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New Technique to Analyze the Breath Sound Spectrum in Children with Asthma

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Objective: Breath sound parameters have been reported as useful biomarkers for evaluating the airway condition.
Methods: The reliability of breath sound analysis using an improved method was investigated. Eighty-three asthmatic children were included in the present study. After adjusting the 0 level based on the background noises of the breath sound spectrum, the total area under the curve of the dBm (A_T), the roll-off from 600–1200 Hz (Slope), the ratio of the third and fourth area to the A_T (A_3/A_T and B_4/A_T), and the ratio of power and frequency at 50% and 75% of the highest frequency (RPF_{75} and RPF_{50}), were evaluated before and after β_2 agonist inhalation. Spirography and the forced oscillation technique were also used to evaluate all subjects.
Results: Using the new method, A_3/A_T, B_4/A_T, RPF_{75} and RPF_{50}, were significantly increased after β_2 agonist inhalation. The increase in A_3/A_T and B_4/A_T were significantly correlated with the increase in FEV_1 and FEE_{25-75}, and the increase in RPF_{75} was reversibly correlated with that in R5–R20.
Conclusions: The spectrum curve indices using the adjusted 0 level can indicate bronchial dilation with β_2 agonist inhalation. These parameters may be useful for the assessment of bronchial reversibility in asthmatic children.

Key words: asthma, breath sound analysis, β_2 agonist, children, bronchial reversibility

INTRODUCTION

Clinically, an objective response to bronchodilators has been used to evaluate bronchial reversibility [1, 2]. Because of its safety, it has often been used especially in children. However, most infants and preschool children are not able to voluntarily perform the physiological maneuvers [3]. Because of this disadvantage, the diagnosis of childhood asthma remains difficult for all physicians [1].

Recently, the analysis of breath sounds has advanced [4, 5]. It has been reported that the breath sounds are sensitive to airway changes and recent developments have improved the possibility of extracting clinically relevant information from every breath sounds [6–8]. Furthermore, the breath sound analysis of breath sounds is expected to be a safe and simple method that can be applied in the clinical assessment of airway changes even in infants and preschool children [9, 10].

Although one of the problems with the analysis of breath sounds is that breath sounds are affected by the airflow rate and the pulmonary function [11, 12], useful analytical methods that are mostly unaffected by the airflow rate have been defined and their clinical usefulness has been reporte [13, 14]. Using such a method, we could confirm the bronchial reversibility using β_2 agonist inhalation in infants [10].

Another drawback is that the operation of the breath sound analysis system is not fully automatic. The analysis of the sound spectrum can be performed automatically it two or more specialists visually determined the highest frequency of the breath sound spectrum, the 0 point on the y-axis of the spectrum, in each sound spectrum [7].

The previous method has shown reliable reproducibility in various aspects, from the collection of breath sounds to the calculation of parameters [7, 10]. However, a simple, stable method is required for multi-center studies or daily medical treatments. Thus, looking back over the last decade of breath sound research, we devised an improved method for the analysis of breath sounds. The aim of the present study was to evaluate the reliability and usefulness of the new method in evaluating bronchial reversibility in asthmatic children.

PATIENTS AND METHODS

Study subjects

Eighty-three pediatric outpatients (Mean age, 9 years; range, 6–15 years; male: female, 53: 30) who were treated and well-controlled at Tokai University Hospital from January 1, 2012 to March 31, 2016 and

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who agreed to participate in our previous our studies were included in this retrospective study. In all cases, atopic-type asthma was diagnosed by a pediatrician. The inclusion criteria were as follows: >1 positive specific IgE value (> 0.7 UA/ml), recurrent wheezing and bronchial hyperresponsiveness on methacholine inhalation challenge, or bronchial reversibility [15, 16].

In all subjects, the absence of respiratory symptoms and wheezing or crackles was confirmed by auscultation by a physician during breath sound sampling. All drugs were withdrawn overnight before the test. None of the subjects had respiratory symptoms on the day of testing. The study protocol was approved by the institutional review board of Tokai University Hospital (No. 17R-161, approval date: October 18, 2017). In previous studies, written informed consent was obtained from all of the children or their legal guardians and the study protocol was approved by the institutional review board of Tokai University Hospital (No. 11R-158, approval date: December 21, 2011 and No. 14R-133, approval date: October 23, 2014).

