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CONFLICT OF INTERESTS

NRL is a patent co-inventor for methods treating vascular barrier dysfunction licensed to Navigen Pharmaceuticals which is unrelated to the Nrf2 pathway. NRL holds a small amount of stock in Navigen Pharmaceuticals which is currently of no value. NRL is a consultant for Cooltech Inc. The remaining authors declare no competing financial interests.

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ORCID

Nyall R. London  <https://orcid.org/0000-0002-2902-4407>

Nyall R. London Jr¹ 

Anuj Tharakan¹

Michelle Mendiola¹

Mengfei Chen¹

Alex Dobzanski¹

Thomas E. Sussan²

Michael Zaykaner¹

Andrew H. Han¹

Andrew P. Lane¹

Venkataramana Sidhaye²

Shyam Biswal²

Murugappan Ramanathan Jr¹

¹Johns Hopkins Department of Otolaryngology - Head and Neck Surgery, Baltimore, Maryland

²Department of Environmental Health Sciences, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

Correspondence

Murugappan Ramanathan Jr, Johns Hopkins Department of Otolaryngology - Head and Neck Surgery, Baltimore, MD.

Email: mramana3@jhmi.edu

Nyall R. London, Jr and Anuj Tharakan contributed equally to this work

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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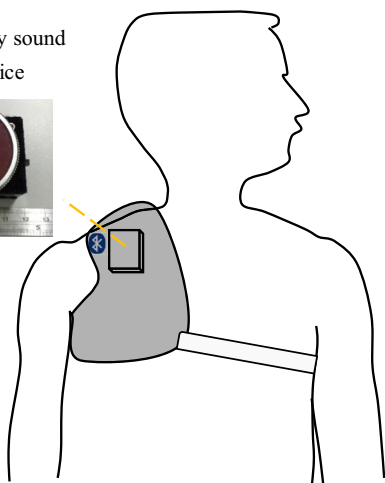
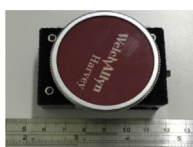
Spectrogram for childhood asthma detection and analysis

1 | INTRODUCTION

Asthma is defined as a chronic inflammation of the lower airways and can easily result in bronchoconstriction and even dyspnea. Every year, hundreds of million people around the world suffer from asthma and are unable to work or attend school due to their uncontrolled symptoms.¹ Wheezing is an obvious breathing sound that portrays airflow interference between the lungs and the bronchus

and is often considered a primary feature of an acute asthma attack, along with coughing, shortness of breath, and chest tightness. Acute exacerbation or asthma attacks using wheezing sounds have been detected by physicians both with and without stethoscopes. Designs for breathing sound monitoring systems and real-time wheeze detection systems have also been reported.² Trubel *et al* used mono-frequent forced oscillation to measure oscillatory airway resistance and calculate variability in order to separate asymptomatic children

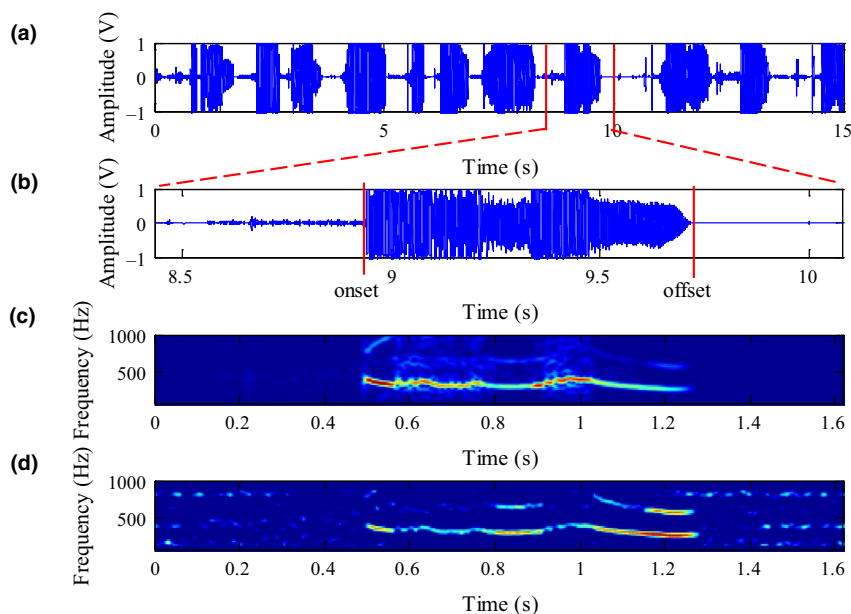
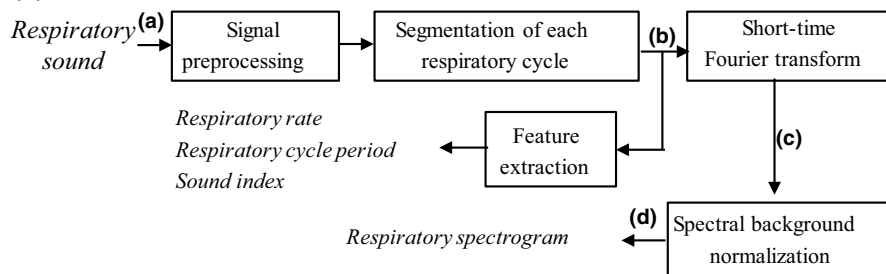
(A)

