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# Signal Quality and Patient Experience with Wearable Devices for Epilepsy Management

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### **Summary:**

Non-invasive wearable devices have great potential to aid the management of epilepsy, but these devices must have robust signal quality, and patients must be willing to wear them for long periods of time. Automated machine learning classification of wearable biosensor signals requires quantitative measures of signal quality to automatically reject poor quality or corrupt data segments. In this study commercially available wearable sensors were placed on patients with epilepsy undergoing in-hospital or in-home electroencephalography (EEG) monitoring, and healthy volunteers. Empatica E4 and Biovotion Everion were used to record accelerometry (ACC), photoplethysmography (PPG), and electrodermal activity (EDA). Byteflies Sensor Dots were used to record ACC and PPG, the Activinsights GENEActiv watch to record ACC, and Epitel Epilog to record EEG data. PPG and EDA signals were recorded for multiple days, then epochs of high quality, marginal quality, or poor quality data were visually identified by reviewers, and reviewer annotations were compared to automated signal quality measures. For ACC, the ratio of spectral power from 0.8 to 5 Hz to broadband power was used to separate good quality signals from noise. For EDA, the rate of amplitude change and prevalence of sharp peaks significantly differentiated between good quality data and noise. Spectral entropy was used to assess PPG, and showed significant differences between good, marginal, and poor quality signals. EEG data were evaluated using methods to identify a spectral noise cutoff frequency. Patients were asked to rate the usability and comfort of each device in several categories. Patients showed a significant preference for the wrist-worn devices, and the Empatica E4 device was preferred most often. Current wearable devices can provide high quality data and are acceptable for routine use, but continued development is needed to improve data quality, consistency, and management, and acceptability to patients.

### **Key Points:**

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- Automated measures of signal quality are important for chronic monitoring with wearable biosensors
- Signal quality metrics for ACC, EDA PPG and EEG can discriminate good from marginal quality data and noise
- People with epilepsy on average have a positive overall response to the use of wearable devices and report a preference for wristbands
- Continued development of devices is needed to improve data quality and consistency, and subject comfort and acceptability

# 1 Introduction

Wearable devices are increasingly common tools for seizure counting and management in clinical epilepsy, among other health applications<sup>1</sup>. This provides tools to help people with epilepsy and their physicians better understand, and ultimately treat their seizures, and track treatment outcomes. Patient under-reporting of seizures is a well-recognized problem in epilepsy<sup>1,2</sup>, and objective seizure counting based on wearable devices may result in more effective management of medications and neuromodulation therapy, and may help in assessing candidacy for surgery. Despite extensive efforts in the field of seizure prediction<sup>3</sup>, the unpredictability of seizures remains a significant difficulty for people with epilepsy regardless of seizure frequency<sup>4</sup>. Non-invasive prediction of seizures through the tracking of temporal cycles<sup>5-8</sup>, physiological signals<sup>9,10</sup>, or their combination could prove transformative for many patients.

A key concern with wearable devices is the quality of the data recorded<sup>11</sup>. This becomes increasingly important in long-term device use, both for use in clinical trials and ongoing epilepsy management. Automated analysis of signals with algorithms requires the ability to exclude data epochs corrupted by artifacts or without physiological content. Comparison between devices often focuses on seizure detection performance rather than objective and fundamental signal quality measures<sup>12,13</sup>. Signal quality measures are simple to compute and allow for direct comparison of similar sensors from data recorded with or without seizures. Signal quality indexes (SQIs) are useful to validate the quality of devices before the commencement of trials, and to compare across trials at different centers or with different endpoints. Furthermore, longitudinal analysis of signal quality from individual devices is useful to assess device adherence and maintenance requirements. The use of these methods along with automated data transfer and analysis can provide reports to physicians, people with epilepsy, and researchers to improve clinical care and advance epilepsy research.

Another important aspect of wearable technologies use is device design. Although various studies have surveyed people with epilepsy and their caregivers about their views on various aspects of wearable devices<sup>14-16</sup>, these studies have not always focused on people with an experience of using

wearable devices for epilepsy management. People with epilepsy who have personal experience with wearable devices may be able to provide more insightful feedback on preferences and concerns of long-term device use.

The present study addresses both of these problems of measuring device signal quality and assessing the preferences of people with epilepsy while using wearable devices. These results will guide future work on the long-term use of wearable devices for seizure detection and forecasting.

## 2 Methods

### *2.1 Study Design*

Commercially available research-grade wearable devices were used by patients undergoing video-EEG monitoring in both in-patient and at-home environments for durations of up to 10 days. Physiological signals utilized were: accelerometry (ACC) to evaluate limb acceleration in 3-axes, electrodermal activity (EDA) to measure skin conductance (which varies with perspiration, reflecting sympathetic tone and psychological arousal), photoplethysmography (PPG) to evaluate microvascular blood volume changes, and EEG to measure cerebral electrical activity. Four commercially available, research-grade wearable biosensors with the ability to record ACC, EDA, and PPG, along with one sensor capable of recording scalp EEG were assessed with patients with epilepsy undergoing EEG monitoring and healthy volunteer subjects. Patients were recruited at Mayo clinic, King's College Hospital, Freiburg hospital, and Seer Medical (Melbourne, Australia). Consecutive patients undergoing stereoelectroencephalography (SEEG) surgery, and those who were admitted to Epilepsy Monitoring Units (EMU) or were scheduled for at-home ambulatory monitoring were recruited for the study unless there were clinical reasons to omit patients, and patients with a range of seizure types (focal, generalized and electrographic) were included. From ACC, EDA, PPG and EEG data, signal quality metrics were assessed retrospectively, and benchmarked against data recorded while not being worn. At the end of the recording period, patients were provided with a survey to assess their preferences and comfort with using wearable devices for seizure prediction.

