Automated Prediction of the Apnea-Hypopnea Index using a Wireless Patch Sensor

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***Abstract*— Polysomnography (PSG) is the gold standard that manually quantifies the apnea-hypopnea index (AHI) to assess the severity of sleep apnea syndrome (SAS). This study presents an algorithm that automatically estimates the AHI value using a disposable HealthPatch^{TM} sensor. Volunteers (n=53, AHI: 0.1−85.8) participated in an overnight PSG study with patch sensors attached to their chest at three specified locations and data were wirelessly acquired. Features were computed for 150-second epochs of patch sensor data using analyses of heart rate variability, respiratory signals, posture and movements. Linear Support Vector Machine classifier was trained to detect the presence/absence of apnea/hypopnea events for each epoch. The number of epochs identified with events was subsequently mapped to AHI values using quadratic regression analysis. The classifier and regression models were optimized to minimize the mean-square error of AHI based on leave-one-out cross-validation. Comparison of predicted and reference AHI values resulted in linear correlation coefficients of 0.87, 0.88 and 0.92 for the three locations, respectively. The predicted AHI values were subsequently used to classify the control-to-mild apnea group (AHI$<$15) and moderate-to-severe apnea (AHI$\geq$15) with an accuracy (95% confidence intervals) of 89.4% (77.4−95.4%), 85.0% (70.9−92.9%), and 82.9% (67.3−91.9%) for the three locations, respectively. Overnight physiological monitoring using a wireless patch sensor provides an accurate estimate of AHI.**

***Index Terms*— Apnea-Hypopnea Index, Heart rate variability, Actigraphy, Respiration, Machine Learning.**

I. INTRODUCTION

Sleep apnea syndrome (SAS) is a chronic sleep disorder highly prevalent worldwide. SAS disorder affects health and quality of life, and also leads to serious health consequences such as cardiovascular disease, neurocognitive dysfunction, and respiratory failure. Overnight polysomnography (PSG) is the gold standard that quantifies the apnea-hypopnea index (AHI) to assess the severity of SAS disorder. However, overnight PSG performed in a sleep laboratory involves many challenges for SAS screening. The laboratory-testing environment might significantly affect normal sleep patterns and may cause more apnea/hypopnea events in some patients as compared to their home environments. The patients might also be more apprehensive and suffer from sleeplessness due to the first night effect [1]. Furthermore, the PSG may not be suitable for SAS screening due to its high operating costs, requirement of dedicated facilities, equipment and personnel, inadequate availability, and limited repeatability.

Home sleep tests using portable monitors have been gaining attention for screening of moderate-to-severe sleep apnea. However, failure rates for home testing are significantly high, leading to inconclusive studies with no interpretable data [2]. Reasons for such failures include the complex sensor attachments, obtrusiveness, compliance issues (such as failure to turn on the monitor), and detachment of sensors during tosses and turns. The costs of home sleep tests vary greatly with inconsistent coding, billing, and coverage [3]. The patient is required to return the monitor to the clinician's office either by drop-off or mail after the home sleep test. Additionally, a waiting period of at least couple of weeks after the sleep test is commonly required to obtain the results, since the algorithms on PSG and home-based monitors predict AHI based on the laborious sleep physician's visual analysis of events using oxygen saturation and airflow signals.

Given the limitations of currently available tools, we present a novel SAS screening tool that estimates the AHI value automatically by epoch-by-epoch analysis of the HealthPatch^{TM}, a disposable wireless patch biosensor.

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II. MATERIALS AND METHODS

A. Study Group

The study population consists of 53 volunteers of healthy and untreated SAS patients (29 males and 24 females) with age range of 22−73 years. The inclusion criterion to participate in the study was the age limit of $\geq$18 years. The exclusion criteria included surgical treatment for SAS and major behavioral and neurological disorders. The AHI had a range of 0.1−85.8 among these subjects.

