UNIVERSITY OF SYDNEY

DOCTORAL THESIS

Long-term monitoring of respiratory metrics using wearable devices

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School Biomedical Engineering

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Declaration of Authorship

I, Joseph Barry Yoo Sik PRINABLE, declare that this thesis titled, "Long-term monitoring of respiratory metrics using wearable devices" and the work presented in it are my own. I confirm that:

- This work was done wholly or mainly while in candidature for a research degree at this University.
- Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated.
- Where I have consulted the published work of others, this is always clearly attributed.
- Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work.
- I have acknowledged all main sources of help.
- Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself.

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Date:

UNIVERSITY OF SYDNEY

Abstract

Faculty of Engineering
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Doctor of Philosophy

Long-term monitoring of respiratory metrics using wearable devices

by Joseph Barry Yoo Sik PRINABLE

Recently, there has been an increased interest in monitoring health using wearable sensors technologies however, few have focused on breathing. The utility of constant monitoring of breathing is currently not well understood, both for general health as well as respiratory conditions such as asthma and chronic obstructive pulmonary disease (COPD) that have significant prevalence in society. Having a wearable device that could measure respiratory metrics continuously and non-invasively with high adherence would allow us to investigate the significance of ambulatory breathing monitoring in health and disease management.

The purpose of this thesis was to determine if it was feasible to continuously monitor respiratory metrics. To do this, we identified pulse oximetry to provide the best balance between use of mature signal processing methods, commercial availability, power efficiency, monitoring site and perceived wearability. Through a survey, it was found users would monitor their breathing, irrespective of their health status using a smart watch. Then it was found that reducing the duty cycle and power consumption adversely affected the reliability to capture accurate respiratory rate measurements through pulse oximetry. To account for the decreased accuracy of PPG derived respiratory rate at higher rates, a long short-term memory (LSTM) network and a U-Net were proposed, characterised and implemented. In addition to respiratory rate, inspiration time, expiration time, inter-breath intervals and the Inspiration:Expiration ratio were also predicted. Finally, the accuracy of these predictions was validated using pilot data from 11 healthy participants and 11 asthma participants. While percentage bias was low, the 95% limits of agreement was high.

While there is likely going to be enthusiastic uptake in wearable device use, it remains unseen whether clinical utility can be achieved, in particular the ability to forecast respiratory status. Further, the issues of sensor noise and algorithm performance during activity was not calculated. However, this body of work has investigated and developed the use of pulse oximetry, classical signal processing and machine learning methodologies to extract respiratory metrics to lay a foundation for both the hardware and software requirements in future clinical research.

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List of Abbreviations

COPD	Chronic Obstructive Pulmonary Disease
I:E Ratio	Inspiration:Expiration Ratio
ECG	Electrocardiogram
FFT	Fast Fourier Transform
IBI	Inter-breath interval
LSTM	Long short-term memory
PPG	Photoplethsmograph
RR	Respiratory rate
RTV	Relative tidal volume
Texp	Expiratory Time
Tinsp	Inspiratory Time
U-Net	U-shaped Network

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Chapter 1

Introduction

1.1 Introduction

Recently, there has been an increased interest in monitoring health using wearable sensors technologies however, few have focused on breathing. The utility of constant monitoring of breathing is currently not well understood, both for general health as well as respiratory conditions such as asthma and COPD that have significant prevalence in society. Once- to twice-daily measurements of peak flow are used for diagnosis and monitoring in asthma, whereas changes in respiratory rate show promise in detecting onset of exacerbations in COPD. In this thesis, "wearables" refer to devices which can be worn about the user's person/body, and "wearable technology" refers to the technology involved in making such a device possible. Having a wearable device that could measure respiratory metrics continuously and non-invasively with high adherence would allow us to investigate the significance of ambulatory breathing monitoring in health and disease management.

1.2 Aims and Research Questions

The aims of this thesis are to:

1. Identify potential wearable technology to continuously monitor respiratory metrics.
2. Investigate signal processing methods to allow extraction of breathing metrics.
3. Present use of a machine learning framework that that overcomes the limitations of classical signal processing methods.

The research questions are as follows:

- Research Question 1: What wearable sensor technologies are available for acquiring respiratory signals and what signal processing methods exist to extract respiratory signals from sensor technologies?
- Research Question 2: What is the rationale for potential users, both with and without respiratory disease, to adopt new technologies that continuously monitor breathing over time?
- Research Question 3: What are device-specific attributes that would meet the expectation of users, both with and without respiratory disease?
- Research Question 4: What are computing hardware limitations of using a pulse oximeter to derived a breathing signal?

- Research Question 5: Is it feasible to use machine learning (recurrent neural network) to predict tidal volume traces from a pulse oximeter?
- Research Question 6: What are the optimum parameters for using single recurrent neural network to predict respiratory metrics in a larger group of healthy individuals?
- Research Question 7: How do two machine learning approaches (recurrent neural networks vs U-Net) perform in predicting respiratory metrics in health and asthma?

1.3 Thesis Overview

This thesis consists of seven chapters as follows:

- Chapter 1 presents the Introduction of this thesis. The Aim, Objectives and Research Questions are presented, followed by the Thesis Overview and List of Publications.
- Chapter 2 (A review paper under consideration by npj digital medicine) presents a review of literature, covering concepts (cost, size, location etc.) of wearable sensors for the continuous measurement of breathing. The relative strengths and limitations of various signal processing methods are compared, particularly those relevant to the derivation of breathing parameters from a photoplethysmograph (Research Question 1).
- Chapter 3 (Prinable et al. a published journal in JMIR Biomedical Engineering [2]) presents an electronic survey of 134 participants used to determine the rationale for adopting new technologies (in asthma and health groups) to continuously monitor breathing over time and evaluate device-specific attributes that would meet their expectations (Research Questions 2 and 3).
- Chapter 4 (Prinable et al. 3 published conference paper IEEE EMBC [3], IEEE LSC [6] and AAPM) presents feasibility and hardware challenges for capturing photoplethsmograph signals, the results of these experiments and discussion [3] (Research Question 4).

  Furthermore, for the first time a LSTM machine learning methodology is presented to extract a relative tidal volume waveform from a pulse signal [6]. A U-Net method was also implemented to investigate the capability to predict a tidal volume waveform up to 5 seconds in the future (AAPM abstract) (Research Question 5).
- Chapter 5 (Prinable et al. a published journal in JMIR uHealth mHealth [7]) presents measurements captured in a respiratory laboratory from healthy participants, a machine learning framework (LSTM) for extracting breathing signals and indices, the results of these experiments and discussion (Research Question 6).
- Chapter 6 (Prinable et al. a published letter in Biosensors [**?**]) presents clinical measurements on both healthy and asthma participants and compares the performance of LSTM and U-Net machine learning methodologies, the results of these experiments and discussion (Research Question 7).

- Finally, Chapter 7 concludes overall studies from chapter 1 to chapter 6. The answers to the research questions are summarised, the study limitations are explained, the impact of the thesis is discussed, and recommendations of future work are provided. A future research plan to conduct further longitudinal studies is also presented.

1.4 External Publications

During this work I collaborated on several different projects accumulating in several publications. The summary of external collaborations and papers during this thesis is listed below:

- Cochlear (2 months): Investigate a novel mixing formula for permittivity and conductivity of cortical bone IOP BPEX (Prinable et al. [6])
- Dolby Digital (6 months): Investigate hardware failures in microspeakers, generated an internal document that influenced future R&D.
- ACRF Image X (1 year): Investigate long range prediction of respiration for gating radiotherapy devices (Accepted abstract for AAPM 2020). Created novel carotid artery hardware in support of new radiotherapy methodologies [7].
- USYD Physics: Designed of a blood pressure wearable using novel fibre optics [8].
- USYD Biomedical Engineering: Provided guidance on methodology and analysis for two conference papers [9, 10].
- COVID19 workgroup (USYD engineering): Provided advice on how a respiratory related wearable could support COVID19 identification (Paper under review in Nature Biotechnology).

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Chapter 2

Background

2.1 Introduction

This chapter formally introduces the clinical rationale for measuring respiratory related metrics for asthma and health, the respiratory metrics that can be captured and explores different sensor technologies, monitoring sites and signal processing techniques to monitor respiratory metrics. This chapter presents a literature review designed to answer the following research question:

- Research Question 1: What wearable sensor technologies are available for acquiring respiratory signals and what signal processing methods exist to extract respiratory signals from sensor technologies?

Chapter 2 consists of a submitted journal manuscript and is undergoing formal peer review at nature partner journal digital medicine.

Statement of Contributions of Joint Authorship:

- Joseph Prinable (Candidate): corresponding author, providing the main idea, writing, reviewing and editing of the manuscript.
- Peter Jones (Alternate Supervisor): proof reading, reviewing and editing the manuscript.
- David Boland: reviewing the manuscript.
- Alistair McEwan (Principle Supervisor): reviewing the manuscript.
- Paul Young: reviewing the manuscript.
- Euan Tovey: reviewing the manuscript.
- Cindy Thamrin (Alternate Supervisor and lead author): proof reading, reviewing and editing the manuscript.

2.2 Clinical Rationale

Monitoring respiratory signals, especially breathing rate, is an important indicator of health status in the intensive care or sleep setting, providing an opportunity for lifesaving interventions or aiding in the diagnosis of sleep disorders. The breathing pattern may be useful for a clinician's evaluation of a respiratory patient, but breathing metrics are not commonly used, hampered by the availability of technologies for continuous, non-obtrusive monitoring of breathing. Long-term monitoring of lung

health using the "Gold standard" of spirometry/peak flow is possible at home, and even has the potential to assess and predict acute exacerbations and treatment response [1, 2, 3, 4]. However, these measures are usually only performed a couple of times a day, rather than being a continuous, unobtrusive method of monitoring disease. In COPD, respiratory rate and pulse rate are sensitive predictors of upcoming exacerbations, thus enabling early intervention to reduce rate and length of hospitalisation. However again, these studies are based on once- or twice-daily measurements [5, 6, 7, 8]. Developing a wearable device that is capable of continuously monitoring (or monitoring at fixed moments in time) a variety of lung function metrics would enable the investigation of clinical utility in ambulatory monitoring in asthma and/or in younger populations including children. These issues are expanded and analysed in depth in the submitted manuscript to npj digital health, "Continuous respiratory monitoring using wearable technologies: a review".

2.3 Breathing Metrics

Outside the clinical setting it is only possible to continuously record relative measures of many respiratory metrics since specialised equipment required for absolute measures are not suitable for day-to-day use due to their non-passive and obtrusive nature. There are a wide variety of tidal breathing indices/ratios that could be captured. These include respiratory rate (RR), the amount of breaths per minute, inspiratory time (Tinsp), expiratory time (Texp), inter-breath interval (IBI), respiration ratio (Tinsp/Texp), duty cycle (Tinsp/IBI), and relative tidal volume (RTV). From these metrics it may also be possible to determine relative airflow, relative tidal breathing flow-volume loops, and relative end-expiratory lung volume.

2.4 Sensors and Signal Processing Methods for Respiration Monitoring

Out of the modalities examined, respiratory bands and pulse oximetry may offer the best combination of merits in terms of their ability to capture multiple accurate respiratory metrics using mature signal processing methods, commercial availability, power efficiency and monitoring site / perceived wearability. Modalities such as microphones, bone conduction or bio-impedance may be less commercially available or wearable, and all except for bio-impedance offer good to excellent power efficiency, but these technologies may evolve to address these issues. In the next chapter the motivations and key features of a wearable to monitor respiratory metrics of potential users to see if the current technologies are feasible for long term studies are explored.

In 2016, Charlton et al. [1] compared the performance of a combination of several algorithms (using both PPG and ECG signals) including Fast Fourier Transforms (FFT), wavelet transforms, multistage band-pass filters, and adaptive frequency estimators. Extracting respiratory signals based on baseline wander, amplitude modulation and frequency modulation, each coupled with 'Count-orig' breath detection [10] and joined together with Smart fusion [11] yielded 95% LOAs of -5.1 to 7.2 bpm and bias of 1.0 bpm. One explanation for these results is that the underlying mechanism which superimposes respiratory motion on the cardiac waveform tends to decouple at higher respiratory rates [12]. The accuracy of deriving respiratory rate

can further be increased by accurately identifying peaks and troughs [13] and implementing a respiratory signal quality index [14, 15] to select only high fidelity data points for reporting.

In Chapter 4 a machine learning method to help mitigate against this mechanism is proposed. Charlton et al. suggests that ECG rather than PPG is a better method to extract respiratory rate with 95% LOAs of -4.7 to 4.7 bpm and bias of 0 bpm. In the next chapter the user requirements for a wearable device to determine feasibility of PPG vs ECG based wearables are explored.

2.5 Concluding Remarks

In this chapter the clinical rationale for monitoring breathing was formally introduced and breathing metrics that could be continuously monitored were identified. Further, sensors and signal processing techniques available to continuously monitor breathing in a ambulatory setting were critiqued. Work within this chapter addressed Research Question 1 through a literature review paper. In the next chapter, the motivations of users and key feature preferences of a wearable that can continuously monitoring respiration was identified and linked back to the findings of this chapter.

Continuous respiratory monitoring using wearable technologies: A review

Joseph Prinable, Peter Jones, David Boland, Alistair McEwan, Euan Tovey, Paul M Young and Cindy Thamrin

***Abstract*—Continuous tracking of physical activity and other physiological signals is rapidly attracting interest; however, monitoring respiratory metrics is still not common. Improved technology now has the potential to continuously monitor respiratory related conditions in day-to-day activity and may be useful for general health monitoring and in an ambulatory setting for both healthy and disease populations**

Out of the modalities examined, respiratory bands and pulse oximetry, may offer the best combination of merits in terms of their ability to capture multiple accurate respiratory metrics using mature signal processing methods, commercial availability, power efficiency and monitoring site / perceived wearability.

Modalities such as microphones, bone conduction or bio-impedance may be less commercially available or wearable. However, all except for bio-impedance offer good to excellent power efficiency such that these technologies may evolve to address these issues.

Future work should seek to investigate longitudinal trends in data obtained from these modalities to identify potential utility in long-term monitoring, and/or the ability to detect detrimental changes to patient health and allow timely intervention.

150-250 words

***Index Terms*—respiration monitoring, asthma, COPD**

I. INTRODUCTION

CONTINOUS tracking of physical activity and other physiological signals is rapidly attracting interest. However, real time monitoring of breathing is still not common in either fitness applications in health or day-to-day management of respiratory patients; instead, it is restricted to specialized laboratory or clinical settings. This reflects the fact that currently there are very few established means to monitor breathing signals directly in a continuous, ambulatory manner. The lack of available monitoring technologies in turn restricts the ability to determine the clinical utility of continuous monitoring of breathing, explaining the paucity of research demonstrating such utility. Nevertheless, there is suggestion from retrospective analyses of clinical trial data that monitoring of lung function measures over weeks and months can yield insights into pathology [3-5], and that monitoring of breathing metrics could detect upcoming exacerbations [7].

There is a growing body of work focused on wearable technology and signal processing, with the potential to continuously monitor respiratory related conditions in day-to-day activity. Thus, the purpose of this review is to summarise the development of new wearable sensors and signal processing methods. This review focuses on five types of wearable devices and analyses their potential based on commercial availability, wearability, and the feasibility of signal processing to extract respiratory metrics.

II. RATIONALE FOR MONITORING BREATHING

Monitoring respiratory signals, especially breathing, is an important indicator of general health status in the clinical setting. Within the intensive care unit (ICU), monitoring of oxygenation, ventilation and mechanical lung function has the potential for predicting catastrophes; this provides an opportunity for interventional lifesaving measures. The analysis of continuous measures of airflow and respiratory effort is also used to inform diagnosis of a sleep related disease within sleep studies.

The utility of monitoring respiration in the ambulatory setting (i.e. outside of clinical setting) is less established. Emerging evidence suggests that respiration monitoring can indicate the degree of perceived physical exertion [10-13] and is linked to a variety of physiological, psychological and environmental stressors [14-16]. This has led to a growing interest in monitoring respiration driven by performance in sports, wellness [18, 19], and for indications of general health status [22]. However, there is still a lack of mainstream monitoring in part due to the lack of commercially available devices.

In respiratory disease, the status of the airways is assessed using the "gold standard" of spirometry. Spirometry measures the volume a subject is able to forcibly expel from the lungs within 1 second (FEV1), the maximum volume of air expelled (forced vital capacity, FVC), and the peak expiratory flow (PEF) [24]. These measures allow the assessment of airway obstruction or lung restriction (via the ratio FEV1/FVC), airway hyperresponsiveness, and diagnosis of diseases such as asthma and chronic obstructive pulmonary disease (COPD) [7]. Long-term monitoring of lung health using spirometry/peak flow is possible at home, and even has the potential to assess and predict treatment response [3, 26-28]. However, there are several limitations: due to the forced manoeuvres involved, not everyone can perform spirometry/peak flow easily, especially patients with severe

obstructive lung disease or contra-indications such as recent surgery or pre-existing conditions; some people can experience faintness or dizziness during testing. The test relies on the ability to follow instructions and is effort-dependent, making it unsuitable for e.g. young children. By its nature it can only be performed a couple of times a day, rather than being a continuous, inobtrusive method of monitoring disease.

A passive, non-obtrusive and continuous measure of lung function, especially respiratory rate, would be highly desirable for ambulatory monitoring of those with a known respiratory disease. Some of the most promising evidence for this comes from COPD, where unlike in asthma, the utility of home monitoring of peak expiratory flow or spirometry is not well demonstrated. Respiratory rate, along with pulse rate, has been shown in several studies to be a sensitive predictor of upcoming exacerbations [7, 31-33], thus enabling early intervention to reduce rate and length of hospitalisation. However, these studies are based on once- or twice-daily measurements from either a stationary pulse oximeter or a home oxygen supply line, hence why utility of breathing metrics is more feasibly demonstrated in COPD patients, who are typically older and less mobile. Creating or modifying devices capable of continuously monitoring a variety of lung function metrics would enable the investigation of clinical utility in ambulatory monitoring in asthma and/or in younger populations including children.

III. BREATHING METRICS

In the ICU, respiratory rate, volume and pressure are critical to determine and titrate ventilation settings [36]. In sleep studies, excursions in the airflow trace are used to determine partial and total pauses in breathing, for the diagnosis of e.g. obstructive sleep apnea [38, 39]. Relative tidal volume excursions of the thorax and abdomen can provide information on breathing asynchrony. In asthma, short-term breathing metrics have not proven useful in clinical monitoring during an acute exacerbation [40]. In COPD, increased respiratory rate showed high sensitivity and specificity in predicting hospitalization within 48 hours [7]. Tidal breathing flow-volume loops (TBFVL) have been used to classify disease state in infants, and relative measures could be derived from the captured signals aforementioned [7, 42-44]. For infants and neonates, end-expiratory lung volume is highly dynamic, providing us with an indication of health or disease. Advanced analyses of tidal volume and inter-breath intervals show specific patterns [47] which change with maturation [48] and show evidence of system "resetting" during sighs [56].

Outside the clinical setting it is only possible to continuously record relative measures of many respiratory metrics since specialised equipment required for absolute measures are not suitable for day to day use due to their non-passive and obtrusive nature. There are a wide variety of tidal breathing indices/ratios that could be captured. These include respiratory rate (RR), the amount of breaths per minute, inspiratory time (Tinsp), expiratory time (Texp), inter-breath interval (IBI), respiration ratio (Tinsp/Texp), duty cycle (Tinsp/IBI), and relative tidal volume (RTV). From these metrics it may also is possible to determine relative airflow, relative tidal breathing flow-volume loops, and relative end-expiratory lung volume.

IV. MEASUREMENT MODALITY

Here we present five modalities that could be used for long-term monitoring of respiratory metrics: microphones, bone conduction, bio impedance, pulse oximetry as well as respiratory bands. We directly compare these modalities to illuminate their potential for adoption.

A. Contact Microphones

A variety of contact microphones have been used to capture respiratory related sounds [59, 60] from which relative measures of airflow can be derived [34, 61, 62]. In addition to measures of flow, both the inspiration and expiration period can be derived [63-65].

It has been suggested that the right thorax region in the seventh intercostal space and the trachea are optimal monitoring sites [66]. However, other sites have also been proposed such as either side of the spinal cord 3 cm below the bottom tip of the shoulder blades [67].

Breathing sounds typically occur in the frequency band from 200 Hz to 800 Hz [68] with sound intensity being flow rate dependent [69], microphone type and recording site [35, 70]. Respiratory signals are typically recorded at 44.1 kHz down sampled to 16 kHz, which is standard practice to reduce the computational requirements of a signal processing unit without loss of core information [67].

Current signal processing related challenges lie with filtering unwanted noise since thoracic lung sounds fall within the same frequency range as human voice (200 Hz - 450 Hz [71]) and heart sounds (150 Hz superimposed on breathing [1, 72]). A variety of signal processing techniques have been used to remove noise including; wavelets, adaptive filtering with a recursive least squares algorithm, time/frequency filtering, reconstruction, autoregressive / mobile average estimation (ARMA) in time/frequency domain of wavelet coefficients, independent component analysis and the entropy-based method [73]. Of these methods, the best results were obtained with adaptive filtering, time/frequency filtering, and ARMA estimation [74]. Martin et al. used a denoising method to reduce external industrial noise [75]

Reported accuracy for deriving respiratory metrics with microphones is generally high. Larson et al used a microphone from a mobile phone compared to an ATS certified clinical spirometer and found the root mean squared error (RMSE) to be 5.2%, 4.8%, 6.3%, and 4.0% for FVC, FEV1, PEF, and FEV1/FVC, respectively [76]. Yadollahi et al reported that respiratory flow measured from the trachea was within 5% of the flow obtained using a pneumotachograph [34]. However, it should be noted that these studies were conducted on subjects either during sleep or at rest.

B. Bone Conduction Microphones

Bone Conduction Microphones (BCM) capture acoustician transmitted through bone vibrations within the body. Historically, these microphones have been used to acquire speech signals with application to military police and rescue situations [77] for communication in high noise environments [78, 79]. Recently, they have been used to capture respiratory

related signals [80].

Several locations have been suggested including the mandibular condyle and the mastoid process [81, 82], the manubrium of the sternum [83], and the external ear canal [71]. However, the throat was found to give the maximum power (dB) for all types of non-vocal body sounds, except eating [2].

Bone Conduction Microphones in conjunction with other modalities have been shown to improve the accuracy of RR derived from respiratory sounds. The fusion of both electret and bone conduction microphones led to a 94.7% accuracy rate as opposed to without the BCM (78.9%), no details were provided for BCM alone [83]. Given the limited scope of the previous studies it is unclear whether tidal volume or any other respiratory metrics can be extracted.

Unlike contact microphones discussed in the previous section, a wavelet transform of sound captured using a bone conduction microphone reveals that breathing sounds are detected in the 700-1400 Hz frequency range. However, other low frequency noises also can also be observed, indicating that the bone conduction microphone reduces but does not eliminate all background noise [84]. In fact, a constraint in adapting a BCM to a wearable platform is the ability to extract the breathing signal as the amplitude of the recorded time domain signal alone is not sufficient to evaluate breathing since it is within the noise floor. Further signal processing power is required to probe the frequency spectrum identifying spectral power centered near 1 kHz, as the absolute value of the signal intensity fluctuates with breathing. To date, all bone conduction data has been captured and post processed [71, 83], with the exception of work by Rahman et al. who implemented a real-time solution on an embedded device [2].

C. Bio-Impedance

Bio impedance (also known as electrical impedance tomography) refers to the measurement of impedance (Z) presented by a biological medium to the flow of an applied alternating current. An AC current propagates between outer electrodes while a voltage differential is measured across the middle electrodes. Breathing effort can be measured as the lungs expand and contract causing a changing impedance depending on the respiratory phase determined [85]. While the primary focus of this modality has been to measure heart rate variability and pulse wave velocity, a linear correlation was found between bio-impedance and spirometry measurements as early as the 1970s [86]. More recent work has highlighted the feasibility of using this modality to derive respiration rate and tidal volume [9, 87, 88].

Krueger-Ziolek et al examined several electrode placement locations and found that the caudal (6th and 7th intercostal space) may be a better monitoring location than the cranial (3rd and 4th intercostal space). This is due to the close proximity to the diaphragm giving rise to a greater measurable lung tissue shift [6].

The accuracy of a four terminal system bio impedance system was found to have a high respiratory rate correlation ($r = 0.944 \pm 0.999$) to a pneumotach. Pulse rate was also found to have high correlation ($r = 0.971 \pm 0.998$) to a clinical ECG system [89]. Additionally, systolic and diastolic blood pressure has been captured at the wrist with good accuracy [90].

The signal processing chain for a bio impedance device is relatively simple, generally only involving an amplification stage and a band pass filter stage to remove unwanted noise [89]. With the advent of artificial neural networks, there was an improvement over linear models with a mean absolute percentage error improving from 9.08% to 8.74% [91].

D. Pulse Oximetry

Pulse oximeters are provided as a standard of care in most clinical settings to allow clinicians to obtain accurate heart rate and S_pO_2 readings [92, 93]. In pulse oximetry, a light source at both red (660nm) and infrared (940nm) wavelengths propagate through tissue and a photoplethysmogram (PPG) signal is captured via a light dependent resistor [50]. The PPG signal's amplitude, frequency, and baseline are modulated by breathing periodicity [25, 53, 94] and effort [95]. This allows respiratory metrics to be derived [17, 20, 50-55, 57, 58, 94, 96-98].

Several locations have been investigated to determine optimum locations to derive heart rate and SpO2 [99]. In adults the left fingertip [99] showed the strongest strength and for neonates the anterior fontanelle may be the best site [100]. The ear may also be suitable locations for a wearable sensor [101]. However, site suitability for respiratory metrics suggest the forearm and ear region rather than the finger may result in more accurate estimations [102, 103].

Respiratory rate can be extracted with bias of one and with two standard deviations of -5.1 to 7.2 (breaths per minute) [25].

There is a wide body of research detailing how to derive respiratory rate from a PPG. Many studies use a Fast Fourier Transform (FFT) [50-52], wavelet transforms [53-55], multistage band-pass filters [57], correntropy spectral density [20], adaptive frequency estimators digital [58] as well as filtering methods to find respiration rate. These methods have been compared extensively by Charlton et al. and an open source Matlab toolbox is available [25]. Karlen et al "fused" several methods together to yield higher respiratory rate estimates [94, 97]. The same group then ported this fusion to a smart phone, where a camera was able record the pulse and respiration rate was derived [98]. To date, these algorithms have not looked at other respiratory related metrics such as IBI, Tinsp and Texp.

E. Respiratory Belts

Respiratory inductive plethysmography (RIP) uses two belts to determine spontaneous tidal breathing by measuring ribcage and abdomen deformation due to inspiration and expiration phases. RIP offers a benefit over the gold standard of spirometry by reducing the bias associated with breathing through a mask or mouthpiece [104].

Respiratory inductive plethysmography uses two belts, one thoracic and one abdominal. Konno and Mead propose that the chest is a system containing two compartments with one degree of freedom each. As such any volume change in the abdomen must be equal and opposite to the rib cage [105].

Retory et al found the bias to be low at 0.04 L for tidal volume, 0.02 s for inspiration period and acceptable at <0.1 s for expiration period [106]. For inspiratory volumes, RIP generally underestimates volume at the start of inspiration and overestimates volume at the end of inspiration [107]. Additionally, the accuracy of RIP decreases up to 30% from supine to sitting for abdominal breathing [107]. Heyde et al demonstrated that after RIP was calibrated to a flow meter 96% of all breathes were detected within +/-10% of limits of equivalence [108].