Wireless respiratory sound
recording device

Host system

FIGURE 1 A, Basic scheme of the proposed medical assistant system. B, Flowchart of the proposed respiratory sound analysis algorithm: (a) raw respiratory sounds, (b) segmented respiratory cycle, (c) original respiratory spectrogram, and (d) respiratory spectrogram with spectral background normalization [Colorfigure can be viewed at wileyonlinelibrary.com]

(B)



with asthma from healthy controls.³ Meanwhile, Lin *et al* used 2D bilateral filtering to enhance the spectral feature of wheezing sounds.⁴ Içer *et al* used three signal-processing methods to obtain the frequency ratio $f_{\min}/f_{\max}$, average instantaneous frequency, exchange time of the instantaneous frequency, and eigenvalues to distinguish various pathological lung sounds.⁵ Furthermore, Habukawa *et al* compared sound parameter indexes, including median, range,

and mean values, from the amplitude of inspiratory lung sounds at 700 Hz, which were obtained from both an asthma and a nonasthma group.⁶ Nevertheless, sufficient information is still lacking with regard to both the time and frequency domains for real-time wheezing sounds of asthma detection. In this study, we used a device to record and analyze the wheezing sounds of childhood asthma patients in both time and frequency domains.

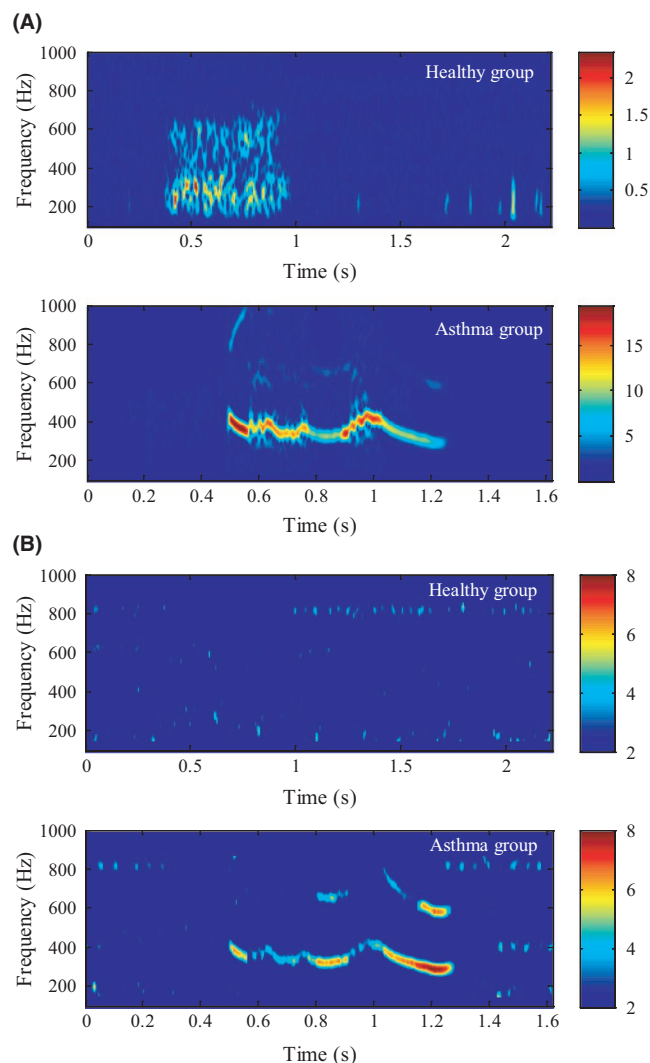


FIGURE 2 Respiratory spectrogram (A) without background normalization and (B) with background normalization corresponding to the different groups

2 | METHODS

The medical assistant system is shown in Figure 1A. The bell of the stethoscope on a wireless respiratory sound recording device was placed on the upper left anterior chest at the first intercostal space on the midclavicular line to collect a 15-second respiratory sound trial, which was then wirelessly transmitted to the host system via Bluetooth. As defined by the American Thoracic Society (ATS), a single wheezing waveform must be greater than 250 milliseconds in the time domain and at least 400 Hz in the frequency domain.⁷ To effectively obtain the characteristics of respiratory sounds, we developed a respiratory sound analysis algorithm, as shown in Figure 1B. The raw respiratory sound is first preprocessed through a band-pass filter with a frequency band of 150–1000 Hz to preserve a meaningful respiratory signal. We segmented each respiratory cycle and extracted its characteristics, including respiratory rate, respiratory cycle period, and sound index. We defined sound index (SI) as the

sum of the sound amplitude per unit time,⁸ the respiratory rate as the number of respiratory cycles per one minute, and the respiratory cycle period as the time between the onset and offset of a respiratory cycle. We obtained a spectrogram of the segmented respiratory sound using the short-time Fourier transform (STFT) and then used order truncate average (OTA) to eliminate background noise.⁹