B. Polysomnography System

The Sapphire 22-channel PSG system (CleveMed, Inc., Cleveland, OH, USA) was used to collect the standard PSG data. Sleep physicians performed sleep scorings in accordance with American Academy of Sleep Medicine (AASM) guidelines. Hypopneas were identified as $\geq$50% reduction in airflow lasting for $\geq$10 s with a 3% desaturation or an arousal. Apneas were identified as the absence of airflow ($\geq$90% of baseline) for $\geq$10 s. Apnea-hypopnea index (AHI) is calculated as the average number of apnea/hypopnea events per hour to quantify the SAS severity.

C. HealthPatch^{TM} Sensor

The HealthPatch^{TM} sensor is a disposable adhesive patch biosensor worn on the chest that incorporates two surface electrodes with hydrogel on the bottom, a battery, an electronic module with the embedded processor, micro-electromechanical system (MEMS) tri-axial accelerometer and Bluetooth Low Energy (BLE) transceiver. The patch sensor facilitates continuous monitoring of ECG and actigraphy signals at a sampling rate of 125 Hz and 62.5

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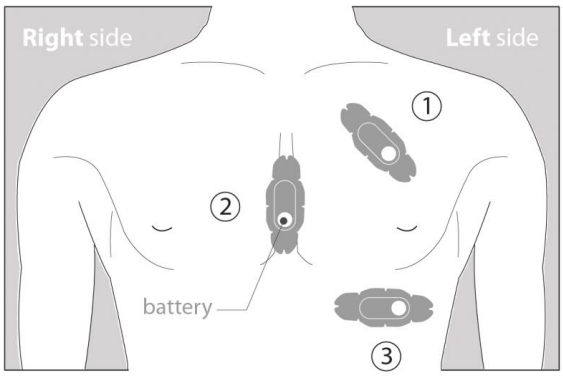

Fig. 1: The disposable HealthPatch^{TM} sensors are attached to three recommended chest locations for the overnight sleep study. However, the user will attach only one sensor at one of the three locations for regular use.

Hz, respectively. The firmware algorithms on the electronic module process the raw waveforms and transmit a stream of processed physiological variables via the BLE link as encrypted data to a relay such as a smartphone, where the live streams of data can be viewed and stored. More details about the patch sensor's physiological monitoring capabilities and its clinical validation can be found in [4].

D. Sleep Study Protocol

An institutional review board (IRB) committee approved the protocol of an attended overnight PSG study with patch sensors. The subjects provided informed consent and specific information including height, weight, age, gender, and neck circumference, and filled out standard sleep questionnaires. A registered PSG technologist hooked up the PSG sensors and adhered three patch sensors to the subject's chest at specified locations and orientations as shown in Fig. 1. The standard procedures for an attended overnight PSG study were followed and PSG data were collected. Each wireless patch sensor was paired with a smart phone and patch data were simultaneously acquired. PSG and patch data extracted between the lights-out and lights-on time period were analyzed offline for development of the AHI prediction algorithm.

E. AHI Prediction algorithm

The AHI prediction algorithm includes six major blocks: 1. Sensor streams, 2. Preprocessing, 3. Feature extraction, 4. Classification module, 5. Regression module, and 6. Display. The details of each block of the algorithm are as follows.

1. Sensor Streams: Heart rate variability (HRV), QRS wave amplitude (RWA), and QRS wave area (RA) were the sensor streams derived from ECG signal. The sensor streams derived from tri-axial acceleration signals included the MEMS-based respiration signal (RESP$_{MEMS}$) [4], signal magnitude area (SMA) as an activity metric, and polar angles of posture. The body impedance value was also measured between the two electrodes. ECG derived signals were recorded on a beat-to-beat basis. SMA, posture angles and body impedance signals were sampled every 4 seconds. RESP$_{MEMS}$ signal was uniformly sampled at 4 Hz.

2. Preprocessing: The preprocessing of sensor streams involved elimination of patch off instances using body impedance, and removal of posture induced low frequency trend artifacts using a moving average filter with N beats, where N=3$\times$user's average beats per minute. Further, outliers of sensor streams were identified and eliminated, if they lie outside the range mean $\pm$ 3$\times$standard deviation of the overnight signals. The respiratory signals were normalized to unit variance with reference to a 3-minute moving window. The preprocessed overnight sensor streams were transformed into nonoverlapping epochs of 150 s window. The expert's event-annotations were mapped to epoch-annotations with reference to the duration of apnea/hypopnea events on a given epoch. A threshold of $\geq$5 s duration was chosen that effectively mapped the shortest events to epoch labels.

