Mini-Symposia Title:

ADVANCES IN SLEEP BIOENGINEERING II: Novel methods for improved diagnostics and assessing adherence to therapy in obstructive sleep apnea

Mini-Symposia Organizer Name & Affiliation:

Philip de Chazal, USyd, Sydney; Thomas Penzel, Charite University Hospital, Berlin; Michael C.K. Khoo, USC, Los Angeles

Mini-Symposia Speaker Name & Affiliation 1:

Dwayne Mann, The University of Queensland, Brisbane, Australia.

Mini-Symposia Speaker Name & Affiliation 2:

Lynne E. Bilston, University of New South Wales, Sydney, Australia.

Mini-Symposia Speaker Name & Affiliation 3:

Jeff P. Armitstead, ResMed Ltd. & Univ. of Sydney, Sydney, Australia.

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Philip de Chazal, University of Sydney, Sydney, Australia.

Mini-Symposia Speaker Name & Affiliation 5:

Mini-Symposia Speaker Name & Affiliation 6:

Theme:

- ○ 01. Biomedical Signal Processing
- ○ 02. Biomedical Imaging and Image Processing
- ○ 03. Micro/ Nano-bioengineering; Cellular/ Tissue Engineering &

- ○ 04. Computational Systems & Synthetic Biology; Multiscale modeling
- ⦿ 05. Cardiovascular and Respiratory Systems Engineering
- ○ 06. Neural and Rehabilitation Engineering
- ○ 07. Biomedical Sensors and Wearable Systems
- ○ 08. Biorobotics and Biomechanics
- ○ 09. Therapeutic & Diagnostic Systems and Technologies
- ○ 10. Biomedical & Health Informatics
- ○ 11. Biomedical Engineering Education and Society
- ○ 12. Translational Engineering for Healthcare Innovation and Commercialization

Mini-Symposia Synopsis— Max 2000 Characters

Insufficient or fragmented sleep has been identified as a public health epidemic. The most prevalent causes include chronic insomnia and obstructive sleep apnea (OSA), which affect almost a billion people. OSA is associated with increased risk of developing a rapidly expanding list of medical comorbidities such as hypertension, cardiac arrhythmias, ischemic heart disease, stroke, diabetes, learning and attention deficits, and depression and mental illness. While the underlying pathophysiology of various endotypes of OSA and their impact on other organ systems remain to be completely understood, the availability of low-cost "smart" technology, along with increasing computational power, are fueling novel advances in improved methods of nonintrusive diagnostics and therapeutic management of the syndrome. In this series of 3 minisymposia, established experts in the fields of cardiorespiratory and sleep research will present their latest findings in a broad spectrum of areas in sleep medicine. This proposal continues the tradition of similarly themed minisymposia series on sleep that we have organized for EMBC over the past 8 years, which have attracted considerable interest among EMBC attendees. This second minisymposium session will focus on the use of novel techniques for signal and image analysis in OSA, as well as the management of "big data" for monitoring compliance with therapy.

Brief speaker biographies:
(1) Dr Dwayne Mann PhD, Postdoctoral Research Fellow, The University of Queensland
(2) Prof. Lynne E. Bilston, PhD, Senior Principal Research Scientist, The University of NSW
(3) Dr Jeff P. Armistead, PhD, Vice President Medical Affairs, ResMed & Univ. of Sydney
(4) Prof. Philip de Chazal, PhD, Professor of Biomedical Engineering, The University of Sydney.

Quantification of Airflow Limitation in the Clinical Sleep Environment

Dwayne L Mann[1,2,3,5], Thomas Georgeson[1], Shane A Landry[3,4], Bradley A Edwards[3,4], Ali Azarbarzin[5], Daniel Vena[5], Lauren Hess[5], Andrew Wellman[5], Susan Redline[5], Scott A Sands[5], Philip I Terrill[1]

[1]School of Information Technology and Electrical Engineering, The University of Queensland, Brisbane, Australia. [2]Institute for Social Science Research, The University of Queensland, Brisbane, Australia. [3]Department of Physiology, School of Biomedical Sciences and Biomedical Discovery Institute, Monash University, Melbourne, Australia. [4]School of Psychological Sciences and Turner Institute for Brain and Mental Health, Monash University, Melbourne, Australia. [5]Division of Sleep and Circadian Disorders, Department of Medicine, Brigham & Women's Hospital & Harvard Medical School, Boston, MA, USA.

I. INTRODUCTION

The apnea-hypopnea index (AHI) is currently used to describe the severity of sleep disordered breathing, as the frequency of obvious episodic hypoventilation (count of apneas and hypopneas per hour of sleep). However, the AHI is not sensitive to more covert, clinically concerning, patterns of ventilation that occur such as sustained airflow limitation and also periods with increased ventilatory drive.