Signals can be captured at 200 Hz [29, 30] and passed through a FIR filter 0.2Hz-0.4Hz [41]. On occasion it's noted that a wavelet filter with a 0.5 s sliding window is also used to remove noise [45].

F. Other modalities

Other technologies have been used for monitoring of respiratory rate, for e.g. smart T-shirts have used a number of different novel modalities such as flex sensors [109-111], near-field coherent sensing [Wearable radio-frequency sensing of respiratory volume, and heart rate] and carbon black elastomers [112]. An example is Hexoskin that has been shown to valid and reliable with 1-6% error for respiratory rate in a small elite cyclist cohort [110]. These are emerging technologies and as such are not included for comparison; larger studies cohorts are required to determine the optimum flex sensor design, long term smart T-shirt durability and compliance.

V. FEATURES RELEVANT TO WEARABLE MONITORING OF BREATHING

As with any technology, there are trade-offs associated with each modality listed. Here various factors are relevant to continuous monitoring of breathing; the ability to capture a wide range of metrics will enable researchers to study and determine which breathing features have the highest sensitivity or specificity for a particular disease or application (however, this may increase signal processing complexity). Increasing the complexity of the signal processing toolchain may represent a drain on finite battery or computational resources. Selection of a specific measurement site that allows more difficult metrics to be captured may also reduce user compliance due to discomfort. Decreasing the cost of the modality means reducing the quality and features available.

Our analysis was split into several themes which are shown in Table I. In the Table of Merit, a score of 1-3 was subjectively assigned for low, medium and high respectively with the analysis of each theme discussed in more depth. Note that this represents the current state of the art of each technology, which may evolve over time,

A. Ability to capture multiple respiratory metrics

All the modalities explored can obtain continuous measures of respiratory rate. Microphones can capture relative measures of airflow and direct measures of inspiration and expiration period. From these metrics' derivation of relative measures of tidal volume, TBFVL, and IBI are achievable. It is unclear if bone conduction microphones can sufficiently extract other respiratory metrics. Bio-impedance, pulse oximeters and respiratory bands all capture relative measures of tidal volume. From this signal, all other metrics are able to be ascertained.

TABLE I
TABLE OF MERIT

Modality	Microphones	Bone conduction	Bio impedance	Pulse oximetry	Respiratory bands
Ability to capture multiple respiratory metrics	High	Low	Medium	High	High
Accuracy to derive respiratory metrics	Medium	Medium	Medium	Medium	High
Maturity of signal processing methods	High	Low	Medium	High	High
Commercial availability	Low	Low	Medium	High	High
Power efficiency	High	High	Low	Medium	High
Monitoring site/ perceived wearability	Low	Low	Medium	High	Medium
Total score	72% (13/18)	50% (9/18)	62% (11/18)	89% (16/18)	94% (17/18)

Each modality in all categories was scored either high (3 points), medium (2 points) or low (1 point).

B. Accuracy to derive respiratory metrics

In general, all modalities show promising feasibility in terms of accuracy when the signals are captured under ideal, stationary conditions. Respiratory belts which directly measure thoracic movement have the highest accuracy for capturing respiratory metrics and are clinically established as the gold standard in sleep studies.

It is critical to highlight however that accuracy reduces when motion is not constrained, which is the case with usual human behaviour. While it is possible to reduce power consumption and acquire repeated measures during periods of no motion, further investigation is required to determine if this achieves satisfactory outcomes. Noise can be reduced by either an accelerometer and adaptive FIR filters or through quadrature-based methods [113]. The former requires many filter weights to be continuously updated, while the later requires only two per frequency. Both methods require additional hardware.

Another issue pertaining to these systems is the trade-off between accuracy and wearability. A bioimpedance system with 16 electrodes will yield a higher accuracy than a four-electrode system, however, setup complexity and associated

cable interference may inhibit uptake.

TABLE II
SIGNAL PROCESSING PIPELINE FOR DIFFERENT MODALITIES

Modality	Microphones	Bone conduction	Bio impedance	Pulse oximetry	Respiratory bands
Sampling	3.675 kHz [1]	8 kHz [2]	40 Hz [6], 256 Hz [8], 300 Hz [9]	75.7 Hz [17], 100 Hz [20, 21], 125 Hz [23], 500 Hz [25]	200 Hz [29, 30]
Down sampling	N/A	N/A	32 Hz	25 Hz	N/A
Pre-process filtering	0.5Hz – 5 kHz [34], 75-2 kHz [35], low pass @ 100 Hz [37]	N/A		0.006 Hz- 10 Hz [25], HP @0.03Hz[23], LP @5.5Hz [17]	0.2Hz-0.4Hz [41], 0.5 s sliding wavelet filter [45]
Extraction of respiratory metrics	FFT based [1, 35, 37, 46]	Linear Discriminant Classifier [2]	DFT [49]	Fast Fourier Transform (FFT) [50-52], wavelet transforms [53-55], multistage band-pass filters [57], Correntropy spectral density [20], adaptive frequency estimators digital [58]	N/A

C. Maturity of signal processing methods

A direct comparison between modalities show comparable accuracy, however the sample size of participants used in the various studies was very different. This could be an indicator of the maturity within the research area. For example, only a handful of studies have been undertaken with bone conduction. Perhaps this is due to difficulty of extracting respiratory metrics combined with the limited and high cost of hardware. In contrast, the accuracy of readily available, and cheaper, microphones have been validated in larger cohorts consisting of over 200 participants, as has pulse oximetry.

Long term monitoring of physiological signals presents a variety of challenges throughout the signal processing pipeline. A typical signal processing pipeline for each of the modalities is presented in Table II.

Audio captured with air conducting or bone conduction microphones are typically sampled at high rates and issues arise with the ability to capture and process the corresponding quantity of data at speed with energy efficient devices. To date, small wearable technologies do not have the necessary compute power to support this modality in real-time, though this may become feasible with advances in FPGA technology. In comparison, bio impedance with a significantly lower sample rate can use Bluetooth technology to offload processing to a smart phone [114]. On the other hand, smart watches with embedded pulse oximeters have sufficient compute power to both capture and process the PPG-derived respiratory signals.

In most cases pre-process filtering is used to remove baseline wander and other unwanted signals. As a consequence, there is an added delay, however, it is unclear if this will have a material influence when determining correlation between respiratory metrics and health outcomes. Typically, a pulse oximeter is used to derive Sp02 and both a low pass filter and automatic gain control (AGC) is implemented in specialised hardware, however, using this hardware does not facilitate the accurate extraction of respiratory metrics.

Extraction of respiratory metrics using microphone, bone conduction and bioimpedance require FFT and DFT, and can be implemented with a low cost system on a chip (SOC) as well as highly optimised software implementations. Conversely, there has been significant effort to develop algorithms that extract respiratory metrics from a PPG. Perhaps one area of concern is that the underlying mechanism that superimposes respiratory motion on the cardiac waveform tends to decouple at higher respiratory rates, and this would need to be addressed in future work, potentially using machine learning. However, similar to FFT and DFT implementations, these algorithms can be run in real time on low cost wearable hardware to facilitate long terms studies using this modality.

D. Power efficiency

All five modalities require power to operate and it is important to be aware of the power requirements in a wearable context, since battery life is finite. Perhaps the most power efficient modality is an off-the-shelf MEMS microphone requiring only 16 μW at 1V [115] due to its passive nature. Respiratory belts offer similar efficiency with a power consumption of 75 μA [116]. Other modalities such as a bioimpedance system captures respiratory response in response to a known input signal [8]. While such devices initially required 1.3 mA to inject 100-350 mA [117], there have been improvements which have reduced this to consuming 270 μA to inject 250 μA [118]. Similarly, a pulse oximeter also relies on a non-passive sensor. In order to meet the low energy requirements of a long-term monitoring wearable, the LED current pulses can be reduced, while still retaining sufficient quality of PPG signal [119-121]. With improvements to microelectronics, it is likely that power efficiency will continue to improve. One area that facilitate wearables is battery technology and it is likely that this too will continue to improve in the future.

E. Monitoring site

The monitoring site that yields the highest quality respiratory signal should not be the single motivating factor. It is also important that the location should be selected such that it is not stigmatising, doesn't affect normal daily behaviour and has a minimal risk of detaching, to increase user compliance [122]. There is evidence of compliance with patch-based devices on the chest [123] which gives rise to the potential implementation of microphones, bioimpedance systems and respiratory belts. Conversely, smart watches have also high compliance rates for long term monitoring, with the majority of missed data capture due to times where the devices were removed for charging [124]. Prinable et al., report that that wrist worn devices are more desirable than other methods [22]. Locations such as the neck and ear, that yield high quality signals for microphones and bone conduction, are potentially unfeasible due to their conspicuous nature, though this may change over time as the technology matures to take

advantage of formats such as wireless in-ear devices (e.g. Apple Airpods) which are gaining popularity.

F. Commercially available modalities

While there are a variety of modalities that show potential to provide long term monitoring of respiratory metrics, many are still in their infancy in terms of commercial availability. To date, several commercial devices exist with larger technology companies such as Fitbit, Apple, Garmin, Withings and Samsung, adding pulse oximeters to smart watches in attempt to capture an emerging target market segment of health and fitness enthusiasts. Of these products only Garmin provides continuous measures of respiration rate. To date, there are no commercially available bone conduction modalities on the market that monitor physiological signals. Meanwhile, Microsoft backed BodyScope technology based on microphone technology for respiratory rate capture, but unfortunately the product failed to come to market. EKO health has released an FDA approved microphone-based product for COVID19 patient monitoring, but it is only suitable for repeat measures. Furthermore, it requires user intervention for respiratory sound capture, as opposed to continuous monitoring. TomTom and Jawbone released commercial watches that make use of bio impedance technologies, though they only measure pulse and not respiration metrics. There are several companies that make CE approved respiratory straps including Phillips and Polar. Additionally, in the recreation and sport space Vernier Go Direct and BIOPAC have also developed commercial products.

G. Implications of current wearable technology to ambulatory monitoring

Both respiration bands and wrist worn pulse oximeters show promise for ambulatory monitoring. There are several implications for wearable technology in an ambulatory setting.

Firstly, these devices may be useful for those with sleep related disorders to determine partial and total pauses in breathing and may provide feedback on how interventions effect quality of sleep.

In asthma cohorts where repeat measures of peak expiratory flow were found to be an indicator for deterioration of lung function, these bands provide the capability to explore other metrics that may require less user interaction than a home monitoring setup and still provide indicators of health.

In health, monitoring respiration metrics may yield further insight into performance gains in sports, wellness, and for indications of general health status.

In particular, the high compliance in smart watch users is allowing general population trends to be uncovered. Data from 200,000 fitbit users linked season flu patterns to increased resting heart rate and increased sleep levels [125]. Of note, changes to respiratory rate measured during the night may be an early predictor of COVID19 [126]. Another area that smart watch technology could be implemented is in children where continuous measures are difficult. Respiratory is a more accurate predictor of clinical deterioration in children than other vital signs.

CONCLUSION

There are multiple promising technologies currently available for continuous monitoring of respiratory metrics, each with its own trade-offs in terms of accuracy, signal processing and power considerations, commercial availability and wearability. In parallel with the continual development of these technologies, the key motivations and user preferences of both the clinician and the device wearer need to be established. In the latter case, factors around device size, weight, location, and cost need to be identified so that high user compliance rates can be achieved; for example, previous work suggest users prefer smart watch technology, the ability to synchronize breathing data with a mobile phone or tablet, overnight power charging, and a cost of ≤Aus $100 [22].

From a clinical perspective such a study would help motivate longitudinal experimental studies that could further elucidate the efficacy of these modalities [127]. Additionally, and more importantly, future work should seek to identify the benefits of these modalities over repeated clinical measures where a higher degree of accuracy could be attained. Potentially, any reduction in the accuracy of specific measures such as respiratory rate obtained from a wearable platform could be accepted, to a degree, if the underlying longitudinal trends in data obtained from such a platform could flag potential detrimental changes to patient health and allow adequate time to intervene prior to hospitalisation.

There have been considerable advances in technology that can allow the continuous monitoring of respiratory metrics. Overall respiratory bands and to a slightly lesser degree smart watch technology with embedded pulse oximeters seem to offer the best compromise between capturing multiple accurate respiratory metrics using mature signal processing methods, commercial availability, power efficiency and monitoring site/ perceived wearability.

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Chapter 3

User Motivations and Device Preferences for Monitoring Breathing with Wearable Technologies

3.1 Introduction

In the previous chapter it was identified that a plethora of sensors could be utilised for respiratory rate monitoring dependent on potential monitoring sites, power constraints, and size. This chapter explores the willingness of people to adopt new wearable technologies for the express purpose of monitoring breathing. In addition we highlight the device features that are important to the user. This chapter presents a user survey designed to answer the following research questions:

- Research Question 2: What is the rationale for potential users, both with and without respiratory disease, to adopt new technologies that continuously monitor breathing over time?
- Research Question 3: What are device-specific attributes that would meet the expectation of users, both with and without respiratory disease?

Chapter 3 consists of a published peer-reviewed article which is reproduced under the terms of Creative Commons Attribution 4.0 licence:

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Statement of Contributions of Joint Authorship:

- Joseph Barry Yoo Sik Prinable (Candidate): corresponding author, providing the main idea, writing, reviewing and editing of the manuscript.
- Juliet Foster: proof reading, reviewing and editing the manuscript.
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3.2 User Survey

A survey was completed by 134 participants (males: 39%, median age group: 50-59 years, asthma: 57%). Of those who completed the Asthma Control Test, 61% (47/77) had suboptimal asthma control. Of the 134 participants, 61.9% (83/134) would be willing to wear a device to monitor their breathing, in contrast to 6.7% (9/134) who would not. The remaining 31.3% (42/134) stated that their willingness depended on specific factors. Regardless of whether or not they were willing to use a wearable, participants were asked to indicate one or more factors that would make them consider using a wearable. Out of all participants, more people who did not have asthma indicated "curiosity" (23%, 13/57 vs 10%,7/77; P=.028) or "I would like to track my performance during exercise" (30%, 17/57 vs 10%, 8/77; P=.004) as a motivating factor to wear the device than those with asthma. Participants with asthma most commonly cited their asthma as motivation for using a wearable; the most common motivation for use in those without asthma was curiosity. More than 90% of total participants would use the device during the day, night, or both day and night.

Design preferences among all users included a wrist watch (nominated by 92.5% [124/134] for both day and night use, out of four body sites), the ability to synchronize breathing data with a mobile phone or tablet (81.3%, 109/134), overnight power charging (33.6%, 45/134), and a cost of $\leq$ Aus$100 (53.7%, 72/134). Of the explored modalities in the previous chapter, pulse oximetry, ECG, and bio impedance may be suitable as a sensor within a wrist worn device. Interestingly, the more accurate respiratory band was not desired by the user population. Given the prevalence of pulse oximeter sensors embedded in smart watches used to monitor heart rate, it would be useful to leverage off this technology.

In the first instance, it would be useful to record respiratory metrics at several time points during the day in an asthma cohort to identify if they are predictors of hospitalisations or acerbations. However, it is also feasible to extend this to include other disease states or even healthy participants as a method to identify if these respiratory metrics correlate to heart arrhythmias.

3.3 Concluding Remarks

One aim of this thesis was to determine the rationale for participants to adopt new technologies to continuously monitor breathing over time. Work within this chapter addressed the question through a user survey in a group of 134 participants. While a small sample size may not allow conclusions to be drawn across all demographic groups, statistical evidence linking the rationale for device usage to a participant's health condition, age and gender was found. Additionally, participant preferences towards device attributes were identified. However, these preferences present both fiscal, time management and technological challenges for a small engineering research group. In the next chapter, some of these technological challenges are explored.

Original Paper

Motivations and Key Features for a Wearable Device for Continuous Monitoring of Breathing: A Web-Based Survey

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Abstract

Background: Analysis of patterns of breathing over time may provide novel information on respiratory function and dysfunction. Devices that continuously record and analyze breathing rates may provide new options for the management of respiratory diseases. However, there is a lack of information about design characteristics that would make such devices user-friendly and suitable for this purpose.

Objective: Our aim was to determine key device attributes and user requirements for a wearable device to be used for long-term monitoring of breathing.

Methods: An online survey was conducted between June and July 2016. Participants were predominantly recruited via the Woolcock Institute of Medical Research database of volunteers, as well as staff and students. Information regarding the survey, a consent form, and a link to a Web-based questionnaire were sent to participants via email. All participants received an identical survey; those with doctor-diagnosed asthma completed an extra questionnaire on asthma control (Asthma Control Test). Survey responses were examined as a group using descriptive statistics. Responses were compared between those with and without asthma using the chi-square test.

Results: The survey was completed by 134 participants (males: 39%, median age group: 50-59 years, asthma: 57%). Of those who completed the Asthma Control Test, 61% (47/77) had suboptimal asthma control. Of the 134 participants, 61.9% (83/134) would be willing to wear a device to monitor their breathing, in contrast to 6.7% (9/134) who would not. The remaining 31.3% (42/134) stated that their willingness depended on specific factors. Participants with asthma most commonly cited their asthma as motivation for using a wearable; the most common motivation for use in those without asthma was curiosity. More than 90% of total participants would use the device during the day, night, or both day and night. Design preferences among all users included a wrist watch (nominated by 92.5% [124/134] for both day and night use, out of four body sites), the ability to synchronize breathing data with a mobile phone or tablet (81.3%, 109/134), overnight power charging (33.6%, 45/134), and a cost of ≤Aus $100 (53.7%, 72/134).

Conclusions: We have explored the motivations and likelihood for adopting wearable technologies for the purpose of monitoring breathing and identified user preferences for key design features. We found participants were motivated to adopt a wearable breathing monitor irrespective of health status, though rationale for use differed between those with and without asthma. These findings will help inform the design of a user-acceptable wearable device that will facilitate its eventual uptake in both healthy and asthma populations.

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KEYWORDS

asthma; wearable; breathing; e-health

Introduction

Asthma is a serious public health problem affecting over 300 million people globally. Management challenges include the early prediction or warning of asthma attacks and optimizing the pharmaceutical management of the disease.

Monitoring of lung function over time is a widely accepted component of the assessment of asthma, both in clinical management of the disease as well as in research trials [1]. Some studies suggest it may also yield insights into the pathology of respiratory diseases and predict future risk of exacerbations [2-4]. In asthma, monitoring is usually based on standard lung function testing involving forced breathing maneuvers assessed periodically in a specialized respiratory laboratory, or by peak expiratory flow measured in a general practice and then in the patient's home either daily or during periods of worsening symptoms. There is a paucity of research on continuous, real-time monitoring of breathing for general health or for management of asthma or other chronic diseases. This may be due in part to the lack of commercial technology to enable such monitoring in a manner that would be acceptable to users. One study has shown that monitoring respiratory rate could help predict the onset of exacerbations in chronic obstructive pulmonary disease [5]. However, it is not known whether monitoring of breathing could aid diagnosis or monitoring of asthma. Breathing monitoring may also provide rapid feedback to a patient during physical exertion or breathing exercises during exacerbation episodes.

Several studies have investigated desirable features for a wearable device for health monitoring, from both a technical [6] and human-centered [7-11] perspective. These studies have provided guidelines on wearable design [7-9] and determined that user acceptability was dependent on factors such as fundamental needs/demonstrated benefit, enjoyment, and social value [10,11]. However, none of these studies sought to specifically determine the desired features for a wearable device used for long-term respiratory monitoring. At present, there are several modalities and locations on the body identified for respiratory monitoring: the ear, throat region, finger, wrist, and chest [12-14]. In the design and development of a device for this purpose, it is important to first identify, understand, and consider user preferences to increase user acceptance, satisfaction, and engagement [8,15].

The purpose of this study is to (1) explore the reasons why participants with or without asthma would potentially adopt new technologies to monitor breathing over time, and (2) evaluate device-specific attributes that would meet the expectation of users within these two groups. We chose to additionally study healthy individuals, not only as a basis for comparison with those with asthma to identify those preferences that are specific to asthma, but also due to the increasing interest in personal health monitoring in the general population as evidenced by the uptake of wearable devices that measure activity and other physiological life signs.

Methods

Study Design and Overview

An online survey was conducted between June and July 2016. A link to the survey was sent electronically to a subset (n=569) of the Woolcock Institute of Medical Research Volunteers Database based on the availability of a valid email address on record, as well as to staff and students at the Woolcock Institute. During the recruitment period, two rounds of recruitment emails were sent to the two lists, followed by a subsequent reminder email for each round. The Volunteers Database consists of members of the public who have previously given consent to be contacted about participation in research. The database comprises both healthy individuals (n=256) as well as those with asthma (n=1173). The exact number reached may differ due to constant additions or withdrawals from the database and the possibility of family members sharing a common email address. Inclusion criteria were (1) provision of informed consent, (2) completion of all responses, (3) no respiratory illness reported (for the healthy group), and (4) self-reported doctor's diagnosis of asthma (for the asthma group). No incentives were offered for participation. The protocol for this study was approved by Northern Sydney Local Health District Human Research Ethics Committee (ethics approval #LNR/16/HAWKE99).

Survey

After clicking on the link to the survey, participants who provided informed consent proceeded to fill out an online questionnaire (see Multimedia Appendix 1) that took approximately 10-15 minutes to complete. The survey was designed to assess participant's current use of technology, to explore their readiness to use a wearable, and to understand their attitude toward the potential usefulness of wearable technologies for monitoring breathing. Specifically, the survey aimed to identify usage preferences (eg, how long the user wishes to wear the device during the night/day) and feature preferences, such as the device form factor (eg, band, sticky patch, earpiece), body location (eg, wearable for neck, chest, ear, wrist), display, charge time, and price.

The survey also included demographic questions such as age, gender, educational and socioeconomic status, and doctor-diagnosed health conditions. Those who reported having a doctor diagnosis of asthma completed the Asthma Control Test (ACT) [16], a well-validated scale [17], which comprises five questions that assess asthma symptoms, use of medication, and the effect of asthma on daily functioning to determine overall asthma control status. The total score ranges from 5 (poor control of asthma) to 25 (complete control of asthma); a score of ≤19 indicates suboptimal control.

Statistical Analyses

Participant demographics were summarized using descriptive statistics. Results were compared between participants with self-reported doctor-diagnosed asthma versus those without

asthma, using *t* tests or Wilcoxon signed rank sum test depending on whether the data were normally distributed. Participants who were "unsure" of their asthma status were grouped with those participants without asthma. Questionnaire responses were compared between asthma and no asthma, between gender, and between age groups using chi-square tests. Statistical analyses were performed using SPSS v. 23 (IBM Corp.), and graphs were generated using Prism v. 7 (GraphPad Software Inc.).

Results

Demographics

In total, 156 participants responded but 2 did not provide informed consent and 20 failed to complete more than 50% of the survey and were omitted from analysis. Of the 134 participants who completed the survey (ie, 85.9% completion rate), 131 provided demographic information as shown in Table 1. Just under a third (29.1%, 39/134) of participants were male, and nearly two-thirds (60.0%, 79/134) had a university education. More than 10 participants were obtained in each age group. The average time to complete the survey was 13 minutes.

A total of 61.2% (76/134) participants reported doctor-diagnosed asthma: mean (SD) ACT score was 17.4 (5.2). Nearly two-thirds (62%, 47/76) of these had suboptimal asthma control based on the ACT.

Technology and Device Use

Participants demonstrated a high level of technology use: 88.8% (119/134) used a smart phone, 29.9% (40/134) used health monitoring devices such as a Fitbit, and a small percentage of participants used smart watches (5.2%, 7/134). Nearly two-thirds (59.7%, 80/134) used only one form of technology, 26.9% (36/134) used two forms of technology, and 3.0% (4/134) used three or more forms of technology. Examples of other specific technology or gadgets used were fitness trackers (11.9%, 16/134), tablet computers (11.9%, 16/134), music players (3.0%, 4/134), conventional mobile telephones (1.4%, 2/134), and electronic books (1.4%, 2/134). Only 8 participants (5.9%, 8/134) used no "other forms of technology or electronic gadgets". Levels of technology use were similar in those with and without asthma.

Motivation for Wearable Use

Nearly two-thirds (61.9%, 83/134) of the total participants indicated that they would be willing to wear a device to monitor their breathing, 7.4% (10/134) would not, and the remaining 30.5% (41/134) stated that their willingness depended on specific factors, described later in this section. There were no significant differences in willingness to adopt a wearable device for monitoring breathing between the 40 participants who currently used health monitoring devices and the 94 who did not (P=.265). Participants with asthma were more willing to wear a device to monitor their breathing, compared to those without asthma: 70% (54/77) versus 51% (29/57), P=.071.

Regardless of whether or not they were willing to use a wearable, participants were asked to indicate one or more factors that would make them consider using a wearable. These are detailed in Figure 1. Out of all participants, more people who did not have asthma indicated "curiosity" (23%, 13/57 vs 10%, 7/77; P=.028) or "I would like to track my performance during exercise" (30%, 17/57 vs 10%, 8/77; P=.004) as a motivating factor to wear the device than those with asthma.

Females were more likely to use the device to track breathing patterns during stress and meditation compared to men (16%, 15/92 vs 3%, 1/39; P=.003). Females were also more likely to use the device when they get breathless (9%, 8/92 vs 5%, 2/39; P=.002) or if they had a known respiratory disease other than asthma compared to men (8%, 7/92 vs 0%, 0/39; P=.031).

The ability to track breathing patterns during stress and meditation was a more common rationale for device use in younger than older age groups: 18-39 (37%, 7/19), 30-39, (4%, 1/27), 40-49 (13%, 2/15), 50-59 (19%, 5/26), 60-69 (3%, 1/31), older than 70 (0%, 0/13); P=.003. Curiosity was also a more common rationale for use in younger people: 18-39 (42%, 8/19), 30-39 (22%, 6/27), 40-49 (7%, 1/15), 50-59 (4%, 1/26), 60-69 (6%, 2/31), older than 70 (8%, 1/13); P=.003.

A larger proportion of the 40 participants who already used a health monitoring device would wear one to monitor their breathing for their asthma or to track patterns during stress (48%, 19/40 for both), compared to those out of the 94 who did not currently use a device (29%, 27/94 for both; P=.036).

Participants were asked to indicate whether any respiratory illnesses other than asthma were part of their motivation to wear a wearable. Only 8 reported that this was a motivating factor.

Table 1. Participant demographic information for the wearable survey study, stratified by health status.

Characteristic	Total, n (%) (n=131)[a]	No asthma, n (%) (n=55)[b]	Asthma, n (%) (n=76)[c]
Gender: Male	39 (29)	22 (40)	17 (22)
Age			
18-29	19 (15)	14 (25)	5 (7)
30-39	27 (20)	13 (23)	14 (18)
40-49	15 (11)	8 (15)	7 (9)
50-59	26 (20)	6 (11)	20 (26)
60-69	31 (24)	6 (11)	25 (33)
70+	13 (10)	8 (15)	5 (7)
ACT, mean (SD)[d]	—	—	17.4 (5.2)
Highest level of education[e]			
Secondary school	21 (16)	6 (11)	15 (20)
Higher certificate or diploma	30 (23)	9 (16)	21 (28)
Bachelor degree or higher	79 (60)	39 (71)	40 (52)
Prefer not to say	1 (1)	1 (2)	0 (0)
Socioeconomic status: Low SES[f]	25 (19)	9 (16)	16 (32)
Employment status[g]			
Employment, full or part time	80 (63)	36 (65)	44 (61)
Employment, casual	12 (10)	7 (13)	5 (7)
Currently unemployed	34 (27)	11 (20)	23 (32)
Household income (Aus $)[h]			
$26,000	12 (9)	4 (7)	8 (11)
$26,000-$51,999	20 (15)	8 (15)	12 (16)
$52,000-$72,799	19 (14)	9 (16)	10 (13)
$72,800-$103,999	21 (16)	6 (11)	15 (20)
$104,000-$155,999	9 (7)	3 (5)	6 (8)
≥$156,000	23 (18)	15 (27)	8 (11)
Prefer not to say	27 (21)	10 (18)	17 (21)
Language other than English spoken at home	19 (15)	11 (20)	8 (11)

[a]131/134 participants who completed a survey provided demographic data.