### *2.2 Physiological Data Collection*

ACC data were recorded by the Empatica E4, Byteflies Sensor Dot, Biovotion Everion and Activinsights GENEActiv devices, which were placed on the wrist, chest, arm and wrist respectively. For each device, several days of visually-assessed good quality ACC data from at least 4 patients was identified and compared with data recorded while the device was not worn by the subject. EDA was recorded by the Biovotion and Empatica devices, each from 5 patients. A few hours of data were recorded with each device placed on the subject over a cloth wrap, not in contact with the subject's skin, to represent poor quality data. PPG data was collected from patients wearing the Empatica, Byteflies, and Biovotion devices. Segments representing noise with the absence of physiological activity for each

device were obtained by a device not worn by a subject, but at rest on a stable surface. EEG data was recorded by the Epitel device. This device is attached to the patient's forehead, close to the hairline, using a provided adhesive sticker with saline gel cutouts over the electrodes, and records a bipolar EEG channel from two electrodes.

### *2.3 Data Labeling*

Ten-minute, non-overlapping segments of ACC data were scored using a binary scale, identifying segments as good quality data (on patient) or noise (not on patient). Ten-minute epochs were chosen for ACC to accommodate sleep or sedentary periods, where movements may be infrequent. PPG data were scored over 1-minute non-overlapping segments by reviewers using a three-point scale, identifying segments as good quality (physiology easily visible with limited noise or artifact content), marginal quality (some physiology apparent but frequently obscured by noise or artifacts), or poor quality (no physiology apparent and signal dominated by noise or artifact). For both ACC and PPG, segments were reviewed and labeled using a custom software written in Matlab (Natick, MA). The Byteflies and Biovotion devices provide PPG data with red, green, and infrared (IR) light sources. To minimize reviewer burden, the IR and green channels for ByteFlies and Biovotion devices respectively were scored by the reviewers, and these scores were applied to all three PPG signals to calculate SQIs. The IR PPG signal for the Byteflies device and green PPG for the Biovotion device each showed the greatest physiological signal component on visual inspection<sup>17-19</sup>. The Empatica does not provide raw PPG values but rather provides a Blood Volume Pulse (BVP), a derived signal calculated from the red and green raw PPG signals. The BVP shows pulsatile blood flow features but is similar to the PPG signal as the slowly-varying respiratory component are removed. Therefore BVP was analyzed using the PPG metrics. For EDA, data segments with less than 4 seconds of artifact were labeled good quality. Marginal quality data segments had both tonic and phasic EDA components, but each segment contained at least 4 seconds of artifacts (sharp changes<sup>17</sup>). The Empatica E4 device returns values less than 0.05  $\mu\text{S}$  when not in contact with skin (for example, with a garment under the device), and zero when entirely off the subject. The Biovotion Everion returns 0.047 mS when it is not in contact with skin and not on the patient. Data segments with amplitude at or below these values, and segments with amplitude changes less than 0.01  $\mu\text{S}$  (0.01 mS for Biovotion) within one minute, were classified as bad. EEG data were scored using a threshold method. All data with a maximum bandwidth (defined below) of over above 75 Hz were considered good quality<sup>20</sup>, and data above 35 Hz acceptable for recording epileptiform activity<sup>21</sup>.

### *2.4 Signal Quality Indices*

#### *2.4.1 Accelerometry*

Prior studies have classified subject activities such as rest, walk and run based on the frequency components of the ACC data acquired from wireless sensors<sup>22</sup>. They showed the highest amplitude of the frequency spectrum of ACC data for these movements is in frequencies below 5 Hz. In order to

exclude low frequency noise components, the power spectrum is calculated for frequencies above 0.8 Hz. To avoid ambiguity regarding the directional orientation of movement the signal quality metrics were calculated on the root mean square (RMS) of the acceleration components of the three axes ( $ACC_x$ ,  $ACC_y$ ,  $ACC_z$ ):

$$RMS = \sqrt{\frac{1}{3}(ACC_x^2 + ACC_y^2 + ACC_z^2)} \quad (1)$$

The signal quality metric for human movement in RMS accelerometry was defined by the ratio of the narrow spectral band covering the normal physiological range (0.8 - 5 Hz) to broadband spectral power (Power Ratio):

$$SQI_{PR} = \frac{P_{[0.8\ 5]}}{P_{[0.8\ F_n]}} \quad (2)$$

Where  $F_n$  is the Nyquist limit frequency for the device. The power ratio of the signal was estimated as the power in the frequency range between [0.8 5] Hz divided by the broadband power from 0.8 Hz to the Nyquist frequency. The Empatica E4 records acceleration with a sampling frequency of 32 Hz. Since the sampling frequency of the Byteflies, Biovotion and GENEActiv devices (48, 51.2 and 1000 respectively) are higher than the Empatica E4, the Empatica E4 Nyquist frequency limit (16 Hz) was used for all devices in order to allow direct comparison between devices. This power ratio should peak when physiological movements dominate the power spectrum, and should take on low values when there is little physiological movement present. The power spectrum was calculated for non-overlapping 4 second segments, and average values over consecutive 10-minute segments are reported. Figure 1. (a) shows the scaled RMS ACC signal in blue and the quality metric in red. The power spectrum of the RMS signal shows higher power in the range of [0 - 5] Hz (Fig 1. (b)).