Here we describe a clinically applicable, non-invasive model to quantify airflow limitation by accurately categorizing each breath as either *certain* flow limitation, *possible* flow limitation or *normal*, providing a mechanism to objectively describe the frequency of obstructive sleep disordered breathing that is otherwise unreported.

II. METHODS

We visually scored a library of breaths (N=117,871; N=40 individuals with suspected or diagnosed sleep apnea) into airflow limitation categories, using the shape of the airflow signal and complimentary physiological signals (e.g. diaphragm EMG).

We then developed an ordinal regression model to predict the visually scored airflow limitation category based upon 23 features extracted from the airflow signal (both time and frequency domain). The final model provides both categorical and continuous output for each breath.

III. RESULTS

There was a strong association between the 3-class regression model predicted airflow limitation category and the visual scoring (kappa = 0.572, Table 1).

Similarly, when continuous model output was compared with visual scoring, there was clear separation between Certain flow limitation and Normal breaths (Fig 1). Across all individuals, airflow limitation was associated with AHI, however this varied widely (R^2=0.23). Interestingly, airflow

limitation occurred frequently in some individuals during arousal breaths and also during stable breathing periods, a proportion of the night previously considered to be without flow limitation.

TABLE I.   MODEL CLASSIFICATION PERFORMANCE

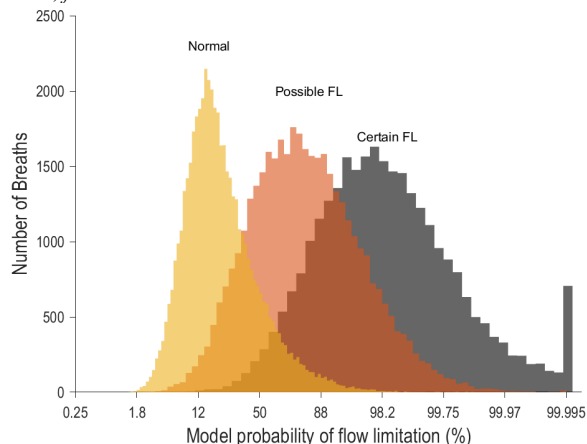| Model Predicted	Visual Scoring		
	Certain-FL	*Possible-FL*	*Normal*
Certain-FL	19025	9545	510
Possible-FL	7303	23502	8248
Normal	217	6914	42607

FL, flow limitation.

Figure 1. Histogram illustrating differences in breaths from each visually scored airflow limitation category with the flow-shape model continuous output. (FL, flow limitation).

IV. DISCUSSION & CONCLUSION

In addition to developing a carefully scored library of training breaths, the current study presents a simple regression model that accurately predicts airflow limitation category from features in the airflow signal alone, fulfilling the clinical need for non-invasive quantification of the certainty and frequency of airflow limitation during sleep.

Novel Imaging Approaches to Understanding Obstructive Sleep Apnoea and Therapy Response

Lynne E Bilston, Neuroscience Research Australia and Prince of Wales Clinical School, University of New South Wales, Sydney, NSW, Australia

Obstructive sleep apnoea (OSA) is a common respiratory sleep disorder where the upper airway collapses either completely (apnoea) or partially (hypopnea) repeatedly during sleep. OSA is a multifactorial disorder, with physiological, anatomical, and biomechanical contributing factors, which vary widely between individuals. While there has been considerable research studying the physiological and anatomical factors, the biomechanical factors are less well understood. Dynamic imaging can provide insight into the biomechanics of the upper airway musculature, for understand the mechanisms of OSA and how OSA therapies work.

Tagged MRI uses a spatially modulated magnetization to superimpose a 'contrasting grid' on soft tissues, whose motion can then be followed with cine-MRI sequences. These grids stay with the tissue as it moves, and their deformation can be tracked using Harmonic Phase (HARP) methods. Here, we used tagged MRI to quantify the movement of the upper airway muscles during quiet breathing in OSA patients and matched controls, lying supine in a 3T MRI scanner (Philips 3TX, Best, The Netherlands). MRI imaging and breathing signals are logged concurrently. Similar data is collected with a mandibular advancement splint to assess the effect that MAS have on upper airway muscle function, to complement anatomical imaging. These data are analysed using custom MATLAB scripts.

In this talk, the relationships between upper airway anatomy, OSA status, and mandibular advancement splint usage will be shown, and the implications of the findings for OSA pathophysiology and treatment efficacy discussed.