[b]55/57 participants who did not have doctor-diagnosed asthma provided demographic data.

[c]76/77 participants who had doctor-diagnosed asthma provided demographic data.

[d]A score of ≤19 indicates suboptimal asthma control.

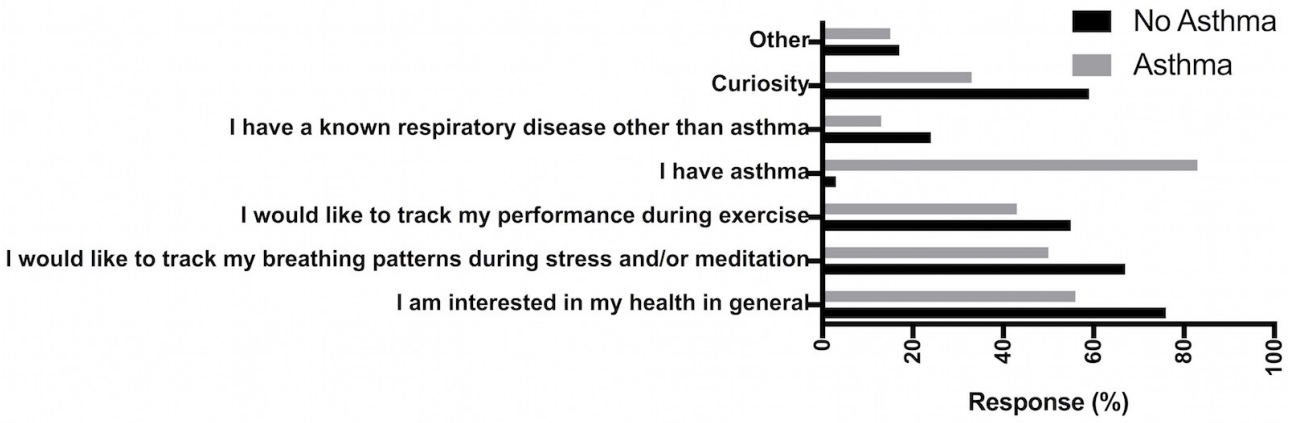
[e]1/131 participants who provided demographic data did not report their education status.

[f]Socially disadvantaged at patient's home address: "Disadvantaged" Socio-Economic Indexes For Area (SEIFA) quintile <3, "Advantaged" SEIFA quintile: 4-5 [18].

[g]2/131 participants who provided demographic data did not provide employment information; "Currently unemployed" includes unpaid or volunteer work, engagement in home duties, or not being in the labor force.

[h]27/131 participants who provided demographic data did not provide household income information.

Figure 1. User motivation for those willing to use a wearable device, stratified by self-reported, doctor-diagnosed asthma status.



Those Willing to Use a Wearable Device

When we restricted our analyses to the subgroup of those willing to use a wearable device only (61.9%, 83/134), the most common motivating factor to wear a device for those without asthma was "curiosity" (59%, 17/29; *P*=.026). The most common motivating factor for people with asthma was "I have asthma" (83%, 45/54; *P*<.001). No significant differences were observed between those with and without asthma in the other provided reasons. Figure 1 shows user motivation across this subgroup, stratified by self-reported, doctor-diagnosed asthma status, with participants able to select multiple responses.

Those Who Would Not Use a Device

In this subgroup (6.7%, 9/134), those without asthma stated they would not wear a device because they did not understand why monitoring breathing was important (eg, "I can't see a reason why I would want to monitor my breathing").

The reasons for not using the device in the four participants with asthma were that they felt their asthma was under control (eg, "Asthma is under control," "I don't get bad asthma attacks, just slight, not worth the bother"), or due to travel or cost ("I am overseas at this time," "Such devices are too expensive").

Those Whose Willingness Depended on Specific Factors

In this subgroup (31.3%, 42/134), 19 had asthma and 23 did not. The most common motivating factor for wearing a device in people with asthma was "I have asthma" (83%, 14/19; *P*<.001). No significant factors were found for those without asthma in this subgroup.

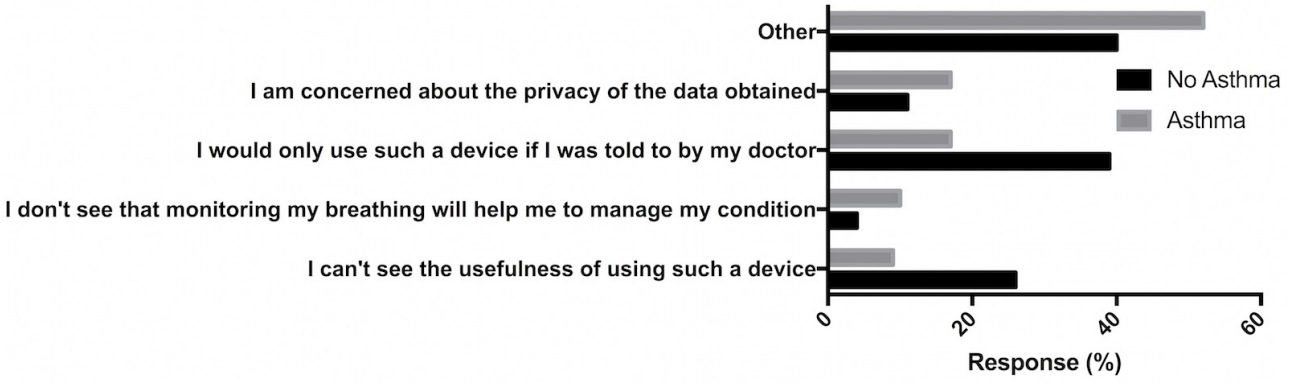
Factors Affecting Wearable Use

The factors affecting wearability mentioned across all participants included design issues and user perception issues. In terms of design, the physical size, location, weight, and bulk of the device were common concerns. Related to these were user perception issues, such as comfort and inhibition of movement, discreetness, and how the device would be fitted to the body. Example of factors provided were "how comfortable and discrete the device is," "how it's worn," "size would it inhibit normal movements and is it 24/7?"

Unappealing Factors

All participants were asked to select which factors would cause them to consider a wearable device unappealing (Figure 2). Of note, 26% (15/57) of participants without asthma did not see the usefulness of the device, compared to 9% (7/77) of those with asthma (*P*=.008). More participants without asthma would use a device to monitor breathing only if they were told to by a medical professional compared to those with asthma (39%, 20/49 vs 17%, 13/77; *P*=.005).

Figure 2. Unappealing factors for wearing a device, stratified by self-reported, doctor-diagnosed asthma.



Device-Specific Features

The device-specific features were themed into five different categories: wearability, cost, power features, display, and data synchronization. All 134 survey participants completed this section. In general, there were no differences between those who were current users of health monitoring devices and those who were not, in preference for form factor, length of usage, cost, display or data storage time preferences, unless otherwise indicated below.

Wearability

A majority (94.0%, 126/134) of respondents (with or without asthma) would use a wearable device during the day, night, or both day and night. Most users preferred to wear the device 5 nights/days a week or more (Figure 3). However, more out of those who already used a health monitoring device indicated they would use the device for 5 days or more a week (83%, 33/40), compared to those who did not already use a monitoring device (60%, 56/94; *P*=.01).

Furthermore, those with asthma said they would wear the device more often than those without asthma during both the night and day: 82% (63/77) with asthma versus 46% (26/57) without asthma would wear the device 5 days or more a week; *P*<.001. Those without asthma were also more likely to wear the device only during training: 26% (15/57) versus 5% (4/77); *P*=.001. No significance differences were found between health status and form factor for daytime use.

Frequency of daytime and nighttime use was higher in older people. For example, older participants predicted they were more likely to wear the device 5 days a week or more during the night: 18-39 (37%, 7/19), 30-39, (59%, 16/27), 40-49 (53%, 8/15), 50-59 (81%, 21/26), 60-69 (74%, 23/31), older than 70 (77%, 10/13); *P*=.026. Younger age groups were more likely to use the device during exercise than older age groups: 18-39 (47%, 9/19), 30-39 (15%, 4/27), 40-49 (7%, 1/15), 50-59 (4%, 1/26), 60-69 (10%, 3/31), older than 70 (8%, 1/13); *P*=.001.

There was a clear preference for a wrist band over other formats such as earbuds, and preferences were similar for day versus nighttime use (Figure 4). Men were more likely to wear a chest band during the day (38%, 15/39 vs 20%, 18/92; *P*=.043) compared to women. At night, men were also more likely to wear an ear bud in the ear (28%, 11/39 vs 16%, 15/92; *P*=.044) but less likely to wear a wrist band (90%, 35/39 vs 97%, 89/92; *P*=.039) compared to women.

Figure 3. Total participant preference for how often the device is to be worn, separated by day and night use.

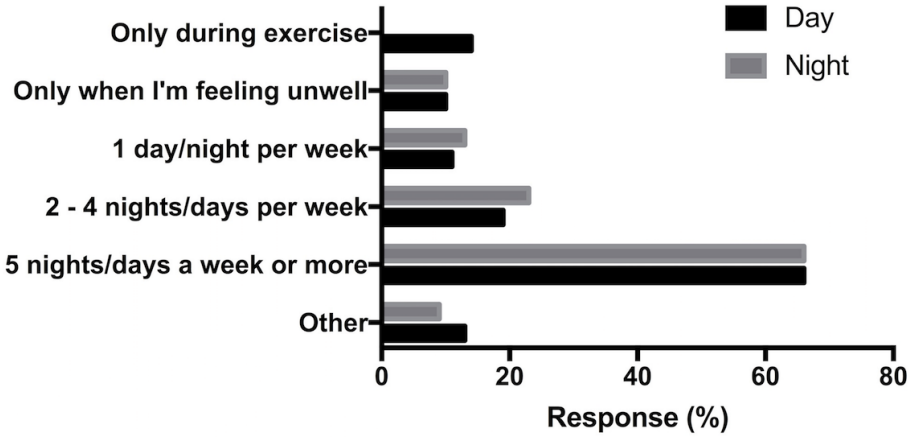
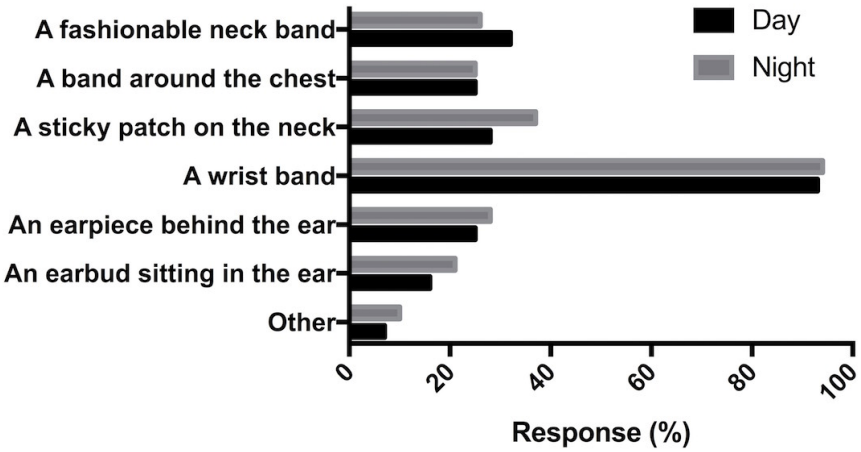


Figure 4. Total participant preference for the form of the device to be worn, separated by day and night use.



Cost

Over half (53.7%, 72/134) of the total participants would be happy to pay up to Aus $100 for a wearable respiratory monitor, 20.8% (28/134) would pay over Aus $100, and the remaining 25.3% (34/134) would use it only "if it were free." No statistically significant differences were observed in responses by health status, different household income, age, or gender.

Power Features

The most popular waiting time for the device to charge was overnight (45/134, 33.6%) as opposed to within 2 hours (22.3%, 30/134), 1 hour (23.1%, 31/134), 30 minutes (11.1%, 15/134), or other (10.4%, 14/134). Charging time did not appear to be a critical factor in user preferences, with other responses provided as: "As long as it takes. Good if the recharging was no more than 2 hours" or "However long it took to charge." No differences were observed between those with or without asthma.

Display

Participants selected between the three different displays shown in Figure 5, representing different formats to display current and past breathing data. No preference was found between display type (numerical information, 48/134; bar graph, 39/134; line graph, 47/134). There was no difference in display preference between those with asthma and without asthma, or between different age or gender groups.

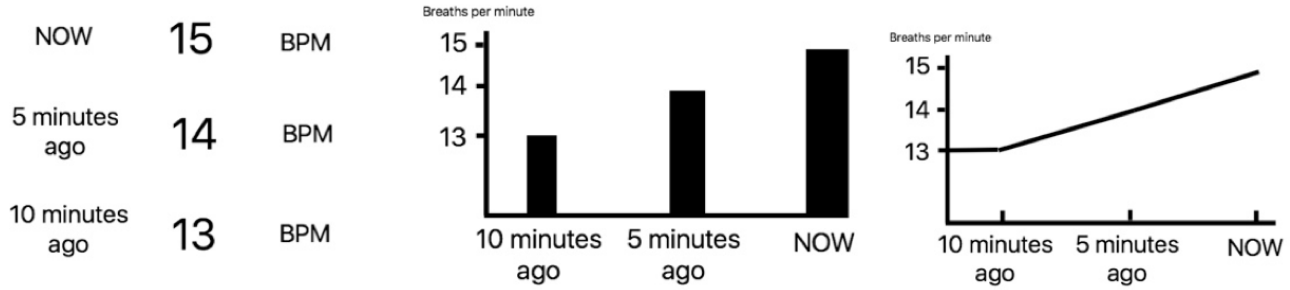
Participants indicated that they would like to receive alerts when their breathing was problematic. Alerts were more popular in those with asthma than those without asthma: 79% (61/77) versus 63% (36/57); *P*=.048.

Syncing and Data Storage

The majority of participants (79.8%, 107/134) reported wanting to sync the device to their phone/tablet. The proportion was higher among those who already use a monitoring device (93%, 37/40). Less than half (45.5%, 61/134) wanted to sync the device with their computer. Those who selected "other" responded with "remote analysis and syncing with my GPs office," "sync with sleep study," or "cloud service." Younger participants were more likely to report wanting to sync their breathing data (number of breaths per minute) with a phone or tablet than older participants: 18-39 (100%, 19/19), 30-39 (100%, 27/27), 40-49 (87%, 13/15), 50-59 (77%, 20/26), 60-69 (68%, 21/31), older than 70 (54%, 7/13); *P*=.001.

The majority of participants reported wanting to save their data for at least 1 week (58.9%, 79/134).

Figure 5. A display of breathing data by numerical information (left), bar graph (middle), and line graph (right).



Discussion

Principal Findings

In this survey, we identified a number of reasons to adopt new technologies to monitor breathing in participants with or without asthma. In participants without asthma, the main factor that influenced motivation for using a wearable was curiosity. The ability to track breathing patterns during stress or meditation and fitness tracking were motivational factors for younger participants. In asthma, the main motivations for use were "having asthma" and the ability to track breathing patterns during periods of breathlessness. We found that most users were willing to wear the device continuously both day and night and that the most preferred device format was a wrist band, regardless of health status. Other desired features were alerts when breathing is problematic (for both asthma and non-asthma groups), the ability to synchronize data with a phone or tablet, a recharging period of every 24 hours, and cost of≤Aus $100.

Motivation for Wearable Use

Previous studies have found that perceived value has a significant influence on both potential and actual customers, with perceived value as an important factor influencing the consumer's decision to adopt new products or services [7,11]. One of the most influential factors for people without asthma was curiosity, a factor that in previous research has been thought to increase initial interest and subsequent user engagement [19].

As might be anticipated, motivation for using a wearable device in asthma was different to those without asthma. In people with asthma, there appeared to be a desire to use breathing monitoring to gain greater control over the management of their asthma, particularly during episodes of breathlessness. An episode of extreme breathlessness during a respiratory exacerbation is often extremely frightening to both patients and their family members [20]. Provided that there has been sufficient testing and development of safe and reliable markers, detailed self-tracking breathing metrics could potentially help provide patients with an objective identifier or predictor of such episodes. This is especially important given that self-perception of airway narrowing is known to be poorer during an asthma exacerbation than at other times [20]. For family members, real-time monitoring may allow them to assist in supporting their relative with asthma in identifying symptom worsening and deciding when to seek emergency care, alongside traditional indicators.

Patients are known to employ a number of strategies to cope with breathlessness episodes, including breathing techniques and reduction of physical exertion [21]. A simple wearable device to measure breathing may provide objective monitoring and feedback during use of breathing techniques, and with the guidance of a health professional, has the potential to support patients to increase their physical activity in a safe manner. A monitor that directly and continuously measures breathing might provide a unique capability for immediate feedback that may not be achieved with currently available devices, such as those measuring wheezing sounds, peak flow, or lung mechanics. There are precedents for monitoring and feedback in asthma, for example, monitoring and feedback of medication use is acceptable and has been shown to increase medication use in adults and children [22,23].

The observed difference in the rationales for using a breathing monitoring device between participants with and without asthma indicates the need to collect separate data on the motivation for use and the utility and feasibility of wearables (for breathing or other purposes), in people with and without (different) health conditions. Conversely, the rationale for choosing not to adopt a wearable device for breathing monitoring was similar between those with and without asthma. The main reason given was a lack of perceived purpose or need for such a device, for example, because asthma was already "under control." Indeed, there is a lack of direct evidence showing that the ambulatory monitoring of breathing patterns over time is useful for asthma. This is despite the disease being characterized by shortness of breath. However, indirect support comes from measurements made using breathing-based lung function tests [24], recent developments in the monitoring of wheeze [25], and data showing breathing patterns predictive of chronic obstructive pulmonary disease exacerbations [5]. The availability of a suitable wearable will enable further work showing utility in asthma management.

User Preference for Device Features

To the best of our knowledge, this is the first time user preferences for a wearable device aimed at respiratory health monitoring have been investigated. This is important as desired design features often come at a technical cost. The results of this study inform us which features are of high value and which features could be compromised in exchange for technical tradeoffs. Furthermore, acceptance of a new technology may be affected by the perceived risk or inconvenience posed by the device. Previous research suggests that factors such as wearability design, physical size, location, weight, and bulk may negatively impact perceived device value. Costly and complicated recording devices may result in low compliance [10].

There are little data available to suggest what constitutes acceptable levels for these features and for human factors in a breathing monitor wearable. In this study, we found significant user perception issues around comfort and inhibition of movement, discreetness, and where the device fits on the body. Our study also revealed that more than 90% of participants would wear the device both day and night, and more than 90% preferred a wrist-worn device. Comfort and frequency of use are likely to interact, with more comfortable devices used for longer.

Most users preferred a wrist band over other formats for site of monitoring; however, this may have been influenced by the type of devices most commonly available on the market at the time. We note that chest bands and ear buds were also identified as next preferred formats for monitoring and may have been selected by participants with existing exposure. Device design choice needs to be made in terms of both user acceptability as well as signal quality. Further study is required to determine the relative feasibility and accuracy in obtaining the breathing signal from these various sites. We did not find significant differences between health groups and their device form preferences.

We found that young participants were more likely to use the device for exercise, but we do not know the reasons why older people were less likely to use such technology for exercise. This could be due to overall lower exercise rates in older people or to less engagement or familiarity with exercise tracking.

Cost can be a barrier to the uptake of monitoring devices, but more than half of our participants would be happy to pay up to Aus $100 (approximately US $80) for a wearable that tracks breathing rate. At this price point, such a breathing wearable would be comparable to lower end activity trackers currently on the market and would require a simple design. While creation of a wearable is feasible at this price point, sacrifices in both reliability and comfort may arise. One area of cost reduction could be eliminating a display from the wearable. Any display could be viewed on an external screen such as a mobile phone, while alerts could be processed locally on the device.

Another consideration is device battery life, that is, power consumption must be carefully managed as a small form factor places constraints on battery life [26]. We found device charge time was negotiable, while device use time should be maintained at a minimum of 24 hours. With the size constraint of a wearable, providing this power may be difficult [6]. However, given that the majority of younger participants would like to synchronize data to their mobile phones or tablet, designers may be able to shift data processing functionality to the phone. Furthermore, since participants would like at least a week's worth of data capacity on the device, the requirement for continuous data transmission may also be reduced.

Given the user requirement for data synchronization and data storage, it is recommended that any wearable device should primarily capture and store data. Data transmission to a mobile phone or tablet can take place secondarily by participant demand or when local device storage is full. Any advanced data processing should also take place post transmission.

User security or privacy could potentially be compromised by continuous monitoring [27,28]. We investigated privacy as an unappealing factor in this study but found no observable difference between those willing or unwilling to adopt a breathing monitor. A sample size of 10 for those who would not adopt the device prevented our analyzing a statistically significant difference between the "willingness" groups.

Limitations

There are factors limiting the applicability of our findings. The first relates to whether the sample was representative of the population in general. There was a relatively high level of technology use over the population sampled, though only a third of participants were specifically current users of health monitoring devices. Also, 60% had a university education, a high percentage of respondents were female, and the ages of the study sample were not normally distributed. Although we measured educational level, we did not measure the health literacy of the participants, which may have impacted their responses to the survey. These demographics may not be representative of the general population, and there may have been a selection bias in those who chose to complete the survey (eg, 24% of those invited from the volunteers database agreed to participate). While we acknowledge there is a potentially high selection bias in those who chose to complete the survey towards those who were already motivated to adopt a wearable, the primary aims of the survey included determining specific user motivation and their preferences for usage and features they wish to have in such a wearable. The population captured was arguably the most appropriate to answer those questions.

Second, while we were able to show differences in the survey responses of those with and without asthma, people without asthma were younger than those with asthma, making it difficult to disentangle the effects of age and disease status. There is some suggestion that older users are more ready to adopt health-related technologies, but the reasons for this require further investigation [29]. More than half of participants with asthma also had suboptimal asthma control.

Third, display preferences were examined in a rudimentary manner in this survey, to determine whether graphical displays were preferred over text. Furthermore, we did not assess in detail whether participants understood how the information was presented, for example, by asking whether they thought the display indicated that their breathing was stable. Once wearable technology is established to measure breathing over time, another study to determine a suitable display of information from the participant's perspective should be explored.

Finally, we did not collect data on whether those who used other health monitoring devices were current or former users, or the reasons for discontinuation of use. Information on how long and why people stay engaged beyond curiosity would have provided major insight into user psychology as well as device development.

Conclusions

We have explored the motivations for, and the likelihood of, adopting wearable technology for the purpose of breathing monitoring and identified user preferences for key design features. We found participants were motivated to adopt a wearable breathing monitor regardless of health status, yet there were distinctly different rationales for use between those with and without asthma. There is a clear need to identify the benefits of monitoring breathing in health and asthma. Next steps will require the development and testing of reliable breathing metrics or indicators that can be safely used by people with asthma for monitoring breathing over time or that assist in the identification of symptom worsening and asthma exacerbations. These findings will help inform the design of a user-acceptable wearable device that will facilitate its eventual uptake in both healthy and asthma populations.

Acknowledgments

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Conflicts of Interest

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Multimedia Appendix 1

Online questionnaire.

[PDF File (Adobe PDF File), 326KB-Multimedia Appendix 1]

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Abbreviations

ACT: Asthma Control Test

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Chapter 4

Hardware and Software Methodology

4.1 Introduction

In the previous chapter it was found that participants, irrespective of health condition would prefer a watch form factor to measure breathing. It is clear that user requirements present certain technological challenges including power constraints, the size of the monitoring device and cost.

In this chapter an investigation of how reducing the power consumption of a pulse oximeter impacts derived accuracy is performed before turning focus to how machine learning methods that could be useful in deriving measures of respiration. The pulse oximeter was selected as hardware technology existed to rapidly implement a prototype. Additionally, this was backed up by the literature review and survey findings. This chapter explores hardware and software methodologies to answer the following research questions:

- Research Question 4: What are computing hardware limitations of using a pulse oximeter to derived a breathing signal?
- Research Question 5: Is it feasible to use machine learning (recurrent neural network) to predict tidal volume traces from a pulse oximeter?

This section consists of two published peer-reviewed conference papers:

Prinable, J., Jones, P., Thamrin, C., & McEwan, A. (2017, July). A novel hardware implementation for detecting respiration rate using photoplethysmography. In Engineering in Medicine and Biology Society (EMBC), 2017 39th Annual International Conference of the IEEE (pp. 726-729). IEEE.

Prinable, J. B., Jones, P. W., Thamrin, C., & McEwan, A. (2017, December). Using a recurrent neural network to derive tidal volume from a photoplethsmograph. In 2017 IEEE Life Sciences Conference (LSC) (pp. 218-221). IEEE.

Statement of Contributions of Joint Authorship:

- Joseph Barry Yoo Sik Prinable (Candidate): corresponding author, providing the main idea, writing, reviewing and editing of the manuscript.
- Peter Jones (Alternate Supervisor): proof reading, reviewing and editing the manuscript.

- Alistair McEwan (Principle Supervisor): proof reading, reviewing and editing the manuscript.
- Cindy Thamrin (Alternate Supervisor): proof reading, reviewing and editing the manuscript.

4.2 Hardware Methodology

Novel hardware was created for the capture and storage of a PPG signal. The Light Emitting Diode (LED) duty cycle was altered to determine the effect on respiratory rate accuracy. The duty cycle of a pulse oximeter was changed between 5%, 10% and 25% at a sample rate of 500 Hz. Where duty cycle refers to the sampling time as a percentage of total time. A PPG signal and reference signal was captured for each duty cycle. At a 25% duty cycle the Root Mean Squared Error (RMSE) was <2 breaths per minute for the top performing algorithm. The RMSE increased to over 5 breaths per minute when the duty cycle was reduced to 5%. The power consumed by the hardware for a 5%, 10% and 25% duty cycle was 5.4mW, 7.8 mW, and 15 mW respectively. For clinical assessment of respiratory rate, a RSME of <2 breaths per minute is recommended. Further work is required to determine utility in asthma management. However for non-clinical applications such as fitness tracking, lower accuracy may be sufficient to allow a reduced duty cycle setting.

4.3 Rationale for Changing to Software Based Research

In Chapter 2, it was identified that manufacturers such as Apple, Fitbit and Garmin make wrist worn devices with embedded pulse oximeters. To have a bigger impact in the field it was prudent to turn away from hardware development and investigate how software could be developed to advance the field of long term respiratory monitoring.

4.4 Software Methodology

For the first time a Long Short-Term Memory (LSTM) architecture was used to predict normalised relative tidal volume from a PPG signal. The RMSE between actual and derived normalised tidal volume traces over the test set was 0.202. The RMSE between peak to peak intervals was 0.7 s. This suggests the LSTM was capable of predicting time-based breathing measures to a higher degree than the amplitude of the normalised tidal volume signal, though these findings are limited due to only having data from a single participant collected over a one month period. In the next chapter the model is extended with more training data and look to other respiratory metrics that could have clinical significance.