#### 2.4.2 Electrodermal Activity

EDA provides time series recording of skin conductance, which is characterized by a slow varying tonic component (skin conductance level, SCL) and a fast-varying phasic component (skin conductance response, SCR). SCR has abrupt phasic increases in the conductance of the skin and usually has a faster rise time than decay time<sup>23</sup>. The SCR amplitude is defined as the difference between the SC values at peak and the preceding trough. Here a minimum SCR amplitude of 0.01  $\mu$ S is used to distinguish between physiological data and noise<sup>24</sup>. Also, the frequency of nonspecific SCR (NS-SCR) has been suggested to measure tonic activity<sup>25</sup>. Typically the NS-SCR rate per minute is at least one (1-3 during rest and more than 20 in high arousal situations)<sup>25,26</sup>.

The EDA signal was recorded using the Empatica E4 and Biovotion Everion in micro Siemens ( $\mu$ S) and kilo Ohms ( $k\Omega$ ), respectively. The EDA in  $\mu$ S is related to resistance in  $k\Omega$  as its reciprocal ( $EDA(\mu S) = 1/R(M\Omega) = 1000/R(k\Omega)$ ). For analysis the Biovotion Everion data was converted to mS to have its data in a same dynamic range as the Empatica E4 data. The sampling frequencies for the Empatica E4 and Biovotion Everion are 4 Hz and 1 Hz, respectively. The quality metric for EDA was called Rate of Amplitude Change ( $SQI_{RAC}$ ), and is the percent amplitude change calculated in

concurrent one-second windows. Sharp changes in signal amplitude of more than a 20% increase or 10% decrease per second are often correlated with subject motion and poor electrical contact with the skin,<sup>27,28</sup> and these values are interpreted as artifact, or poor quality data. If the amplitude of EDA changes less than 0.01  $\mu$ S for the E4 signal and 0.01 mS for the Biovotion signal over a one minute epoch, the device is likely not recording physiological signals, and the SQI of that minute of data was set to be zero. Fig. 1 (c) shows the scaled EDA signals from an E4 recording of a healthy subject, with the calculated SQI<sub>RAC</sub>. During the day when the subject is moving, the EDA signal has many sharp increases and decreases in amplitude, which represent motion artifacts. During the night while the subject is relatively still, the SQI<sub>RAC</sub> stays within the normal range due to consistent contact between the EDA electrodes and the skin.

#### 2.4.3 Photoplethysmography

Signal quality of PPG was assessed by calculating spectral entropy which measures the ‘peakedness’ of the frequency spectrum<sup>29,30</sup>. Due to its oscillating nature, a good quality PPG signal exhibits a peaked power spectrum and has lower spectral entropy than a PPG signal corrupted by noise, which exhibits a more flat spectrum with less pronounced spectral peaks, and correspondingly higher spectral entropy. Because most of the physiological PPG signal power lies within  $f_1 = 1$  Hz and  $f_2 = 3$  Hz (see Figure 2) it is possible to limit the spectrum for calculating the spectral entropy (SE) to the frequency range of 1 – 3 Hz:

$$SQI_{SE}(f_1, f_2) = - \frac{\sum_{f_1}^{f_2} \hat{P}(f) \cdot \log_2 \hat{P}(f)}{\log_2(N)} \quad (3)$$

where  $\hat{P}(f)$  is an estimate of the power spectral density at frequency  $f$  and  $N$  is the number of frequency bins in  $[f_1, f_2]$ . Note that  $\hat{P}(f)$  is normalized such that it sums to one in the frequency band  $[f_1, f_2]$  and, in order to get a smooth estimate, we took the average of  $\hat{P}(f)$  over 15 non-overlapping 4-second windows (resulting in 1-minute segments) before calculating SQI<sub>SE</sub>. Fig. 2 shows a typical Empatica E4 on-patient PPG signal with corresponding spectrogram and calculated metric. Values of SQI<sub>SE</sub> close to one indicate noise segments (e.g., day 2, 10:01 AM to 5:59 PM). Low values of SQI<sub>SE</sub> correspond to high quality data (e.g. day 1, between 9.54 PM and 11:14 PM). PPG signals corrupted by e.g. motion artifacts show values of SQI<sub>SE</sub> close to 0.8 (e.g. day 1, 10:09 AM to 7.29 PM).

#### 2.4.4 Electroencephalography

Signal quality of EEG was assessed by calculating the maximum bandwidth, a measure that estimates the highest frequency at which the recorded signal power is significantly different from background noise<sup>31,32</sup>. It was calculated as the highest frequency with power greater than a threshold,

$$P_t = 1.5 \times (Q_{75}(P_{Noise}) - Q_{25}(P_{Noise})) + Q_{75}(P_{Noise}) \quad (4)$$



where  $Q_n(P)$  is the  $n$ th quantile of  $P$  and  $P_{Noise}$  is the mean of the frequency power in the 200-255 Hz band calculated every 10 seconds in a 10 minute window. The power spectrum was calculated from the squared amplitude of the Fourier transform. Noise was defined in this way as it was the highest spectral band below the Nyquist frequency (256 Hz) which can be assumed to have minimal scalp EEG power. Although  $P_{Noise}$  could contain a small amount of physiological information, we have approximated the noise in this way in lieu of hardware based testing of the device.

## 2.5 Survey Collection

Patients with epilepsy undergoing clinical EEG monitoring were recruited to use wearable devices for the duration of their monitoring. Some patients were willing to wear multiple devices, wearing up to four devices at a time. Monitoring lasted at least three days in all cases. Some healthy controls were recruited as well to wear devices for a similar duration. At the end of the recording period subjects completed a survey on a tablet device, answering questions about basic demographics, device preference (if multiple devices were worn) and impression of comfort. In the case where multiple devices were worn, device impression was only completed for the preferred device. Questions were answered on a 7-point Likert scale.

