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Digital Phenotyping of Autoimmune Diseases Using Non-Contact Radio Frequency Sensing: A Longitudinal Study Comparing Systemic Lupus Erythematosus and Healthy Participants

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ABSTRACT

Recent ubiquitous sensing technologies make it possible to capture streaming digital data that reports aspects of a patient's physiology, behavior, and symptoms both quantitatively and in real time. As a result, it may be possible to develop streaming disease readouts that are more accurate and less obtrusive than relying on patient and caregiver reports alone. This study investigates the feasibility of leveraging physiological and behavioral signals extracted from a radio frequency sensing device to characterize metrics indicative of breathing, mobility, and sleep patterns. We investigate the variations in these signals between individuals with Systemic Lupus Erythematosus (SLE) and healthy participants in a 6-months longitudinal, exploratory, in-home study involving 19 SLE and 28 healthy participants. Results show that many signals (e.g., breathing rate, sleep efficiency, and gait speed) significantly distinguish SLE and healthy participants and demonstrate the potential of using

remote sensing as an unobtrusive low-burden tool to assess disease symptoms continuously and in real time.

CCS CONCEPTS

• **Human-centered computing** Empirical studies in ubiquitous and mobile computing;

KEYWORDS

Digital Phenotyping, Non-Contact Sensing, Systemic Lupus Erythematosus

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1 INTRODUCTION

Chronic autoimmune diseases such as Systemic Lupus Erythematosus (SLE) [20] are characterized by abnormal immune responses that target various organs and tissues in the body. SLE in particular

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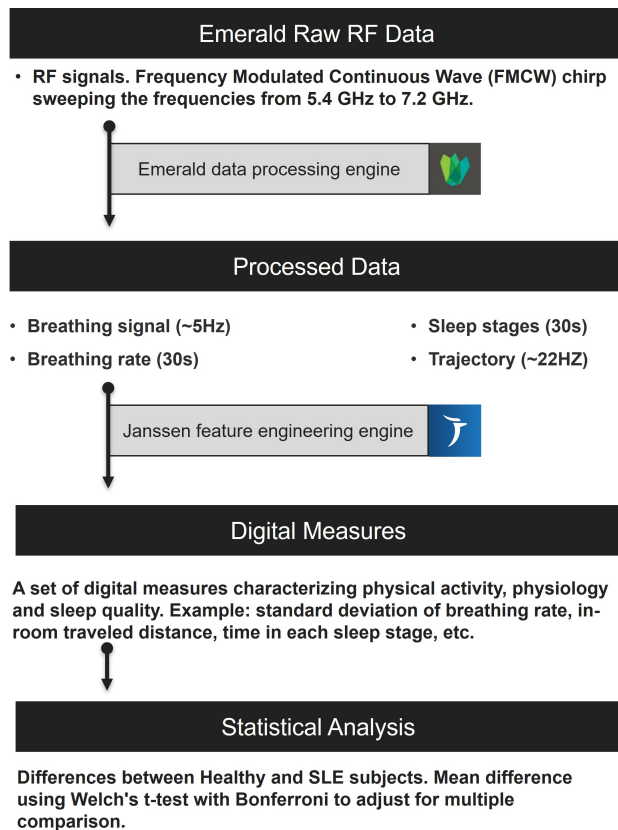


Figure 1: The proposed data processing pipeline.

can cause a wide range of symptoms such as pain, fatigue, and sleep disturbance that impair quality of life [13, 17, 23, 28]. Current methods to assess SLE symptoms are largely based on self-reported measures [10, 15, 28] that suffer from various limitations such as subjectivity, response bias and memory limitations in addition to relying on active engagement of participants which was shown in the literature to decrease over time [4, 6]. It is then important to investigate other methods to address these limitations.

Technology innovations have transformed and enhanced momentary data collection in natural settings enabling researchers to collect more detailed and accurate data in real-world environments. For instance, passive sensing can offer several advantages as an alternative or complement to self-report measures such as rich contextual information, longitudinal monitoring, objective data and ecological validity [2, 3, 5, 9, 14, 25]. Passive sensing involves collecting data about individuals' behaviors, activities, and physiological responses through sensors embedded in various devices, such as smartphones, wearables, or environmental sensors [25]. Furthermore, non-contact sensing [16], which involves capturing information about individuals without contact, is an emerging technology due to its non-invasiveness and convenience (e.g., no burden related to charging the device) but its use in a clinical setting for SLE subjects is under investigated. The goal of this study is to investigate the use of a non-contact sensing method using the Emerald Radio Frequency (RF) sensor [1] to capture differences between

SLE and healthy participants in their homes. We propose to extract meaningful features from Emerald signals and investigate how they differ when compared between SLE and healthy participants. This can help identify distinct patterns of activity and sleep parameters in the home environment that are indicative of disease state and could be used to better understand the impact of therapy on patients' daily lives. This work is important to inform future development of remote symptoms monitoring through non-contact sensing that could be used to assess disease trajectory and recovery over time.