Study protocol

The assessments were performed before and 15 minutes after β_2 agonist inhalation. Each subject was requested to take tidal breaths. It was confirmed that the breath sound samples included no wheezes, crackles or spikey outside noises based on auscultation and the breath sound analyzer image [7]. After the sound analysis, the patients' pulmonary function was tested using spirometry and the forced oscillation technique (FOT) [3].

Breath sound samples were obtained two times; before and 15 minutes after β_2 agonist inhalation. Each personal breath sound parameter was analyzed conventionally, using a sample with the median value from three tidal breaths.

In *Study 1*, in order to examine the reliability of the parameters obtained by the new method, one doctor measured these variables in the same sample twice to determine the intra-observer variability. In order to examine the validity of the measurements, two physicians measured the parameters in the same subjects to determine the inter-observer variability [17].

In *Study 2*, the sound spectrum samples of asthmatic children who agreed to participate in our previous studies and underwent a breath sound analysis to evaluate airway reversibility were retrospectively analyzed. We assessed the correlations between the respiratory function tests and each pulmonary sound parameter before and after β_2 agonist inhalation [14].

Pulmonary function tests

As the pulmonary function of the participants, spirometry test (Chestgraph HI-105, Chest Co., Tokyo, Japan) was determined. In each subject, the resting baseline was selected using the best-of-three resting results based on the highest sum of the FVC and FEV_1. The results are based on the percent predicted value of Japanese children [18].

For the measurement of the FOT parameters, an FOT system (Master- Screen-Impulse Oscillometry System, Jaeger CO, Wurzburg, Germany) was used [5]. The measurements were made in the standing position with a nose-clip on. Real-time recordings of mouth pressure and flow signals pulsed through the 5–20-Hz spectrum were superimposed over tracings of the tidal breathing. Measurements of respiratory resistance (Rrs) at 5 and 20 Hz and their difference (R5, R20, and R5-R20) and respiratory impedance at 5 Hz (X5) were recorded.

β_2 agonist inhalation

All subjects inhaled β_2 agonist solution (procaterol [30 μg] in 2.0 ml of saline) [14]. The assessments were performed before and 15 minutes after β_2 agonist inhalation.

Basic breath sound analysis

The breath sound analysis was performed as described previously [7, 14]. Breath sounds were recorded for ≥ 10 seconds in a silent room using a handheld microphone. The microphone was placed on the second intercostal space along the mid-clavicular line. A sound analysis of the inspiration phase was performed using an LSA-2000 sound spectrometer (Kenz Medico Co., Saitama, Japan).

The sound-amplifying unit was found to be effective for analyzing sounds in the range of 100–2500 Hz. The recorded sounds were analyzed according to a fast Fourier transformation. The sampling frequency was 10,240 Hz and the spectra were obtained using a Hanning window. The sounds were displayed as a spectrograph (Suppl. Figure a). The dBm values were plotted on the Y axis and the Hz values were plotted on the X axis. To evaluate the dBm-based spectrum images, we decided to set the zero point of the Y axis (dBm) based on the mean of the background noise (at $>2{,}500$ Hz) for all subjects. The mean background noise in our silent room was -88.1 ± 5.0 dBm. Thus, the 0 point (0 dB) for the calculation of the dBm-based area under the curve (AUC) was considered to be -90 dBm of the original dBm recorded by the sound spectrometer [7, 14].

The point of maximum frequency during inspiration in the sound spectrogram was used for the sound spectrum analysis. A five-point moving average was used as a smoothing technique to determine the suitable dBm value for identifying some checkpoints in the slope of each sound spectrum. After the 0 point was visually determined by 2 or more physicians, these data were automatically calculated using a home-made calculation software program. Slope indicates the roll-off of the middle spectrum curve (-dBm/octave) [19, 20]. The A_T, A_3 and B_4 values were conventionally calculated according to the dBm and Hz (1 arbitrary unit [dBm・Hz] on a spectrum image) [7, 14]. The spectrum curve indices, the A_3/A_T, B_4/A_T, RPF_{75} and RPF_{50} values, were also calculated.

The new breath sound analysis

The new method has the same basic procedure as the previous method. In the new method, the 0 level (0 dB of breath sound spectrum) was visually corrected based on the breath sound spectrums in each sample before the 0 point (the frequency at 0 dB) was decided (Figure).