## 2.6 Statistical Methods

A  $t$ -test was used to evaluate metric performances for ACC, PPG and EDA data. Survey results were assessed by computing the mean response for each question and for each device. A 2-way ANOVA was conducted to assess the effects of age and gender for each question. For each response, interaction between gender and age group was not found to be significant ( $p < 0.05$ ). Hence, gender and age groups were analyzed as independent factors. No significant difference was found between recruitment sites hence these were aggregated for analysis.

# 3 Results

## 3.1 Accelerometry Data Analysis

Data from 19 patients with epilepsy were included in the analysis of ACC data extracted from Empatica E4, Byteflies, Biovotion and GENEActiv devices. Normal data was recorded with the device on the patient, while noise segments represent data recorded by a device resting on a stable surface (not worn). The  $SQI_{PR}$  (eq. 2) has higher values when the subject is physically active. The mean and standard deviations of the power ratio across 10-minute segments from patients wearing the device are reported in Table 1. Both average and standard deviation together could be considered as a metric to distinguish noise from acceptable data, as well as classifying the physical activities. During sleep however, the

metric may falsely classify the signal as noise when the subject shows no movement. In this case, tracking the metric over a longer time period is suggested (Fig 1. (a) 22:43 to 12:00, second day,  $\text{avg} \pm \text{std} (\text{SQI}_{\text{PR}}): 0.29 \pm 0.003$ ). Shorter time periods may be used during sleep if other signals, such as EDA and temperature, can be associated with ACC data to confirm the device is being worn. For example, in Fig 1. (a) from 0:44 to 1:19 am (first day), data is classified as noise based on ACC metric, and zero EDA signal in Fig 1. (c) supports that. However, from 1:34 to 1:54 am on the first day, which is classified as noise (not on patient) using the proposed ACC SQI, the EDA signal has high-quality data suggesting the device is being worn while the subject is still. All four devices reported in Table 1 show similar quality of ACC data and are able to capture movement with comparable ability.

### 3.2 Electrodermal Data Analysis

Data from 10 patients were selected for EDA analysis. The average and standard deviation of the  $\text{SQI}_{\text{RAC}}$ , the amplitude change per second, for positive (amplitude increasing) and negative (amplitude decreasing) SQIs separately, were reported for both devices in Table 2. The SQIs were compared with the reviewer labels and showed an average agreement of 86% and 90% between the labels and SQIs for the Empatica and Biovotion, respectively. A  $t$ -test showed a significant difference in the  $\text{SQI}_{\text{RAC}}$  for data labeled as good quality compared to low quality (bad and marginal) classes with  $p < 0.001$ . Moreover, the SQIs of the data collected with the electrodes not in touch with the skin was compared with normal data including good and marginal ( $p < 0.05$  for Empatica and  $p < 0.001$  for Biovotion, reported in Table 2). For the Empatica device, the EDA signal is zero when it is not on the patient's wrist, and the Biovotion device records a constant value of 21 k $\Omega$  (0.047 mS) in our experiments, where the device was on patient but not in contact with skin. As measured by the marginal and noise percentage of data reported in Table 2, the Empatica E4 recorded EDA data with highest quality on average in our cohort.

### 3.3 Photoplethysmography Data Analysis

PPG data was analyzed from 15 patients. BVP data from Empatica E4 and PPG data with 3 light sources from Byteflies and Biovotion devices were analyzed. Table 3 summarizes the mean and standard deviation of the spectral entropy  $\text{SQI}_{\text{SE}}$  for good, marginal and noise data, respectively. As expected, good quality data exhibit the lowest spectral entropy of all classes. Noise has the highest spectral entropy with values close to one, in correspondence with a flat spectrum in the 1-3 Hz frequency band. Marginal quality data epochs show values in between good and noise  $\text{SQI}_{\text{SE}}$  values. The green PPG for Biovotion and IR light PPG for Byteflies devices were scored by reviewers, and these scores were used to classify the remaining PPG signals. Although the Empatica BVP data is preprocessed, Byteflies and Biovotion devices also provide good quality data for at least one light source.

### 3.4 EEG Data Analysis

A total of 405 days of Epitel Epilog EEG data from 21 patients were analyzed by calculating the signal's maximum bandwidth, which is an estimate of the highest frequency at which the recorded

signal is significantly different from noise. The results show that 21.4% of EEG data were classified as good (maximum bandwidth above 75 Hz), 33.3% classified as acceptable (maximum bandwidth between 35 Hz and 75 Hz), and 45.3% of data were marginal (maximum bandwidth below 35 Hz).

### 3.5 Data Validation

The proposed SQIs were computed over a larger set of acquired data including ACC, EDA and PPG signals. The analysis showed 71% of Empatica EDA data (34 patients, 89 days) and 13% of Biovotion EDA data (10 patients, 7 days) was classified as acceptable quality (rate of amplitude change stays within [-10% 20%] limit). 90% of Empatica ACC data (39 patients, 117 days) was classified as acceptable quality, and 91% of Empatica BVP data (28 patients, 71 days) was classified as acceptable quality. 94% of Biovotion ACC data (1 patient, 1 day) had acceptable quality. Results of analysis of Biovotion PPG data shows that 95%, 91% and 58% of green, IR and red lights were classified as acceptable data.

### 3.6 Patient survey analysis

Patients were provided with a survey at the end of data recording to evaluate wearable device acceptability. Table 4 presents the demographics of the patient cohort that completed device acceptability surveys. All respondents completed the entire survey. The majority of respondents identified as female, and the most represented age cohorts are 20-29 and 30-39 years of age.

