

A New Modality Using Breath Sound Analysis to Evaluate the Control Level of Asthma

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ABSTRACT

Background: Reliable symptom assessment is essential in asthma management. We developed new technology for analyzing breath sounds and assessed its clinical usefulness for monitoring asthmatic children.

Methods: Eighty asthmatic children and 59 non-asthmatic children underwent breath sound analysis in an asymptomatic state. Their asthma control was assessed by the Asthma Control Test™ or Childhood ACT™ scores and divided into two groups, namely, well-controlled (perfect) ($n = 19$) and not well-controlled (not perfect) ($n = 61$). Breath sounds were recorded using two sensors, located on the right anterior chest and trachea. We calculated the acoustic transfer characteristics between the two points, which indicated the relationship between frequencies and attenuation during breath sound propagation. Two indices of sound parameters, the chest wall sound index (CWI) and the tracheal sound index (TRI), were calculated from the transfer characteristics and tracheal sounds. We also developed a new parameter, the breath sound index (BSI), on a 2-dimensional diagram of CWI and TRI and tried to determine whether BSI may clarify asthma control better than CWI or TRI alone.

Results: There was a significant difference in TRI and BSI between asthmatic and non-asthmatic children ($p = 0.007$, $p < 0.001$). There was a significant difference in CWI and TRI between the well-controlled and not-well-controlled groups ($p < 0.001$). BSI discriminated between the two groups accurately ($p < 0.001$). The sensitivity and specificity of BSI for asthma control were 83.6% and 84.2%, respectively.

Conclusions: Asthma control could be evaluated using a new index calculated from breath sound analysis.

KEY WORDS

airway management, asthma, BSI, children, CWI, TRI

INTRODUCTION

The goals of asthma control are to achieve minimal or no symptoms all day long as well as full physical activity, including exertion, and prevent exacerbation.¹ In addition, well-controlled subjects should show normal lung function.¹ Asthma control should apply not only to clinical manifestations but also to the objective parameters of airflow limitation and airway inflammation. However, it is difficult to perform lung function tests in small children. Reliable assessment of asthma control is essential to manage asthma efficiently.² Therefore, objective monitoring is a useful tool in the management of asthmatic small children.

When asthma is not well-controlled, airway inflammation and flow limitation may not be well-controlled. Airway inflammation and flow limitation are associated with mucus hypersecretion and airway edema, which causes airway narrowing and affects breath sounds. Even in the absence of adventitious sounds, recent developments in signal processing methods have improved the possibilities of extracting physiologically and clinically relevant information from breath sounds.³⁻⁵

The change in the high frequency component of breath sounds corresponded with changes in the objective parameters of airflow limitation.⁵ Recently, breath sound analysis that uses the acoustic transfer

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Table 1 Patient characteristics

	Asthma			Non-asthma
	Total (n = 80)	Well controlled (n = 19)	Not-well controlled (n = 61)	(n = 59)
Gender M/F	57/23	14/5	43/18	27/32
Average age (years)	10.3 ± 3.0	11.2 ± 2.7	10.0 ± 3.1	11.0 ± 3.4
Height (cm)	136 ± 28	141 ± 17	138 ± 19	140 ± 17
Weight (Kg)	33 ± 13	40 ± 15	35 ± 13	35 ± 11
Severity				
Intermittent	14	3	11	
Mildly persistent	24	8	16	
Moderately persistent	33	6	27	
Severely persistent	9	2	7	

characteristics of the pulmonary system became available. The transfer characteristics are expressed as the ratio between the magnitude of the output signal and the magnitude of the input signal in a certain frequency domain. It has been reported that the transfer characteristics may be affected by airway wall compliance, airway diameter, and energy dissipation caused by motion.⁶⁻⁸

In this study, we sought to determine whether breath sound analysis could be used to detect changes in transfer characteristics and change in the high-frequency component of tracheal sounds according to the control level of asthma and its potential for evaluating the control level of asthma.

METHODS

SUBJECTS AND STUDY DESIGN

The baseline patient characteristics are listed in Table 1. The study subjects were 80 pediatric asthmatic outpatients in the Minami Wakayama Medical Center and 59 non-asthmatic children. Non-asthmatic children attended the center for a health screening. The diagnosis and classification of asthma were made according to international guidelines.^{9,10} Subjects with mild, moderate, and severe persistent asthma were treated continuously with inhaled corticosteroid and/or leukotriene receptor antagonists.

An asthma specialist used the Asthma Control Test™ (ACT) or Childhood ACT™ (C-ACT) for all asthmatic children in the outpatient department.