2 METHODS

In this study we investigate the use of non-contact sensing (Emerald system) to remotely capture breathing, sleep and mobility in a natural environment. The Emerald system consists of a general-purpose wireless sensor that transmits radio frequency (RF) signals and then captures their reflections. The Emerald sensor employs frequency-modulated continuous-wave (FMCW) radar and antennae arrays and receives reflections from nearby people [24]. The high degree of water content in the human body (60%) facilitates the reflection of the radio signals and modulates them with the person's movements [12, 29]. The Emerald RF sensor is manufactured by Emerald Innovations, Inc. [1] and the dimensions of the sensor are 30×35×5 cm (Figure 2).

2.1 Preprocessing

As depicted in Figure 1, the Emerald system processes the raw RF signals, which is constituted of a Frequency Modulated Continuous Wave (FMCW) chirp sweeping the frequencies from 5.4 GHz to 7.2 GHz. Details of how Emerald is extracting these signals can be found in previous research [11, 12, 29]. Emerald's system extracted breathing signal at 5Hz (body displacement due to breathing), breathing rate every 30 seconds, sleep stages every 30 seconds (i.e., awake, light, Rapid Eye Movement (REM), and deep sleep), and trajectory data at 22Hz. Time series of (x, y) coordinates of the subject when they are moving within the range of the Emerald Device. Details of how Emerald is extracting these signals can be found in previous research [11, 12, 29]. Note that because the Emerald sensor placement was chosen to focus on sleep (2 to 3 meters from the bed), measures of breathing are only captured during in-bed periods while measures of mobility are related to movements in and around the bed area

2.2 Feature Extraction

Our feature extraction engine processes Emerald's breathing, sleep stages and trajectory signals to extract meaningful features of breathing, mobility, and sleep. A representative features set is presented in Table 1. Note that this is not an exhaustive list and that we chose to only present few features (11 out of 33 extracted features) due to the lack of space. A more established feature list will be discussed in future works.

2.2.1 Breathing. To characterize breathing patterns, we extracted daily average and standard deviation of breathing rates to investigate if breathing rate and variations in breathing differ between the two cohorts.

Signal	Feature	Description
Breathing	AVG breathing rate	Average breathing rate
	SD breathing rate	Standard deviation of breathing rate
Mobility	AVG speed	Average gait speed
	SD speed	Standard deviation of gait speed
	Traveled distance	Total traveled distance within the field of view of the Emerald sensor
Sleep	Duration of sleep stages	Time spent awake, in light, deep, or REM sleep
	Sleep efficiency	The amount of time the participants spend asleep while in bed
	Entropy of sleep stages	Sample entropy of sleep stages

Table 1: Features characterizing breathing, mobility, and sleep patterns extracted on a daily level then averaged across the 6-month

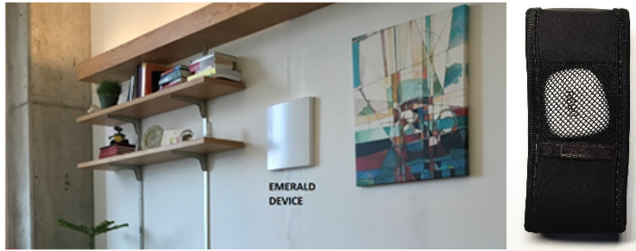


Figure 2: (Left) Emerald RF Sensor. The sensor was mounted on a bedroom wall within typically 2-3 meters of the bed. (Right) An ankle accelerometer was worn for the first 14-30 days of the study to associate the RF signals with the study participants.

2.2.2 Mobility. Because it has been demonstrated in the literature that physical activity levels can correlate with SLE symptoms [20, 22], we chose to extract average and standard deviation of speed captured in participants’ trajectories in the bedroom area. We also measured the total daily in-room traveled distance from trajectory data to characterize activity levels.