Statistical analyses

All statistical analyses were conducted using the

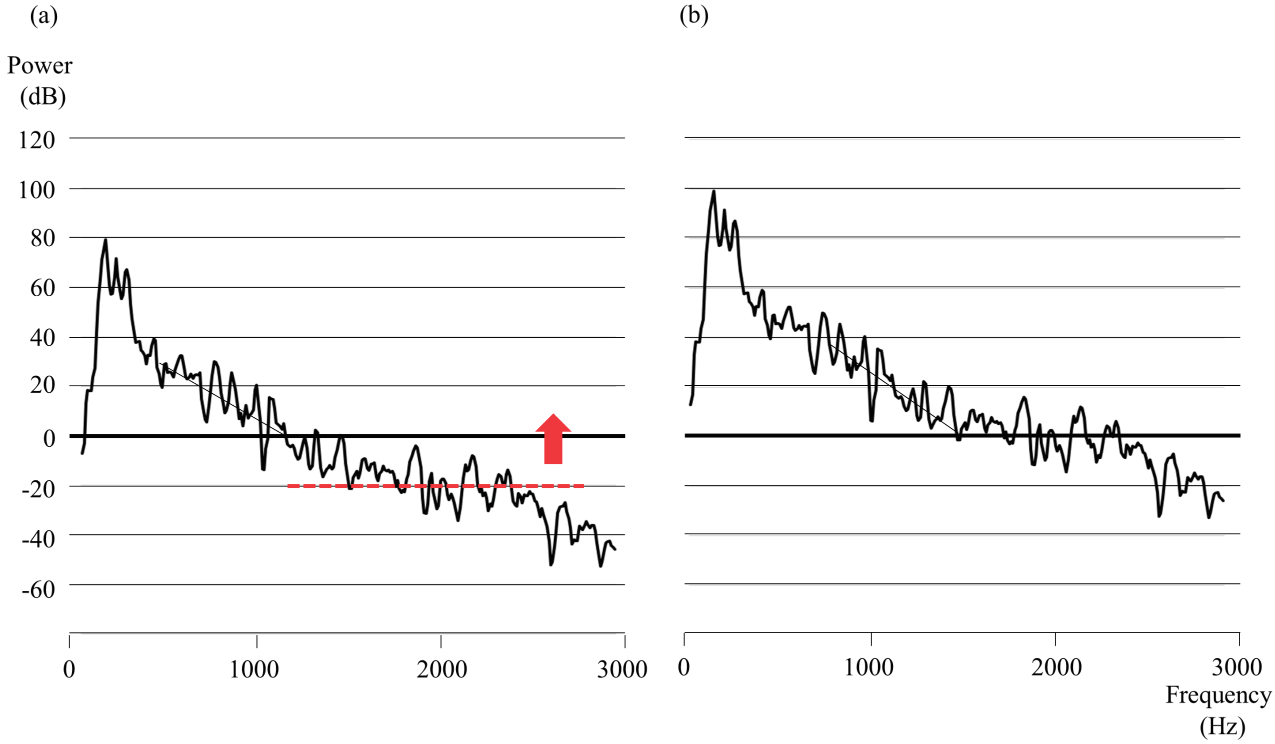

Figure The new breath sound analysis method
In the new method, the 0 level was visually corrected based on the breath sound spectrums in each sample (arrow) before the 0 point was decided.

SPSS software program (IBM SPSS Statistics, Version 22 for Windows; IBM Corp., Armonk, N.Y., USA). Paired parameters were compared using Wilcoxon's signed-rank test. P values of < 0.05 were considered to indicate statistical significance. Correlations between individual breath sound parameters and other measurements were determined using Pearson's correlation coefficient.

RESULTS

The pulmonary function and breath sound analyses

All 83 subjects (median age, 9 years, boys: girls, 53: 30) underwent spirometric analyses. Chest auscultation by pediatric respiratory specialists revealed no adventitious sounds. In each of the 83 subjects, the breath sound spectrum parameters were also successfully calculated. None of the breath sound images showed wheezing [21], rales or distinct outside noises. The shape of the sound spectrum showed good similarity in the same patients.

Repeatability of the breath sound analysis

In the 32 subjects, the repeatability of the common and spectrum curve indices was evaluated. The intra-observer and inter-observer correlation coefficients for the common parameters and spectrum curve indexes showed relatively good repeatability (Table 1). Using the Bland-Altman method, revealed that with the exception of RPF_{75}, there was a small degree of variation in the 0 point, common parameters and spectrum curve indices determined by the observers (data not shown).