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Digital Health Applications and Patient Reported Outcomes in the Treatment of Sleep Disorders

Jeffrey P. Armitstead, ResMed Ltd and the University of Sydney, Sydney, Australia

Abstract— **Digital health applications offer the promise of improved adherence to therapies for chronic respiratory disorders such as sleep apnea. This paper reports on insights gleaned from a database analysis of telemonitored therapy devices which included patient reported outcomes.**

I. INTRODUCTION

Sleep apnea is a major global public health epidemic. A recent estimate puts the global prevalence of obstructive sleep apnea (OSA) alone in the order of 900 million people [1] and the cost of untreated OSA has been estimated to be in the billions annually in a recent Australian report [2]. Continuous positive airway pressure (CPAP) is the gold standard therapy for OSA and has recently been shown to improve quality of life cost-effectively, reduce health care utilization, increase workplace productivity, and diminish accident risk [3]. However, adherence with any therapy for chronic disease can be challenging especially at initiation and over the longer term. We have recently shown using a large aggregated database analysis using data from connected CPAP devices that adherence is high in the first 90 days of therapy [4].

Patient-reported outcomes (PROMS) are an increasingly important aspect of clinical care; they allow assessment of treatment effectiveness and the potential for the personalisation of care. A recent review has highlighted the promise of digital health applications to improve adherence and personalize care in respiratory disorders [5] while another report has highlighted the potential of data-driven insights to achieve the same end [6]. We sought to use both approaches and investigate their potential in patients with OSA combining electronically captured PROMS with CPAP device telemetered data.

II. METHODS

We examined de-identified data of US OSA patients on PAP therapy in the AirView database (ResMed, San Diego). Therapy data was acquired from wirelessly connected AirSense 10 platforms (CPAP and APAP modes). To be included patients needed to register in the myAir database and complete pre- and post-PAP questionnaires via the myAir app. Self-reported age, gender, degree of sleepiness (simple 5-point scale), and primary reason for therapy were captured at baseline. Additionally, patients reported the degree of sleepiness at 7, 14, 21, 28 days on therapy, allowing assessment of symptom change. The study was reviewed by

an institutional review board (IRB) and deemed exempt from IRB oversight.

III. RESULTS

Approximately 200,000 patients commenced CPAP or APAP during the analysis period, and 17,920 patients (8.8%) met the selection criteria and had complete data. The mean age was 47.6±12.4 years and 61.5% were male. Sleepiness was the most commonly reported reason for therapy (60.2% of patients), and 77.4% of patients reported "moderate" to "extreme" sleepiness at baseline. Baseline sleepiness did not influence PAP adherence. Self-reported sleepiness improved with PAP therapy in most patients over the 28-day assessment period, with 61.7% of patients reporting "no" or "slight" sleepiness.

IV. DISCUSSION & CONCLUSION

Aggregated data from telemonitored therapy devices provides insights into challenges to CPAP adherence. Combining machine-derived metrics with electronically reported patient outcomes enriches the framework immensely. Future work will look to utilize such data to potentially personalize care and to strengthen patient engagement with therapy. An engaged patient combined with a data-rich care team has the potential for excellence in joint care decision making.

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Identifying the Site of Upper Airway Collapse in Obstructive Sleep Apnoea Patients Using Snore Signals

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I.   INTRODUCTION

The information regarding the site-of collapse could assist clinicians in choosing the most appropriate treatment for obstructive sleep apnoea (OSA) patients. Conventional methods in determining the site-of-collapse involve the use of an endoscope or a pressure catheter during drug-induced or natural sleep. Unfortunately, these methods are not well tolerated by patients, and inconsistency of the obstruction site identified with natural sleep and drug-induced sleep, which in turn limit their clinical application. Therefore, the crux in identifying the site-of-collapse is to find a simple, non-invasive method with minimal impact on patients during natural sleep.

Previous studies have shown that acoustic analysis of snoring can assist in the diagnosis of OSA and in estimating OSA severity. A few studies have been conducted in finding the relationship between snoring and site of collapse. However, this requires an additional burden to the patients undergoing a sleep test.

II.   METHODS

The patient's respiratory sound signals were recorded by a ceiling micro-phone (about 1.5m above the patient's bed) concurrently with the routine PSG recordings. The probable site-of-airway collapse was determined by manual analysis of the shape of the airflow signal during hypopnoea, which has been reported to correlate with the site of collapse. Various time and frequency features of the snoring during hypopnoea were extracted and to automatically annotate the site-of-collapse of each hypopnoea event into different sites-of-collapse. The predominant site-of- collapse for a sleep period was then determined from the individual hypopnoea annotations. Also, a clustering model was developed to analyse the correlation between the clusters generated and the site-of-collapse.

III.   RESULTS AND DISCUSSION

Our results reveal that the snore signal during hypopnoea can provide information regarding the predominant site-of-collapse in the upper airway. We believe that it is an important first step in establishing the feasibility of a practical non-invasive, low-cost diagnosis tool for improving the selection of appropriate therapy for OSA patients without any additional burden to the patients undergoing a sleep test