All the participants then underwent breath sound recording for at least 30 seconds. The asymptomatic period was defined as that without any respiratory or systemic symptoms, including asthma attack, upper or lower respiratory infections, and upper respiratory infections with cough. Confirmation that the breath sounds did not include wheezing or crackles was obtained on the basis of auscultatory findings and breath sound analysis.

Control of asthma condition was assessed by the ACT or C-ACT scores; the subjects were then divided

into two groups, well-controlled (perfect) or not well-controlled (not perfect).¹¹ ACT was applied for children 12 years old or older. C-ACT was applied for children younger than 12 years old. There were no significant differences in age, body weight, and height between the groups.

Written informed consent was obtained from all subjects or their legal guardians, and the study protocol was approved by the ethics committee of Minami Wakayama Medical Center.

SOUND RECORDING AND SIGNAL PROCESSING

A schematic block diagram of the recording system is presented in Figure 1. The recording and signal processing method in this study is the same as that described previously.¹²

Breath sounds were recorded on the right upper anterior chest at the second intercostal space in the midclavicular line and on the tracheal anterior cervical triangle (these recorded sounds are referred to as chest sounds and tracheal sounds, respectively) using sound sensors (TA-701T; NIHON KOHDEN, Tokyo, Japan). Breath sounds were recorded for at least 30 seconds while the patients breathed freely.

Breath sounds were re-sampled to 6 kHz, and 512-point fast Fourier transformation (FFT) was performed with a 75% overlap into adjacent segments using a Hanning data window. The acoustic transfer characteristics of the pulmonary system were calculated on the basis of a cross-spectrum method using chest and tracheal sounds. The values of indices (explained in the following section) were calculated for all inspiratory breath sounds, and the median was then calculated.

CHEST WALL SOUND INDEX (CWI)

To detect a change in the attenuation of breath sounds between the trachea and the chest wall, we calculated the acoustic transfer characteristics between these two points. We assessed the attenuation

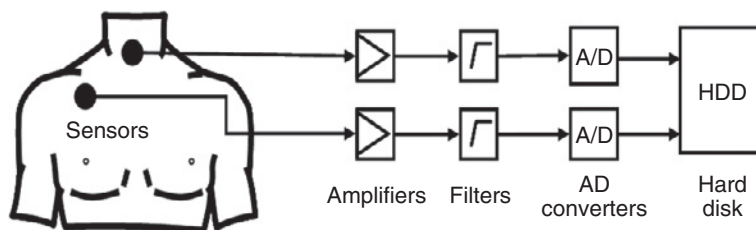


Fig. 1 Block diagram of the recording system. Breath sounds are measured at two locations. The breath sounds are amplified and high-pass-filtered. After that, breath sounds are converted from an analog to a digital form and stored on a hard disk. A/D, analog-to-digital converter; HDD, hard disk.

of breath sounds in the transition region of the transfer characteristics. We studied the relative attenuation at a high frequency with reference to the attenuation at a low frequency within the transition region of 100 to 400 Hz. The transfer characteristics at the transition region were calculated from the tracheal and chest sounds. The relative attenuation is called CWI. To measure attenuation at a low frequency (LoFreqAtt), we used a frequency corresponding to the beginning of the transition region. Transfer characteristics are relatively flat below 100 Hz and start to be attenuated over 100 Hz. The beginning of the transition region varied depending on the individual and ranged from 100 to 200 Hz. Therefore, we measured the average attenuation from 100 to 200 Hz at the transition region for LoFreqAtt. Frequency below 200 Hz can be influenced by heart sounds. However, this influence is negligible because LoFreqAtt is calculated by averaging processing from 100 to 200 Hz in the frequency domain.

To measure attenuation at a high frequency (HiFreqAtt), we used frequency corresponding to the higher frequency at the transition region. We adopted 400 Hz as high frequency because transfer characteristics over 400 Hz are unstable and not attenuated linearly in most recordings owing to the lower power of breath sounds in the chest. Therefore, for HiFreqAtt, we measured attenuation at 400 Hz of the transition region.

Generally, when a ratio of physical quantities is calculated in sound wave analysis, the expression of ten times the common logarithm of the ratio is used (unit is dB). As breath sounds are also sound waves, we used dB to express CWI.

$$\text{CWI} = 10 \times \log_{10} (\text{HiFreqAtt}/\text{LoFreqAtt}) \text{ [dB]}$$

TRACHEAL SOUND INDEX (TRI)

According to the shape of the spectrum distribution of tracheal sounds, we determined the power ratio of two frequency bands between 100 and 1300 Hz. Figure 2 is an example of the spectrum distribution of tracheal sounds in a 12-year-old girl. As shown in Figure 2, the spectral shape of tracheal sounds has a low-