3. Feature Extraction: Features were computed based on the epochs of preprocessed sensor streams using time-domain, frequency-domain, and nonlinear techniques. The time-domain features were obtained for the series of HRV, RWA, RA, RESP$_{MEMS}$, and SMA that included median, standard deviation, coefficient of variation, mean absolute deviation, kurtosis, interquartile range, dispersion metric as the difference between 90th and 10th percentiles, and approximate entropy. The beat-to-beat HRV data were further analyzed to obtain the root mean square and standard deviation of the successive differences of NN intervals and percentage of successive NN intervals differ by 50 ms and nonlinear Poincare plot features.

The frequency-domain features were extracted from the uniformly sampled (4 Hz) series of HRV, RWA, RA, and RESP$_{MEMS}$. A power spectral density estimate was obtained using Welch's averaged, modified periodogram method with 50% overlap and Hamming windows. Following are the computed frequency-domain features: total, very low frequency (VLF), low frequency (LF), and high frequency (HF) band powers and their normalized values, LF/HF ratio, spectral kurtosis, spectral entropy, and peak-to-mean ratio. The accelerometer data were used to obtain the posture related features: the mean overnight posture, mean posture polar angles, and the number of overnight posture transitions. All the above physiological features and patient information were combined to form the feature vector (F_v) that was input to the epoch classification stage.

4. Classification Module: Linear Support vector machines (SVM) have been one of the very popular machine learning classifiers due to their flexibility, computational efficiency, and capacity to handle high dimensional data [5]. In the current settings, a linear SVM classifier model was trained to classify each epoch with absence/presence of apnea/hypopnea events using the feature vector F_v and the reference epoch class labels $y_i \epsilon \{-1, 1\}$. The trained binary classifier model was later used to predict the epochs with apnea/hypopnea events for a given feature vector of a test data set. The number of epochs with events per hour (EPH) was calculated based on the predicted labels. EPH value can

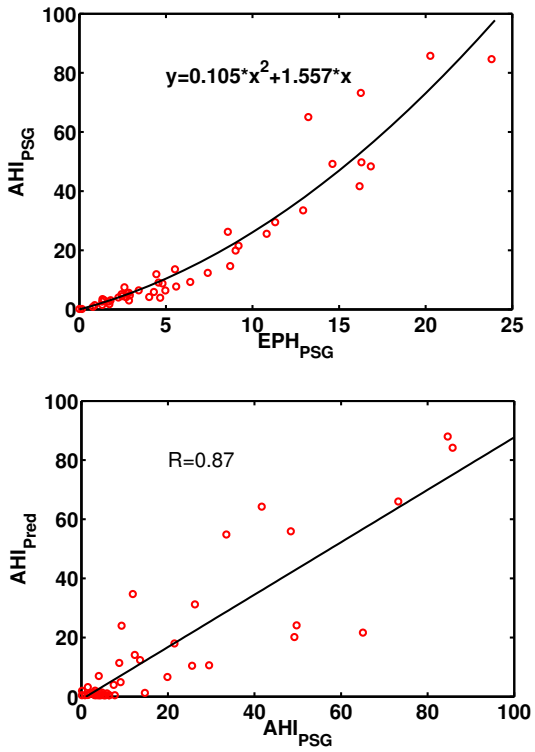

Fig. 2: Quadratic regression model trained with epochs with events per hour (EPH) and apnea-hypopnea index (AHI) of PSG data (top); Comparison of the predicted vs. reference AHI values shows high linear correlation (bottom).

be obtained by the equation,

$$EPH = \frac{P}{(P+N)} \times \frac{3600}{WL} \tag{1}$$

where, P is the number of positive epochs, N is the number of negative epochs, and WL is the epoch window length.