2.2.3 Sleep. We extracted multiple features to represent sleep quality including sleep efficiency which represents the amount of time the participants spend asleep while in bed [18]. It is calculated by dividing the amount of time spent asleep (light, REM, and deep) by the total amount of time in bed (higher values indicate better sleep quality). Furthermore, we measure the time spent in every sleep stage (i.e., awake, light, rapid eye movement (REM), and deep stages) in minutes per day. We also measured the complexity of sleep cycles using sample entropy [19]. It is defined as the probability that two matching sleep stage series will continue to match at the next stage segment. A match is defined as two segments having corresponding data points within a certain small range, described by the tolerance factor r [27]. When two matching series do not continue to match in the following segment, the sample entropy increases, hence a higher sample entropy reflects that the sleep stage segment is less predictable, i.e., indicates a higher variability of the sleep stage signal. Our approach for measuring sample entropy is as follows: (1) we first attribute a numerical value to each sleep cycle (1=awake, 2=REM, 3=light, 4=deep), (2) create time series of sleep stages with no repetitions (e.g., a typical awake, REM, light, deep transition

would look like this: 1-2-3-4 regardless of how many seconds they spend in a given stage), and finally (3) measure the sample entropy using the following formula: $SamEn = -\log(C(m + 1, r)/C(m, r))$ where: m is the length of the pattern or template (set to 1), r is the tolerance threshold (the maximum allowable difference between data points for them to be considered similar and is set to 20% of the standard deviation (SD) of the sleep stages, $C(m, r)$ represents the number of similar m -length template matches found in the data, and \log denotes the natural logarithm.

2.3 Statistical Analysis

To analyze the difference between SLE and healthy participants, we average the daily features for each participant over the course of the study and we perform a Welch’s t-test [8] while correcting for multiple comparisons using the Bonferroni correction method [26]. Effect size is estimated using Hedges’ g value [7, 21]. As reported in the literature [7], 0.15, 0.40, and 0.75 are used as thresholds to interpret small, medium, and large effects.

3 STUDY DESIGN

$N=47$ participants (1 male, 46 female), aged 48 on average ($SD=10.5$) were recruited in a 6-month, prospective, non-interventional, exploratory study for digital measure data profiling in healthy ($N=28$) and SLE ($N=19$) participants. Healthy participants were demographic matched to the disease cohort. The study did not restrict or introduce any medical interventions including medications. Participants were 38% white, 38% black or African American, 15% Asian, 2% multiple, and 6% chose not to report their ethnicity. Note that this data is a subset of a larger dataset including other cohorts, other measures such as actigraphy data and patient reported data measures of health-related quality of life. The Emerald RF sensor was mounted on a bedroom wall (placed approximately 1.15 meters from the floor) on the side of the bed on which the participant sleeps typically within 2 to 3 meters of the bed, and the sensor did not require the participant to interact with it. In some cases, the wall was not suitable for mounting and the sensor was mounted on a portable stand instead (see Figure 2). Study participants agreed to sleep on a consistent side of the bed with no other people allowed on their side of the bed and no pets allowed in the bedroom for the duration of the study to ensure the algorithms can accurately quantify sleep, breathing, and trajectory. The exact layout of the bedroom as well as the Emerald sensor location were recorded for

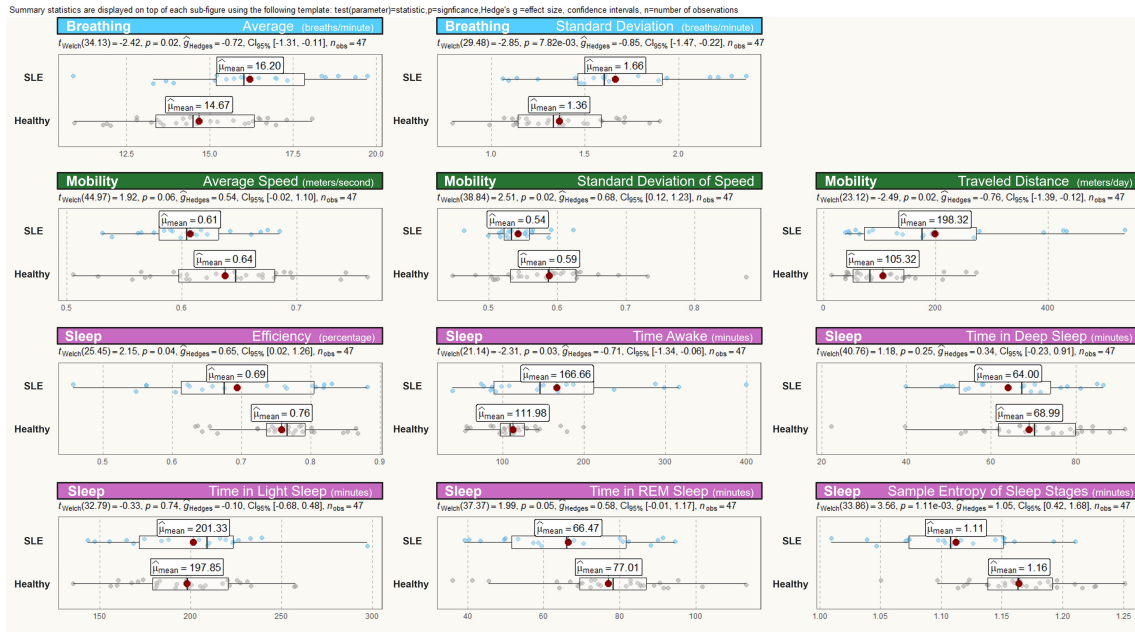


Figure 3: Results describing differences in breathing (in blue), mobility (in green), and sleep (in magenta) between SLE and healthy participants. A summary statistic is presented in each sub-figure and a template for the summary is presented in the top of the figure.