Differences in the lung function before and after β_2 agonist inhalation

With the exception of FVC, all spirometric parameters showed a significant increase after β_2 agonist inhalation (Table 2). Furthermore, all of the FOT parameters, R20, R5 and R5−R20, showed a significant decrease, and X5 showed a significant increase after β_2 agonist inhalation (Table 2).

Differences in the breath sound parameters before and after β_2 agonist inhalation

With the exception of common parameters, A_T and Slope, in both the previous method and the new method, an analysis of the data revealed that the median values of the spectrum curve indices showed significantly changes after β_2 agonist inhalation (Table 3).

In Table 4, the data obtained using the previous method and the new method were compared (Table 4). The values of A_T in the new method were increased; however, they were well-correlated with the values obtained with the previous method. The B_4/A_T values with the new method did not differ from those obtained using the previous method, and showed no correlation with the values obtained with the previous method.

The relationship between the pulmonary function parameters and the breath sound parameters before β_2 agonist inhalation

The parameters of the pulmonary function and the FOT, FVC, FEV_1, $FEF_{25\text{-}75}$, $\dot{V}_{50}$, $\dot{V}_{25}$, R20, R5, R5−R20 and X5 values showed no significant correlations with the breath sound parameters (A_3/A_T, B_4/A_T, RPF_{75} and RPF_{50}) (data not shown).

Table 1 Intra- and inter-observer variability in the breath sound analysis parameters

		SDD	RC	CC
A_T (dBm・Hz)	Intra-observer	462.1	924.2	0.932
	Inter-observer	773.4	1546.8	0.793
0 point (Hz)	Intra-observer	98.5	197.0	0.731
	Inter-observer	73.6	147.2	0.839
A_3/A_T (%)	Intra-observer	1.49	2.98	0.693
	Inter-observer	1.48	2.96	0.680
B_4/A_T (%)	Intra-observer	1.22	2.44	0.630
	Inter-observer	1.17	1.34	0.628
RPF_{75} (dBm/Hz)	Intra-observer	0.90	1.80	0.839
	Inter-observer	1.05	2.10	0.834
RPF_{50} (dBm/Hz)	Intra-observer	0.44	0.88	0.936
	Inter-observer	0.70	1.40	0.831

SDD, SD of the difference between the first and second measurements made by the same observer (intra-observer) and those made by a different observer (inter-observer); RC, repeatability coefficient (the 95% confidence limit of difference); CC, correlation coefficient. n = 32.

Table 2 The results of the pulmonary function tests

	Before β_2 inhalation	After β_2 inhalation	P value
FVC (%pred)	80.4 (71.7, 89.0)*	82.7 (73.7, 88.4)	0.225
FEV_1 (%pred)	91.5 (85.3, 95.4)	92.9 (88.1, 96.4)	**0.001**
FEF_{25-75} (%pred)	97.0 (78.1, 110.0)	105.0 (92.7, 123.4)	< **0.001**
$\dot{V}_{50}$ (%pred)	92.1 (76.8, 109.0)	103.2 (85.3, 119.6)	< **0.001**
$\dot{V}_{25}$ (%pred)	94.7 (73.1, 120.7)	109.8 (83.5, 131.1)	< **0.001**
R20 [kPa/(L/s)]	0.46 (0.39, 0.57)	0.40 (0.33, 0.47)	< **0.001**
R5 [kPa/(L/s)]	0.51 (0.39, 0.64)	0.42 (0.33, 0.54)	< **0.001**
R5−R20 [kPa/(L/s)]	0.16 (0.12, 0.25)	0.12 (0.07, 0.19)	< **0.001**
X5(Hz) [kPa/(L/s)]	−0.19 (−0.23, −0.15)	−0.18 (−0.22, −0.14)	**0.029**

n = 83, paired t-test; *, Median (1st quartile, 3rd quartile)