The feasibility to predict future measures of relative tidal volume from a past respiratory signal history in a cohort of 10 cancer patients undergoing radiotherapy treatment was investigated. Pearson correlation between the reference and the derived metric was above 0.8 for t = 0s and fell below 0.6 at t = 1.5s. These findings fall in line with previous studies [1]. This provides insight into the difficulty to create an early warning system based on a minute by minute predictive model where high degrees of accuracy is required. This model was trained on a substantial amount of data (2.3 million examples or 28 hours worth of respiratory traces) and while longitudinal studies are still required to determine the how respiratory metrics correlate

to asthma acerbations or COPD flareups, it is unlikely, at this stage, that an accurate model based on past relative tidal volume would be sufficient. In the next chapter, other metrics that could be derived from a pulse oximeter are explored.

4.5 Concluding Remarks

An important part of this thesis was to determine how hardware characteristics influence breathing parameters derived from a pulse oximetry. Power should not be saved by reducing the duty cycle rate of a pulse oximeter as it led to unacceptable reduction in respiration rate accuracy. This means that there will be a trade off between monitoring time, battery size and usability. For the first time it was shown that machine learning techniques could predict relative tidal volume from a pulse oximeter. Additionally, predictions of relative tidal volume past 1.5 seconds into the future may be unsuitable for clinical use. The next chapter seeks to build on these preliminary finding in larger cohorts and expand further investigation potential methodology.

A novel hardware implementation for detecting respiration rate using photoplethysmography

Joseph Prinable[1], Peter Jones[1], Cindy Thamrin[2], and Alistair McEwan[1]

***Abstract*— Asthma is a serious public health problem. Continuous monitoring of breathing may offer an alternative way to assess disease status. In this paper we present a novel hardware implementation for the capture and storage of a PPG signal. The LED duty cycle was altered to determine the effect on respiratory rate accuracy. The oximeter was mounted to the left index finger of ten healthy volunteers. The breathing rate derived from the oximeter was validated against a nasal airflow sensor. The duty cycle of a pulse oximeter was changed between 5%, 10% and 25% at a sample rate of 500 Hz. A PPG signal and reference signal was captured for each duty cycle. The PPG signals were post processed in Matlab to derive a respiration rate using toolbox by Charlton et al. [4]. At a 25% duty cycle the RMSE was <2 breaths per minute for the top performing algorithm. The RMSE increased to over 5 breaths per minute when the duty cycle was reduced to 5%. The power consumed by the hardware for a 5%, 10% and 25% duty cycle was 5.4 mW, 7.8 mW, and 15 mW respectively. For clinical assessment of respiratory rate, a RSME of <2 breaths per minute is recommended. Further work is required to determine utility in asthma management. However for non-clinical applications such as fitness tracking, lower accuracy may be sufficient to allow a reduced duty cycle setting.**

I. INTRODUCTION

Asthma is a serious public health problem affecting over 300 million people globally [1]. Management challenges include the early prediction or warning of asthma attacks and optimising the pharmaceutical management of the disease.

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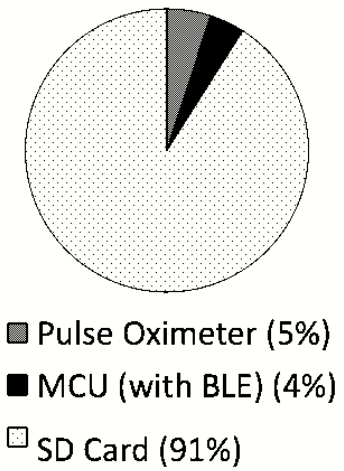

Fig. 1. Power consumption comparison

Monitoring of lung function over time is a widely accepted component of the assessment of asthma, both in clinical management of the disease as well as in research trials [1]. However, there is a paucity of research on continuous, real-time monitoring of respiratory rate for general health or for management of asthma or other chronic diseases. This may be due in part, to the lack of commercial technology to enable such monitoring in a manner that would be acceptable to the clinical community in terms of both accuracy and long term continuous monitoring capabilities.

There is no published data on the accuracy requirements of devices to assess breathing in human adults. However, international device standards for infant lung function testing have been recommended for flow based sensors [2].

In addition to flowmeters, respiratory rate (f_R) may be determined from a photoplethsmogram (PPG) acquired using a pulse oximeter [3]. Charlton et al. analysed the accuracy of several algorithms against an oral nasal pressure sensor and provided a test suite to analyse datasets [4].

Minimum device sampling rates are determined by Shannon's theorem. Frey et al. recommend devices used to measure f_R should be able to measure between 10-80 breaths per minute for an infant [2]. Bates et al. suggest a sample rate of 200 Hz for the accurate determination of inspiratory/expiratory times for infants and children using a flowmeter [5]. Algorithms such as an Incremental Merge Sort (IMS) algorithm [6], identify pulse peaks creating 'windows' for further processing steps used to derive f_R from a PPG. Therefore, f_R derived from a PPG require higher sampling rates compared to a flowmeter in order to meet Shannon's theorem.

The long term operation of wearable devices for f_R detection using a pulse oximeter is constrained by battery capacity making power optimisation critical. Figure 1 shows a percentage power consumption comparison between a Texas Instruments CC2540 MCU with BLE capability (11.5mW), pulse oximeter (15mW) and SD card (300mW) with reported power consumption sourced from Dieffenderfer et al [7] and the manufacturer datasheet for the SD card used in this study (SanDisk microSD OEM Product Manual Revision 2.0 Document No.80-36-03335 March 2010). While the SD card power consumption is the highest of three components, future development will likely introduce BLE and discrete SPI flash memory functionality to mitigate against this issue.

This paper seeks to determine how changing the duty cycle at a fixed sample frequency (500 Hz) of a pulse oximeter affects the accuracy of f_R detection.

II. METHOD

A. Reference Signal

A reference E-Health Platform V1 Airflow Sensor (Libelium Comunicaciones Distribuidas S.L., Zaragoza, Spain) was used to detect actual respiratory rate. This sensor interfaced to an Arduino Uno and the captured signal was saved to a DELL Optiplex 9010 (DELL, Round Rock, Texas, USA).

B. Sensor Technology

A transmission based pulse oximeter (B-M-310715-0126 Texas Instruments, Dallas, TX) was controlled by an AFE4490 (Texas Instruments, Dallas, TX). The duty cycle was set at 1%, 5%, 10%, and 25%, where the maximum allowable duty cycle was 25% as set by the manufacturer. The LED current was fixed at 5.88 mA, with a reference voltage of 0.75 V. The IR LED was disabled and no IR PPG signal was captured and saved. The AFE4490 sampled the PPG signal at 500 Hz, 22 bit resolution (stored as 32 bit unsigned number) and was transmitted via a SPI interface to the Main Control Unit (MCU). The AFE4490 did not high pass filter (either in hardware or software) the PPG signal as is common with many commercial pulse oximeter circuits. If required, the raw PPG could be filtered in software.

C. MCU

For this study, a SmartRF06 Evaluation Board for the CC2650 (Texas Instruments, Dallas, TX, USA) was used. The CC2650 is an amalgamation of an ARM Cortex -M3 running at 2.4 GHz, an ARM Cortex -M0 running an RF core for Bluetooth functionality, Sensor controller, and several GPIO modules such as 2 x SSI, I2S, UART, and I2C. The MCU runs a TI-RTOS environment. The CC2650 is the successor of the CC2540 used by Dieffenderfer et al. [7].

D. Participant Data Collection

Ethics was approved under HREC reference: LNR/16/HAWKE/99. Data was acquired from 10 healthy volunteers, ages 20 - 48. The volunteers were seated with both hand resting palm down on the desk in front of them. A pulse oximeter was placed on the left index finger and the participant was instructed to breathe at a constant tidal breathing rate 20 breathes per minute (BPM) for 2 minutes. Twenty BPM is within the normal f_R for a resting adult. The subjects were shown a "loop timer" visualisation on a laptop for cadence. Further, volunteers were also asked not to talk, cough, swallow, sneeze, and any other activity that could interrupt their breathing pattern. Several correct breathing cycles were observed before recording began.

E. Data Storage

The SD card was formatted prior to each data capture. Then, the raw PPG signal data was buffered from the AFE4490 (AFE) into a "Ping Pong" style FIFO on the MCU and sent via a secondary SPI to a SD card (SanDisk Ultra 64 GB Class 10). The use of dual FIFO and SPI channels was used to mitigate against potential long delays (up to 350 ms) between page writes often found with most SD cards. The SD card implements a FAT32 file system based on Chan's FatFs ANSI C library (Available at: http://elm-chan.org/fsw/ff/00index_e.html) which limits file sizes to 4 GB allowing a theoretical maximum of approximately 25 days of PPG data per file to be stored.

F. Signal Processing

Data was processed in MATLAB R2016a using a toolbox "RRest" created by Charlton et al. [4] (Available at: http://peterhcharlton.github.io/RRest).

1) Preprocessing: The reference signal was preprocessed into a vector containing the time (seconds) of each breath peak. Both PPG and reference data were formatted to conform with the RRest toolbox. Raw PPG signals were inverted for convention.

2) Filtering and Signal Processing Algorithms: For more in depth explanation of the signal processing algorithms and filters used please refer to to Charlton et al. [4].

3) Statistical analysis: The toolbox ranks the performance of different algorithms based on limits of agreement (LOA). The top two performing algorithms (lowest 2SD) at a 25Hz duty cycle were selected to determine if accuracy changes with duty cycle.

G. Power consumption

The AFE4490 and the MCU are powered from two separate USB cables connected to a 5V, 2A rated source. DC current was measured using a HP 34401A Digital multimeter (Hewlett Packard, Palo Alto, USA). Power consumption was tested as shown by Table I to determine the power consumption at different duty cycles of the AFE. The power consumption of the MCU and SD card was also tested.

III. RESULTS

A. Participant Data Collection

Data was acquired from 10 subjects. The median (lower,upper quartiles) ages of the analysed subjects was 25.5 (23.7, 32.25) years. One participant was female.

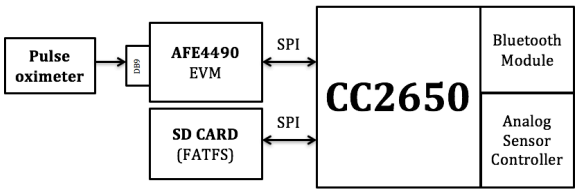

Fig. 2. Hardware Block Diagram

TABLE I

POWER CONSUMPTION TEST PROTOCOL

Test	State	Duty Cycle (%)
1	AFE capture	25
2	AFE capture	10
3	AFE capture	5
4	AFE capture	1
5	AFE idle	N/A

TABLE II

RESPIRATION RATE RMSE VERSUS DUTY CYCLE

Duty Cycle	Al1	Al2
25	2.0	3.5
10	4.4	7.5
5	5.1	7.9

B. Signal Processing

The raw PPG signals at the different pulse oximeter duty cycles for a typical participant is shown in Figure 3. Figure 4 shows the PPG signals for a participant that have been normalised between 0 and 1.

C. Respiration Rate Accuracy

At a 1% duty cycle the measured PPG signal was not large enough to be observed over the systems' noise. Consequently this data was omitted from further analyses. Two algorithms were chosen for analysis as they had the lowest 2SD at the 25Hz duty cycle. The first algorithm (AL1 or $E_{T4}F_{M1}$), was a combination of breath detection using "count-orig" Schäfer et al. [10] and "Smart Fusion" by Karlen et al. [11] and had 2SD of 3.42. The second algorithm (AL2 or $E_{T5}F_{M1}$) was a combination of breath detection by "peak detection" [10] and Smart Fusion by Karlen et al. [6] and had a 2SD of 5.43. The root mean square error (RMSE) of derived f_R was compared between 5%, 10%, and 25% is shown in Table II. It can be seen RMSE increases as duty cycle decreases.

D. Power Consumption

The power consumption of the AFE4490 was tested and the results are shown in Table III. The measured power in the idle state was 3.3 mW and falls within a reasonable range given the manufacturer claims $<$ 2.3 mW at 3.0-V supply. The CC2650 drew 20 uA current while the SD card current ranged between 119 mA to 121.3 mA.

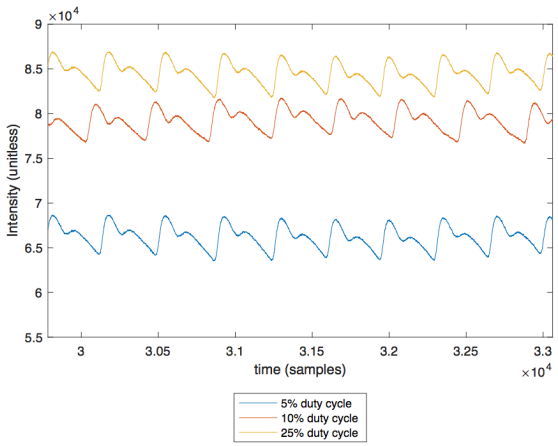

Fig. 3. Typical participant signals at 5%, 10%, and 25% duty cycle

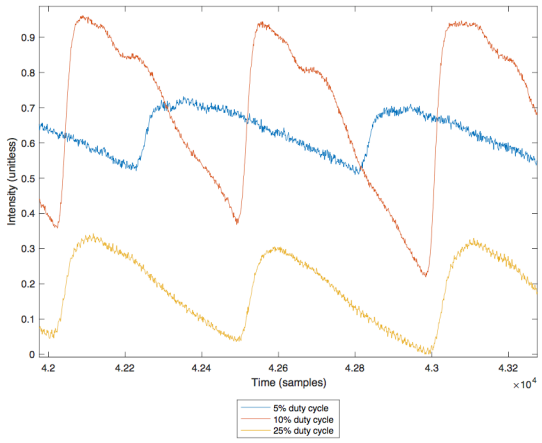

Fig. 4. Normalised participant PPG signals at 5%, 10%, and 25% duty cycle

TABLE III

POWER CONSUMPTION RESULTS

Test	Duty Cycle (%)	Current (mA)	Power (mW)
1	25	5	15
2	10	2.6	7.8
3	5	1.8	5.4
4	1	1.2	3.6
5	0	1.1	3.3

Using MATLAB R2016Bs curve fitting toolbox, the duty cycle (%) to power (mW) can be shown to be linear (R^2 = 0.99), given by Equation 1.

$$Power = 0.47 * dutycycle + 3.1 \quad (1)$$

IV. DISCUSSION AND FUTURE WORK

In this paper we sought to determine if reducing the duty cycle of pulse oximeter would affect the accuracy of derived f_R in order to minimise power consumption. For both algorithms (Al1 and Al2) it was observed that the RMSE decreased as the duty cycle increased from 5% to 25%. Additionally, the top performing algorithm at both 5% and 10% duty cycles was breath detection by "peak detection" [12] coupled with "Smart Fusion." [6].These findings support Charlton et al. [4] findings that smart fusion and time-domain breath detection estimations techniques performed well against spectral based algorithms.

In figure 4 the dicrotic notch is readily identifiable at a 10% duty cycle but not at either 5% or 25%. The absence of such dicrotic notches are also seen in the MIMIC and Controlled Breathing databases [12]. These databases contain reference respiratory information and PPG signals used in several studies [4],[6],[11]. The systolic peaks are identifiable at all duty cycles and were used within the IMS algorithm to create windows [11]. We saw PPG shape variability at

different duty cycles for a most participants though with such a small participant size it is unclear what may cause these factors.

To date, there are no clinical guidelines on the minimum accuracy required to measure f_R in adults, particularly on devices that do not directly measure flow. We have assessed the accuracy of our device against a nasal flow sensor, the accuracy of which is unspecified. A nasal flow sensor is standard for assessment of breathing during clinical sleep studies, but further validation should include comparisons against other standard measures of flow of higher accuracy, e.g. a pneumotachograph or respiratory inductance plethysmography.

The observed RMSE at a 25% duty cycle may be sufficient for non-clinical applications such as fitness tracking where coarser granularity of respiratory rate is more acceptable. For example, a device that informs the user of increased, decreased, stationary, sedentary respiratory information.

A. Power consumption

The power consumption of 15 mW was observed at the duty cycle of 25%. During this study only one sample was taken per duty cycle. It is possible to average several samples over a given duty cycle however at no extra power cost. However, given the shape of a PPG and a heart rate of 200 beats per minute, 500 samples per second allows the key features to be derived so we did not average during this study.

We recommend that the use of a SD card is limited to storing only critical information for data redundancy. Discrete SPI flash memory could be used that would offer the advantages over an SD card in terms of device real estate reduction, power and speed advances. This type of memory is constrained by storage size and would have to be used primarily as a buffer before being wirelessly transmitted over a protocol such as BLE. The effect of lost data due to a BLE link disconnecting must be examined to determine if the resultant data is clinically acceptable.

V. CONCLUSIONS

In this paper we presented a novel hardware implementation for the capture and storage of a PPG signal. The LED duty cycle was altered to determine the effect on respiratory rate accuracy. A PPG signal and reference breathing signal was captured for each duty cycle. The PPG signals were post processed in Matlab to derive are respiration rate using toolbox by Charlton et al. [4]. For clinical assessment of respiratory rate, a RSME of <2 breaths per minute is recommended. Further work is required to determine utility in asthma management, e.g. in predicting onset of an asthma attack, assessing disease status, and providing feedback for breathing exercises. However for non-clinical applications such as fitness tracking, lower accuracy may be sufficient to allow a reduced duty cycle setting. This would in turn save power and reduce the overall weight and size of the device.

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Using a recurrent neural network to derive tidal volume from a photoplethsmograph

Joseph B. Prinable[1,2], Peter W. Jones[1], Cindy Thamrin[2], and Alistair McEwan[1]

Abstract— **There is increasing interest in monitoring health using wearable sensors, however very few technologies have focussed on breathing. The ability to monitor breathing indices may have indications both for general health as well as respiratory conditions such as asthma, where long-term monitoring of lung function has shown promising utility.**

In this paper we designed hardware to capture photoplethysmograph (PPG) signals, and a Long Short-Term Memory (LSTM) architecture was trained to predict normalised tidal volume from a PPG signal. A pulse oximeter was mounted to the left index finger of a healthy subject who breathed at a comfortable rate through a pneumotachograph for fifteen minutes. The test was repeated once a week for four weeks. The RMSE between actual and derived normalised tidal volume traces over the test set was 0.202. The RMSE between peak to peak intervals was 0.7 s. This suggests the LSTM was capable of predicting time-based breathing measures to a higher degree than the amplitude of the normalised tidal volume signal. For clinical assessment of breathing pattern, a trained LSTM model may be acceptable if validated on a larger population. With access to a larger dataset, there is potential that a LSTM can be trained to provide reliable predictions of changes in breathing patterns over time.

I. INTRODUCTION

There has been increasing interest in monitoring health using wearable sensors. However, very few technologies have focused on obtaining breathing metrics. While the ability to measure breathing metrics may be beneficial for assessing general health, it would be especially beneficial for real-time monitoring of asthma, which is a health condition that affects over 300 million people globally [1]. Monitoring of lung function using specialised metrics such as peak expiratory flow, have been shown to be useful for predicting risk of an asthma episode [2]; however this can be difficult to perform for patients as it involves forced manoeuvres. It remains to be seen whether metrics derived from simple breathing might provide similar utility in asthma.

The availability of a sensor which can measure breathing continuously and in an ambulatory manner would facilitate studies to establish clinical utility. One potential sensor is a pulse oximeter which obtains a photoplethsmogram (PPG). The PPG signal's amplitude, frequency, and baseline is modulated by breathing periodicity [6], [7], [8] and effort [5], allowing respiration rate to be continuously monitored in an ambulatory setting. In addition to respiratory rate, other breathing metrics such as tidal volume or even the shape of the volume profile may be of interest and provide further information of changes in the breathing pattern over time.

Extraction of breathing metrics from the underlying PPG waveform can be achieved using a recurrent neural network (RNN). A form of RNN which is well-suited to processing time series having varying duration between key features is the Long Short-Term Memory architecture (LSTM) [12]. The LSTM approach has been applied to other biomedical field's time series problems such as predicting blood pressure [9] and respiration monitoring using a video system [10] and may allow a continuous tidal volume waveform to be predicted from a PPG.

This is a preliminary study to determine the feasibility of extracting tidal volume from a PPG using a LSTM and may inform future studies that seek to determine breathing patterns over in an ambulatory manner.

II. METHOD

A. Participant Data Collection

Test measurements were conducted on a single healthy participant, as pilot data to inform a future larger study in healthy volunteers and patients with lung disease. The protocol for this study was approved by Northern Sydney Local Health District Human Research Ethics Committee (#LNR/16/HAWKE99 ethics approval).

At each session, the participant was seated and instructed to breathe at a comfortable rate for 15 minutes through the experimental setup. A pulse oximeter was placed on the left index finger and the PPG was obtained. Each session was repeated once a week for four weeks.

B. Standard Measure of Flow

The pneumotachograph was used to obtain reference breathing tidal volume data for comparison. The experimental setup comprised a 32-mm diameter breathing tube connected to a 0-400 L min^{-1} pneumotachograph (Series R4830B, Hans Rudolph Inc., Kansas City, MO, USA) and bacterial filter mouthpiece (SureGard RJVKB2, Bird Healthcare, Port Melbourne, VIC, Australia). Flow across the pneumotachograph was measured using a $\pm$2.5 cm H_2O solid-state pressure transducer (Sursense DC001NDC4, Honeywell Sensing and Control, Golden Valley, MN, USA). The setup description, calibration and validation have been previously described [11]; for this study only the flow signal was used. While the flow signal was sampled at 300 Hz, data was down-sampled for recording at 6 Hz, which is considered to be sufficient resolution for the purposes of breathing rate and tidal volume extraction.

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C. Hardware

In this section we describe the hardware used to capture a PPG in this study. The hardware consists of the following modules; four sensor modules, a data aggregation module, and a PC . To note, only one of the four channels was used in this study. 3D printed cases allowed the hardware to be mounted in the 3.5 inch bays of a computer case.

The sensor module comprised an AFE4490 pulse oximeter shield for Arduino -V2 (Protocentral, Bangalore, India) used to control a commercial reusable transmission-based pulse oximeter (Nellcor, Minneapolis, MN) and an Arduino Uno (Arduino, NY, USA). On a shield-generated interrupt, the pulse signal was captured at 500 Hz, 24 bit resolution via SPI by an Arduino Uno (Uno). The SPI channel operated at 1 MHz. The signal was stored on the Uno as a unsigned 32 bit number. Once the signal was saved on the Uno, an interrupt was generated. The interrupt alerts the data aggregation module that a signal was ready to be sent via an I2C transmission. This interrupt occurs irrespective if the last I2C sample was successfully transmitted.

The data aggregation module comprises an Arduino Mega (Mega). The Mega is hardware interrupt driven by each sensor module. On interrupt, the Mega samples from the corresponding Uno (sensor module) via I2C. The I2C bus operated at 400 KHz. The sample was stored in a 10 element circular FIFO register. The data aggregation module communicates to a laptop (Macbook Pro, Apple Inc., Cupertino, California, USA) via a UART channel operating at 320,400 bits/s.

The laptop initiates a handshake protocol with the data aggregation module. The protocol consists of a request to begin test, followed by the length of the test in seconds, and a start command. The computer buffers streaming data and then saves the data in a .csv file format.

The average time elapsed between sampling the pulse signal and storing it on the Uno was measured.

D. Signal Processing using a Long Short Term Memory Model

1) Feature Generation: In this study we generated thirty features from the raw PPG signal as shown in Figure 1. The features were generated as follows:

- Features 1-10: The captured PPG signal was passed through ten parallel 2nd order Butterworth band-pass filters ranging from 0.1 Hz to 1 Hz, in 0.1 Hz increments. This resulted in 10 signals that were named feature 1-to-10. The low pass cutoff frequency for all filters was 2 Hz.
- Features 11-20 were the upper envelope of the filtered signals 1-10.
- Features 21-30 are the lower envelope of the filtered signals 1-10.

The first four minutes of data was discarded to allow the effect of the filter to be eliminated. The signal was then down sampled to 6 Hz in line with the pneumotachograph. Each feature was then normalised between -1 and 1.

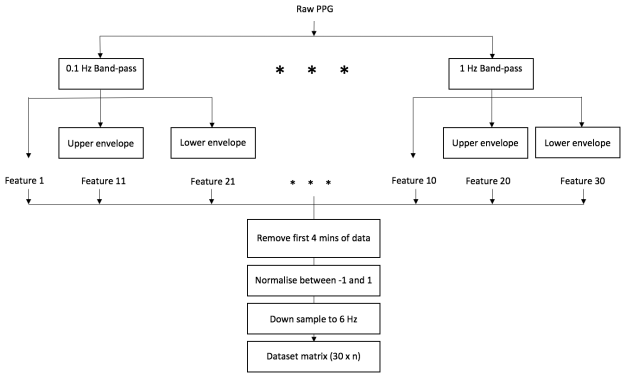

Fig. 1. The raw PPG signal is passed through 10 parallel band-pass filters and features 1-10 are extracted. The upper and lower envelopes of features 1-10 form features 11-20 and 21-30 respectively. The features are joined and the first four minutes of data are removed. The feature set is then normalised and downsampled. This results in a dataset matrix of 30 x (n - $trunc$). Where n is the length of the raw PPG signal. $trunc$ is the amount of data samples that were removed in the first four minutes

2) Datasets: Two dataset were created during this study. The first dataset combines data from all four weeks in the study and should result in the most accurate model, while the second dataset is used to determine how generalisable a trained model will perform over time. The datasets were created as follow:

- Data Set 1: A random 5% window of each session's data were combined together to form the test set. The remaining data was randomised with 80% used for the training set and 20% for validation.
- Data Set 2: Week one through three's data was randomised and split 80% / 20%, for training and validation respectively. Week four's data was used as the test set.

For both datasets, training and validation sets were then duplicated 7 times, each with varying Gaussian noise added with a mean of zero and a standard deviation ranging from 0.1 to 0.7 in 0.1 deviation steps to reduce overfitting.

The target set for both datasets consisted of a tidal volume trace from the pneumotachograph, which was normalised between -1 and 1 resulting in a relative tidal volume.

3) Long Short Term Memory (LSTM) Model Parameters: A LSTM architecture is a type of recurrent neural network with specialised internal states. These states allow for long-term dependencies (memory) to be incorporated when making a prediction.

An open source Python 3.5 library called TensorFlow r1.3 was used to create and train the LSTM model [12]. Each LSTM cell consists 1550 units. Cells were layered sequentially five times with a dropout layer after each. The dropout rate was set to 0.5 between layers to reduce over fitting. There was a dense fully connected layer at the end. AdamOptimizer was used to train the LSTM using the default learning rate of 0.001. A batch size of 128 was used during training, 256 for validation, and 756 for testing. The sequence length was 70 and chosen as this is the approximate size of one breath cycle. The model was trained for 50 epochs on a Dell Optiplex D810 having an i7 processor, 30 GB

RAM, and two NVIDIA Titan Xp graphics cards. An epoch is one run over the entire training and validation dataset.

E. Model Validation

The training weights and biases were saved after every epoch resulting in 50 models being generated. Validation data was applied to each model with the model resulting in the lowest RMSE between real and derived tidal volume being chosen for testing.

F. Model Testing

The test set was applied to the best model found in the model validation stage and the RMSE between the actual and derived relative tidal volume signals was recorded.

G. Peak to Peak Intervals of the Tidal Volume Waveform

The time difference in seconds between two consecutive peaks within the relative tidal volume signal was calculated. This was done using a library 'find peaks' in Matlab (The MathWorks, Natick, Massachusetts, U.S.A) which was visually inspected for correctness. The RMSE between actual and derived peak-to-peak intervals was recorded.

