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Journal of Medical Devices. Received March 07, 2021;
Accepted manuscript posted December 06, 2021. doi:10.1115/1.4053160
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RestEaze: An Emerging Technology to Characterize Leg Movements during Sleep

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Journal of Medical Devices. Received March 07, 2021;
Accepted manuscript posted December 06, 2021. doi:10.1115/1.4053160
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ABSTRACT

Several sleep disorders are characterized by periodic leg movements during sleep including Restless Leg Syndrome, and can indicate disrupted sleep in otherwise healthy individuals. Current technologies to measure periodic leg movements during sleep are limited. Polysomnography and some home sleep tests use surface electromyography to measure electrical activity from the *anterior tibilias* muscle. Actigraphy uses 3-axis accelerometers to measure movement of the ankle. Electromyography misses periodic leg movements that involve other leg muscles and is obtrusive because of the wires needed to carry the signal. Actigraphy based devices require large amplitude movements of the ankle to detect leg movements (missing the significant number of more subtle leg movements) and can be worn in multiple configurations precluding precision measurement. These limitations have contributed to their lack of adoption as a standard of care for several sleep disorders. In this study, we develop the RestEaze sleep assessment tool as an ankle-worn wearable device that combines capacitive sensors and a 6-axis inertial measurement unit to precisely measure periodic leg movements during sleep. This unique combination of sensors and the form-factor of the device addresses current limitations of periodic leg movements during sleep measurement techniques. Pilot data collected shows high correlation with polysomnography across a heterogeneous participant sample and high usability ratings. RestEaze shows promise in providing ecologically valid, longitudinal measures of leg movements that will be useful for clinicians, researchers, and patients to better understand sleep.

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INTRODUCTION

Sleep is associated with a general inhibition or decrease in motor activity in most land-based mammals. Dysfunction in this inhibitory neural circuitry during sleep can manifest as leg movements during sleep (LMS). There are different types of LMS that are related to various conditions making their characterization a useful biomarker. For example, periodic leg movements during sleep (PLMS) can reflect arousals characterized by large, transitory increases in blood pressure and heart rate and significant changes in brain activity [1–4]. The characteristic features of PLMS (number, inter-movement interval, autocorrelation, distribution pattern over the night, intensity) can aid in identifying these underlying conditions, e.g. restless legs syndrome (RLS) [5], periodic leg movement disorder (PLMD) [6] sleep apnea [7], and REM behavior disorder [8,9]. PLMS in children occur commonly with attention deficit hyperactivity disorder [10,11] and RLS [11] which can indicate functional brain iron deficiency. In these children, PLMS may be a key biomarker for this particular type of iron deficiency, because it can occur with low-normal serum ferritin and can be treated with oral iron, improving their ADHD symptoms [12,13]. Collectively, the ability to measure and characterize LMS in an ambulatory setting has the potential to significantly improve the diagnosis and management of sleep disorders associated with LMS.

Currently, the standard of care to measure LMS is polysomnography (PSG). PSG is not optimized to measure LMS because it is costly and thus not approved for many patients, obtrusive (patients are connected to multiple wires), and typically used for a single night. Because PLMS vary over multiple nights [14] and because of the first night effect of PSG [15] the accuracy precision of estimating PLMS through PSG is lacking. Alternatives

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have been developed for ambulatory LMS monitoring including the PAM-RL [16] and other accelerometry-based devices [17]. However, using ankle-worn devices that solely rely on accelerometers to detect LMS is problematic because (1) the movement of the lower limb needs to be of sufficient

amplitude to exceed the baseline noise of the accelerometers (thus small yet significant LMS may not be detected) (2) there is insufficient information in the accelerometers to detect rotations or other movements of the lower limb that occur during LMS. These deficits have led to the realization that individual adjustment and parameterization is needed to use these devices [18] potentially leading to their limited to non-existent use in clinical settings.