5. Regression Module: The EPH values are subsequently mapped to AHI values using regression analysis. The relationship between the EPH values and AHI values is found to be nonlinear because the EPH value reaches a plateau as a function of AHI value based on the epoch window length. Therefore, a second order regression model is trained for fitting the relationship between EPH and AHI values as,

$$y = \beta_2 x^2 + \beta_1 x + \beta_0 \tag{2}$$

where, x is the EPH value, y is the nonnegative AHI value, β_2 is the quadratic effect parameter, β_1 is the linear effect parameter, and the intercept β_0 is set to be zero. The reference EPH_{PSG} and AHI_{PSG} values of training data set were used to obtain the quadratic regression model using least squares estimation as shown in Fig. 2 (top). Based on the trained regression model, the predicted EPH value was mapped to a predicted AHI value. The optimization process of the classifier and regression models is described below.

Optimization process of AHI prediction: The classifier and regression models were optimized to minimize the mean square error (MSE) of AHI prediction with reference to AHI_{PSG} based on leave-one-out cross-validation (LOOCV). The optimization process involved identification of the optimal penalty factor (C) for the linear SVM classifier model that can accurately predict the epoch's binary classes, and minimize the MSE of the predicted AHI. For each value of a predefined C array, the EPH_{Pred} values were obtained from linear SVM classifier, applied to the trained quadratic regression model, and AHI values were predicted for $(L+1)$ LOOCV cycles, where L is the number of training subjects. The MSE of predicted AHI was computed with respect to the AHI_{PSG} values and stored in an array of same size of C. The MSE values were similarly obtained for all the other C values using LOOCV. The optimal penalty parameter for linear SVM classifier was found to be the one that offered the least MSE error of AHI. Such optimization process ensures to provide highest performance and improved generalization capabilities.

6. Display: The implementation of the AHI prediction algorithm on the sensor/smartphone can compute the AHI value by the end of sleep test and display it on the smartphone application screen. Based on the predicted AHI value, the user can be categorized into either control or subgroups of apnea as per AASM. The results of the apnea screening can be notified to the patient and the physician's office.

F. Data Analysis

The nonparametric Kruskal-Wallis test with Dunn's multiple comparison tests were performed to investigate significant differences ($P<0.05$) with patient specific information among the control, mild apnea, and moderate-to-severe apnea groups. The patch sensor data collected simultaneously on each of the three chest locations were found to have unique morphology and characteristics of raw and derived signals. Hence, three independent classifier models combined with regression analysis were trained and optimized separately to produce accurate prediction of AHI with respect to each patch location. In the current study, the predicted AHI values were used to classify the subjects as moderate-to-severe apnea ($AHI \geq 15$) vs. control-to-mild apnea ($AHI < 15$). The algorithmic performance of sleep apnea screening was evaluated by comparing the predicted subject labels with the reference lables based on AHI_{PSG}. The performance measures included specificity, sensitivity, and accuracy with their 95% confidence intervals.

III. Results

Table 1 shows the patient specific information among the control, mild apnea and moderate-to-severe apnea groups. The gender ratio among three groups indicated a higher prevalence of apnea in males than females. The patient information such as height, weight, age, BMI, and neck circumference values were progressively increased from control group to moderate-to-severe apnea group. The Kruskal−Wallis test indicated significant differences ($P<0.05$) in these patient specific measures among three groups. Thus, the patient specific features are highly valuable for AHI prediction.

TABLE I: Patient information among control, mild apnea, and moderate-to-severe apnea groups.

Info.	Control AHI<5	Mild (5≤AHI<15)	Mod.-severe (AHI≥15)	P value
Subjects	21	17	15	N/A
Gender(M/F)	6/15	10/7	13/2	N/A
Height(cm)	167.8±1.9	174.5±2.6	178.1±1.9*	<0.01
Weight(kg)	67.4±2.4	80.2±4.5	97.8±7.1*	<0.001
Age	36.7±2.4	41.3±3.4	51.3±3.8*	<0.05
BMI	24.0±0.9	26.3±1.3	30.7±2.0*	<0.01
NeckCirc(cm)	36.5±0.6	38.2±0.9	43.6±1.4*†	<0.001
AHI	2.8±0.3	8.8±0.8‡	44.3±5.7*†	<0.001

* and ‡ denote P<0.05 compared to the control group. † denote P<0.05 compared to the mild apnea group.