Table 3 The results of the breath sound analysis

	Before β_2 inhalation	After β_2 inhalation	P value
[Previous method]			
A_T (dBm・Hz)	7074 (5886, 8268)*	7372 (6188, 8613)	0.110
Slope (-dBm/octave)	23.6 (15.9, 29.3)	24.6 (15.7, 32.5)	0.805
A_3/A_T (%)	11.8 (10.7, 13.2)	13.7 (12.4, 14.8)	< **0.001**
B_4/A_T (%)	7.0 (6.2, 8.0)	8.2 (7.3, 9.2)	< **0.001**
RPF_{75} (dBm/Hz)	5.7 (4.7, 7.0)	7.3 (6.1, 8.9)	< **0.001**
RPF_{50} (dBm/Hz)	5.9 (5.0, 6.6)	6.8 (6.1, 8.1)	< **0.001**
[New method]			
A_T (dBm・Hz)	7786 (6672, 9222)	7844 (6616, 9198)	0.723
Slope (-dBm/octave)	22.8 (15.4, 30.5)	23.7(16.5, 32.2)	0.823
A_3/A_T (%)	12.2 (11.0, 13.4)	13.0 (12.0, 14.0)	**0.002**
B_4/A_T (%)	7.6 (6.4, 8.4)	7.8 (7.2, 8.7)	**0.006**
RPF_{75} (dBm/Hz)	5.7 (4.4, 6.6)	6.9 (5.7, 8.1)	< **0.001**
RPF_{50} (dBm/Hz)	5.6 (5.1, 6.6)	6.8 (5.8, 7.4)	< **0.001**

n = 83, P value; Wilcoxon signed rank test; *, Median (1st quartile, 3rd quartile)

Table 4 The relationship between the data of the previous method and the new method

	Previous method	New method	P value	
			Wilcoxon	Pearson
A_T (dBm・Hz)	7074 (5886, 8268)*	7786 (6672, 9222)	< **0.001**	< **0.001**
Slope (-dBm/octave)	23.6 (15.9, 29.3)	23.7 (16.5, 32.2)	0.596	< **0.001**
A_3/A_T (%)	11.8 (10.7, 13.2)	13.0 (12.0, 14.0)	0.052	**0.003**
B_4/A_T (%)	7.0 (6.2, 8.0)	7.8 (7.2, 8.7)	**0.028**	0.080
RPF_{75} (dBm/Hz)	5.7 (4.7, 7.0)	6.9 (5.7, 8.1)	0.436	**0.004**
RPF_{50} (dBm/Hz)	5.9 (5.0, 6.6)	6.8 (5.8, 7.4)	0.203	< **0.001**

n = 83, Wilcoxon, Wilcoxon signed rank test, Pearson; Pearson's correlation coefficient; *, Median (1st quartile, 3rd quartile)

Table 5. The relationship between changes in the lung function data and breath sound parameters

		⊿FVC (%pred)	⊿FEV1 (%pred)	⊿FEF_{25-75} (%pred)	⊿$\dot{V}_{50}$ (%pred)	⊿$\dot{V}_{25}$ (%pred)	⊿R20 [kPa/(L/s)]	⊿R5 [kPa/(L/s)]	⊿R5−R20 [kPa/(L/s)]	⊿X5 [kPa/(L/s)]
[Previous method]										
⊿A_3/A_T	CC	−0.083	−0.063	−0.083	−0.089	−0.049	−0.016	−0.034	−0.286	0.112
	P	0.485	0.588	0.471	0.440	0.670	0.888	0.765	**0.011**	0.324
⊿B_4/A_T	CC	−0.140	−0.055	−0.104	−0.101	−0.073	−0.095	−0.010	−0.171	0.090
	P	0.220	0.633	0.386	0.380	0.530	0.406	0.928	0.131	0.428
⊿RPF_{75}	CC	−0.058	−0.091	−0.060	−0.066	0.043	−0.033	−0.240	−0.122	−0.052
	P	0.627	0.445	0.617	0.579	0.721	0.778	**0.037**	0.294	0.652
⊿RPF_{50}	CC	0.002	0.017	−0.038	−0.065	−0.032	0.125	0.148	0.071	0.008
	P	0.985	0.890	0.754	0.594	0.793	0.291	0.210	0.548	0.946
[New method]										
⊿A_3/A_T	CC	0.290	0.279	0.224	0.198	−0.093	−0.069	0.046	−0.190	0.295
	P	**0.010**	**0.014**	**0.049**	0.083	0.514	0.544	0.685	0.092	**0.008**
⊿B_4/A_T	CC	0.363	0.387	0.327	0.324	0.294	−0.112	0.049	−0.144	0.289
	P	**0.001**	**< 0.001**	**0.003**	**0.004**	**0.009**	0.324	0.668	0.203	**0.009**
⊿RPF_{75}	CC	0.120	0.022	0.089	0.090	0.030	0.002	−0.009	−0.273	0.091
	P	0.297	0.848	0.442	0.434	0.799	0.987	0.940	**0.015**	0.426
⊿RPF_{50}	CC	−0.012	−0.033	−0.044	−0.050	0.016	0.161	0.196	0.052	−0.114
	P	0.920	0.774	0.703	0.661	0.892	0.155	0.081	0.644	0.314