RestEaze (Figure 1) is an emerging, enabling technology that detects and characterizes leg movements during sleep (including PLMS), and can classify leg movements during sleep (LMS) associated with cortical micro-arousals. LMS are critical features of sleep that are either entirely ignored (e.g. wrist based actigraphy) or poorly characterized (e.g. using EMG or ankle-based actigraphy) with current systems. Therefore, currently, there are no good solutions for longitudinal characterization of leg movements during sleep. One of the key innovations of the RestEaze system is enhancing the characterization of LMS using textile-based, displacement capacitive sensing. This sensor enables more complex measurement of the LMS some of which is entirely missed by current approaches. Specifically, the capacitive sensors can detect subtle movements of the lower limb as changes in the electric field detected by the capacitor. This permits the detection of gross movements of the lower limb (e.g. flexion/extension of the knee) but also subtle movements (flexion/extension of the great toe), and some movements of the

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opposite lower limb. The data provided by the capacitive sensors provides additional information to classify LMS that are associated with arousals from those that are not [19]. Finally, the RestEaze device itself is a light, comfortable band worn on the ankle and therefore useful for longitudinal evaluations as it is significantly less disruptive than PSG.

This manuscript reports the results of an initial feasibility study that was performed to develop algorithms for the detection and classification of LMS and other sleep features. Six subjects wore the RestEaze device in addition to overnight PSG. This enabled the initial development of algorithms for the detection of LMS, PLMS, micro-cortical arousals, standing/lying position, and wake/sleep times. These classifications support the calculation of important sleep metrics. e.g., In-Bed Times, Sleep Times (Onset and Offset), Wake After Sleep Onset (WASO), Sleep Efficiency (SE), Periodic Leg Movement during Sleep Index (PLMSI), Arousals Index (ARI). These sleep metrics determined by our system are highly correlated with PSG measurement. Additionally, usability testing among users indicated a high ease of use and acceptance rating.

METHODS

RestEaze System Description

A complete discussion of the ankle-worn device, its power consumption, and additional technical details can be found in Bobovych et al 2020 [20].

RestEaze consists of an ankle-worn textile band, mobile application, and backend server for the collection, storage, and analysis of sleep movement data. Machine learning algorithms detect critical sleep features for in-home sleep assessment. The multi-sensor

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ankle bands are worn overnight, in-home, and the data are relayed from the sensors to a smartphone application, then to the backend server where the data are analyzed and visual presentation of the results are available.

The unique component of RestEaze is an array of textile capacitive sensors built into the ankle band. This sensing technique is based on the principle of a parallel plate capacitor, where the conductive fabric and the user's body serve as two plates of a virtual capacitor. The change in distance between the capacitor plates at the ankle and the user's foot - and toes (mostly the large toe) - produces a measurable change in capacitance. The standard arousal movement of flexor at the ankle is well captured by these sensors. The capacitive sensing augments the inertial measurement unit (IMU) data to give measures of both device and environment motion, allowing the capture and classification of more complex movements. Figure 1 provides a picture of the current prototype RestEaze device and recordings from the accelerometers and capacitive sensors. These data (in addition to the gyroscopy) are used to detect and classify LMS. Using these time-series data, algorithms have been developed that detect and classify LMS, specifically targeting the PLMS that are associated with cortical arousals[19].

In addition to the RestEaze sensor platform, a complete software suite has been developed for secure data storage, analysis, visualization, and subject management (Figure 2). These visualizations show the analyzed data that reflect metrics of LMS and other critical sleep features over several nights.

Feasibility Study Description

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The initial feasibility study used training data from standard all-night PSG recordings at Johns Hopkins sleep laboratories. They include 6 channels of EEG, 2 channels of EOG, and 2 channels of EMG activity. The bi-lateral *anterior tibialis* EMG and the video recording of legs and feet provided ground truth of leg movements during sleep. During these studies, participants wore the RestEaze device on both ankles. These recordings supported the algorithm development and are presented here. In this study, PSG data from 2 adults (one RLS patient off medications and another normal subject with no sleep complaint) and 4 children (3 children with ADHD not on medication and one child with no sleep complaints) (see Table 1) were used.

All PSG sleep measures used in the following analyses were obtained by visual scoring of the sleep studies by trained technicians with a careful review and adjustment of the results as needed by a board-certified sleep professional (RPA) who was also an experienced expert in leg movement and arousal recordings and measurements. All scoring followed the rules established by the American Academy of Sleep Medicine (AASM)[21] except the leg movement scoring from the EMG which followed the newer revised standards of the International Restless Legs Syndrome Study Group (IRLSSG) and the World Association of Sleep Medicine (WASM) [22]. Detailed methods for how various sleep measures were scored and labeled using PSG data is provided in the Supplemental Materials. Ultimately, RestEaze system output was compared to PSG using difference measures and Pearson correlation which are reported in Table 2.