TABLE II: Algorithmic performance for the classification of (AHI<15) and (AHI≥15) based on the predicted AHI.

Location	Specificity%	Sensitivity%	Accuracy %
1	93.9 (83.3, 98.0)	78.6 (64.9, 87.9)	89.4 (77.4, 95.4)
2	92.9 (80.6, 97.6)	66.7 (51.2, 79.2)	85.0 (70.9, 92.9)
3	84.6 (69.4, 93.1)	77.8 (61.7, 88.4)	82.9 (67.3, 91.9)

The values in parentheses indicate the lower and upper bound of 95% confidence intervals.

The predicted AHI values demonstrated high correlation with the reference AHI_{PSG} values. Fig. 2 (bottom) shows a strong correlation of 0.87 between the AHI_{Pred} and AHI_{PSG} values for the patch pool of location 1. The linear correlation coefficients for patch locations 2 and 3 were found to be 0.88 and 0.92, respectively. The predicted AHI values were subsequently used to classify the control-to-mild apnea group (AHI<15) vs. the clinically significant moderate-to-severe apnea group (AHI≥15) with an accuracy of 89.4%, 85.0%, and 82.9% for the three locations, respectively. The algorithmic performance including specificity, sensitivity and accuracy with 95% confidence intervals (Table 2) showed no significant differences among the three chest locations. Hence, the patch sensors can be used at any of the three locations for accurate AHI estimation and effective SAS screening.

IV. Discussion

Overnight physiological monitoring with an adhesive HealthPatch^{TM} sensor provides an accurate estimate of AHI values compared to the gold-standard of PSG.

Wristwatch, wristband, and bracelet commercial devices offer sleep-awake patterns primarily based on actigraphy signals, but most of these devices do not appear to have the functionality of AHI quantification or sleep apnea screening [6]. A wrist worn commercial device Watch-PAT200 that derives AHI value using blood oxygen saturation, heart rate, and actigraphy signals has shown a correlation of 0.87 as compared to PSG's AHI, and demonstrated 0.93/0.73 as the specificity/sensitivity for the detection of SAS with AHI threshold of 15 in 30 adults [7]. The RUSleeping RTC, a single-channel portable device that measures airflow has reported the specificity/sensitivity of 0.83/0.70 to screen SAS subjects with AHI≥15 in 34 adults [1]. The performance of the current algorithm of AHI prediction using ECG and actigraphy signals alone and without blood oxygen saturation/airflow signals is highly comparable to the aforementioned studies.

Overnight PSG is not suitable for mass screening of sleep apnea due to many challenges. Furthermore, determining AHI values using PSG is generally not an automated process. It requires manual identification of start and end time periods for each event by visual analysis of oxygen saturation and airflow signals. In contrast, the patch sensor is disposable, inexpensive, unobtrusive, simple to attach and easy to connect/pair wirelessly with the user's smartphone. The encrypted data is transmitted via a BLE link to the smartphone and stored there overnight. After the overnight recording, the recorded data can be automatically analyzed on the smartphone processor, and the results can be displayed on the application screen. From the smartphone, the analysis report can be easily sent to a physician or a family member. The user can wear the sensor for multiple nights in a row. This biosensor solution is novel and can be easily used for widespread sleep apnea screening. Given the current obesity epidemic and high prevalence of Type-2 diabetes, the proposed automated sleep apnea screening system can be obtained from primary care practitioner offices, diabetic clinics, or by a physician's referral.

In conclusion, SAS screening using HealthPatch^{TM} sensor could provide a convenient and inexpensive wireless solution for continuous multi-night sleep apnea assessment that can increase the confidence in the predicted AHI value and the overall SAS screening outcome.

ACKNOWLEDGMENT

The authors thank A. Chan and L. Aga of Vital Connect Inc, and the team of the California Sleep Institute, CEI Medical Group, Palo Alto including S. Lawson, M. Cushing, F. Arguelles, and S. Kirkland for managing various aspects of the sleep study.

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