machine learning (AI/ML)-based analysis models as part of the Preprocessing protocols and that process signals to detect sleep events: Nox BodySleep, Nox Respiratory Analysis, PSG Sleep Staging, PSG Arousal Detection.

The training data for the models consisted of signals of healthy patients and patients diagnosed with sleep disorders acquired from different US, EU and Asian sites.

DeepRESP models are not adaptive continuous learning algorithms. The models are locked so that they do not change as a result of user input.

Clinical Performance

The clinical performance of DeepRESP was validated by a retrospective study. It used manually scored sleep recordings, originating from sleep clinics in the United States, performed as part of routine clinical work matching indicated use of the study device and patient population.

The performance of DeepRESP with regards to scoring of sleep recordings with electroencephalography (EEG) (i.e. Type I and II), and sleep recordings without EEG (i.e. Type III) was validated. Two separate studies were conducted, one to validate DeepRESP with scoring of Type I-II recordings and a second one with scoring of Type III recordings. The studies were done by evaluating the agreement in scoring and clinical indices resulting from the automatic scoring by DeepRESP compared to manual scoring. The performance of DeepRESP was compared to the agreement of the automatic scoring of the predicate device to manual scoring. The same collection of sleep recordings and same manual scoring were used when comparing the automatic scoring of DeepRESP and the predicate device. The study method was a retrospective data study comparing paired differences.

In both studies DeepRESPs performance with regards to sleep state estimation and respiratory event scoring was validated against the Nox Sleep System (K192469). For evaluation for performance of arousal scoring, Sleepware G3 (K202142) was used as a comparator.

For validating scoring performance for Type I recordings, a total of 2,224 Type I recordings were used. For validating scoring performance for Type III recordings, a total of 3,488 sleep recordings were used, including 2,213 Type I recordings and 1,275 Type II recordings. The Type I and II recordings were processed as Type III recordings by utilizing only the subset of signals from them that are common to Type III recordings.

The recording collection used for validation of Type I scoring consisted of 46% Females, had individuals in all age groups (22-35, 36-45, 46-55, 56-65, 65+), and all BMI groups (<25, 25-30, <30). The recording collection used for validation of Type III scoring consisted of 33% females, had individuals in all age groups (22-35, 36-45, 46-55, 56-65, 65+), and all BMI groups (<25, 25-30, <30). The Type I and II sleep recordings were collected as part of standard clinical care for patients suspected of suffering from sleep disorders. The patients came from urban, suburban, and rural areas with a high-level of race/ethnicity diversity (Caucasian or White, Black or African American, Other, Not Reported). The patient population was therefore considered as representative of patients seeking medical services for sleep disorders in the United States.

Results:

In the retrospective study intended to validate DeepRESP for Type I recordings:

- In comparison to the primary predicate device with regards to severity classification of sleep recordings, with AHI ≥5 and AHI ≥15 as severity thresholds, the study device showcased non-inferiority against the primary predicate device. Additionally, for OPA (overall percentage agreement) and PPA (positive percentage agreement) the study device achieved superiority for AHI ≥15 and AHI ≥5.
- In comparison to the primary predicate device with regards to overall respiratory event scoring the study device showcased non-inferiority for all endpoints, additionally achieving superiority for OPA.
- In comparison to the primary predicate device with regards to sleep state estimation the study device showcased non-inferiority for PPA, NPA, and OPA.
- In comparison to the additional predicate device with regards to arousal event scoring, the study device achieved non-inferiority.

The performance agreement of DeepRESP for type I studies compared to manual scoring can be seen in table 2.

Table 2. Performance agreement of DeepRESP compared to manual soring. Scoring of Type I recordings.

	PPA% [95% CI]	NPA % [95% CI]	OPA % [95% CI]
AHI ≥5	87.5 [86.2, 89.0]	91.9 [87.4, 95.8]	87.9 [86.6, 89.3]
AHI ≥15	74.1 [72.0, 76.5]	94.7 [93.2, 96.2]	81.5 [79.9, 83.3]
AHI ≥30	66.8 [63.6, 70.1]	97.9 [97.2, 98.6]	86.7 [85.3, 88.0]
Respiratory events	72.0 [70.9, 73.2]	94.2 [94.0, 94.5]	87.2 [86.8, 87.5]
Wake	95.4 [95.1, 95.6]	94.6 [94.4, 94.9]	94.8 [94.6, 95.0]