each participant. The data was compressed and transmitted after encryption via Wi-Fi to a secure server for further storage and analysis. The participants were also asked to wear a small accelerometer for 14 to 30 days at the beginning of the study (see Figure 2). Accelerometer and bed layout data are used to create an algorithmic filter that recognizes motion patterns from the RF signals. This filter is used by the Emerald platform to remove irrelevant information and retain only data specific to the participants.

4 RESULTS

4.1 Breathing

As presented in Figure 3, the average breathing rate was significantly different between SLE (AVG=16.2 breaths/minute) and healthy (AVG=14.67 breaths/minute) with SLE participants having 1.6 breaths/minute higher than healthy participants ($p=0.02$, Hedge's $g=-0.72$) with a medium to large effect size. The standard deviation of breathing rate was also found to be significantly different with a large effect size ($p<0.01$, $g=-0.85$) indicating less stable breathing for SLE participants. Note that we did not explore in this work if breathing is mediated by another effect such as lower sleep quality. This will be investigated in future work.

4.2 Mobility

SLE participants exhibited slower speed ($p=0.06$, $g=0.54$) and lower standard deviation of speed ($p=0.02$, $g=0.68$). SLE participants were also found to have a significantly higher total in-room traveled distance ($p=0.02$, $g=-0.76$) where SLE participants were found to have almost double in-room traveled distance than healthy participants (see Figure 3). This may indicate that SLE participants

spent more time in their bedrooms due to the lack of ability to perform other activities of daily living. It can also be due to more frequent awakening at night. Further analysis of the spatiotemporal distribution of trajectory data will be performed in future work to further investigate these findings.

4.3 sleep

SLE participants had significantly lower sleep efficiency with a medium to large effect size ($p=0.04$, $g=0.65$) with SLE participants having 7% lower sleep efficiency than healthy participants. Looking at time spent in different sleep stages, we can observe that there is no statistical difference in time spent in deep ($p=0.24$) and light sleep ($p=0.74$). However, SLE participants were found to have more awake time in the order of 55 minutes on average higher than healthy participants. They were also found to spend about 11 minutes less in REM stage ($p=0.05$, $g=0.58$) per night (see Figure 3). The sample entropy of sleep stages reveals a significant and large effect size ($p<0.001$, $g=1.05$) with SLE participants having lower entropy than healthy participants. Lower entropy indicates less complex sleep stage trajectories. This is justified by the fact that SLE participants spent less time on REM stage making the sleep stage traces look less complex given most of the time, the sleep is alternating between awake and light sleep instead of alternating between the four stages (see Figure 3 where we record more time in awake and light stages and less for deep and REM in SLE).

5 DISCUSSION AND CONCLUSION

This paper discussed the use of non-contact sensing to extract physiological and behavioral signals that can characterize symptoms of autoimmune diseases such as Systemic Lupus Erythematosus (SLE).

We presented a set of features that represent breathing, mobility and sleep patterns and explored how they differ between SLE and healthy participants in a 6-months in-home study including 19 SLE and 28 healthy participants. Results suggest that many features are significantly different between the two cohorts. SLE participants were found to have significantly higher breathing rates, slower gait speed, and less steady gait patterns. SLE participants were also found to have significantly less efficient sleep and were found to have less REM sleep and being more awake when in bed indicating poorer sleep quality than healthy participants. These results are in line with previous research [2, 17] showing poor sleep quality in SLE participants using actigraphy devices. When ranking the features based on the absolute value of their effect size, we find that the top three features that best separate SLE and healthy participants are: (1) sample entropy of sleep stages ($g=1.05, p<0.001$), (2) standard deviation of breathing ($g=-0.85, p=0.01$), and (3) in-room traveled distance ($g=-0.76, p<0.05$). This potentially suggests that breathing, mobility, and sleep are all dysregulated in SLE and demonstrates the importance of multi-modal sensing at capturing multiple dimensions of disease state. These findings are in line with the known symptoms of SLE that can cause fatigue, fevers, pain and swelling and that significantly impact the quality of life and effect participants' mobility and sleep quality [10, 15, 22, 23]. These findings provide preliminary evidence of the utility of using passive sensing and non-contact sensing to monitor disease activity of SLE. Future work will explore how daily self-reported symptom measures correlate with the objective sensing features and investigate how these signals can be combined together to provide a holistic view of symptoms that can ultimately predict disease trajectory remotely and continuously.

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