III. RESULTS

1) Sensor Module: The mean (standard deviation) of time elapsed between sampling the pulse signal and storing it on the Uno was 2.005 ms $\pm$ 0.004 ms.

2) Model Training: The training set consisted of 124,524 examples. Figure 2 shows the training RMSE over 50 epochs that decreased and reached a plateau assessed visually of 0.02. Each epoch took 18 minutes to train.

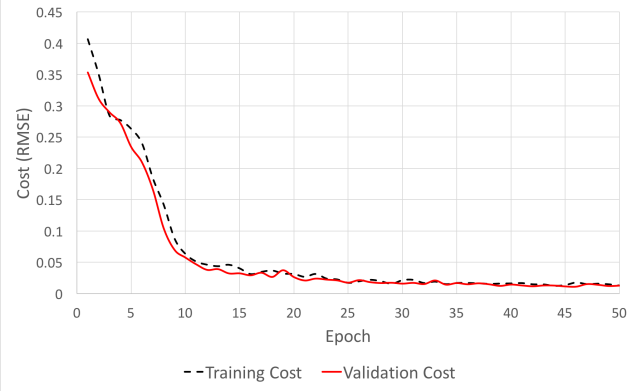

Fig. 2. Training cost function over 500 epochs

3) Model Validation: The validation set consisted of 31,125 examples. Figure 2 shows the validation cost function over 50 epochs. The lowest RMSE of 0.01 occurred at epoch 46.

4) Model Testing: The test set consisted of 756 examples. For clarity, the four set of test data were merged into one image. Figure 3 shows the predicted (dashed) versus actual (solid) relative tidal volume. The test set RMSE was 0.202. Pearson's correlation coefficient between the two tidal volume waveforms was 0.84.

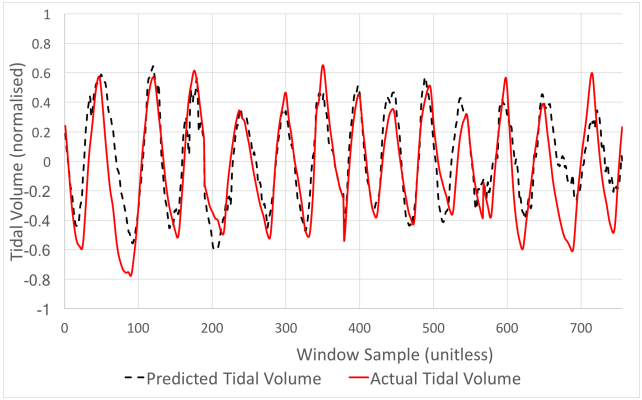

Fig. 3. A normalised window of 756 predicted (orange) vs actual (blue) points of a relative tidal volume signal

5) Peak to Peak Intervals of the Tidal Volume Waveform: There were 12 peak-to-peak intervals over the 756 sample test window as shown in Figure 3. The RMSE was 0.7 s.

A. Model Generalisability Over Time

The test set consisted of 3024 samples shown in Figure 4. The RMSE was 0.2904. The whole test is presented to show overall trends.

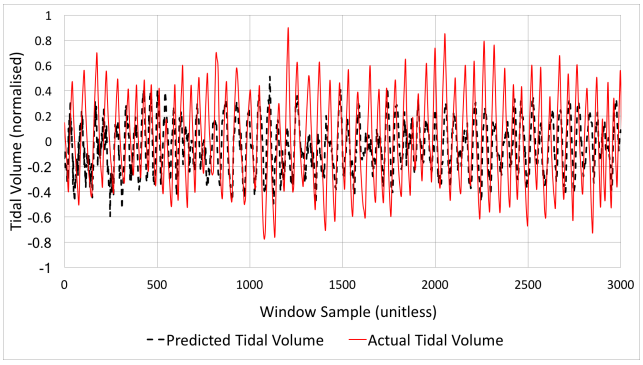

Fig. 4. A normalised window of 3024 predicted (orange) vs actual (blue) points of a relative tidal volume signal

IV. DISCUSSION AND FUTURE WORK

This was a preliminary study to determine the feasibility of extracting a relative tidal volume from a PPG using a LSTM. A four sensor device was created to measure the PPG signal. During this study only sensor 1 was used to capture a PPG from a single participant once a week for four consecutive weeks. We measured the variation of sample time for this sensor and found that there is a potential to miss between 0.45 to 4 seconds of data over a 15-minute period. This can be explained by the tolerance of the clocking oscillator to the AFE4490. This was deemed acceptable given that the data was eventually down sampled to 6 Hz. Further use with this equipment, especially when comparing one sensor to another, should be done at a lower frequency rate to mitigate against mismatched sample periods. Future work with this equipment

will enable the investigation on how multiple measurement sites effect the accuracy of a derived relative tidal volume waveform.

In this study we used a LSTM architecture to predict relative tidal volume amplitude from a PPG. There was a Pearson correlation of 0.84 between the derived and actual tidal volume waveforms which compares favourably to existing amplitude measures [10]. Upadhya et al. report respiration rates derived from the tidal volume waveform have less than $\pm$ 3 breaths per minute error and a RMSE of $<$3.3 BPM for more than 95% of their test cases. A trained LSTM model with dataset 1 was shown to predict a relative tidal volume signal from a PPG signal with a RMSE of 0.202 in a controlled environment. The test error was higher than the validation error over the 50 epochs which may be a consequence of the dropout layers in the LSTM which are activated during training and deactivated when validating.

Figure 3 shows high frequency noise which makes accurate quantification of tidal volume attributes difficult. We found the RMSE between peak-to-peak intervals of the relative tidal volume signal to be 0.7 s and while we did not implicitly derive respiration rate from the relative tidal volume waveform, we expect this breathing parameter would compare favourably to the state-of-art [8]. While the periodicity of the derived relative tidal volume may be acceptable, Figure 3 shows that there is a subtle differences in peak heights. It may be possible to determine breathing metrics such as flow (differential of tidal volume) or shape and variability of the flow signal if accurate peak heights can be derived in the future.

We investigated how generalisable a trained model will perform over time to predict tidal volumes using dataset 2 and report a RMSE of 0.2904. During this study we did not use k-fold validation and it is possible the model using dataset 1 results in an over estimation of true accuracy. This is supported by the difference of a 0.08 RMSE between the two datasets models. Figure 4 shows that the periodicity between the relative tidal volume signals are similar however, the difference in amplitude is large. It is therefore posited that breathing parameters such as inspiration period, expiration period, inter-breath-intervals and respiratory rate which rely primarily on the periodicity of the relative tidal volume signal may be predicted over time and could help inform future studies consisting of different health groups.

Previously we found that participants would prefer a wearable to have a watch form factor [3]. In this paper we did not look at the feasibility of implementing a LSTM in this type of form factor. The model required a powerful machine with GPU capability for training however, it is expected that an embedded platform could perform the required processing to obtain real-time predictions using a trained model. Future work should determine the feasibility of implementing a trained LSTM in a watch in terms of power consumption, bill of material (BOM) costs, and size.

We have presented pilot work using LSTM to predict a breathing trace - future work will examine optimising the model parameters for speed and accuracy. One further limitation of this study was that the target set was normalised between 1 and -1 which results in a derivation of a relative tidal volume. This means that we can only quantify changes in an individual's breathing pattern relative to their own baselines, which is adequate for personal monitoring. If an accurate LSTM model was trained on a non-normalised target set, direct comparisons between individuals based on their health condition could be examined in the future. In this study we collected data from a single participant at a resting breathing rate and future studies should test the efficacy of a LSTM model at a range of breathing rates over multiple individuals.

V. CONCLUSIONS

In this paper we presented a novel hardware implementation for the simultaneous capture and storage of four PPG signals. We applied a LSTM to a single PPG channel and were able to predict a relative tidal volume signal with a minimum RMSE of 0.202. We additionally derived peak-to-peak intervals and found the error to be 0.7 s. For clinical assessment of inter-breath-intervals a trained LSTM model may be acceptable. However, with a larger dataset a LSTM model may be able to predict other breathing metrics which could provide further information on changes in the breathing pattern over time.

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Realtime long range respiratory prediction

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INTRODUCTION

Adaptive imaging and gated radiotherapy treatment involves making decisions in response to patient respiratory phase. Therefore, the ability to accurately determine phase is paramount and is constrained by adequate past information to inform a model as shown in Figure 1.

Current state of the art struggles to predict beyond a 500 ms horizon which is problematic as current hardware and software latencies are 250 ms.

The aim of this work was to investigate if a 5s phase prediction horizon can be achieved.

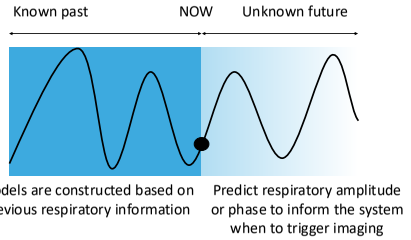


Figure 1: Imaging is triggered based on phase models

METHOD

A 24 lung cancer patient study with ~22 hours of RPM data and CAPNOBASE (42 patients, ~6 hours) datasets [3,4] were fused, resulting in a dataset containing ~2.3 million training/validation examples.

A machine learning (UNET) architecture [2] was trained using reinforcement learning to predict a 5-second respiratory window. The model performance was tested on a 20 respiratory traces from 10 patients acquired through 4DCBCT.

We assessed the performance of the UNET in terms of RMSE and Pearson correlation to the actual respiratory displacement and phase. State-of-art baseline and phase estimation is based on elliptical shape tracking in augmented state space and Poincaré sectioning principle [1]. For comparison we used a state-of-the-art phase prediction method [1].

RESULTS

In Figure 2, the predicted respiratory displacement from the UNET shows a good approximation of the actual displacement (r>0.6 up to 1.5 s). From this prediction, respiratory phase was calculated.

The state-of-the-art phase predictor incorrectly estimated the phase between the 100th and 180th sample due to the previous respiration cycle being smaller (50 vs 150). The UNET calculates the respiratory phase incorrectly in the middle (50th -100th samples) at the end of the respiratory cycle (150th-160th samples) due to incorrectly calculated turning points.

The RMSE linearly increased until 1.5s while the Pearson correlation remained above 0.6 (Figure 3).

Overall, the UNET did not offer any benefit compared to state-of-the-art method to predict phase with RMSE of 0.084 vs 0.019 [1].

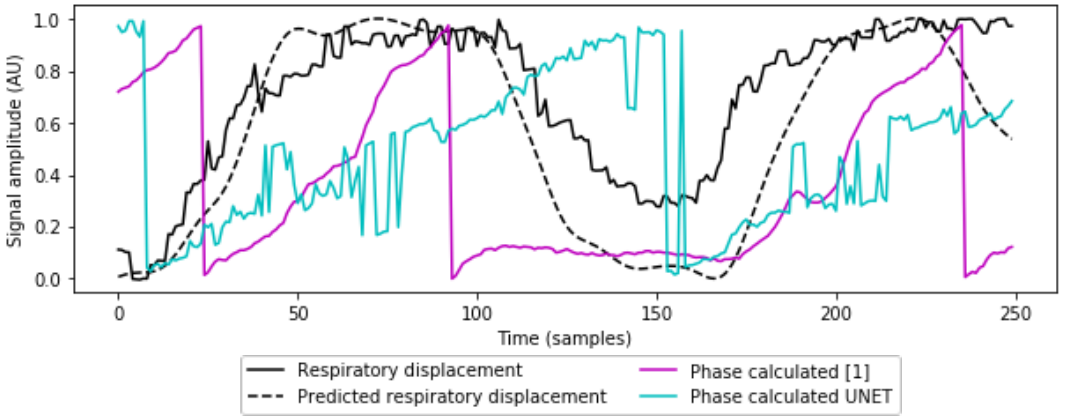
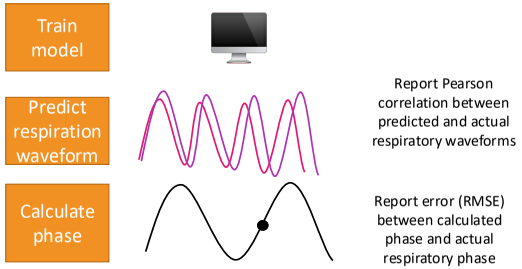


Figure 2: Respiratory displacement and phase calculations



RESULTS

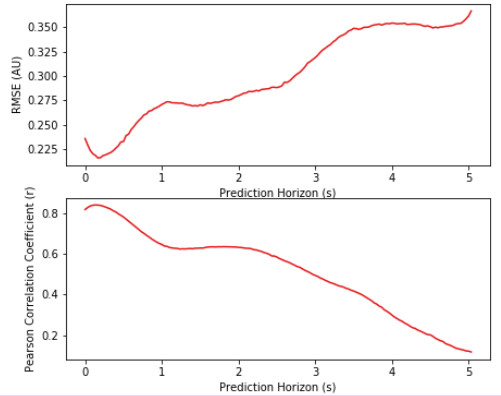


Figure 3: RMSE vs prediction horizon (top). Pearson correlation vs prediction horizon (bottom)

CONCLUSIONS

This is the first implementation of machine learning to predict respiratory phase. While the overall prediction was not better than the state of art [1], we believe that it would could offer benefits during erratic breathing.

With an increasing demand to perform more complex computations on the fly to improve image quality, it is likely that an associated system lag would increase. Therefore, mitigating against this lag will become more important in the future.

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Chapter 5

Extracting breathing indices in healthy populations

5.1 Introduction

In the previous chapter the technological challenges faced when developing hardware to continuously monitor breathing was explored. Then a potential machine learning approach to measure respiratory rate was introduced. Chapter 5 presents a machine learning framework leveraging off the model presented in Chapter 4 that can be applied to extract breathing indices in healthy populations to answer the following research question:

- Research Question 6: What are the optimum parameters for using single recurrent neural network to predict respiratory metrics in a larger group of healthy individuals?

Chapter 5 consists of a published peer-reviewed journal paper which is reproduced under the terms of Creative Commons Attribution 4.0 licence:

Prinable, J., Jones, P., Boland, D., Thamrin, C., & McEwan, A. Derivation of breathing metrics from a photoplethysmograph at rest.

Statement of Contributions of Joint Authorship:

- Joseph Barry Yoo Sik Prinable (Candidate): corresponding author, providing the main idea, writing, reviewing and editing of the manuscript.
- Peter Jones (Alternate Supervisor): proof reading, reviewing and editing the manuscript.
- David Boland: proof reading, reviewing and editing the manuscript.
- Alistair McEwan (Principle Supervisor): proof reading, reviewing and editing the manuscript.
- Cindy Thamrin (Alternate Supervisor): proof reading, reviewing and editing the manuscript.

5.2 LSTM Methodology

In this chapter it was found that a recurrent neural network could predict tidal volume from a pulse oximiter. The model presented in Chapter 4 was extended to

include ten healthy participants. A single recurrent network could predict a variety of breathing metrics that hadn't been derived previously in literature. Over a 40 second window the LSTM model predicted breathing metrics with a bias and Limits of Agreement for inspiration time 0.03 s(-1.14, 1.20), expiration time 0.05 s (-1.07, 0.96), respiratory rate 0.12 (-1.5,1.75), inter-breath intervals -0.06 s (-1.29, 1.16) and the I:E ratio 0.00 (-.45, 0.46) A constraint of using machine learning in this context was the small datasets used to generate a model. However, these findings especially respiratory rate outperform all classical signal processing methods to date. In terms of respiratory rate, the new approach outperforms the ECG derived approach that had a bias of 0 bpm and Limits of Agreement of -4.7 to 4.7 bpm presented by Charlton et al. [1]. Large biomedical technology companies are better positioned to capture large quantities of data across many demographic groups and potentially improve the accuracy of derived breathing metrics using the methodology described in this chapter.

5.3 Concluding Remarks

In this chapter a machine learning framework was presented that could derive a series of respiratory metrics from 10 healthy participants. Importantly, this new framework allowed an improvement of accuracy for respiratory rate and potentially overcomes the physiological decoupling of respiratory motion on the cardiac waveform at higher respiratory rates. The results of this chapter will be useful for other groups as a benchmark by which to compare new machine learning approaches (or other classical signal processing techniques). In the next chapter, the ability to discern between asthma and health groups by comparing the breathing indices is investigated.

Original Paper

Derivation of Breathing Metrics From a Photoplethysmogram at Rest: Machine Learning Methodology

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Abstract

Background: There has been a recent increased interest in monitoring health using wearable sensor technologies; however, few have focused on breathing. The ability to monitor breathing metrics may have indications both for general health as well as respiratory conditions such as asthma, where long-term monitoring of lung function has shown promising utility.

Objective: In this paper, we explore a long short-term memory (LSTM) architecture and predict measures of interbreath intervals, respiratory rate, and the inspiration-expiration ratio from a photoplethysmogram signal. This serves as a proof-of-concept study of the applicability of a machine learning architecture to the derivation of respiratory metrics.

Methods: A pulse oximeter was mounted to the left index finger of 9 healthy subjects who breathed at controlled respiratory rates. A respiratory band was used to collect a reference signal as a comparison.

Results: Over a 40-second window, the LSTM model predicted a respiratory waveform through which breathing metrics could be derived with a bias value and 95% CI. Metrics included inspiration time (–0.16 seconds, –1.64 to 1.31 seconds), expiration time (0.09 seconds, –1.35 to 1.53 seconds), respiratory rate (0.12 breaths per minute, –2.13 to 2.37 breaths per minute), interbreath intervals (–0.07 seconds, –1.75 to 1.61 seconds), and the inspiration-expiration ratio (0.09, –0.66 to 0.84).

Conclusions: A trained LSTM model shows acceptable accuracy for deriving breathing metrics and could be useful for long-term breathing monitoring in health. Its utility in respiratory disease (eg, asthma) warrants further investigation.

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KEYWORDS

photoplethysmogram; respiration; asthma monitoring; LSTM

Introduction

There has been increasing interest in monitoring health using wearable sensors. However, very few technologies have focused on the breathing signal. The ability to monitor breathing may be beneficial for general health and particularly for asthma, which is a health condition that affects over 300 million people globally [1]. Monitoring of lung function using specialized metrics such as peak expiratory flow has been shown to be useful for predicting risk of an asthma episode [2]; however, this can be difficult to perform for patients as it involves forced maneuvers. It remains to be seen whether continuous monitoring of simple breathing metrics such as the interbreath interval (IBI) and the inspiration-expiration (I:E) ratio could provide further information on asthma control [3] and disease status [4].

The availability of a noninvasive sensor that measures breathing continuously and in an ambulatory manner would facilitate studies to establish clinical utility. One sensor of interest is the pulse oximeter that is commonly used in a clinical setting to measure both arterial blood oxygen saturation (SPO_2) and heart rate. A tidal breathing method exists that also shows promise for clinical prediction [5]; however, these methods are unsuitable

for continuous monitoring (eg, during walking or exercise). It was recently shown that a pulse oximeter can also be used to continuously monitor respiratory rate in a clinical setting [6]. This is possible because breathing periodicity [6,7] and effort [8] modulate photoplethysmogram (PPG) amplitude, frequency, and baseline wander [9,10]. Filtering and feature-based signal processing approaches can be applied to the PPG signal to extract a surrogate respiratory signal. This in turn can be processed to derive breathing rate (BR) with varying degrees of accuracy [7].

Unfortunately, there is poor amplitude correlation between the surrogate respiratory waveform and a gold standard respiratory trace. This poor correlation may make the I:E ratio difficult or impossible to derive using existing methods. In this work, we sought to address this using machine learning. In a previous pilot study [11], we demonstrated how a long short-term memory (LSTM) approach could predict a respiratory waveform from which BR could be derived. LSTM is a type of a recurrent neural network that can capture long-term, time-based dependencies in data [12]. Through the LSTM, we showed that the Pearson correlation coefficient between the derived respiratory waveform and a pneumotachograph trace had similarly high r values (r>0.8) to existing methods. In this paper, we built on this study by investigating the accuracy to which IBI, I:E ratio, and BR respiratory metrics can be attained from a PPG-derived surrogate respiratory waveform using an LSTM. We show that, in comparison to existing approaches, we can derive breathing metrics to a higher degree of accuracy from a pulse oximeter.

Methods

Datasets

Data Collection

Measurements were recorded from a group of 10 healthy participants who provided informed consent. The protocol for this study was approved by Northern Sydney Local Health District Human Research Ethics Committee (LNR/16/HAWKE/99 ethics approval). Participants conducted 5 randomized breathing serials at a rate of 6, 8, 10, 12, or 14 breaths per minute (BPM). Each serial was conducted for 5 minutes. Each participant was coached to breath one full inhalation and exhalation in time with a visual prompt.

An Alice PDx (Philips Respironics, Murrysville, PA) portable sleep diagnostic system was used to measure physiological signals during this study. The supplied pulse oximeter was attached to the index finger of the nonmaster hand, allowing the capture of a raw PPG trace, SPO_2, and pulse rate data. The Alice PDx reported calculated values for SPO_2 and pulse rate 3 times per second. PPG signals were sampled at 75 Hz.

Respiratory inductance plethysmography is a method to measure relative tidal volume (RTV) as a function of the chest and abdominal wall movement [13]. In this study, inductance bands were placed around the abdomen and ribcage according to the manufacturer's guidelines, allowing RTV to be estimated as the weighted sum of the chest and abdominal wall inductance signals. The Alice PDx system reported an RTV signal based on the contribution of both respiratory bands and was captured at 100 Hz.

Description of Available Features

The Alice PDx system outputs three independent time series: PPG, SPO_2, and pulse rate. The SPO_2, processed PPG, and pulse rate signals were up-sampled to 25 Hz while the RTV was down-sampled to 25 Hz before normalizing between ±1. The sampling rate of 25 Hz was selected to ensure respiratory rate accuracy [7,14] and so that all time series data had the same time scale.

In addition to the three time series given by the Alice PDx system, a bandpassed PPG time series was generated by passing the original PPG signal through a sixth order Butterworth bandpass filter with a center frequency corresponding to the respiratory rate of the signal with a bandwidth of 0.002 Hz. This additional time series was included because our previous findings suggested that this feature could improve model prediction [11].

Altogether, the available features used within our model are as follows:

- Feature 1: PPG
- Feature 2: bandpassed PPG
- Feature 3: SPO_2
- Feature 4: pulse rate

We previously determined experimentally that the inclusion of SPO_2 and pulse rate values helped inform the network when decoupling between the pulse signal and respiratory signal occurs [11]. The exact underlying physiological mechanisms are unclear.

Derivation of a Respiratory Waveform Time Series

For comparison purposes, RRest toolbox [15] was used to extract respiratory waveforms from a PPG using 10 feature-based and filter-based algorithms as shown in Figure 1. The resulting respiratory waveforms were temporally aligned to correspond with the reference respiratory waveform in the test set for comparison purposes. The techniques used to derive the respiratory waveforms, as well as our LSTM method, are described in Table 1.

Figure 1. Using existing filter-based and feature-based methods, 10 relative respiratory waveforms were derived from a photoplethysmogram (PPG) signal, and another relative respiratory waveform was derived using a long short-term memory (LSTM) that accepts PPG, arterial blood oxygen saturation (SPO2), band-passed (BP) PPG, and pulse rate inputs. BR: breathing rate; I:E: inspiration-expiration ratio; IBI: interbreath interval.

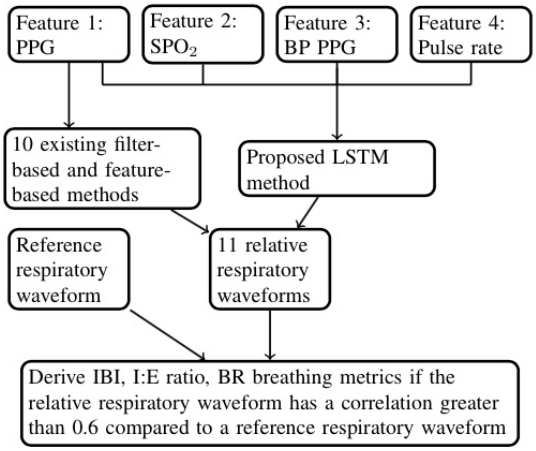


Table 1. Techniques for the extraction of respiratory signals from a photoplethysmogram (adapted from Charlton et al [15]).

Respiratory signal	Description
Filter-based	
X_{A1}	Bandpass filter between plausible respiratory frequencies
X_{A2}	Maximum amplitude of the CWT[a] within plausible cardiac frequencies (30-220 beats per minute) [16]
X_{A3}	The frequency corresponding to the maximum amplitude of the CWT within plausible cardiac frequencies [16]
Feature-based	
X_{B1}	Mean amplitude of troughs and proceeding peaks [7]
X_{B2}	Difference between the amplitudes of troughs and proceeding peaks [17]
X_{B3}	Time interval between consecutive troughs [17]
X_{B4}	Mean signal value between consecutive troughs [18]
X_{B5}	Peak amplitude [17]
X_{B6}	Trough amplitude [18]
X_{B10}	PPG[b] pulse width estimation using a wave boundary detection algorithm [19]
Machine learning–based	
X_{LSTM}[c]	Proposed LSTM method

[a]CWT: continuous wavelet transform.

[b]PPG: photoplethysmogram.

[c]LSTM: long short-term memory.

LSTM Architecture and Parameters

We propose the use of an LSTM model as an alternative to the signal processing methods described in Table 1. In this section, we discuss our training and validation procedures to determine an appropriate LSTM architecture to predict a respiratory waveform.

The core component of an LSTM architecture is a memory cell whose characteristics allow long-term data dependencies to be captured. A single LSTM cell uses gate mechanisms to forget irrelevant parts of a previous state, selectively update the current cell state, and to output the cell state [12]. Each cell contains a number of hidden units that define the dimensionality of both the current and output states. Increasing hidden units within a model may lead to overfitting. Conversely, reducing hidden units below a certain threshold will not allow a model to be trained.

Hyperparameter Search

We first conducted a structured, though nonexhaustive, hyperparameter search to determine suitable values for our final LSTM architecture. We then performed more extensive training to maximize the performance of our final architecture.

Hyperparameter Exploration

An open-source Python 3.5 library called TensorFlow r1.3 was used to train the LSTM model on a Dell Optiplex D810 (i7, 32 GB RAM; Dell Inc, Round Rock, TX) and two Titan Xp (Nvidia Corp, Santa Clara, CA) graphics processing units (GPUs).

The AdamOptimizer class of Tensorflow was used to train the LSTM using a learning rate of 0.0005 for 100 epochs with a batch size of 128. We explored the effect of changing the amount of cells (100, 300, 500), hidden units within a cell (500, 1500, 2500), and layers (1, 2, 3) and compared the results against a default model containing 100 cells, 500 hidden units, and a single layer. For this study, cells were layered sequentially two times to improve model accuracy and robustness [20]. The dropout layer was placed between each layer with a dropout rate of 0.5 to reduce overfitting [21]. There was a single dense, fully connected layer at the end.