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RESULTS

Table 2 provides a summary of the results of the feasibility study. Additional detail for each metrics is provided in subsequent sections.

Leg Movement Classification

A random forest regressor was trained for the classification of movement windows as leg movements of interest as determined by EMG and visual scoring. The regressor showed a ROC curve with AUC of 0.95, as shown in Figure 2. The results of the leg movement classifier were promising, showing an accuracy, precision, recall, and f1 score of 93.65%, 79.64%, 80.22%, and 79.93%, respectively, where the f1 score is optimized. f1 is determined by:

$$f1 = \frac{tp}{tp + \frac{fp + fn}{2}} \quad (1)$$

where tp = true positive, fp = false positive, and fn = false negative.

This corresponds well with the interscorer rating agreement lower limit of 75%, indicating the level of intrinsic human accuracy limits in defining the ground truth by the manual labeling process. It is anticipated that a larger data set, more representative of the population, will allow improvement in this classifier, but a level of accuracy meeting inter operator error is already certainly acceptable. It demonstrates the feasibility of using

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RestEaze to detect all significant LM, including those not detected by the anterior tibialis recordings.

Relationship of RestEaze LMS detections to *anterior tibialis* EMG LM detections

The Leg Movement classification of the RestEaze system defines an onset and offset of a movement by the deviation of a sensor from steady state, as seen by the IMU and capacitive sensors. The PSG system marks the onset and offset of movements based on EMG activity from the anterior tibialis or from video recordings showing visible movement. Because RestEaze uses capacitive sensing it can detect complex leg movements that include multiple muscle activations beyond the *anterior tibilias*. RestEaze data demonstrated that leg movements tend to have a longer duration and earlier onset than those marked in PSG studies through activation of the anterior tibialis EMG. A prior study using multiple EMG recordings found that about 45% of LM started with muscle contractions other than the anterior tibialis[21]. Figure 3 shows the differences between RestEaze and anterior tibialis EMG LMS detections for the duration of the events and for onset times. The actual total LMS recorded by RestEaze occurs earlier and lasts longer.

PLMS are determined by fixed criteria applied to LMS. These are determined explicitly from the features of LMS detected from anterior tibialis EMG. The PLM criteria relate to their duration, distance to neighboring movements, and bilateral nature. Specifically, they have a duration requirement of 0.5-10 seconds for monolateral movement and 0.5-15 seconds for bilateral movements, and an inter-movement interval (the time from the onset of one LM to the onset of the next LM) requirement of 10-90 seconds. These criteria

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were developed for EMG recordings of the anterior tibialis. The RestEaze measurements would detect these movements, and thus about 50% of the cases should have an earlier onset than from the PSG measures of only the anterior tibialis EMG. The end of a leg movement (LM) ankle flexor includes a short period when the foot drops after the end of the anterior tibialis contraction, and RestEaze LM durations will, therefore, generally extend beyond the time when the EMG is active. Thus, the actual LM compared to the EMG will often both start earlier and commonly end later, making them longer than those measured from the anterior tibialis EMG. RestEaze records the actual movement and is, therefore, as expected longer than the anterior tibialis recording. These recording differences require altering the RestEaze PLM criteria for both inter-movement interval (IMI) between PLM onsets and the maximum duration of a single significant LM. These differences, shown in Figures 3 indicate that the IMI criteria for RestEaze measures need to be reduced by 5 seconds to account for the onset differences, and the maximum duration needs to be increased by 5 seconds from 10s to 15s for unilateral movements and accordingly increased from the 15s to 20s for bilateral movements. *This finding could have a significant influence on how LMS are characterized and ultimately how they are incorporated into diagnoses/management of sleep disorders.*

Arousal Classification

A random forest regressor was trained for the classification of leg movements during sleep related to the presence of an arousal; where arousal was determined by EEG and arousal relation was determined by a less N second difference between the presence of a LMS and arousal. The regressor showed a ROC curve with AUC of 0.80, as shown in Figure 4. The results of the arousal classifier were promising, showing an accuracy,