Survey results are summarized in Table 5. Patients who wore multiple devices were asked which device they preferred, and only responded to the survey for the preferred device. The Empatica E4 was the preferred device more often than other devices. The Biovotion device had the most positive results for both ease of manipulation and usability, followed by the two wrist-worn devices, the Empatica E4 and GENEActiv. GENEActiv had the most positive results for both long-term comfort and comfort during sleep. The Byteflies sensor dots were most preferred for potential seizure prediction. However, all devices generally had positive responses.

Being in the 60-69 year old age group was significantly correlated with more negative usability responses ( $p < 0.05$ ). Being in the 30-39 year old age group was significantly correlated with more positive long-term comfort responses ( $p < 0.01$ ). No significant effect was found with gender for response to any question.

## 4 Discussion

Automated, objective measures of signal quality are important for large-scale data acquisition and management systems, such as are needed for epilepsy monitoring and management systems. Here we

describe and validate quantitative signal quality metrics for ACC, PPG, EDA and EEG. As a quality metric for ACC data the power ratio of the signal in the frequency range between  $[0.8 - 5]$  Hz over  $[0.8 - 16(F_n)]$  Hz, was estimated. According to the results reported in Table 1, the average and standard deviation of the proposed  $SQI_{PR}$  (eq. 2) can be used as a metric to decide if the device is on the patient or not. However, for short segments classified as noise, observing other signals like EDA and PPG (and many devices also record temperature) is suggested to identify times when subjects may be physically still (for example, during sleep). All devices tested showed significant differences in  $SQI_{PR}$  between normal use and device removal, and any of the devices tested would perform well. The rate of amplitude change (%) was defined as a quality metric for EDA data, which for good data is between 20% increase and a 10% decrease, discarding data with amplitude smaller than  $0.05 \mu S$  (equal to  $0.047 \text{ mS}$  for Biovotion) and 1-minute segments with amplitude changes less than  $0.01 \mu S$  for the Empatica E4 ( $0.01 \text{ mS}$  for Biovotion). In some special cases, this range would be slightly different<sup>25</sup>. Note that in our study cohort the arm-worn Biovotion device recorded a greater proportion of marginal and poor quality EDA data (and a lower proportion of good quality data) compared to the wrist-worn Empatica device. It is unclear whether this is due to the difference in sensor placement, differences in sensor design, or other factors.

The signal quality of PPG was evaluated by spectral entropy to measure the peakedness of a spectrum. Good PPG signals have lower spectral entropy than a noisy PPG signal. The t-test was used to evaluate the metric's performance and it showed metrics can classify data into good and noise (or not on the patient) classes with a  $p < 0.05$  for all signals. A direct comparison of the individual green, red, and IR PPG channels from the Byteflies and Biovotion devices to the aggregated PPG signal from the Empatica device is perhaps unclear, although the spectral entropy ranges observed for the green and infrared signals from the Biovotion and Byteflies devices gave similar results, suggesting a similar aggregated measure from these devices may be quite similar to the Empatica BVP. The Biovotion device's IR channel showed less change in  $SQI_{SE}$  amplitude and the red channel showed almost no change between good, marginal, and poor data compared to the other devices. In general, EDA and PPG together can be used to robustly detect if a device is worn or not with the individual quality metrics. The SQI of ACC data could be used to distinguish between periods of device on vs. off body, however special care needs to be put towards not misclassifying sleep as device not worn. Signal quality in a modular, ambulatory EEG device has somewhat different characteristics than a typical wired EEG setup, where line noise may dominate as an indicator of poor signal quality. The SQI reported here has been used widely in intracranial EEG<sup>31–33</sup> and showed good ability to differentiate signal quality in this study.

There is a large number of devices commercially available for epilepsy management, and an increasing number is receiving regulatory approval for detection of specific seizure types<sup>8</sup>. Automated monitoring of data quality in long-term use, will be of great importance for clinical and research applications. Long-term use of wearable devices will also necessitate robust online data transfer to

minimize the need for manual data management. Such systems exist for many consumer grade wearable devices, and will minimize compliance and technically related errors. Online connectivity can also provide the opportunity to give direct feedback to users about their compliance and data quality. This in turn may have a positive effect on increasing compliance. However many devices currently available have deficiencies in design that limit their acceptability to the user, negatively impacting adherence. It is necessary that people with epilepsy and their caregivers are integrated into the development process of wearable devices, such that interest in the device is not solely based on medical benefits. It is encouraging that all average survey responses were positive to the tested devices, although not reflected in these results were occasional refusals by subjects to use devices. Surveys of larger populations will be required in order to appropriately power such studies.

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## Disclosure of Conflicts of Interest

EN and DF are employees of Seer Medical Pty. Ltd. MC and DF are shareholders of Seer Medical Pty. Ltd. No other authors have conflicts to declare.

## Ethical Publication Statement

We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

## References

1. Elger CE, Hoppe C. Diagnostic challenges in epilepsy: seizure under-reporting and seizure detection. *Lancet Neurol.* 2018; 17:279–288.
2. Cook MJ, O’Brien TJ, Berkovic SF, et al. Prediction of seizure likelihood with a long-term, implanted seizure advisory system in patients with drug-resistant epilepsy: a first-in-man study. *Lancet Neurol.* 2013; 12:563–71.
3. Kuhlmann L, Lehnertz K, Richardson MP, et al. Seizure prediction—ready for a new era. *Nat Rev Neurol.* 2018; :1.