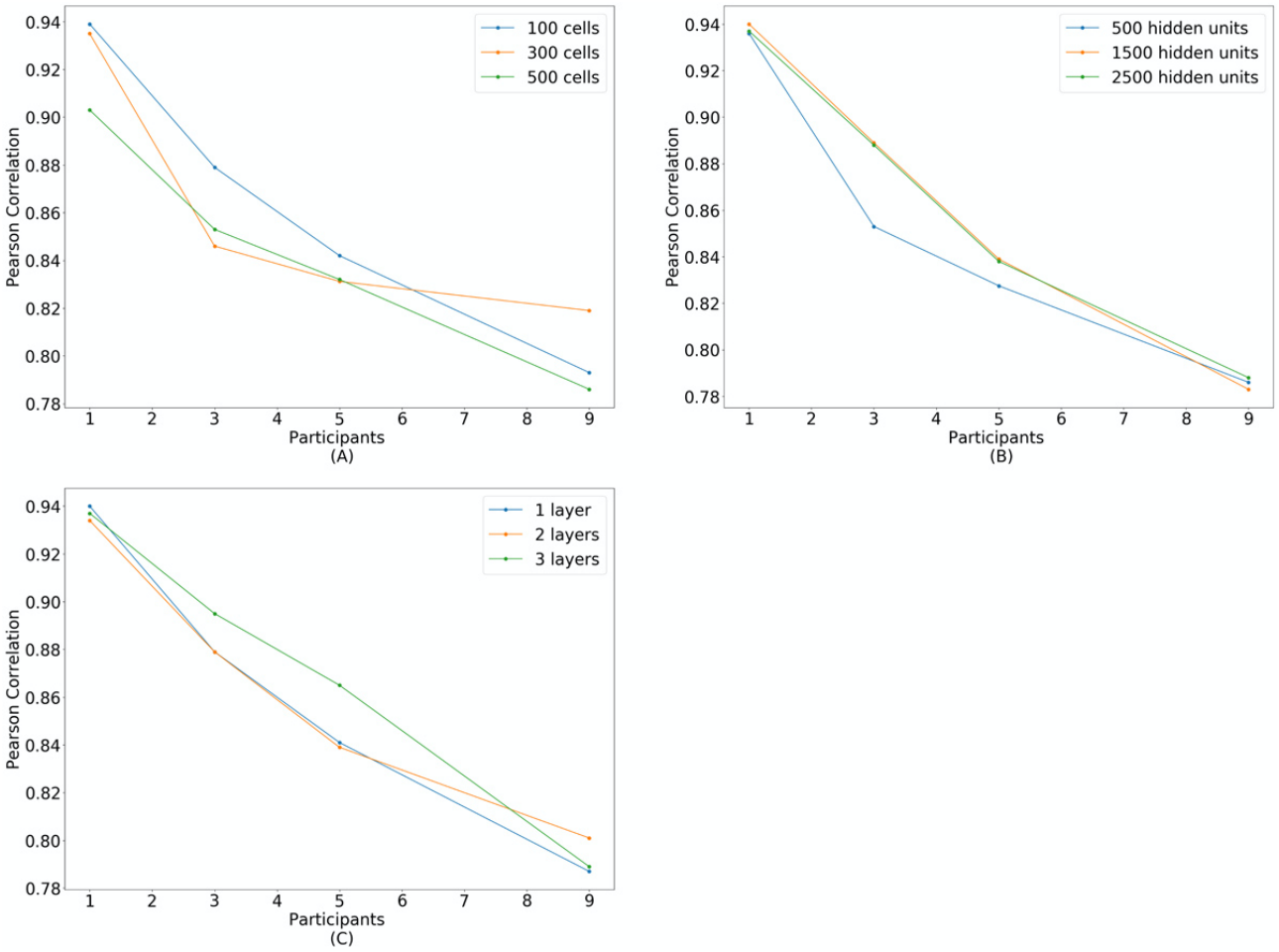
To minimize training time for hyperparameter exploration, 4 smaller training datasets were created from the original 45 unique datasets (9 participants, each with 5 breathing serials). These datasets contained data from 1 participant (7), 3 participants (3, 5, 7), 5 participants (1, 3, 5, 7, 9), or 9 (1, 2, 3, 4, 5, 6, 7, 8, 9) participants. This allowed us to compare model performance as the number of participants increased for the various configurations. To further reduce training time, each dataset was reduced to 1 minute of data, splitting 70%, 15%, and 15% into training, validation, and test sets, respectively. To assess the performance of the model, we conducted 5-fold cross validation. To reduce computational time that typically results in higher error bias but lower variability, we chose 5 folds over 10 folds [22]. We investigated permutations of the available features and found that accuracy increased with the number of features with a minimal cost in terms of execution time.

Table 2 shows the training time in minutes as a function of participants and the hyperparameter. The Pearson correlation coefficients between the derived and reference respiratory waveforms are plotted as a function of increasing number of participants for the chosen cell values (Table 2) in Figure 2A, hidden unit values in Figure 2B, and layer values in Figure 2C. The highest correlation was achieved with 300 cells and 2 layers for 9 participants. For hidden units, the correlation was similar between the quantities, with 2500 hidden units only slightly better than 500 (0.786 vs 0.788). Due to the minimal difference, the latter was selected as it required significantly less training time (211 minutes vs 1213 minutes) for comparable performance.

Table 2. Training time (minutes) for the hyperparameter search.

Hyperparameters	1 participant	3 participants	5 participants	9 participants
Cells				
100	24	75	110	208
300	54	200	272	505
500	84	313	542	932
Hidden units				
500	24	69	150	211
1500	52	161	264	482
2500	131	402	665	1213
Layers				
1	24	65	116	220
2	35	125	190	366
3	48	158	271	470

Figure 2. Pearson correlation values between derived and reference respiratory waveforms, given a dataset containing n participants, for a long short-term memory (LSTM) with (A) cells of size 100, 300, and 500; (B) hidden units of size 500, 1500, and 2500; (C) layers of size 1, 2, and 3.



Final Model Training

The final model had around 8257 trainable parameters consisting of 300 cells, 2 layers, and 16 hidden layers. To train our final model, we used AdamOptimizer with an initial learning rate of 0.02 and batch size of 256. We conducted 5-fold cross validation with approximately 223,786 training examples per fold with early stopping.

Extraction of Breathing Metrics

We defined a valid window when the Pearson correlation coefficient was >0.6 between the gold standard respiratory waveform and derived tidal volume waveform (TVW) in the window. For test sets that contained valid windows, we extracted peaks and troughs in MATLAB R2016b (MathWorks Inc, Natick, MA). To find the maximum points, 'findpeaks' was used, and we used a linear search algorithm to find the global minimum between 2 consecutive peaks. Using the peak and trough data, we extracted the following: IBI (the period in seconds between 2 consecutive peaks within the TVW signal), inspiration time (period in seconds between a trough and peak within the TVW signal), expiration period (period in seconds between a peak and trough within the TVW signal), and I:E (ratio between consecutive inspiration time and expiration period).

We then evaluated the Bland-Altman agreement [13] between the derived respiratory metrics to reference metrics.

Additionally, the root mean square error between hypothesized RTV signal y(t) and the true RTV Y(t) was calculated for each person and respiratory rate and subsequently averaged across the 5 folds.

Results

Data Collection

Data were acquired from 10 healthy subjects. One subject was excluded because of incomplete recordings due to an SD card save error on the Alice PDx. Therefore, data for 9 subjects were analyzed. The median (lower, upper quartiles) age of the analyzed subjects was 28 years (24.5 to 33.0 years). Median BMI was 23.59 kg/m^2 (21.28 to 30.04 kg/m^2), and 3 subjects (3/9, 33%) were female. In total, we recorded 3.75 hours of data, consisting of 5 minutes * 5 breathing rates * 9 participants.

Model Validation

The weights and biases were saved for each epoch during training. Training was stopped when the validation error diverged to avoid overfitting. Early stopping occurred when the validation cost did not improve for 5 epochs.

Derivation of Breathing Metrics

In total, 225 unique test sets were created from 9 participants, at 5 respiratory rates, over 5 folds. Each test set was a window of 1000 samples (40 seconds) in length. We plotted the number of valid windows as a function of increasing Pearson correlation coefficients between derived and reference respiratory waveforms in 0.2 increments in Figure 3. For a Pearson correlation coefficient ≥0.6, our approach, X_{LSTM}, was valid for 191/225 (85%) windows, while the next highest performing algorithm, X_{A1}, was valid for 128/225 (57%) windows, followed by X_{A2}, which was valid for 119/225 (53%) windows. Other algorithms were excluded from further analysis due to a small percentage of valid windows: 21/225 (9%) for X_{A3}, 56/225 (25%) for X_{B1}, 38/225 (17%) for X_{B2}, 36/225 (16%) for X_{B3}, 23/225 (10%) for X_{B4}, 65/225 (29%) for X_{B5}, 52/225 (23%) for X_{B6}, and 11/225 (5%) for X_{B10}.

Breathing metrics were averaged over each 40-second test set. The mean (SD) between derived and gold standard metrics and their associated *t* test results are shown in Table 3. The Bland-Altman agreement between derived and gold standard metrics for all subjects and respiratory rates are reported in Table 4. In the case of X_{LSTM}, a Savitzky-Golay filter was used to smooth the derived respiratory waveform prior to extracting the breathing metrics.

The Bland-Altman plot for the derived breathing metrics of inspiration time, expiration period, IBI, BR, and I:E across all participants (1-9) and all respiratory rates (6, 8, 10, 12, 14) using X_{LSTM} is shown in Figure 4. For comparison purposes, we report the Bland-Altman plot for derived respiratory rate across all participants and all respiratory rates using the highest performing algorithm found by Charlton et al [7] in Figure 5.

Figure 3. Number of valid windows as a function of increasing Pearson correlation coefficients between derived and reference respiratory waveforms in 0.2 increments. For an explanation of the variables please refer to Table 1.

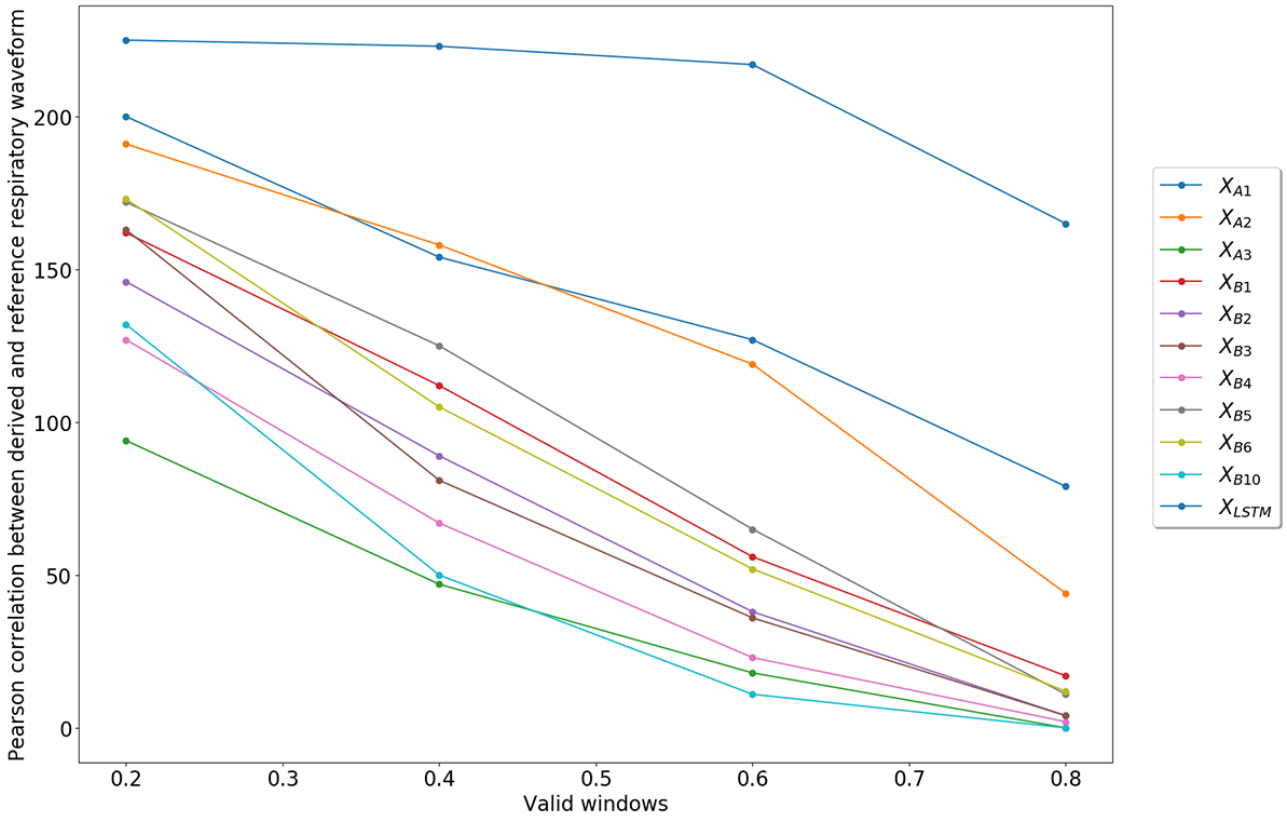


Table 3. Breathing metrics for the reference respiratory band, X_{LSTM}, X_{A1}, and X_{A2} methods, with their associated paired t test results.

Breathing metrics	Respiratory band, mean (SD)	X_{LSTM}[a]			X_{A1}			X_{A2}		
		Mean (SD)	t_{180} test	*P*	Mean (SD)	t_{126} test	*P*	Mean (SD)	t_{118} test	*P*
Tinsp[b] (seconds)	3.28 (1.29)	3.14 (1.15)	2.92	0.004	3.46 (1.31)	1.65	0.103	3.40 (1.42)	0.02	0.99
Texp[c] (seconds)	3.13 (1.01)	3.19 (1.05)	–1.68	0.095	3.38 (1.09)	–3.24	0.002	3.10 (0.95)	–1.44	0.152
BR[d] (BPM[e])	10.28 (2.72)	10.41 (2.74)	–1.39	0.167	9.69 (2.73)	1.93	0.056	10.35 (2.95)	–0.46	0.649
IBI[f] (seconds)	6.40 (1.98)	6.33 (1.96)	1.12	0.262	6.84 (2.09)	–2.18	0.031	6.50 (2.09)	–1.73	0.086
I:E[g]	1.01 (0.36)	1.09 (0.43)	–3.09	0.002	1.03 (0.40)	–2.68	0.008	1.00 (0.29)	–1.50	0.135

[a]LSTM: long short-term memory.

[b]Tinsp: inspiration time.

[c]Texp: expiration period.

[d]BR: breathing rate.

[e]BPM: breaths per minute.

[f]IBI: interbreath interval.

[g]I:E: inspiration:expiration ratio.

Table 4. Derived breathing metrics using the X_{LSTM}, X_{A1}, and X_{A2} methods and associated statistical analyses.

Method	Bland-Altman r^2	*P*	Absolute Bias	95% LoA[a]	Relative Bias (%)	95% LoA
Tinsp (seconds) [b]						
X_{LSTM}[c]	0.70	<.001	–0.16	–1.64 to 1.31	–3.70	–38.44 to 31.05
X_{A1}	0.74	<.001	–0.11	–1.51 to 1.30	–2.35	–35.65 to 30.95
X_{A2}	0.74	<.001	-0.01	–1.46 to 1.46	–0.22	–33.34 to 32.90
Texp (seconds)[d]						
X_{LSTM}	0.54	<.001	0.09	–1.35 to 1.53	2.35	–31.84 to 36.55
X_{A1}	0.41	<.001	0.25	–1.45 to 1.95	6.41	–32.82 to 45.63
X_{A2}	0.43	<.001	0.10	–1.39 to 1.59	2.70	–36.34 to 41.73
BR[e] **(BPM**[f]**)**						
X_{LSTM}	0.83	<.001	0.12	–2.13 to 2.37	1.22	–23.63 to 26.07
X_{A1}	0.92	<.001	–0.13	–1.68 to 1.41	–1.38	–18.42 to 15.65
X_{A2}	0.88	<.001	0.04	–1.94 to 2.02	0.14	–19.35 to 19.62
IBI[g] **(seconds)**						
X_{LSTM}	0.82	<.001	–0.07	–1.75 to 1.61	–0.98	–22.62 to 20.66
X_{A1}	0.88	<.001	0.14	–1.31 to 1.60	2.08	–16.55 to 20.70
X_{A2}	0.91	<.001	0.10	–1.13 to 1.33	1.37	–16.20 to 18.94
I:E[h]						
X_{LSTM}	0.30	<.001	0.09	–0.66 to 0.84	9.91	–63.89 to 83.70
X_{A1}	0.11	<.001	0.09	–0.68 to 0.87	6.65	–61.43 to 74.73
X_{A2}	0.04	<.001	0.05	–0.62 to 0.71	3.41	63.89 to 70.72

[a]LoA: limits of agreement.

[b]Tinsp: inspiration time.

[c]LSTM: long short-term memory.

[d]Texp: expiration period.

[e]BR: breathing rate.

[f]BPM: breaths per minute.

[g]IBI: interbreath interval.

[h]I:E: inspiration:expiration ratio.

Figure 4. Bland-Altman plots for (A) inspiration time (seconds), (B) expiration time (seconds), (C) interbreath interval (seconds), (D) breathing rate (breaths per minute), and (E) inspiration:expiration ratio using the LSTM method.

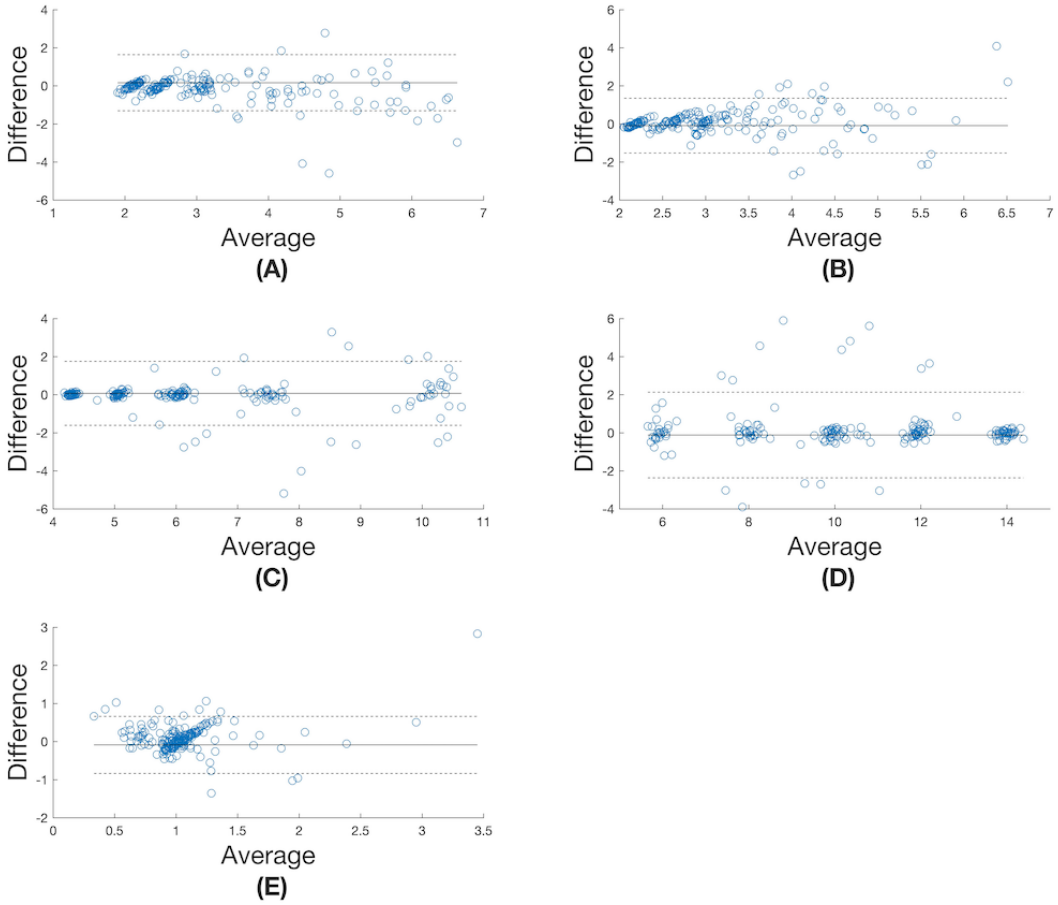
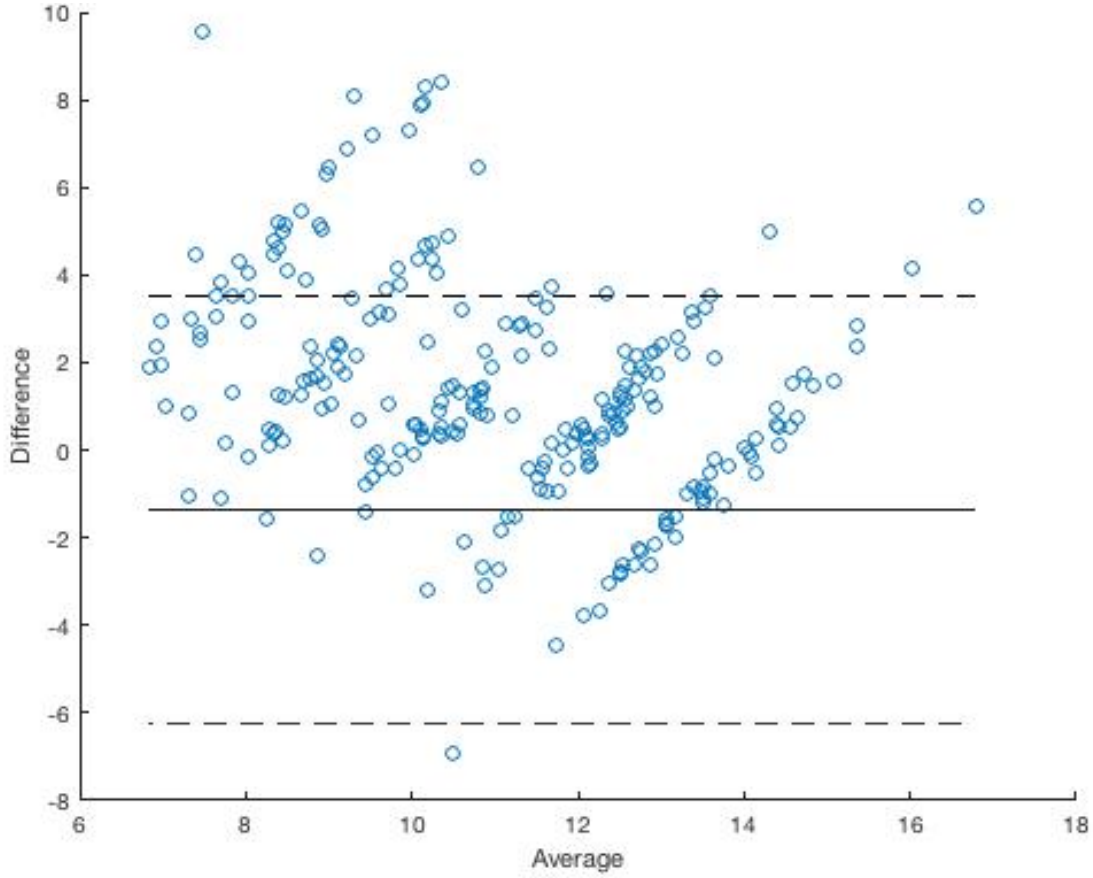


Figure 5. Bland-Altman plot for the highest performing algorithm ($X_{B1,2,3}E_{T4}F_{M1}$) found by Charlton et al [7].



Our model consistently performed comparably to the other methods, showing similar agreement (lower bias) and variability (narrower limits of agreement). The relative bias for our model was <4% for all breathing metrics examined except for I:E ratio (at 9.9%), which is within the limits of accuracy of existing standards on the estimation of breathing metrics using conventional methods [5], although the limits of variability are wide.

The differences for inspiration time are bound within the 95% CIs for average inspiration periods <4 seconds. Distinct clustering can be seen around an inspiration period of 2 seconds (Figure 4A). The differences for expiration period are bound within the 95% CIs for average expiration periods of 2-3 seconds (Figure 4B). For IBI, 4 distinct clusters occur corresponding to intervals of 4, 5, 6, and 7 seconds; however, the clustering weakens above 9 seconds (Figure 4C). For BR, 5 distinct clusters are formed corresponding to expected BRs of 6, 8, 10, 12, and 14 BPM (Figure 4D). There is noticeable clustering for I:Es of 0.8-1 (Figure 4E).

To quantify the accuracy of our model and provide a metric for future comparisons, we report the root mean square error over all participants and respiratory rates for X_{LSTM} for inspiration time (0.77 seconds), expiration period (0.74 seconds), IBI (0.8377 seconds), BR (0.86 BPM), and I:E (1.15).

Discussion

Principal Findings

In this work, we were interested in determining the feasibility of finding continuous measures of inspiration time, expiration period, IBI, BR, and I:E metrics from a PPG. We showed how an LSTM architecture could be used to predict these metrics for 191/225 (85%) test sets comprised of 9 participants at a respiratory rate of 6, 8, 10, 12, or 14 BPM. We conducted Bland-Altman analyses and found the LSTM was able to predict the average inspiration time of –0.16 seconds (–1.64 to 1.31 seconds) and expiration period of 0.09 seconds (–1.35 to 1.53 seconds) over a 40-second window. The LSTM was able to predict an I:E ratio of 0.09 (–0.66 to 0.84), although this was poorly correlated with reference values. However, this is the first time this metric is being reported in the literature as measured from a pulse signal.

The LSTM model was trained to minimize the error between derived and reference respiratory waveforms and was then able to generalize the breathing characteristics of 9 subjects and predict future respiratory waveforms based on PPG data. The ability to “see and learn” a reference signal presents a distinct advantage over existing methods. Through this approach, it was possible to determine the continuous average breathing metrics of inspiration time, expiration period, IBI, and BR for the majority of time (85%), exceeding a Pearson correlation threshold of 0.6. In contrast, these breathing metrics could only be derived, at best, around half the time (56% in the case of

X_{A1}) using existing feature-based and filter-based algorithms that did not rely on any previous reference data. While we directly compared the performance of X_{A1} and X_{A2} to the LSTM method, other methods were excluded from this analysis due to the fact that the correlation between the derived respiratory waveform and the gold standard was <0.6 more than 80% of the time. Feature-based techniques (X_{B1}-X_{B6}, X_{B10}) have performed well in previous respiratory rate algorithm assessments by Charlton et al [7] and would likely have similar performance on this dataset. In the cases where breathing metrics could be extracted for $X_{A1}$and X_{A2}, we found that the metrics of inspiration time, expiration period, and I:E were poorly correlated with the reference metrics, as shown in Table 4.

We conducted Bland-Altman analysis on the highest performing algorithm $X_{B1,2,3}E_{T4}F_{M1}$ found by Charlton et al [7] in his comparison of classical signal processing algorithms for PPG. The bias in our dataset compared to those in the dataset used by Charlton et al [7] was higher (–1.12 vs 1). However, the 95% limits of agreement (BPM) was lower (–2.4 to 2.1 vs –5.1 to 7.2). X_{LSTM} compares favorably to $X_{B1,2,3}E_{T4}F_{M1}$ with similar bias (0.12 vs –1.10) and a smaller 95% limits of agreement (BPM; –2.13 to 2.37 vs –2.63 to 2.44). The bias in our model compares well against existing standards on breathing metric estimation using conventional methods, which stipulate an accuracy of at least 2% for respiratory rate. It is worth noting that the standards are formulated for infant populations who breath faster. The wide variability seen in our model could be improved, although it is lower than that obtained from other methods examined. The high degree of variability could arise from differences in accuracy with different respiratory rates. While there is insufficient data from this study to ascertain this, it justifies use of longer-term data collection for further investigation.