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precision, recall, and f1 score of 76.18%, 74.06%, 88.06%, 80.45%, respectively, where the f1 score is optimized. The results show that there are movement features that can identify arousal related leg movements. These data show feasibility even for this small sample size. The precision is reduced mostly by the number of false positives, but many of these represent arousal occurring shortly after or adjacent to detected LM arousal. The false-positives identify LM-arousals in temporal proximity to correctly identified LM arousals. These false-positive LM-arousal pairing are associated with features indicating a significant underlying arousal process that becomes clearer with nearby LM. These false positives thus tend to reflect a period of increased instability of sleep with LM related to a putative persisting CNS arousal process. *This again raises the issues noted above of expanding the temporal window of the arousal process as was done for the association with cardiac arrythmias*[9].

Sleep Classification

A random forest regressor was trained for the classification of sleep/wake over 1-minute consecutive non-overlapping windows; where wake/sleep was determined by EEG, scored into sleep stages 1, 2, 3, REM). The results were promising, showing a ROC curve with AUC of 0.87, as shown in Figure 5. These very promising results of the sleep classifier showed an accuracy, precision, recall, and f1 score of 83.72%, 85.18%, 93.56%, 89.17%, respectively, where the f1 score is optimized. The classification works well for detecting periods of wake lasting several minutes, but has trouble detecting short awakenings. This classification could likely be improved by additional normalization to account for subject condition and leg movement strength.

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Derived Sleep Metrics

In order to calculate the performance of the sleep metric calculations, classifiers were trained in leave-one-out fashion for each of the subjects; meaning each subject was evaluated using a classifier with similar input features and parameters, but none of the test subjects' data was used in training. The results for sleep state, leg movement sleep and arousal were used to generate standard sleep metrics and compared to the PSG output for a group of 6 subjects. A table describing the subjects in the study is provided in Table 1.

The sleep measures of Arousals, LMS, PLMS, Sleep Efficiency, Sleep Onset/Offset, TST and WASO all show significant correlation across our pool of subjects. There was one outlier for sleep onset for subject #2. This was associated with a prolonged period of wake and partial stage 1 sleep during the first 2.5 hours of the recording. The technician scored this long period as all wake while RestEaze detected short periods of sleep during this time. A later review by a sleep expert and technician both confirmed that there were segments of stage 1 sleep during this time that were not initially scored as sleep by the technologist nor previously detected in the standard review. This scoring difference exaggerates the errors for sleep onset, WASO, arousals, and PLMS. In particular, the correlation between PSG and RestEaze for WASO was 0.66 (Table 2) when including this subject but 0.89 when this subject was excluded. These metrics overall show agreement for the major differences between subjects and overall correlation across subjects >0.85 with allowance for the one problem noted for sleep onset of subject #2.

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WASO demonstrated the lowest correlation among all sleep measures and was underestimated for 4 of the 6 subjects.

Usability Results

We performed an in-Home data collection on 7 subjects for at least 5 days to evaluate the usability of RestEaze use for in-home, multi-night sleep recordings. The goal of the in-home study was to gauge (1) comfort of using the band and the smartphone applications, and (2) ensure that all the data from the device is reliably collected and analyzed at the backend. Participants responded to questions on a Likert scale. The questions were 1) how comfortable it was to wear the band (0 = Uncomfortable... 5 = Comfortable), 2) how much was sleep disrupted using the band (0 = Disrupted... 5 = Uninterrupted), 3) how easy it was to put on the band (0 = Very Difficult... 5 = Very Easy), and 4) how easy it was to use the Android app (0 = Very Difficult... 5 = Very Easy).

The average Likert scale rating was 3.2, 4.5, 4.4, and 4.6 on a scale of 5, respectively. The rating of 3.2 for comfort was less than desired and thus the next version of RestEaze has been industrially designed to be softer and more form fitting to improve comfort. The other indices of usability were at or exceeding our goals.