4. Dumanis SB, French JA, Bernard C, et al. Seizure forecasting from idea to reality. Outcomes of the my seizure gauge epilepsy innovation institute workshop. *eNeuro*. 2017; 4.
5. Karoly PJ, Goldenholz DM, Freestone DR, et al. Circadian and circaseptan rhythms in human epilepsy: a retrospective cohort study. *Lancet Neurol*. 2018; 17:977–985.
6. Baud MO, Rao VR. Gauging seizure risk. *Neurology*. 2018; 91:967–973.
7. Karoly PJ, Maturana MI, Cook MJ, et al. Forecasting Cycles of Seizure Likelihood. *medRxiv*. 2019; :2019.12.19.19015453.
8. Gregg NM, Nasser M, Kremen V, et al. Circadian and multiday seizure periodicities, and seizure clusters in canine epilepsy. *Brain Commun*. 2020; 2:fcaa008.
9. Beniczky S, Conradsen I, Henning O, et al. Automated real-time detection of tonic-clonic seizures using a wearable EMG device. *Neurology*. 2018; 90:e428–34.
10. Regalia G, Onorati F, Lai M, et al. Multimodal wrist-worn devices for seizure detection and advancing research: focus on the Empatica wristbands. *Epilepsy Res*. 2019; .
11. Beniczky S, Ryvlin P. Standards for testing and clinical validation of seizure detection devices. *Epilepsia*. 2018; 59:9–13.
12. Onorati F, Regalia G, Caborni C, et al. Multicenter clinical assessment of improved wearable multimodal convulsive seizure detectors. *Epilepsia*. 2017; 58:1870–1879.
13. Fűrbass F, Kampusch S, Kaniusas E, et al. Automatic multimodal detection for long-term seizure documentation in epilepsy. *Clin Neurophysiol*. 2017; 128:1466–72.
14. Bruno E, Biondi A, Richardson MP. Pre-ictal heart rate changes: A systematic review and meta-analysis. *Seizure*. 2018; 55:48–56.
15. Simblett SK, Bruno E, Siddi S, et al. Patient perspectives on the acceptability of mHealth technology for remote measurement and management of epilepsy: A qualitative analysis. *Epilepsy Behav*. 2019; 97:123–9.
16. Simblett SK, Biondi A, Bruno E, et al. Patients' experience of wearing multimodal sensor devices intended to detect epileptic seizures: A qualitative analysis. *Epilepsy Behav*. 2020; 102:106717.

17. Lee S, Shin H, Hahm C. Effective PPG sensor placement for reflected red and green light, and infrared wristband-type photoplethysmography. In: 2016 18th International Conference on Advanced Communication Technology (ICACT). 2016. p. 556–8.
18. Castaneda D, Esparza A, Ghamari M, et al. A review on wearable photoplethysmography sensors and their potential future applications in health care. *Int J Biosens Bioelectron*. 2018; 4:195.
19. Tamura T, Maeda Y, Sekine M, et al. Wearable photoplethysmographic sensors—past and present. *Electronics*. 2014; 3:282–302.
20. Sinha SR, Sullivan LR, Sabau D, et al. American Clinical Neurophysiology Society Guideline 1: Minimum Technical Requirements for Performing Clinical Electroencephalography. *Neurodiagnostic J*. 2016; 56:235–44.
21. Curtis MD, Gnatkovsky V. Reevaluating the mechanisms of focal ictogenesis: The role of low-voltage fast activity. *Epilepsia*. 2009; 50:2514–25.
22. Sharma A, Purwar A, Lee Y-D, et al. Frequency based classification of activities using accelerometer data. In: 2008 IEEE International Conference on Multisensor Fusion and Integration for Intelligent Systems. 2008. p. 150–3.
23. Benedek M, Kaernbach C. A continuous measure of phasic electrodermal activity. *J Neurosci Methods*. 2010; 190:80–91.
24. Decomposition of skin conductance data by means of nonnegative deconvolution - Benedek - 2010 - *Psychophysiology* - Wiley Online Library [Internet]. [cited 2019]. Available from: <https://onlinelibrary.wiley.com/doi/full/10.1111/j.1469-8986.2009.00972.x>
25. Braithwaite, Jason, Watson, Derrick, Jones, Robert, et al. A Guide for Analysing Electrodermal Activity (EDA) & Skin Conductance Responses (SCRs) for Psychological Experiments. *Psychophysiology*. 2013; 49:1017–1034.
26. Dawson ME, Schell AM, Filion DL. The electrodermal system. In: *Handbook of Psychophysiology*, 2nd Ed. Cambridge University Press; 2000. p. 200–23.
27. Taylor S, Jaques N, Chen W, et al. Automatic identification of artifacts in electrodermal activity data. In: 2015 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC). 2015. p. 1934–7.

28. Kocielnik R, Sidorova N, Maggi FM, et al. Smart technologies for long-term stress monitoring at work. In: Proceedings of the 26th IEEE International Symposium on Computer-Based Medical Systems. 2013. p. 53–8.
29. Misra, Hemant, Ikbali, Shajith, Bourlard, Herve, et al. Spectral entropy based feature for robust ASR. In: IEEE International Conference on Acoustics, Speech, and Signal Processing (ICASSP). 2004. p. I–193.
30. Rezek IA, Roberts SJ. Stochastic complexity measures for physiological signal analysis. IEEE Trans Biomed Eng. 1998; 45:1186–91.
31. Bundy DT, Zellmer E, Gaona CM, et al. Characterization of the Effects of the Human Dura on Macro- and Micro-Electrocorticographic Recordings. J Neural Eng. 2014; 11:016006.
32. Nurse ES, John SE, Freestone DR, et al. Consistency of Long-Term Subdural Electroencephalography in Humans. IEEE Trans Biomed Eng. 2018; 65:344–52.
33. Miller KJ, Sorensen LB, Ojemann JG, et al. Power-law scaling in the brain surface electric potential. PLoS Comput Biol. 2009; 5.