NREM	92.3 [92.0, 92.6]	92.7 [92.4, 92.9]	92.4 [92.2, 92.6]
N1	42.8 [41.6, 43.8]	89.7 [89.3, 90.1]	87.1 [86.7, 87.5]
N2	74.2 [73.4, 74.9]	82.8 [82.3, 83.3]	78.7 [78.3, 79.1]
N3	43.1 [41.4, 44.8]	98.5 [98.4, 98.7]	91.6 [91.3, 91.9]
REM	84.3 [83.6, 85.0]	98.3 [98.2, 98.4]	96.3 [96.2, 96.4]
Arousal events	62.2 [61.2, 63.1]	89.3 [88.8, 89.7]	81.4 [81.1, 81.7]

In the retrospective study intended to validate DeepRESP for Type III recordings:

- In comparison to the primary predicate device with regards to severity classification of sleep recordings, with AHI ≥5 and AHI ≥15 as severity thresholds, the study device showcased superiority for PPA for all thresholds. In the case of NPA, and OPA, the study device showcased non-inferiority compared to the primary predicate device.
- In comparison to the primary predicate device with regards to overall respiratory event scoring the study device showcased non-inferiority for NPA, achieving superiority for OPA and PPA.
- In comparison to the primary predicate device with regards to sleep state estimation the study device showcased non-inferiority for PPA, NPA, and OPA.
- In comparison to the additional predicate device with regards to arousal event scoring, the study device achieved non-inferiority.

The performance agreement of DeepRESP for Type III studies compared to manual scoring can be seen in table 3.

Table 3. Performance agreement for DeepRESP compared to manual scoring. Scoring of Type III recordings.

	PPA% [95% CI]	**NPA % [95% CI]**	**OPA % [95% CI]**
AHI ≥5	93.1 [92.2, 93.9]	81.1 [75.1, 86.6]	92.5 [91.7, 93.3]
AHI ≥15	82.1 [80.6, 83.5]	92.3 [90.5, 94.0]	84.7 [83.5, 85.8]
AHI ≥30	75.9 [73.7, 78.0]	96.8 [96.0, 97.6]	87.2 [86.2, 88.4]
Respiratory events	75.4 [74.6, 76.1]	87.8 [87.4, 88.1]	83.7 [83.4, 84.0]

Wake	76.2 [75.5, 77.0]	96.8 [96.6, 97.0]	92.7 [92.5, 92.9]
NREM	94.5 [94.2, 94.7]	79.0 [78.4, 79.6]	89.2 [88.9, 89.4]
REM	79.1 [78.2, 79.9]	98.1 [98.0, 98.2]	95.4 [95.2, 95.5]
Arousal events	66.8 [65.8, 67.6]	86.8 [86.4, 87.1]	81.8 [81.5, 82.0]

The validation results demonstrate that the predefined clinical performance criteria of DeepRESP against the primary predicate device and additional predicate device have been met for studies with and without EEG signals. DeepRESP is therefore considered as deemed effective in its intended purpose, i.e. categorising sleep related events, that help aid in the diagnosis of sleep related disorders.

Supported File Format

DeepRESP accepts signals from sleep studies in .ndf and .prodobuf format.

Current Version

The client can always ensure they are using the expected version of DeepRESP by calling the "about" endpoint.

Standard Operation

DeepRESP is used through a third-party client application, which provides the user interface for DeepRESP's functionality. No installation is required for the use of DeepRESP.

The third–party client will run a DeepRESP preprocessing protocol to automatically score the uploaded sleep study. After the preprocessing sequence has been followed, the third-party client application can offer the end-user the opportunity to manually review, correct or adjust sleep scoring before requesting DeepRESP to initiate postprocessing to calculate the output parameters, such as the AHI. Please refer to the instructions of the third-party client application for further information.

Decommissioning and Disposal

If there are any questions or assistance is required regarding the decommissioning and/or disposal process, including the retrieval or deletion of user data, please contact support@noxmedical.com.

Security Information

Cloud Environment

DeepRESP is an API-centric, cloud-based software system that automates the analysis of sleep study data using a serverless AWS infrastructure. The operating environment has the following certifications:

- ISO-27001
- SOC2
- HITRUST

Data at Rest

All API processing results are encrypted at rest. All processing results stored in Amazon S3 are encrypted using Server-Side Encryption with Amazon S3-managed keys.

Data in Transit

All data is transferred using encrypted endpoints (on port 443). No non-encrypted endpoints are provided for data communication.

The endpoint encryption uses TLS 1.2 and only clients supporting that level of encryption are supported.

Backups

No data is permanently stored in DeepRESP. Therefore, no backup strategy is needed or implemented in the operating environment.