DISCUSSION

It is expected that RestEaze can significantly improve the management of sleep disorders associated with leg movements. Of particular interest is the diagnosis and management of RLS. RLS is currently diagnosed clinically based on a patient report according to criteria specified by the International Restless Legs Syndrome Study Group (IRLSSG) [23]. There are currently little to no objective data used for the diagnosis of RLS which

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has led to a significant mis-/underdiagnosis of the condition. Some authors suggest results from the ambiguity and indescribable nature of patient symptoms that are misunderstood by clinicians thus leading to mis- or underdiagnosis [24,25]. In one study, this underdiagnosis was approximated at 12.9% [26] (i.e. missing 87.1% of cases) while other studies have shown as little as 2-3% (missing 97%-98%) of expected diagnosis of RLS [26,27]. The proportion of these cases that result from difficulty of symptoms interpretation vs clinical error is unknown, but improved diagnostic capabilities are needed. A study that used PSG to measure PLMS in RLS patients found that measurement of PLMS identified clinically-defined RLS with a specificity and sensitivity of 81% ± 19% [28]. Conservatively estimating the prevalence of RLS in the United States at 3.25% [6], the potential improvement in diagnostic accuracy could be estimated at approximately 68.1% through the use of ambulatory PLMS characterization. Furthermore, PLMS change as a function of treatment in RLS patients and thus can be used as an objective marker for treatment management. Multiple, placebo-controlled, double-blind clinical trials have demonstrated a clear reduction in PLMS after medically treating RLS [29–31]. While clinical improvement will remain the cornerstone of management, objective measurement of PLMS can aid in the management of augmentation or recurrent maintenance insomnia in the already-diagnosed RLS patient.

LMS are a well-recognized, critical feature of sleep that have been extensively researched, however, an adequate ability to monitor them in an ambulatory setting has been lacking. When compared to PSG, as many as 20% of the LM events would be missed by relying on EMG-based *anterior tibialis* recording. This has been previously documented with multiple EMG recordings showing LM often has primary involvement

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of muscles other than the *anterior tibialis* [32], including for some only the hallucis longus producing only extension of the big toe. Multi-lead EMG studies have further confirmed that LMS (including PLMS) are complex movements involving multiple muscles [33]. Our current results suggest that RestEaze will detect these complex movements with its capacitive sensors. It is also encouraging that the differences are relatively small for sleep metrics, including the hard to estimate sleep onset and, to a lesser extent, WASO.

This initial study performed with the ambulatory, RestEaze sleep monitor system show a high correlation with LMS measured by PSG. Further, preliminary evidence suggests that RestEaze (1) can classify LMS associated with cortical arousals, distinct from other types of leg movements and (2) suggests LMS commence earlier and last longer than EMG (PSG) derived estimates. These results provide some initial validation for RestEaze as a key tool for scientists, clinicians, and patients to provide an accurate and convenient method to characterize leg movements during sleep and other critical sleep indicia.

Limitations

The limited number of subjects in this pilot study (n = 6) limits the generality of the results presented. Additional data is needed to further confirm these results across various patient populations. The ground-truth data in this study had an interscorer agreement of 85-90% (10–15% disagreement) of LMS necessarily limits RestEaze classifier accuracy.

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ACKNOWLEDGMENT

Tanzen Medical Inc. is grateful for the time and effort of the participants in these studies. This study was funded by the National Science Foundation, Small Business Innovation Research program through a Phase I Grant, No: 1819626

We are exceptionally grateful for the insights and ideas provided by the late Richard Allen, Ph.D. We thoroughly enjoyed reviewing earlier versions of this manuscript with him and are excited to continue our understanding of sleep pathology based on his work. We are also grateful to our patients for their time.

FUNDING

This work was supported by a grant from the National Science Foundation, Small Business Innovation Research Phase I Grant, No: 1819626.

Conflict of Interest

Authors Justin Brooks, Cody Feltch, Ryan Robucci,, Sanjay Agarwal, and Nilanjan Banerjee are shareholders of Tanzen Medical Inc.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All studies were approved by the accredited Institutional Review Board at Johns Hopkins University.

Disclaimer

Currently, RestEaze is not an FDA approved device. Tanzen Medical Inc is actively engaged with the FDA and welcomes collaboration from interested scientists/clinicians to continue studying leg movements during sleep.