The hyperparameters for the LSTM model were chosen in a structured, although non-exhaustive, manner by comparing a change in the number of cells, hidden units, or layers to a fixed model. Figures 2-4 show a decreasing trend in the correlation between the LSTM-derived respiratory waveform and the reference waveform as the number of participants increased. This trend occurred irrespective of the number of cells, hidden units, or layers. This may be accounted for, in part, by the complexity for which the LSTM model must account as the participant population increases. In the specific case of 300 cells, the correlation curve decreased quasi-exponentially. However, in the case of hidden units and layers, the correlation curve decreased quasi-linearly. It remains to be seen if the minimum correlation is bound between derived and reference respiratory waveforms for a given population. The findings of this paper show that our previous network parameter was much larger than required [11].

In this work, we used the following 4 features: PPG, filtered PPG, SPO_2, and pulse rate. We did not conduct feature selection, which may have helped to improve the overall model performance. It would be useful to see the effect of removing the filtered PPG signal feature to reduce additional preprocessing time and computational power.

Due to a limited participant population, we did not conduct leave-one-out participant cross validation. The shape of each respiratory waveform varied from person to person, and it is unlikely that the LSTM model derived in this work would be able to predict respiratory metrics from an unseen participant. However, with a larger training population, the LSTM model may be exposed to enough data to enable the accurate prediction of respiratory metrics in an unseen participant. Previously, we found that participants would prefer that a wearable sensor device have a watch form factor [23]. In this paper, we did not look at the feasibility of implementing an LSTM in this type of form factor. Currently, LSTM training requires GPU-grade computational power. With current low-power Bluetooth low energy devices [11,24,25], it may be possible to acquire PPG data and stream real-time data to a cloud-based GPU server to run online training. Once the weights and biases of the LSTM architecture are found, it may also be possible for an embedded platform to perform the required processing to obtain real-time breathing metric predictions. At present, field-programmable gate arrays can be used for real-time predictions and benefit from low latency and low power consumption [26]. Additionally, the field-programmable gate array architecture is reconfigurable. This would allow any potential device to be individually tailored to a specific model.

Conclusion

This paper presents the feasibility of monitoring simple breathing metrics such as the IBI, BR, inspiration time, expiration period, and I:E for a person at rest. We hope this proof-of-concept paper will inspire future research to collect further data and develop more powerful machine learning algorithms. In the future, it may also be possible to derive these metrics from a wristworn device that contains a pulse oximeter and accelerometer for a person at rest and support potential longitudinal studies to determine if these metrics can provide further information on asthma type [3] and provide any clinical utility [4].

Conflicts of Interest

None declared.

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Abbreviations

BPM: breaths per minute.
BR: breathing rate.
I:E: inspiration:expiration ratio.
IBI: interbreath interval.
GPU: graphics processing unit.
LoA: limits of agreement
LSTM: long short-term memory.
PPG: photoplethysmogram.
RTV: relative tidal volume.
Texp: expiration period.
Tinsp: inspiration time.
TVW: tidal volume waveform.

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Chapter 6

Proof of Concept in an Asthmatic Population

6.1 Introduction

In the previous chapter a machine learning framework to extract breathing indices from a pulse oximeter was presented. This framework is used to compare the differences in both health (n=10) and asthma groups (n=10 in this chapter). Additionally, in 2019 a U-Net [1] was used to derive respiratory rate from a pulse oximeter. This chapter answers the following questions:

- Research Question 7: How do two machine learning approaches (recurrent neural networks vs U-Net) perform in predicting respiratory metrics in health and asthma?

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Statement of Contributions of Joint Authorship:

- Joseph Barry Yoo Sik Prinable (Candidate): corresponding author, providing the main idea, writing, reviewing and editing of the manuscript.
- Peter Jones (Alternate Supervisor): proof reading, reviewing and editing the manuscript.
- David Boland: proof reading, reviewing and editing the manuscript.
- Alistair McEwan (Principle Supervisor): proof reading, reviewing and editing the manuscript.
- Cindy Thamrin (Alternate Supervisor): proof reading, reviewing and editing the manuscript.

6.2 U-Net and LSTM Methodology Comparison

The LSTM vs. U-Net model provided breathing metrics which were strongly correlated with those from the reference signal (all $p<0.001$, except for inspiratory: expiratory ratio). We found good bias across all metrics, however variability was high

and could be attributed to poor detection at low respiratory rates. The following absolute mean bias (Limits of Agreement) values were observed (in seconds): inspiration time 0.01(-2.31, 2.34) vs.-0.02(-2.19, 2.16), expiration time -0.19(-2.35, 1.98) vs.-0.24(-2.36, 1.89), and inter-breath intervals -0.19(-2.73, 2.35) vs. -0.25(-2.76,2.26). The inspiratory:expiratory ratios were -0.14(-1.43, 1.16) vs. -0.14(-1.42, 1.13). Respiratory rate(breaths per minute) values were 0.22(-2.51, 2.96) vs. 0.29(-2.54, 3.11). While percentage bias was low, the Limits of Agreement was high (35% for respiratory rate).

6.3 Concluding Remarks

In this chapter two state of the art machine learning frameworks were compared to determine their ability to derive a series of respiratory metrics from 10 healthy and 10 asthma participants. The results of this chapter will be useful for other groups as a benchmark by which to compare new machine learning approaches (or other classical signal processing techniques). The code for both models are accessible online (https://github.com/josephprinable/PPGtoRESP) and will provide de-identified data from the study participants upon reasonable request for scientific purposes and subject to ethics approval. In the next chapter a detailed discussion of this thesis is presented.

sensors

MDPI

Letter

Derivation of Respiratory Metrics in Health and Asthma

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Abstract: The ability to continuously monitor breathing metrics may have indications for general health as well as respiratory conditions such as asthma. However, few studies have focused on breathing due to a lack of available wearable technologies. To examine the performance of two machine learning algorithms in extracting breathing metrics from a finger-based pulse oximeter, which is amenable to long-term monitoring. Methods: Pulse oximetry data were collected from 11 healthy and 11 with asthma subjects who breathed at a range of controlled respiratory rates. U-shaped network (U-Net) and Long Short-Term Memory (LSTM) algorithms were applied to the data, and results compared against breathing metrics derived from respiratory inductance plethysmography measured simultaneously as a reference. Results: The LSTM vs. U-Net model provided breathing metrics which were strongly correlated with those from the reference signal (all $p < 0.001$, except for inspiratory: expiratory ratio). The following absolute mean bias (95% confidence interval) values were observed (in seconds): inspiration time 0.01(−2.31, 2.34) vs. −0.02(−2.19, 2.16), expiration time −0.19(−2.35, 1.98) vs. −0.24(−2.36, 1.89), and inter-breath intervals −0.19(−2.73, 2.35) vs. −0.25(2.76, 2.26). The inspiratory:expiratory ratios were −0.14(−1.43, 1.16) vs. −0.14(−1.42, 1.13). Respiratory rate (breaths per minute) values were 0.22(−2.51, 2.96) vs. 0.29(−2.54, 3.11). While percentage bias was low, the 95% limits of agreement was high (~35% for respiratory rate). Conclusion: Both machine learning models show strong correlation and good comparability with reference, with low bias though wide variability for deriving breathing metrics in asthma and health cohorts. Future efforts should focus on improvement of performance of these models, e.g., by increasing the size of the training dataset at the lower breathing rates.

Keywords: asthma; respiratory monitoring; machine learning; U-Net; LSTM

1. Introduction

There has been increasing interest in monitoring health using wearable sensors. However, very few developers have focused on technologies to monitor the breathing signal. While the ability to monitor breathing daily may be beneficial for tracking general health, it may also be especially relevant for respiratory-related diseases such as asthma and chronic obstructive pulmonary disease (COPD). In asthma, monitoring of lung health is often done using standardised lung function tests such as spirometry and peak expiratory flow; the latter has been shown to be useful for predicting the risk of an asthma episode [1,2]. However, these tests can be difficult to perform for patients, even with the availability of digital spirometers and peak flow meters outside the clinical setting, as it involves

forced manoeuvres and training. Although spirometry is important for the diagnosis of COPD, daily monitoring of spirometry/peak flow is considered to be of limited benefit and not commonly used in COPD [3]. The tests are also typically only done once or twice a day, and not suitable for continuous monitoring. In COPD, such tests are of limited benefit and not commonly used [3]. Monitoring respiratory rate has been shown to be useful in predicting upcoming COPD flare-ups [4], but such measurement was only possible via an oxygen monitor in patients who happened to be on home oxygen therapy.

The availability of a non-invasive sensor that measures breathing continuously and in an ambulatory manner would have potentially significant implications on day-to-day disease monitoring. One sensor of interest, and of widespread availability, is the pulse oximeter, which is commonly used in a clinical setting to measure both arterial blood oxygen saturation and heart rate. However, standard commercial pulse oximeters are not suitable for use outside the clinical setting because they require tethered/cabled fixture to the finger and their functionalities are limited during everyday activity, e.g., for walking or exercising, or during daily activities at home. Commercial wearable technologies from companies such as Garmin, Apple, and Fitbit, among others [5], contain pulse oximeters that can continuously monitor respiratory rate, heart rate, and O2 saturation outside a clinical setting, though their accuracy in extracting respiratory rate has not been clinically tested in a large cohort.

One challenge facing reliable application of pulse oximeter sensors is the accurate extraction of the breathing signal from the photoplethysmogram (PPG) signal. State-of-the-art machine learning algorithms have shown early promise in achieving this, in particular the U-shaped network (U-Net) [6] and Long Short-Term Memory (LSTM) architectures [7,8]. In our previous work [8], we demonstrated for the first time that detailed respiratory metrics could also be extracted from a volume trace acquired during normal, tidal breathing using a LSTM network in healthy participants. However, it is unclear how well the U-Net architecture can extract these metrics, nor how either of these methods perform in disease populations.

In this proof-of-concept study, we aimed to determine the feasibility of extracting the breathing signal and respiratory metrics from a PPG signal in both healthy and asthmatic populations, using the U-Net and LSTM machine learning algorithms, and compared the performance of these approaches against a gold standard respiratory band.

2. Materials and Methods

2.1. Study Subjects

Measurements were recorded from a group of participants (11 healthy and 11 with asthma) who provided informed consent. Subjects were volunteers recruited from the Woolcock Institute of Medical Research database. The protocol for this study was approved by Northern Sydney Local Health District Human Research Ethics Committee (#LNR/16/HAWKE99 ethics approval).

2.2. Breathing Data Collection

Participants conducted five randomized breathing serials at a rate of 6, 8, 10, 12, or 14 breaths per minute. Each serial was conducted for five minutes. Each participant was coached to breathe at a specific rate by following a visual prompt shown on a desktop screen. The prompt contained a window that was set to the target time for each breath and a marker showing % through the target time.

An Alice PDx (Phillips Respironics, Murrysville, PA, USA) portable diagnostics system was used to acquire measurements during the day. This provided the reference gold standard volume signal, based on electrical inductance changes arising out of movement detected by two elastic bands of winding coils wrapped around the chest and abdomen, sampled at 100 Hz. The Alice PDx also simultaneously measured the PPG signal sampled at 75 Hz. Both signals were subsequently resampled to 25 Hz to reduce the computational time required to train models.

2.3. Principle of Breathing Signal Extraction from the PPG Signal

It is possible to extract the breathing signal from the photoplethysmogram signal (PPG) generated by the pulse oximeter because breathing periodicity [9–11] and effort [12] modulate the PPG amplitude, frequency, and baseline wander. This is shown in Figure 1.

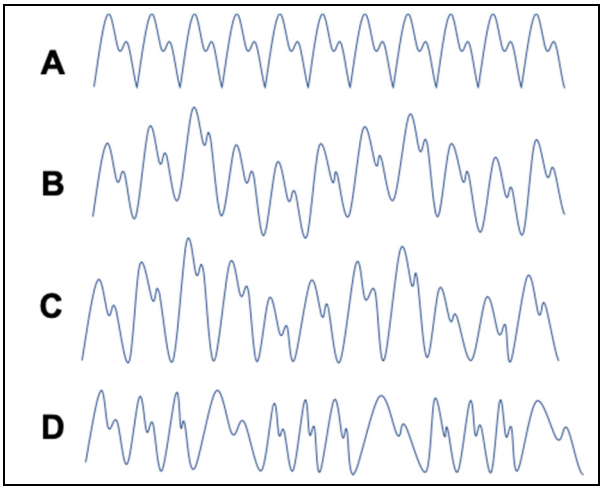

Figure 1. Illustrative examples of the photoplethysmographic signal showing: (**A**) no modulation or wander; (**B**) baseline wander; (**C**) amplitude modulation; (**D**) pulse width modulation potentially induced by breathing cycles.

2.4. Machine Learning Models Used

We compared two machine learning architectures to extract the relative volume trace from the pulse signal: (1) the U-Net architecture, adapted from the original methods described by Rivichandran et al. [6] and (2) an LSTM network, previously described by Prinable et al [8]. The LSTM network is an architecture that has gated connections designed to learn patterns in historical data by regulating information flow, while a U-Net learns patterns by passing information through a series of filters. Both networks were trained on a Dell Optiplex D810, i7, 32 GB RAM, and two Titan Xp (NVIDIA, Santa Clara, CA, USA) graphics cards. Both models were programmed in Python using the Keras open-source library. Each model was trained over multiple epochs with each epoch referring to one run through the whole training dataset. We stopped model training if the performance did not improve after 5 epochs. The dataset was split up using 5-fold cross validation to verify the generalisation of the models.

2.5. Extraction of Key Breathing Metrics from Generated Volume Trace

The output of both the machine learning architectures was a Tidal Volume Waveform (TVW). A Savitzky–Golay filter was used to smooth the trace for both the LSTM and U-Net. We then extracted the following breathing metrics: inspiration period, expiration period, breathing rate, and inter-breath interval. The inspiration to expiration (I:E) ratio was calculated from the inspiration period and expiration period. These metrics are shown in Figure 2.

In this work, we define the previous terms as follows:

- inspiration period (Tinsp): the period in seconds between a trough and a peak within the TVW signal.
- expiration period (Texp): the period in seconds between a peak and a trough within the TVW signal.
- I:E ratio: the ratio between consecutive inspiration time and expiration period. Derived values for Tinsp and Texp are used for this calculation.

- inter-breath interval (IBI): the period in seconds between two consecutive peaks within the TVW signal.
- breathing rate (BR): the amount of breaths per minute (derived independently of IBI).

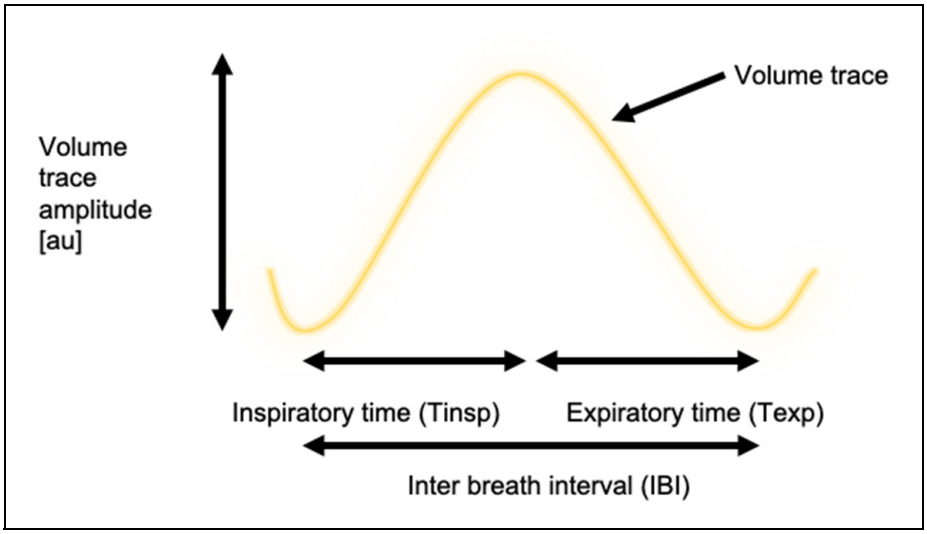

Figure 2. Diagrammatical definitions of respiratory metrics derived from a volume trace.

Since the breathing signal obtained from either the gold standard or the PPG signal is a relative rather than absolute volume trace, i.e., only showing relative changes in volume, we did not consider tidal volume as a metric.

2.6. Performance in Extracting Breathing Traces and Metrics

There was a total of 550 windows obtained from 22 participants, 5 breathing rates, and 5 folds of data. In each window, the reference respiratory metric was extracted and compared to both the LSTM and U-Net predictions. In our previous paper [8], we post-processed the output data and excluded windows that did not meet a specific minimum correlation. In this analysis, we used all the available data as a better representation of the accuracy that could be attained if the system was implemented in real time.

2.7. Statistical Analysis

The volume trace derived from the pulse oximetry sensor and the gold standard were compared using Pearson correlation coefficients. Extracted breathing metrics were compared against the gold standard using paired t-tests and Bland–Altman analyses.

3. Results

3.1. Participant Population

The demographic information of the 22 participants is shown in Table 1. Ten (45%) of the participants were male. The mean (standard deviation, SD) for participant age was 43.8 (18.0) years. Eleven participants reported doctor-diagnosed asthma, with optimal asthma control as a group (mean (SD) 5-point Asthma Control Questionnaire (ACQ5 [13]) score 1.04 (0.94)), though 2 of these had sub-optimal asthma control based on ACQ5 > 1.5. Table 1 shows that they have mild airflow limitation and obstruction based on spirometry (%predFEV1 and FEV1/FVC).

Table 1. Participant information for the study, stratified by health status.

	Status	
Characteristic	**No Asthma (n = 11)**	**Asthma (n = 11)**
Sex: Male n (%)	6 (55)	4 (36)
Age, mean (SD) years	30.1 (7.3)	55.9 (16.3)
BMI, mean (SD) kg/m^2	25.1 (4.8)	26.7 (5.0)
ACQ5, mean (SD)		1.04 (0.94)
%predFEV1, mean (SD)		84.6 (22.1)
%predFVC, mean (SD)		102.8 (15.9)
FEV1/FVC, mean (SD)%		68.3 (15.3)

ACQ5: 5-point Asthma Control Questionnaire; %predFEV1: Forced expiratory volume, percentage of predicted; %predFVC: Forced vital capacity, percentage of predicted; FEV1/FVC: Forced expired volume/forced vital capacity.

3.2. Datasets

An example window for 6, 8, 10, 12, and 14 breaths per minute is shown for Participant 1 in Figure 3.

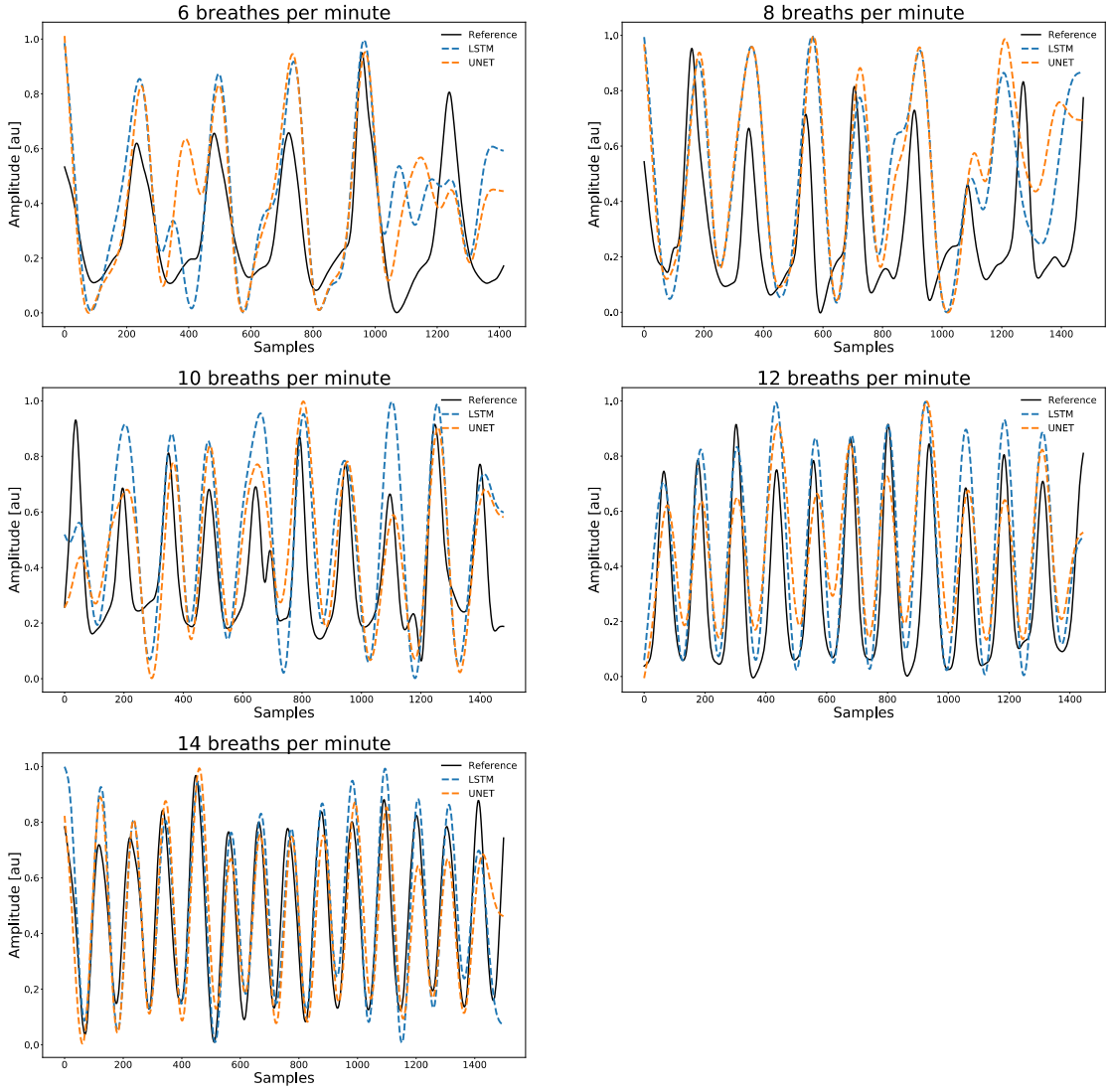

Figure 3. Example window for 6, 8, 10, 12, and 14 breaths per minute is shown for Participant 1.

Training Time

The LSTM trained slower: 18 (3) minutes vs. 11 (4) mins for the U-Net. Both architectures took an input of 320 samples (~13 seconds) and predicted a single sample from the respiratory waveform. Approximately 13 seconds of input data were selected based on previous parameter search optimisation [8]. The results of this comparison led to moderate correlation (r = 0.6) for both networks. The breakdown of windows that exceeded a certain correlation is shown in Figure 4.

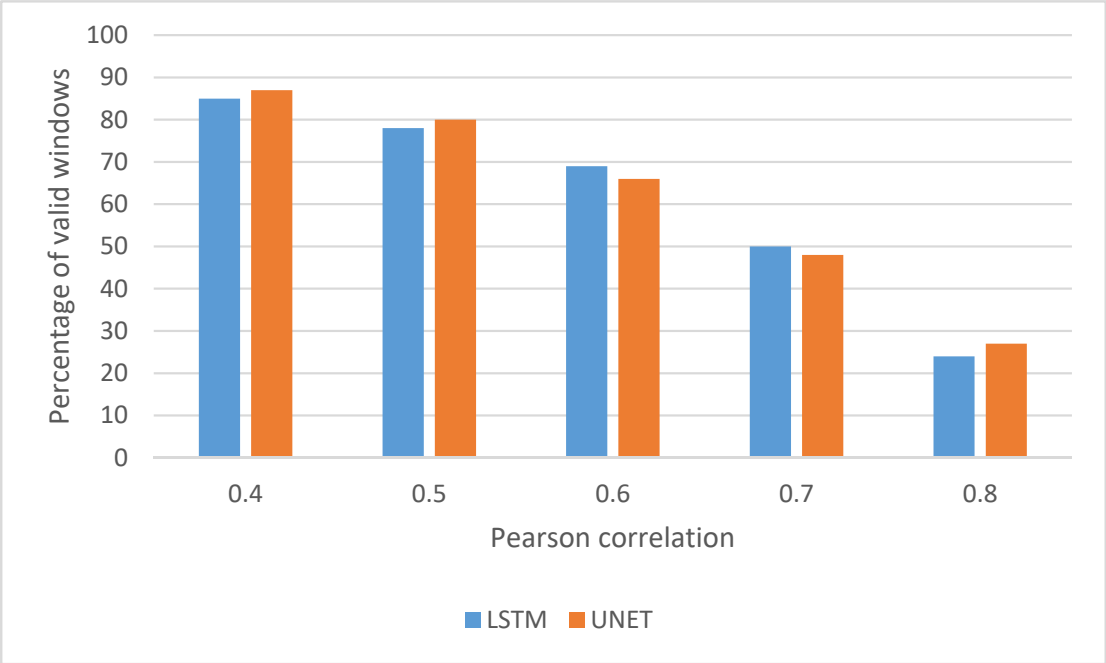

Figure 4. Percentage of valid windows exceeding corresponding Pearson correlation with the reference signal for the Long Short-Term Memory (LSTM) and U-shaped network (U-Net.)

The paired t-test between derived and gold standard metrics for all people and respiratory rates are reported in Table 2.

Table 2. Paired t-test between derived and gold standard metrics for all people and respiratory rates.

Metric	**Reference**	**LSTM n = 550**		**U-Net n = 550**	
	Mean (SD)	**Mean (SD)**	***p*-Value**	**Mean (SD)**	***p*-Value**
Tinsp (s)	3.50 (1.47)	3.51 (1.38)	$p = 0.87$	3.48 (1.33)	$p = 0.83$
Texp (s)	3.28 (1.19)	3.09 (0.88)	$p < 0.05$	3.04 (0.83)	$p = 0.001$
I:E ratio (unitless)	1.11 (0.62)	0.97 (0.20)	$p < 0.001$	0.96 (0.19)	$p = 2.63$
BR (BPM)	9.99 (2.81)	10.21 (2.53)	$p = 0.17$	10.28 (2.52)	$p = 0.07$
IBI (s)	6.77 (2.15)	6.59 (2.05)	$p = 0.14$	6.52 (1.99)	$p < 0.05$

The Pearson correlation and mean bias and 95% limits of agreement (LoA) between derived and gold standard metrics are shown in Table 3.

Table 3. Derived breathing metrics using the LSTM and U-Net methods and associated statistical analyses.

Method	r^2	p	Absolute Bias	95% LoA	Relative Bias (%)	95% LoA
Tinsp (seconds)						
LSTM	0.66	$p < 0.001$	0.01	−2.31 to 2.34	1.89	−52.95 to 56.74
U-Net	0.69	$p < 0.001$	−0.02	−2.19 to 2.16	1.30	−52.15 to 54.74
Texp (seconds)						
LSTM	0.46	$p < 0.001$	−0.19	−2.35 to 1.98	−3.70	−55.21 to 47.80
U-Net	0.47	$p < 0.001$	−0.24	−2.36 to 1.89	−4.97	−56.84 to 46.89
I:E ratio						
LSTM	−0.04	0.39	−0.14	−1.43 to 1.16	−4.65	−87.18 to 77.88
U-Net	0.01	0.89	−0.14	−1.42 to 1.13	−5.30	−87.07 to 76.47
IBI (seconds)						
LSTM	0.81	$p < 0.001$	−0.19	−2.73 to 2.35	−2.39	−32.76 to 27.97
U-Net	0.81	$p < 0.001$	−0.25	−2.76 to 2.26	−3.16	−33.69 to 27.36
BR (BPM)						
LSTM	0.87	$p < 0.001$	0.22	−2.51 to 2.96	2.99	−27.04 to 33.02
U-Net	0.86	$p < 0.001$	0.29	−2.54 to 3.11	3.69	−27.17 to 34.56

The Bland–Altman agreement between derived and gold standard metrics for all people and respiratory rates are shown for the U-Net in Figure 5 and LSTM in Figure 6.