## Figures

**Fig 1.** (a) Scaled accelerometer data of Empatica E4 from a control subject in blue, and average power ratio quality metric over 10-minute segments in red. The Mean  $\pm$  Variance of power ratio  $SQI_{PR}$  is shown in black. Subject performed multiple activities including walking, running, and biking. (b) The corresponding power spectrum of the raw accelerometer data. (c) The corresponding scaled EDA signal (red) and  $SQI_{RAC}$  (black). Zero  $SQI_{RAC}$  shows segments where the amplitude of the EDA signal is less than 0.05  $\mu S$  (no skin contact) or the amplitude change is less than 0.01  $\mu S$  in a 1-minute segment. (d) An 80 second segment of EDA signal from the recording, likely illustrating non-specific SCR periodic changes consistent with high physical activity<sup>25</sup>.

**Fig. 2** Typical on-patient PPG spectrogram depicted in the upper panel recorded with Empatica E4. Note that most of the signal power distributes among frequencies below 5 Hz and that the signal was not recorded continuously (white spaces in upper and lower panel). The corresponding raw PPG signal is depicted in the lower panel (black line) with the calculated  $SQI_{SE}$  on top (red line).



# Tables

**Table 1. Signal quality index (Power Ratio),  $SQI_{PR}$  for accelerometer data from 3 devices; Empatica E4, Byteflies, Biovotion and GENEActive. Acceptable data compared with recorded noise.**

| Device                   | Location | No. of patients | Duration (days) | $SQI_{PR}$<br>avg±std(normal) | $SQI_{PR}$<br>avg±std(noise) | P-value |
|--------------------------|----------|-----------------|-----------------|-------------------------------|------------------------------|---------|
| Empatica E4              | wrist    | 6               | 18              | 0.35±0.086                    | 0.29±0.005                   | <0.001  |
| Byteflies Sensor Dot     | chest    | 4               | 10              | 0.32±0.09                     | 0.27±0.006                   | <0.001  |
| Biovotion Everion        | arm      | 5               | 12              | 0.37±0.10                     | 0.29± 0.0017                 | <0.001  |
| Activinsights GENEActive | wrist    | 4               | 12              | 0.38±0.09                     | 0.30±0.007                   | <0.001  |

**Table 2. Signal quality index (Rate of Amplitude Change),  $SQI_{RAC}$  for EDA data from 2 devices; Empatica E4, and Biovotion. Acceptable quality data compared with recorded noise. The  $SQI_{RAC}$  is between -10% and 20% for good data. Amplitude change of more than a 20% increase (positive values) or 10% decrease (negative values) per second, are caused by artifacts and are often correlated with subject motion**

| Device            | Location | No. of patients | Duration (days) | Amplitude threshold (normal) | $SQI_{RAC}$<br>avg ±std % (good) | $SQI_{RAC}$<br>avg ±std % (marginal) | Average percentage of marginal + noise segments per minute | P-value |
|-------------------|----------|-----------------|-----------------|------------------------------|----------------------------------|--------------------------------------|------------------------------------------------------------|---------|
| Empatica E4       | wrist    | 5               | 16              | SC>0.05μS                    | 2.05±3.18<br>-1.28±1.67          | 124.9±458.2<br>-30.9±22.7            | 35.77                                                      | <0.05   |
| Biovotion Everion | arm      | 5               | 6               | SC> 0.047mS                  | 1.17±1.47<br>-1.08±1.1           | 56.11±50.34<br>-26.18±15.58          | 87                                                         | <0.001  |

**Table 3: Spectral Entropy for PPG data (SQI<sub>SE</sub>) from Empatica E4, Biovotion and Byteflies**

| Device                  | Location | No. of patients | Duration (days) | SQI <sub>SE</sub><br>avg ±std<br>(good) | SQI <sub>SE</sub><br>avg ±std<br>(marginal) | SQI <sub>SE</sub><br>avg ±std<br>(noise) | P-value |
|-------------------------|----------|-----------------|-----------------|-----------------------------------------|---------------------------------------------|------------------------------------------|---------|
| Empatica E4             | wrist    | 5               | 14              | 0.56 ± 0.16                             | 0.82 ± 0.10                                 | 0.98 ± 0.02                              | <0.001  |
| Biovotion<br>Everion    | arm      | 5               | 2               |                                         |                                             |                                          |         |
|                         |          | Green*          |                 | 0.53± 0.13                              | 0.76± 0.2                                   | 0.97± 0.01                               | <0.001  |
|                         |          | Infrared        |                 | 0.79±0.12                               | 0.85±0.06                                   | 0.97± 0.01                               |         |
|                         |          | Red             |                 | 0.92±0.09                               | 0.91±0.06                                   | 0.97± 0.01                               |         |
| ByteFlies<br>Sensor Dot | chest    | 5               | 4.5             |                                         |                                             |                                          |         |
|                         |          | Infrared*       |                 | 0.59±0.14                               | 0.77±0.11                                   | 0.98 ± 0.02                              | <0.001  |
|                         |          | Green           |                 | 0.58±0.13                               | 0.74±0.12                                   | 0.98 ± 0.02                              |         |
|                         |          | Red             |                 | 0.64±0.13                               | 0.80±0.09                                   | 0.98 ± 0.02                              |         |

\*Data quality was scored by reviewers for one PPG channel, and scores were applied to the remaining channels.