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NOMENCLATURE

AASM	American Academy of Sleep Medicine
ADHD	Attention Deficit Hyperactivity Disorder
AUC	Area Under the Curve
EEG	Electroencephalogram
EOG	Electrooculography
EMG	Electromyography
IMU	Inertial Measurement Unit
IRB	Institutional Review Board
IRLSSG	International Restless Legs Syndrome Study Group
LMS	Leg movements of sleep
LMSI	Leg movements of sleep index
PLMS	Periodic leg movements of sleep
PLMSI	Periodic leg movements of sleep index
PSG	Polysomnogram
RLS	Restless legs syndrome
ROC	Receiver Operator Characteristic
TST	Total sleep time
WASO	Wake after sleep onset
WASM	World Association of Sleep Medicine
WSS	World Sleep Society

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Accepted manuscript posted December 06, 2021. doi:10.1115/1.4053160
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Table Caption List

Table 1 Description of the 6 subjects used in this pilot study. Notably, the subjects are highly varied in terms of age and diagnoses.

Table 2 The main result of the feasibility study shows significant correlation with PSG derived measures of sleep. PSG: Polysomnogram; Diff: PSG-RE; ARI: Arousal Index; LMSI: Leg movements of sleep index, PLMSI: Periodic leg movements of sleep index; TST: Total sleep time; WASO: Wake after sleep onset. *min from lights out for sleep excluded, **one outlier excluded (see text).

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Figure Captions List

Fig. 1 The RestEaze ankle band, web interface, and android application (left), comparison on capacitance and accelerometry during common leg movements and foot flexion (center), and a comparison of capacitance change from different magnitude foot flexions (right). In combination with an IMU, the capacitive sensors measure leg movement characteristics such as magnitude, duration, and velocity.

Fig. 2 Data visualization from the RestEaze web application (left) and mobile app (right). These screenshots show visualizations of the data for a representative subjective. The visualizations are customizable to show metrics of interest.

Fig. 3 The difference between the onset (left) and duration (right) between PSG and RestEaze. In each plot, histograms of the differences between leg movement onset (top, left) and leg movement duration (top, right) are displayed for all subjects and leg movements. For leg movement onset the time that PSG detected leg movement onset were generally later than the same leg movement detected by RestEaze. With respect to durations, RestEaze was able to detect leg movements for longer than those estimated by PSG. Collectively, analysis with RestEaze shows that leg movements begin earlier and last longer than when measured by PSG, the current standard of care.

Fig. 4 RestEaze shows a high classification accuracy for determing LMS associated with arousals. TPR = True Positive Rate, FPR = False Positive Rate

Fig. 5 RestEaze can classify sleep from non sleep periods with a high degree of accuracy. TPR = True Positive Rate, FPR = False Positive Rate.

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Subject ID	Age (years)	Gender	Diagnosis
1	36	Female	RLS (no medications)
2	70	Female	No sleep disorder
3	6	Male	ADHD
4	16	Male	ADHD
5	10	Female	No sleep disorder
6	10	Male	ADHD

Table 1.

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SID	System	ARI	Arousals	LMS	LMSI	PLMS	PLMSI	Sleep Efficiency	Sleep Offset (min)*	Sleep Onset (min)*	TST (min)	WASO (min)
1	RestEaze	17.25	111	150	23.32	55	8.55	88	434	21	385	32
	PSG	13.45	77	188	32.84	72	12.58	78	435	20	343	74
	Diff	3.8	34	-38	-9.52	-17	-4.03	10	-1	1	42	-42
2	RestEaze	37.4	145	245	63.19	125	32.24	44	520	24	232	264
	PSG	26.74	86	233	72.44	79	24.56	37	509	218	192	109
	Diff	10.66	59	12	-9.25	46	7.68	7	11	-194	40	155
3	RestEaze	7.01	47	59	8.81	14	2.09	77	517	36	401	81
	PSG	6.33	42	106	15.97	9	1.36	76	518	38	398	81
	Diff	0.68	5	-47	-7.16	5	0.73	1	-1	-2	3	0
4	RestEaze	9.12	69	74	9.78	15	1.98	82	551	28	453	71
	PSG	5.93	40	67	9.94	10	1.48	73	550	23	404	124
	Diff	3.19	29	7	-0.16	5	0.5	9	1	5	49	-53
5	RestEaze	3.18	21	88	13.34	10	1.52	100	395	0	395	0
	PSG	6.45	41	106	16.67	9	1.42	96	393	2	381	11
	Diff	-3.27	-20	-18	-3.33	1	0.1	4	2	-2	14	-11
6	RestEaze	15.9	80	173	34.39	48	9.54	86	349	44	301	4
	PSG	8.05	39	160	33.03	40	8.26	83	349	44	290	14
	Diff	7.85	41	13	1.36	8	1.28	3	0	0	11	-10
Correlation with PSG		**0.96**	**0.87**	**0.93**	**0.98**	**0.89**	**0.96**	**0.98**	**1.00**	**0.99****	**0.97**	**0.66**