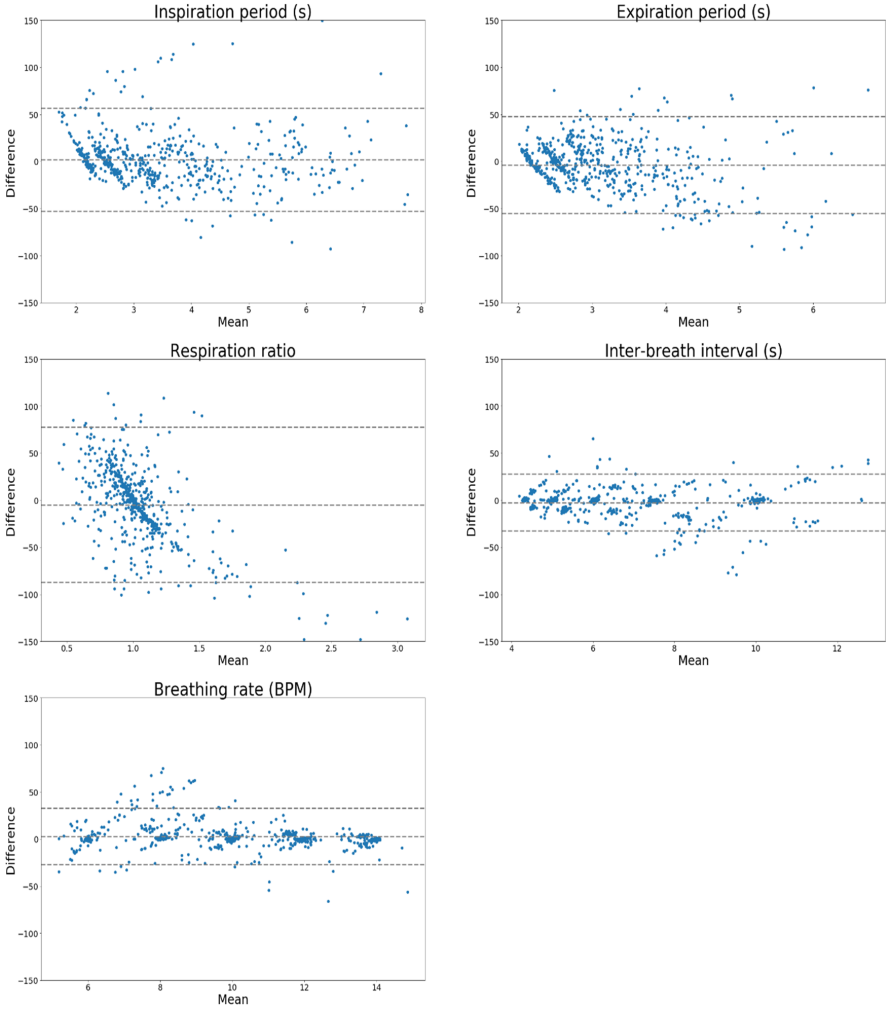

Figure 5. Bland–Altman agreement expressed as percent differences for LSTM architecture.

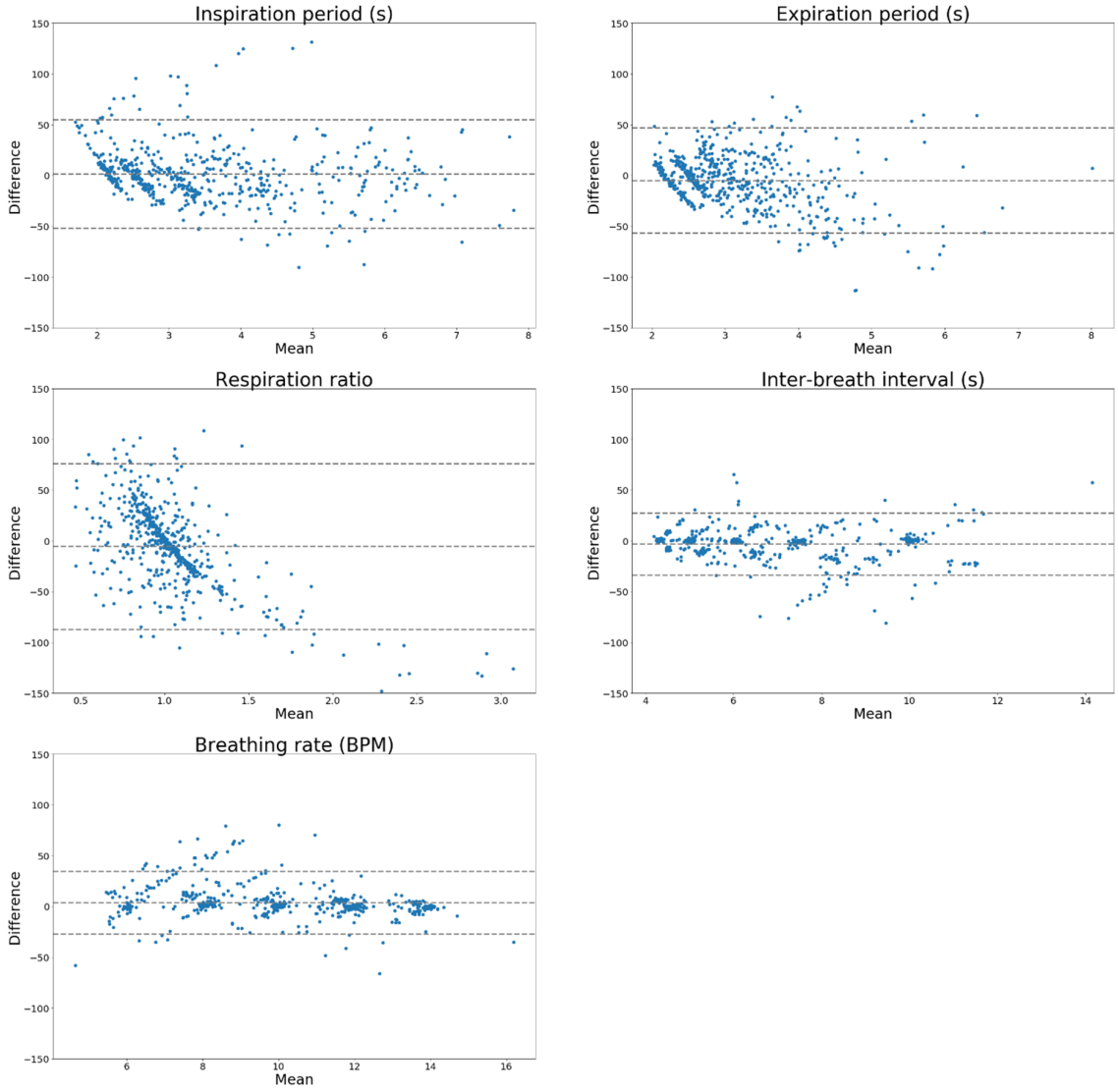

Figure 6. Bland–Altman agreement expressed as percent differences for U-Net architecture.

4. Discussion

This is the first implementation of machine learning methodologies to extract respiratory metrics from a PPG in both asthma and health groups in an ambulatory setting. While the Pearson correlation between the actual and predicted relative tidal waveform was relatively moderate (LSTM r = 0.65, U-Net r = 0.64), the resultant waveforms still contained sufficient information to adequately extract key breathing metrics of inspiration period, expiration period, inter-breath interval, and respiratory rate.

The U-Net showed similar performance to the LSTM in terms of extracted respiratory metrics with the reference signal as shown by the comparable bias for all metrics in Table 2. Both methods provided strong correlations with the gold standard, particularly for breathing rate and inter-breath intervals. However, the variability was very high for most metrics, with limits of agreement up to ±56% (with the exception of I:E ratio which had unacceptable performance overall). Best performance was seen again for the breathing rate and the inter-breath intervals, with limits of agreement up to ~35%.

The Bland–Altman plots (Figures 5 and 6) show evidence of proportional bias, which may be due to the detection of spurious breaths in the extracted volume traces which do not correspond directly to a real breath in the reference volume trace. This may have resulted in large apparent deviations in, e.g., the breathing rate or inter-breath interval compared to the closest available breath from the reference

signal; the deviation thus becomes larger with the size of the breathing rate or inter-breath interval itself. The proportional bias appears centred around each of the breathing rates used to train and test both models.

In the current work, the U-Net architecture required more computational power than the LSTM though it took a shorter time to train. If memory requirements are a major consideration in implementing a machine learning approach in a wearable device, then the LSTM should be selected. Otherwise, the U-Net is a better option to reduce training time with a large dataset.

To date, it is unclear whether continuous measures of breathing metrics such as Tinsp, Texp, IBI, and breathing rate are good predictors of an asthma exacerbation. Further, it is unclear as to how often respiratory measures would need to be captured to have a correlation to asthma exacerbation. If performance can be improved, then the limitation to achieving long-term, continuous monitoring of respiratory metrics to evaluate this will no longer be the algorithms themselves but, rather, the implementation of those algorithms on a wearable device. This will provide us with a tool to investigate the clinical utility of ambulatory respiratory monitoring. Furthermore, the data could be made securely accessible to a respiratory patient's doctor or nurse practitioner in real time for potential early intervention.

An area of concern for long-term monitoring with wearables is compliance. Previously, we found that smart watch technologies are likely to have the highest compliance rate compared to a chest strap or other respiratory monitoring device [14]. It is unlikely that these devices have the processing power to train models though they do have enough computing power to run them.

In practice, regardless of machine learning model used, patient-specific training would be necessary. This could be realised by having the individual wear a chest band in addition to a pulse capture smart watch for an initial "training" period and breathing at a range of respiratory rates, with the chest strap no longer being required after the model was successfully trained. We previously demonstrated that a single model was sufficient to predict respiratory rate for a single participant over the period of a month's time [6].

Our study has a number of limitations. First, breathing metrics derived with both models showed comparable bias across all breathing rates, but the variability was high particularly for inspiration and expiration times, and the respiratory ratio. The causes for this are unknown, but we noted that variability tended to be higher at the lower breathing rates and may be driven by poor breath detection. This, in turn, may be due to insufficient breaths available for training at these lower breathing rates, since fewer breaths are available during a fixed time period. Subsequent efforts should focus on improving the performance at these lower rates, by increasing the presence of low respiratory rate breathing cycles in the training dataset. Another approach to reduce variability would be to assess the quality of the PPG signal and exclude windows with poor quality [10,15], though this would mean loss of information during, e.g., noisy periods. Nevertheless, the bias and standard deviation presented in this work fall in line with our previous findings [8] and perform better in terms of bias and 95% LoAs for respiratory rate in other studies employing larger datasets [10,16–19]. The high variability may limit applicability in the clinical setting, but the performance may be adequate for general long-term monitoring of breathing rate for day-to-day use.

Second, the asthma cohort in this study have mild disease based on their lung function (%predFEV1 and FEV1/FVC). Ambulatory breathing patterns in severe asthma have not been well characterised, highlighting the lack of available tools for such investigations. Studies within clinical research laboratory settings have shown, e.g., no differences in variability during acute vs. refractory severe asthma [20], and yet increased variability of inter-breath intervals in some asthma phenotypes [21]. Further work will be needed to determine how the algorithms perform with severity of disease and irregular breathing, as well as patient factors such as age, BMI, and fitness status. However, we propose that may be partly mitigated with appropriate training based on the patient's own breathing pattern.

In conclusion, this work informs the further development of machine learning models for extracting respiratory metrics from PPG signals, using real-world data from both asthmatic and healthy

groups. We have demonstrated that such a modality is feasible, but training the data appropriately may be the key to successful implementation.

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Chapter 7

Discussion

7.1 Introduction

In this thesis, a number of aspects related to breathing monitoring using wearable technology were explored. A literature search to evaluate available wearable sensors and signal processing schemes suitable for capturing breathing metrics was conducted. Then an online survey of potential users of wearable technology to monitor breathing, both with and without respiratory disease, to find out rationale and preferences for such technology, was conducted and analysed. The feasibility and hardware considerations for acquiring pulse oximetry from a wearable sensor, and a machine learning framework to extract the breathing signal from the photoplethysmograph was explored. Finally, the performances and limitations of two machine learning approaches in both health and asthma volunteers were evaluated.

In this chapter the key findings, impact, limitations and future work arising out of this thesis are discussed. These are presented for the Research Questions posed in the Introduction. Next, framed around the findings of this thesis, areas of impact for smart watch technology that captures respiratory metrics for asthma and COPD populations, and how they may reduce burden to global health care facilities are discussed.

7.2 Key Findings, Impact, Limitations and Future Work

7.2.1 Research Question 1: What wearable sensor technologies are available for acquiring respiratory signals and what signal processing methods exist to extract respiratory signals from sensor technologies?

Overall, respiratory bands and to a lesser degree smart watch technology with embedded pulse oximeters seem to offer the best compromise between capturing multiple accurate respiratory metrics using mature signal processing methods, commercial availability, power efficiency and monitoring site/ perceived wearability.

To the best of our knowledge, there are few reviews relevant to the use of wearable technologies to capture breathing [1]. This review has provided a comprehensive analysis of the state-of-the-art research, and informed subsequent work on this thesis, allowing us to focus on the use of pulse oximetry to obtain breathing metrics for continuous respiration monitoring. In a broader context, this work informs scientists, engineers and clinicians as to the present capability of technology and how they may also facilitate longitudinal studies within and beyond the scope of respiratory diseases such as asthma and COPD.

We aimed to extensively cover all literature pertinent to continuous monitoring of breathing however, we did not review technologies that were not deemed "wearable." For example multi lead ECG. Further, we did not analyse technologies that were in their infancy, for example flex sensors, near field coherent sensing, and carbon black elastomers that are employed in T-shirt-based wearables.

It would be useful to review the current state of implantable sensors, advances to battery management systems, micro-electric circuits and discuss how these technologies could disrupt conventional methods of physiological data acquisition when they mature.

7.2.2 Research Question 2: What is the rationale for potential users, both with and without respiratory disease, to adopt new technologies that continuously monitor breathing over time?

A survey was completed by 134 participants (males: 39%, median age group: 50-59 years) including those who are healthy as well as those with asthma (n=77, 61% with suboptimal asthma control assessed using the Asthma Control Test). Of the 134 participants, 61.9% (83/134) would be willing to wear a device to monitor their breathing, in contrast to 6.7% (9/134) who would not. The remaining 31.3% (42/134) stated that their willingness depended on specific factors. Participants with asthma most commonly cited their asthma as motivation for using a wearable; the most common motivation for use in those without asthma was curiosity. More than 90% of total participants would use the device during the day, night, or both day and night [2].

The motivations and likelihood for adopting wearable technologies for the purpose of monitoring breathing were identified. It was found participants were motivated to adopt a wearable breathing monitor irrespective of health status, though rationale for use differed between those with and without asthma.

There were several limitations to this study. Firstly, the demographics of the sample group may not be indicative of the population in general across age, gender, education and health condition. Secondly, there was potentially high selection bias in those who chose to complete the survey towards those who were already motivated to adopt a wearable. Thirdly, people without asthma were younger than those with asthma, making it difficult to disentangle the effects of age and disease status. Finally, we also did not collect data on whether those who used other health monitoring devices were current or former users, or the reasons for discontinuation of use, which could be used to explore factors affecting adherence.

Frequency of daytime and night-time use was higher in older people. For example, older participants predicted they were more likely to wear the device 5 days a week or more during the night: 18-39 (37%, 7/19), 30-39, (59%, 16/27), 40-49 (53%,8/15), 50-59 (81%, 21/26), 60-69 (74%, 23/31), older than 70(77%, 10/13); P=.026. There is some suggestion from this work that older users are more ready to adopt health-related technologies, but the reasons for this require further investigation. Future studies could gather information on how long and why people stay engaged beyond curiosity, which would provide major insight into user psychology as well as device development."

7.2.3 Research Question 3: What are device-specific attributes that would meet the expectation of users, both with and without respiratory disease?

From the same survey, more than 90% of total participants would use the device during the day, night, or both day and night. Design preferences among all users included a wrist watch (nominated by 92.5% [124/134] for both day and night use, out of four body sites), the ability to synchronize breathing data with a mobile phone or tablet (81.3%, 109/134), overnight power charging (33.6%, 45/134), and a cost of $\leq$ AUD $100 (53.7%, 72/134) [2].

The results of this study inform us of which features are of high value and which features could be compromised in exchange for technical tradeoffs. Furthermore, acceptance of a new technology maybe affected by the perceived risk or inconvenience posed by the device.

There are factors limiting the applicability of our findings. First, display preferences were examined in a rudimentary manner in this survey, to determine whether graphical displays were preferred over text. Also, there was no assessment to detail whether participants understood how the information was presented, for example, by asking whether they thought the display indicated that their breathing was stable.

Once wearable technology is established to measure breathing over time, a focus group could be set up to explore more detailed user interaction features, such as useability, information display and feedback, user incentive/gamification to maximise adherence. These would pave the way towards future longitudinal studies to test feasibility device useability, and adherence in both health and respiratory disease.

7.2.4 Research Question 4: What are computing hardware limitations of using a pulse oximeter to derived a breathing signal?

There was a relatively low error (expressed in terms of the root-mean-square error, RSME) of <2 breathes per minute at 25% duty cycle for the top performing algorithm. However the error increased to over 5 breaths per minute when the duty cycle was reduced to 5%. However, there was a noticeable drop (3 times) in power consumption from a 25% duty cycle compared to a 5% duty cycle [3].

This work provides guidance to hardware developers as to the importance of maintaining higher LED power levels to achieve adequate degrees of accuracy and therefore suggests power consumption to be optimised in other areas.

There are factors limiting the applicability of our findings:

1. To date, there are no clinical guidelines on the minimum accuracy required to measure respiratory rate in adults (in contrast to infants) [4, 5], particularly on devices that do not directly measure flow. Longitudinal studies in adult populations, linking clinically captured respiratory metrics to health status over time would be required to address this issue.

2. Feasibility was assessed in PPG captured from a single participant once a week, albeit for a long period of time (for four consecutive weeks).

A nasal flow sensor is standard for assessment of breathing during clinical sleep studies, but further validation should include comparisons against other standard measures of flow of higher accuracy, e.g. a pneumotachograph (though this is less suitable for long-term monitoring and involves breathing into a mouthpiece) or respiratory inductance plethysmography.

7.2.5 Research Question 5: Is it feasible to use machine learning (recurrent neural network) to predict tidal volume traces from a pulse oximeter?

We explored the use of a Long Short-Term Memory (LSTM) machine learning architecture, and found it could predict normalised/relative tidal volume trace from a PPG signal in a single participant. The RMSE between actual and derived normalised tidal volume traces over the test set was 0.202 while the RMSE between peak to peak intervals was 0.7 s. While these findings are limited by a single participant it shows that with sufficient data it is possible to predict relative tidal volume, at rest, over differing time points [6].

This work showed it was possible to use neural networks to derive measures of respiration from a pulse oximiter and has led other groups to explore machine learning approaches to predict respiratory rate to improve derived respiratory rate accuracy.

There are factors limiting the applicability of our findings:

1. A sample size of one was used in this study.
2. There is a potential to miss between 0.45 to 4 seconds of data over a 15-minute period due to hardware limitations. This could be mitigated with hardware that is appropriately time calibrated.
3. k-fold validation was not implemented and it is possible the results are an over estimation of true accuracy.
4. The target set was normalised between 1 and -1 which results in a derivation of a relative tidal volume. This means that it is only possible to quantify changes in an individual's breathing pattern relative to their own baselines.
5. A bandpass filter specifically tailored to the frequencies of interest was used, thus potentially biasing this study towards reporting higher accuracy.
6. We did not directly compare this method to other existing signal processing methods.

Implementing the model in a larger study cohort is required to draw stronger evidence towards the use of machine learning as a method to be used to derive respiratory rate from a pulse oximeter. These studies should include comparison to existing literature using the same datasets.

7.2.6 Research Question 6: What are the optimum parameters for using single recurrent neural network to predict respiratory metrics in a larger group of healthy individuals?

Over a 40-second window, the LSTM model predicted a respiratory waveform through which breathing metrics could be derived with a bias value and 95% CI. Metrics included inspiration time (–0.16 seconds, –1.64 to 1.31 seconds), expiration time (0.09 seconds, –1.35 to 1.53 seconds), respiratory rate (0.12 breaths per minute, –2.13 to 2.37 breaths per minute), inter breath intervals (–0.07 seconds, –1.75 to 1.61 seconds), and the inspiration-expiration ratio (0.09, –0.66 to 0.84) [7].

This body of work outlines a machine learning framework used to predict a variety of respiratory metrics and sets the basis for other machine learning work to

benchmark against. In particular, this work presented a framework and optimisation of model parameters to predict relative tidal volume from a PPG which have been discussed in detail [7]. Further, through code porting it could be implemented in all current and commercial pulse oximiter enabled smart watches/bands to enable long term studies once accuracy is established.

There are factors limiting the applicability of our findings:

1. Due to a limited participant population, we did not conduct leave-one-out participant cross validation.

2. The shape of each respiratory waveform varied from person to person, and it is unlikely that the LSTM model derived in this work would be able to predict respiratory metrics from an unseen participant.

3. 40 second windows were used in this study and it is unclear of the accuracy if finer time granulation is required.

A study containing asthma participants would show feasibility to predict respiratory metrics in disease, and motivate long term studies to show how changes to respiratory metrics are linked to health status.

7.2.7 Research Question 7: How do two machine learning approaches (recurrent neural networks vs U-Net) perform in predicting respiratory metrics in health and asthma?

The LSTM vs. U-Net model provided breathing metrics which were strongly correlated with those from the reference signal (all $p<0.001$, except for inspiratory: expiratory ratio). We found good bias across all metrics, however variability was high and could be attributed to poor detection at low respiratory rates. The following absolute mean bias (95% confidence interval) values were observed (in seconds): inspiration time 0.01(-2.31, 2.34) vs.-0.02(-2.19, 2.16), expiration time -0.19(-2.35, 1.98) vs.-0.24(-2.36, 1.89), and inter-breath intervals -0.19(-2.73, 2.35) vs. -0.25(-2.76,2.26). The inspiratory:expiratory ratios were -0.14(-1.43, 1.16) vs. -0.14(-1.42, 1.13). Respiratory rate(breaths per minute) values were 0.22(-2.51, 2.96) vs. 0.29(-2.54, 3.11). While percentage bias was low, the 95% limits of agreement was high (35% for respiratory rate) [8].

These results are similar to previously reported findings where PPG derived respiratory rate was acquired with 95% LOAs of -5.1 to 7.2 bpm and bias of 1.0 bpm and ECG derived respiratory rate was acquired with 95% LOAs of -4.7 to 4.7 bpm and bias of 0 bpm. One explanation for these results is that the underlying mechanism which superimposes respiratory motion on the cardiac waveform tends to decouple at higher respiratory rates.

This work directly compared the performance of two state of the art machine learning approaches to predict respiratory metrics. Despite the wide variability, the performance compares well with the literature (Charlton et al.) and it provides information on how to approach poor performance. Additionally, this highlights the key capabilities of each method which importantly informs smart watch companies that there will be a trade off between accuracy, training speed and memory size.

There are factors limiting the applicability of our findings:

- The asthma cohort in this study can be considered to represent a low risk asthma group.

- The original U-Net architecture was modified to have the same amount of trainable weights as the LSTM so that there would be fair comparison between the two models.
- This was a proof of concept study and a larger cohort would be required to draw inference in a general asthma or health population.
- A pneumotachograph trace was not aligned to the predicted respiratory waveform. Therefore, it is unclear at what point the inspiration or expiration takes place."

The asthma cohort in this study can be considered to represent a low risk asthma group based on their asthma control score, %predFEV1, %predFVC and FEV1/FVC. Validation in a larger cohort with a wider spread of asthma control and severity would be necessary.

We speculate that patient-specific monitoring and prediction would improve performance, where custom models would be trained on an individual basis. This might be realised by having the individual wear a chest band in addition to a pulse capture smart watch for an initial "training" period, with the chest strap no longer being required after the model was successfully trained.

During this work a relative tidal volume trace was predicted from which respiratory metrics were derived. It would be useful determine how accurately these metrics can be derived directly from the PPG signal through reinforcement learning. This may potentially increase the accuracy of metrics, in particular the I:E ratio.

Having established feasibility and performance, next steps would be to investigate which continuous measures of breathing metrics such as Tinsp, Texp, IBI and breathing rate, as well as how often to acquire respiratory measures, that are most sensitive to disease status changes, e.g. future exacerbations in asthma or COPD.

This work has demonstrated the potential to acquire respiratory metrics with current technology and machine learning algorithms. It would be clinically useful to conduct long term studies to address two overarching questions:

7.3 Areas of impact for a smart watch capable of continuously monitoring respiratory metrics

7.3.1 Can smart watches that capture respiratory metrics be clinically useful for asthma and COPD populations?

There are four key areas that could benefit from long term monitoring of respiratory metrics in asthma and COPD populations.

1) Awareness: In chapter 3 it was found that regardless of health status there was no clear preference for how respiratory data was presented. Rather than presenting changes to respiratory metrics it may be more useful to report a risk matrix (i.e safe, warning, alert) through which the user can understand how their day/night time activity trends are related to their health status.

2) Reaction: In chapter 7 two machine learning models were presented that derived respiratory metrics. Based on these metrics the early detection of an exacerbation may be possible, which would enable the user sufficient time to change their environment or activity, before requiring an intervention.

3) Remotely testing the response to intervention and/or treatment: It would be useful to retrospectively investigate causal links between respiratory metrics and

intervention and/or treatment. If such links can be established clinicians could remotely monitor the health status of their patients in more rural and remote areas areas.

4) Biofeedback / breathing training: It was found in chapter 3 that biofeedback was important to certain users to track breathing patterns during stress, when they were breathless as well as during meditation. The metrics explored in this thesis would allow further breathing training beyond what is currently offered by smart watch companies with the ability to segment the breathing cycle into an inhale or exhale.

7.3.2 How can smart watches be used to reduce burden to global health care facilities?

The COVID19 pandemic has placed a prolonged burden on health care facilities and in many cases specialised respiratory clinics have been closed. In the future it would be useful to have alternate methods and devices that offer insight into lung and respiratory health without human contact or specialised equipment. While the efficacy of such methods and devices would need to be tested, clinicians may be able to have an indication of how well the prescribed interventions or treatment plans are working without physical visits.

In this current pandemic it is clear that screening methods have been a useful tool to elucidate how COVID19 has spread. While it is unclear as to the effectiveness of screening coupled with the COVIDSafe app issued by the Australian Governement, having additional measures offers further insight that was not previously possible. Especially in the cases where certain respiratory metrics could show indicators of immunity.

Finally, if potential correlations between respiratory metrics and disease status could be established, it may be possible to conduct remote screening across at risk populations at scale. This would allow heat maps of risk areas to be identified and appropriate resources allocated depending on population and risk factors. This large scale approach could yield important information that could inform decisions at a government level.

7.4 Conclusion

I hope this body of work will inspire future research to collect further data and develop more powerful machine learning algorithms. In the future, it may also be possible to derive these metrics from a wrist worn device that contains a pulse oximeter and accelerometer for a person at rest. The availability of this technology would support potential longitudinal studies to determine if these metrics have significant utility in fitness monitoring in health and disease monitoring in asthma, COPD and other respiratory conditions. It may even provide further detailed insight into phenotyping of disease based on continuous breathing metrics, that has not been possible to date.

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