n = 83, CC, Pearson's correlation coefficient.

The relationship between the changes in the pulmonary function parameters and the changes in the breath sound parameters before and after β_2 agonist inhalation

The comparison between FOT parameters and spectrum curve indices using the previous method, the ⊿A_3/A_T value was correlated with the ⊿R5−R20 value, and ⊿RPF_{75} value was correlated with the ⊿R5 value (Table 5). No correlations were observed among the other spectrum curve indices.

On the other hand, the comparison between spirometric parameters and spectrum curve indices revealed that the ⊿A_3/A_T and ΔB_4/A_T values obtained by the new method were significantly correlated with the ⊿FVC, ΔFEV_1 and ⊿FEF_{25-75} values. The comparison between FOT parameters and spectrum curve indices revealed that the ⊿A_3/A_T and ⊿B_4/A_T values were correlated with the ⊿X5 value, and ⊿RPF_{50} value was correlated with the ⊿R5−R20 value (Table 5). No correlations were observed among the other breath sound parameters.

DISCUSSION

A breath sound analysis is expected to be a safe and simple method that can be applied in the clinical assessment of airway changes in children [22]. According to the previous reports, breath sound parameters change during histamine and methacholine inhalation challenges [23, 24], and a strong relationship is thought to exist between increased changes in breath sound parameters and airway narrowing in asthmatic patients [25, 26].

Although one major problem of these methods is that breath sounds are affected by the airflow rate and pulmonary function [11, 12], we have developed a reliable method for the analysis of breath sounds and demonstrated its usefulness in the assessment of bronchial constriction in children [7, 10]. Our previous studies using this method revealed interesting findings regarding a potential application as a biomarker in children with asthma; the effect of risk factors for asthma development on the spectrum curve indices in infants in a large multicenter-prospective study [27] and the bronchial reversibility in the well-controlled asthmatic children with a normal lung function [28].

However, one problem with this system is that its operation is not fully automated. The analysis of sound spectrum can mostly be performed automatically; however, two or more specialists must visually determine the highest frequency of breath sound (0 point) in each sound spectrum. The previous method has sufficient reliability to use for clinical research [13, 14], however, a simple method is necessary for conducting a multi-center participated studies or for applying when patients undergo daily medical treatment.

We think that the first step required for full automation is to adjust the 0 level of background noises in each sample. With the previous method, the examiners could not determine the 0 point with confidence in a small number of samples. One of the reasons for this is that our previous method sets the 0 level as −90 dBm based on the average background noise in large samples in our institute [7]. As a result, when the original 0 level is higher than −90 dBm, the high-pitched area of the lung sound spectrum may be emphasized, and when the original 0 level was lower than −90 dBm, the high-pitched area of the lung sound spectrum may be underestimated. These factors can adversely affect the accuracy of the 0 point.

There may be several reasons why changes in the basaline of spectrum are seen among patients. We considered the influence of wide-ranging noises inside and/or the difference in the force with which each examiner held the microphone. Noises with short-time wide-range frequencies were often seen in the breath sound spectrum like vertical strips [29]. We hypothesized that some of them, which were often observed in a large breath, appeared due to the influence of the upper respiratory tract [29]. Furthermore, when the examiner held the microphone with a small amount of pressure, outside noises with wide-range frequencies may increase.

To resolve these problems, in the present study, the examiners determined a convincing 0 level first and newly corrected the sound spectrums with the new 0 level. They subsequently determined the 0 points. In this study, we have been able to prove that this new method is sufficiently accurate and reliable. The intra-observer and inter-observer correlation coefficients were satisfactory for this simple clinical test, and sensitivity to bronchial change, which was examined in the β_2 agonist inhalation challenge, was also sufficient in comparison to the lung function tests. Furthermore, all examiners seemed to feel that it was easier to determine the 0 points.