Table 2

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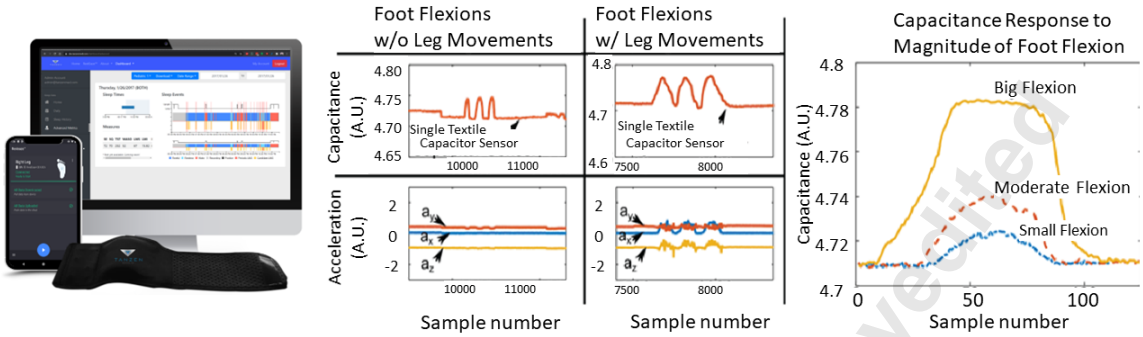

Figure 1

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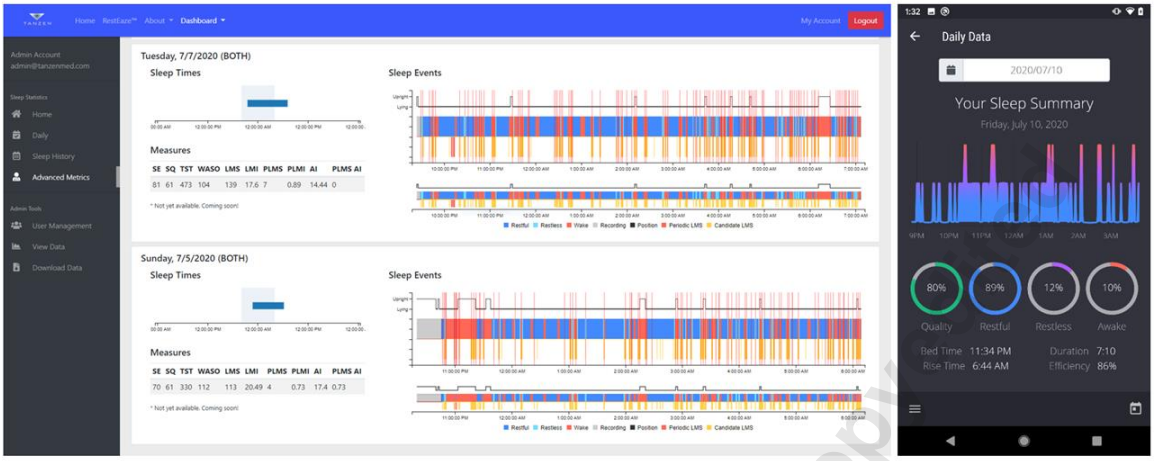