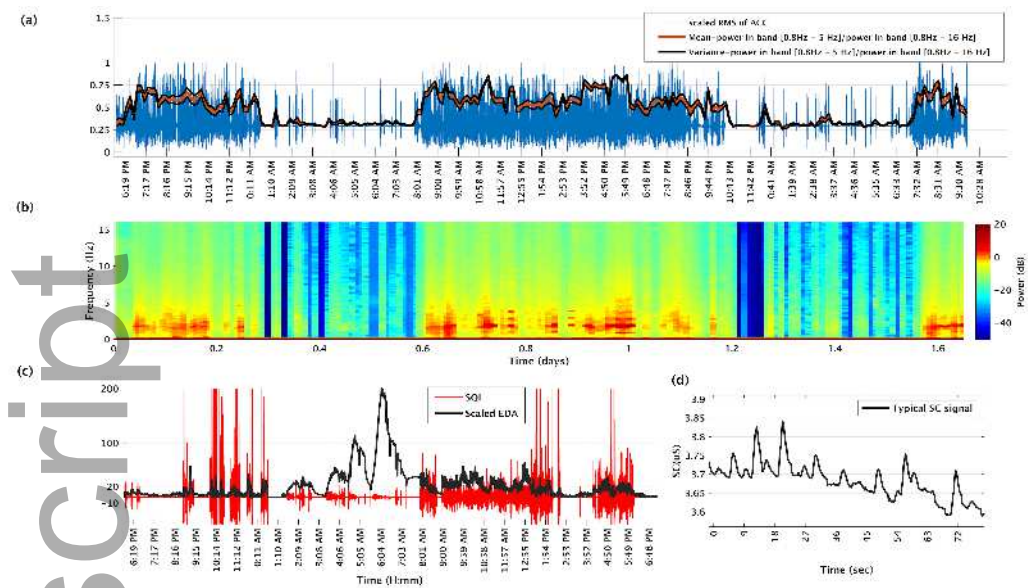
**Table 4: Demographics of patients' survey respondents.**

|                                  |            |
|----------------------------------|------------|
| Total patients                   | N = 70     |
| <i>N (%) using one device</i>    | 25 (35.7%) |
| <i>N (%) using &gt;1 devices</i> | 45 (64.3%) |
| Female (%)                       | 41 (58.6%) |
| Age group - N, (%)               |            |
| <20                              | 11 (15.7%) |
| 20-29                            | 22 (31.4%) |
| 30-39                            | 15 (21.4%) |
| 40-49                            | 9 (12.9%)  |

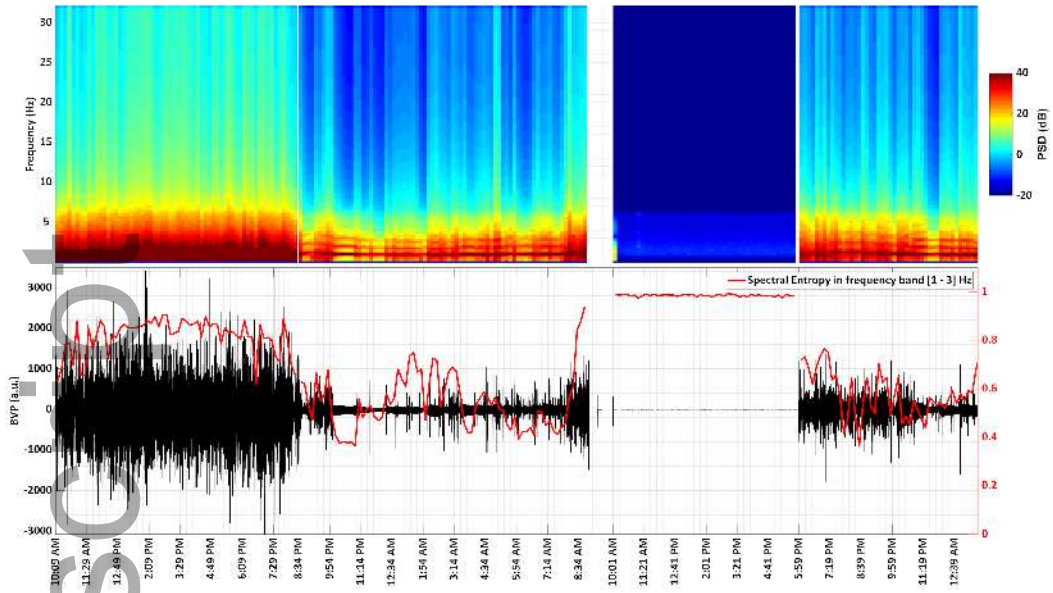
|       |           |
|-------|-----------|
| 50-59 | 8 (11.4%) |
| 60-69 | 5 (7.14%) |

**Table 5: Patient survey results. Values are mean results from 7-point Likert scale: 1- Strongly Agree, 4-Neutral, 7-Strongly Disagree. Bold indicates best result per column.**

| Device                  | Times used (N) | Preferred Device (N) | Preferred Device (%) | Easy to Manipulate | Usable      | Long-term comfort | Comfort During Sleep | Would use for seizure prediction |
|-------------------------|----------------|----------------------|----------------------|--------------------|-------------|-------------------|----------------------|----------------------------------|
| Biovotion Everion       | 9              | 1                    | 11%                  | <b>1.00</b>        | <b>1.00</b> | 3.00              | 1.33                 | 1.67                             |
| Empatica E4             | 40             | 19                   | <b>48%</b>           | 1.82               | 2.25        | 1.89              | 2.14                 | 1.75                             |
| ByteFlies Sensor Dots   | 14             | 3                    | 21%                  | 2.67               | 2.67        | 2.33              | 2.33                 | <b>1.33</b>                      |
| Activinsights GENEActiv | 15             | 4                    | 27%                  | 1.20               | 1.20        | <b>1.00</b>       | <b>1.20</b>          | 1.80                             |
| Epitel Epilog           | 18             | 2                    | 11%                  | 1.50               | 2.25        | 2.00              | 1.75                 | 3.50                             |



epi\_16527\_f1.tiff



epi\_16527\_f2.tiff