In the new method, similarly to the previous method [13, 14], there were no significant relationships between the parameters of the lung function tests, spirometry and FOT, or other breath sound parameters. However, the relationship between the changes in the lung function parameters and the changes in the breath sound parameters, A_3/A_T, B_4/A_T, RPF_{75} and RPF_{50}, were evaluated in the new method. Although lung function tests and the analysis of breath sounds should evaluate different aspects of the respiratory physiology [3], it is a fact that the results of these tests reflect airway constriction. These data suggest that the analysis of breath sounds will introduce very important results in future studies of the airways in infant and preschool children.

The advantage of the new method may be dependent on the correct evaluation of the high-pitched area in each sound spectrum. It has been suggested that when bronchial dilatation is introduced, the main change that occurs is in the high-pitched part of the sound spectrum [7, 13, 14]. The changes in the spectrum curve indices, which are related to the ratio of the high-pitched sound area to the whole area of the lung sound spectrum, are interesting to study in asthmatic children. The reason, why the value of B_4/A_T determined with the new method showed no difference from the previous method and why the values showed no correlation with the values of the previous method (Table 3) may be dependent on the appropriate evaluation of the narrow high-pitched area in the new method.

On the other hand, in Table 3, the value of A_T, total area under the curve, of the new method, was significantly higher than that of the previous method. The previous method used an average of the background noise (−90.0 dBm) which was relatively higher than the actual average of background-noise power (−88.1 dBm) [7]. It seems that the value of A_T increased with the increase in the total lung sound spectrum area after correcting the 0 level. In the Bland-Altman plots, only RPF_{75} showed a tendency of dots to rise to the right. We think that RPF_{75} indicates the fine changes in the high-pitched area of breath sounds [14]; thus, slight changes in the right angle of the breath sound spectrum resulted in the tendency to rise to the right.

The relative noisy and low power breath sound on children made our evaluation difficult. For examiners, it was not so difficult to determine the 0 point in each breath sound spectrum with visual observation. However, some wide-range, wave-like noises around the 0 point of the sound spectrum make an accurate analysis difficult. Although many problems in the collection and analysis of breath sounds remain [10, 13, 27], automation has to be attempted. For a long time, we have studied the automatic analysis of all parameters based on the lung sound spectrum, considering the application of AI [30]. It seems that our results in this study may be useful for promoting full automation in the analysis of breath sounds.

Consequently, the main finding of the present study is that the adjustment of the 0 level before the decision of the 0 point is a useful technique for analyzing the childhood breath sound spectrum more accurately. Furthermore, the breath sound parameters in asthmatic children change significantly after β_2 agonist inhalation. We think that the breath sound spectrum seems to reflect the state of airway narrowing well, from the perspective of respiratory physiology. Although spirometry is the gold standard for assessing the lung function [3], our new method, which is safe and simple to perform during tidal breathing, may facilitate the application of the analysis of breath sounds in the evaluation of bronchial reversibility in young children. Based on the results of this study, we would like to continue to improve our methods with the goal of achieving the fully automated measurement of airway responsiveness based on the analysis of breath sounds.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest in association with the present study.

DISCLOSURE

This study was supported by the Environmental Restoration and Conservation Agency of Japan in 2009–2019.

ABBREVIATIONS

FVC: forced vital capacity
FEV_1: forced expiratory flow and volume in 1 second
FEF_{25-75}: mean forced expiratory flow between 25% and 75% of the FVC
$\dot{V}_{50}$: maximal expiratory flow at 50% vital capacity
$\dot{V}_{25}$: maximal expiratory flow at 25% vital capacity
FOT: forced oscillation technique
Rrs: respiratory resistance
R5: resistance at 5 Hz
R20: resistance at 20 Hz
R5–R20: difference in resistance between 5 Hz and 20 Hz
X5: reactance at 5 Hz
Slope: roll-off from 600 to 1200 Hz
AUC: area under the curve
A_T: total area under the curve of 100 Hz to the 0 point
A_3: third area under the curve
B_4: forth area under the curve
RPF_{50}: ratio of power and frequency at 50% of the 0 point

RPF_{75}: ratio of power and frequency at 75% of the 0 point

0 point: the frequency of inhaled breath sound spectrum at 0 dB

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