Figure 2

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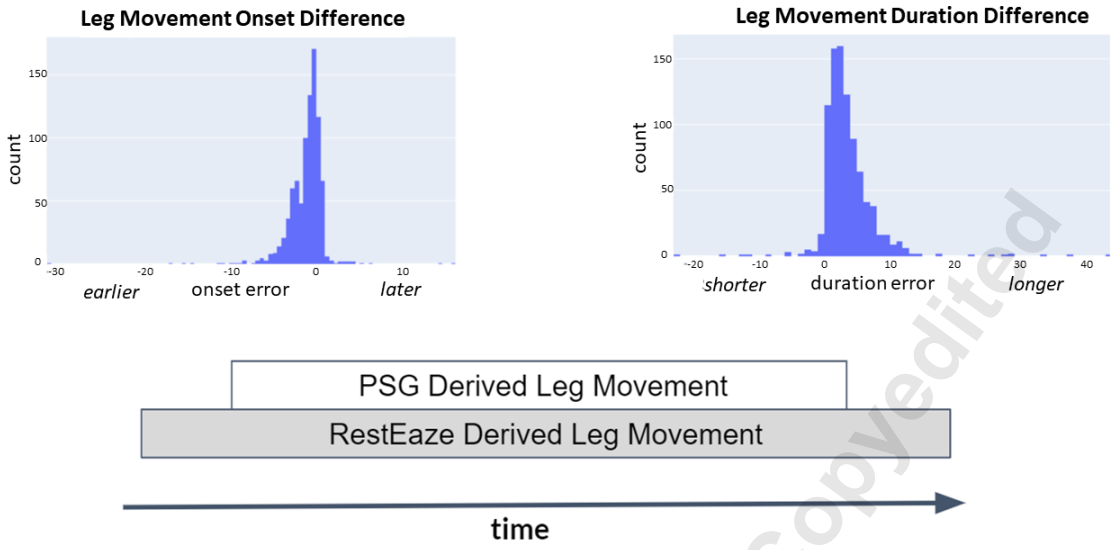

Figure 3

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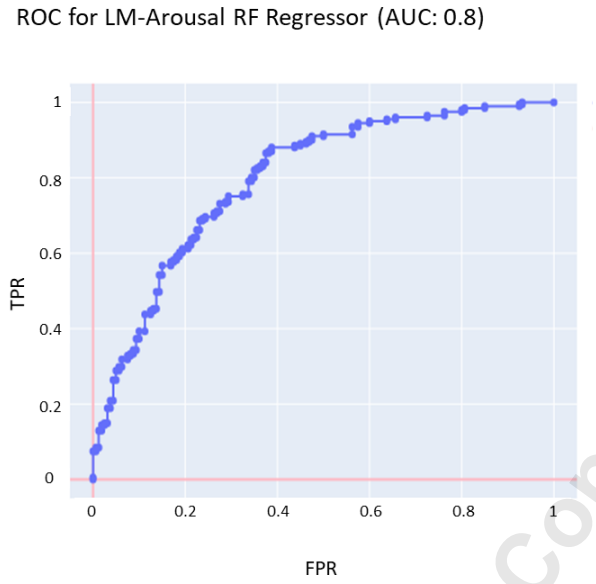

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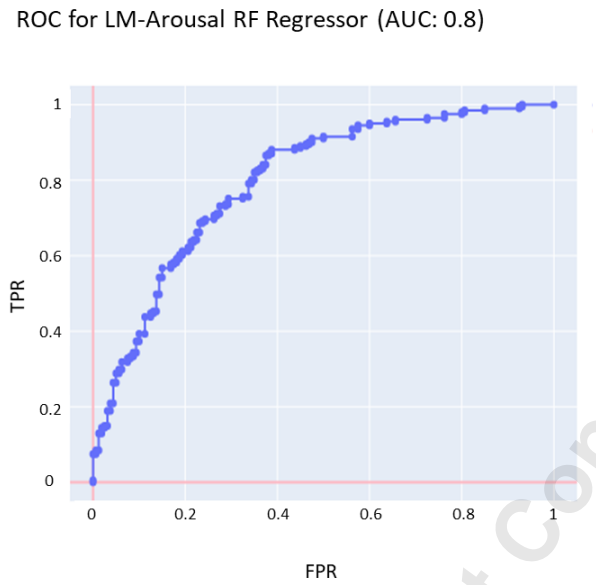

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