In this study, we performed experimental trials with 17 healthy children (14 males and 3 females) and 26 children with asthma (19 males and 7 females) at Kaohsiung Chang Gung Memorial Hospital in Taiwan. The ages of these participants ranged from 0 to 8 years old, and they were either hospitalized or visited the outpatient clinic due to asthma with acute exacerbation. The subjects all had symptomatic asthma and audible wheezing at the time when the sound was recorded. This experiment was approved by the Institutional Review Board (IRB: 104-2415B), and we obtained the written informed consent from the parents or guardians of all participants. We also enrolled a total of 50 other independent participants (37 healthy and 13 asthma children) who had similar characteristics with the experimental trials in order to perform blind testing. The presentation of a specific narrow line pattern (duration > 250 millisecond) in the respiratory spectrogram with OTA was recognized as a wheeze.

3 | RESULTS

We examined respiratory spectrograms with/without OTA normalization corresponding to the different groups (Figure 2) and found that the respiratory spectrogram of the healthy group was distributed between 150 and 700 Hz for 0.5–0.75 seconds, while that of the asthma group was between 200 and 450 Hz for 0.25–0.6 seconds. The respiratory spectrogram magnitude of asthma was stronger than that of the healthy group. Using the OTA technique, we eliminated background respiratory noise and effectively enhanced the wheezing feature with a certain time/frequency pattern (frequency of maximum peak: 353.01 ± 154.62 vs 426.43 ± 139.83 Hz, $P < 0.05$, Figure 2). The average respiratory cycle period of the asthma group (0.64 ± 0.32 second) was significantly shorter than the healthy group (1.03 ± 0.51 second, $P < 0.05$). Furthermore, the average sound index of the asthma group was significantly larger than the healthy group (371.55 ± 171.41 vs 73.95 ± 23.65 au, $P < 0.05$). We also investigated the correlation between the wheezing grade diagnosed by a physician on a scale of 0–3 (indicating none, mild, moderate, and severe condition of wheezing, respectively) and various lung sound features. Our results indicated that the respiratory rate ($r = 0.476$), respiratory cycle period ($r = -0.534$), and sound index ($r = 0.603$) were all significantly related to wheezing grade (all $P < 0.05$ by Spearman's rank correlation). When regarding subgroups by age (<2 years old, $N = 13$) in asthma children, there are no significant difference in sound index and frequency of maximum peak ($P > 0.05$), but female gender asthma patients had a higher frequency of maximum peak than male patients (428.6 ± 119.2 vs 181.7 ± 184.2 Hz, $P < 0.001$).

A blind test with 50 participants showed that our findings had 94% accuracy, 84.62% sensitivity, and 91.67% positive predictive value.

4 | DISCUSSION

Most of the aforementioned methods primarily focused on the features of lung sounds in the frequency domain, but in this study, we explored the relationship in both the time and frequency domains.⁽³⁾ Narrowing bronchial airways also cause an increased intensity or pitch of lung sounds. In the asthma group, the frequency corresponding to the maximum peak in the wheezing sound spectrum was about 350 Hz, while the duration of the wheeze lasted approximately 250 milliseconds. Wheezing sounds can be seen like the sounds of a musical instrument due to airway fluttering caused by airway narrowing. The wheezing grade also demonstrated a significant correlation with respiratory rate, respiratory cycle period, and sound index. Therefore, these elements may have the ability to quantitatively estimate the asthma condition in the future.

In this study, we proposed a device for analyzing childhood asthma and successfully applied it to extract a spectrum of wheezing features in both the time and frequency domains. We developed a wearable, wireless lung sound recording device to improve the convenience of daily monitoring of breathing sounds and detect wheezing in real time to reduce the impact of asthma with acute exacerbation with an overall cost of less than 100 USD.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest to disclose with regard to this article.

FUNDING INFORMATION

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KEYWORDS

asthma, order truncate average, spectrogram, wheezing

ORCID

Ho-Chang Kuo  <https://orcid.org/0000-0002-3295-2984>

Ho-Chang Kuo¹ 

Chi-Chun Lo^{2,3}

Yan-Di Wang⁴

Jheng-Dao Wu⁴

Bor-Shyh Lin⁴

¹Department of Pediatrics and Kawasaki Disease Center, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan

²Institute of Electrical and Control Engineering, National Chiao Tung University, Hsinchu, Taiwan

³Department of Engineering and Maintenance, Chang Gung Memorial Hospital, Kaohsiung, Taiwan

⁴Institute of Imaging and Biomedical Photonics, National Chiao Tung University, Tainan, Taiwan

Correspondence

Bor-Shyh Lin, Institute of Imaging and Biomedical Photonics, National Chiao Tung University, Tainan, Taiwan.

Email: borshylin@gmail.com

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