System Monitoring

Best practices for system monitoring are employed to ensure the security and stability of the system. AWS Inspector, CloudWatch and CloudTrail are used to monitor the systems for vulnerabilities, unusual activities and performance issues. Wazuh is used to monitor the logs for unusual activities or unauthorized file system changes. All these systems can generate alerts and block potentially threatening IP addresses.

Intrusion Detection and Prevention

To ensure that unauthorized people and services do not gain access to the platform, a number of intrusion detection and prevention measures have been implemented.

Log files are monitored to detect and prevent brute force attacks. Log files are also monitored to detect multiple failed attempts to try to access the system and then block the IP of the calling system when this occurs.

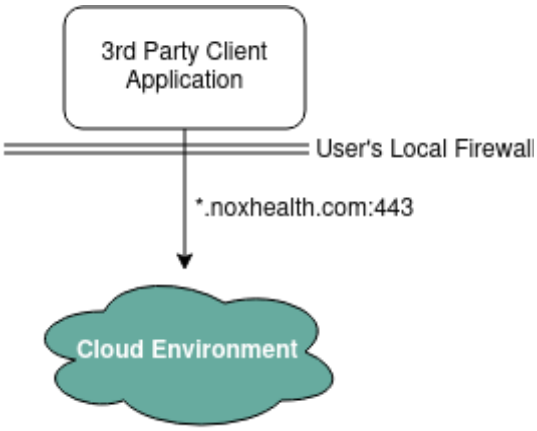
Reporting

In case of a security event is detected that has an impact on the security of the system or data, users are notified via Nox Medical's Customer Relationship Process (SOP-0004)[1].

Client Environment

DeepRESP is an API-centric, cloud-based software system that automates the analysis of sleep study data using a serverless AWS infrastructure. DeepRESP operates without a graphical user interface (GUI). It therefore integrates with third-party clients for data processing and result dissemination, relying on these systems for visualization and reporting.

The user accesses the medical device through a Client Application (third-party system). The following diagram illustrates the security ecosystem of the medical device from a user perspective:



To ensure seamless operation of the 3rd party client application access to DeepRESP, the following security measures shall be implemented by the user:

- Whitelisting of *.noxhealth.com (the asterisk means that subdomains shall be included) in the user's local firewall configuration
- Allowing outgoing traffic on port 443 to *.noxhealth.com in the user's local firewall configuration

No specific anti-malware software configuration is required for the application to operate securely and effectively.

[1] Nox Medical operates an ISO 13485 Certified Quality Management System.

Security Updates

All vulnerabilities notified / detected are assessed using the CVSS[2]. The score ranges between 0 and 10 and Security Updates are issued according to the following:

- CVSS 9.0-10.0: Critical – turn off service until the vulnerability has been patched.
- CVSS 7.0-8.9: High – Fix within 1 week.
- CVSS 4.0-6.9: Medium – Fix within 4 weeks.
- CVSS 0.1-3.9: Low – Fix within 8 weeks.
- CVSS 0: None – No action.

Security Updates are deployed to the Cloud Environment. This ensures that the end user is always using the latest version of the DeepRESP software.

Vulnerabilities

No vulnerabilities have been identified that can affect cybersecurity or safety of the device.

The vulnerability process used complies with the ANSI/AAMI SW96:2023 Standard for medical device security using methods described in the AAMI TIR57:2016 guidance – Principles for medical device security.

Software Bill of Materials (SBOM)

The Software Bill of Material is provided as an IFU Addendum to this user manual. The SBOM may be maintained more regularly than the product under scope and it is therefore recommended to use the latest version when reviewing the content.

Please reach out to support@noxmedical.com for full disclosure **of the latest version** of the SBOM for the product. The SBOM is updated with every product release / patch / vulnerability detection and is available both in a human readable and a machine-readable format.

Description of Abbreviations

AHI	Apnea-Hypopnea Index (AHI)
API	Application Programming Interface
EEG	Electroencephalogram
EMG	Electromyogram

[2] The Common Vulnerability Scoring System (CVSS) is a method used to supply a qualitative measure of severity.

EOG	▸ Electrooculogram
HSAT	▸ Home Sleep Apnea Test
NPA	▸ Negative Percentage Agreement
OPA	▸ Overall Percentage Agreement
PPA	▸ Positive Percentage Agreement
PSG	▸ Polysomnography
SaMD	▸ Software as a Medical Device
(01)15694311112099 (8012)VVvvrr	▸ Unique Device Identifier (UDI): the Application Identifier (01) indicates the device identifier (DI) (i.e. “15694311112099”), the Application Identifier (8012) indicates the software version (i.e. “VVvvrr”) The UDI is accessible from the following REST API method: /v1/about