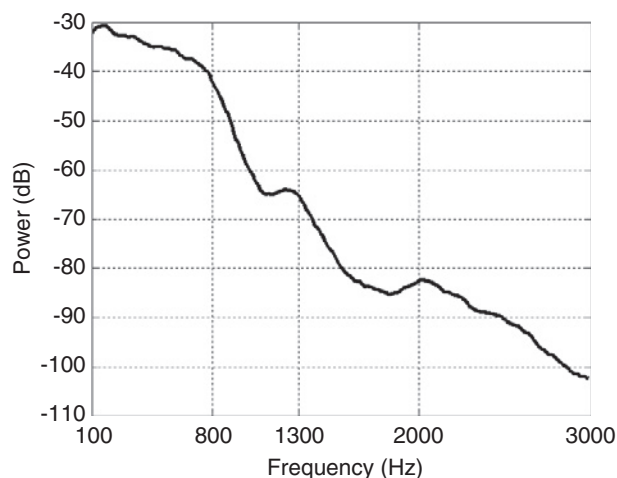


Fig. 2 Spectrum distribution of tracheal sounds. Spectrum distribution of tracheal sounds in a 12-year-old girl is shown. Tracheal sounds below 800 Hz are not largely attenuated. Tracheal sounds over 800 Hz are largely attenuated with increasing frequency.

frequency band where the power is not largely attenuated, as is seen below 800 Hz. It is also apparent that the power is largely attenuated over 800 Hz. Tracheal sounds over 1300 Hz are attenuated for more than 20 dB when compared with those below 800 Hz in most recordings; thus, the tracheal sound power over 1300 Hz is less than 1% of the power below 800 Hz. According to these observations, we used 100 to 800 Hz for a low-frequency band and 800 to 1300 Hz for a high-frequency band. To determine the power ratio according to the spectral shape of tracheal sounds, we measured the low- and high-frequency powers of tracheal sounds (LoPow and HiPow). We calculated the ratio between HiPow and LoPow as well as ten times the common logarithm of the ratio and used dB to express TRI.

$$\text{TRI} = 10 \times \log_{10} (\text{HiPow}/\text{LoPow}^a) \text{ [dB]}$$

We used 1.4174 as a multiplier 'a' of LoPow to reduce the influence of body size, which was determined by the slope of the regression line of LoPow

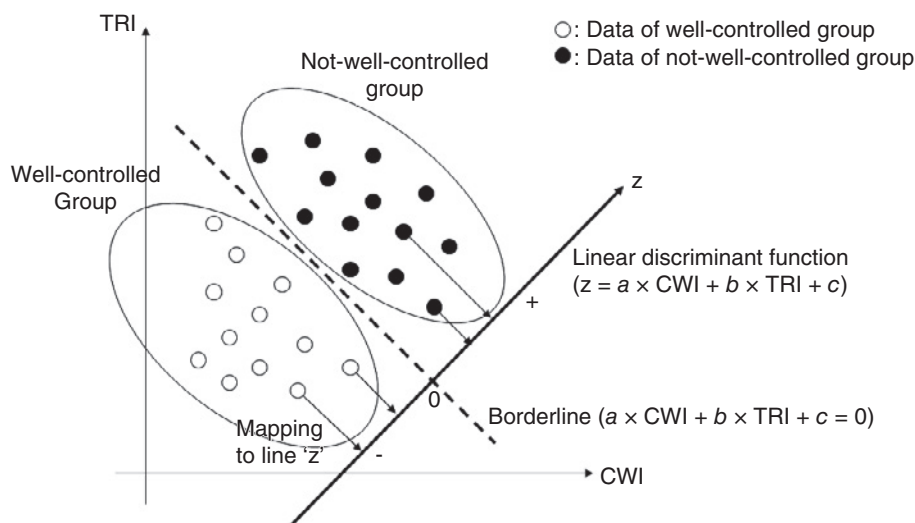


Fig. 3 Explanation of linear discriminant function. Data of the not-well-controlled (black circle) and well-controlled (white circle) groups are plotted in a 2-dimensional diagram of CWI and TRI. Line 'z' is a linear discriminant function. A dashed line of 'z' = 0 is the borderline to distinguish data into two groups. CWI, chest wall sound index; TRI, tracheal sound index.

and HiPow.¹²

BREATH SOUND INDEX (BSI)

As we observed higher CWI and TRI in the not-well-controlled group than in the well-controlled group, we tried to improve the discrimination accuracy by combining these two indices. To combine the discriminative power between the well-controlled and not-well-controlled groups of CWI and of TRI, we introduced a new index named BSI. BSI is determined by a linear discriminant function using CWI and TRI as shown below. Generally, a linear discriminant function is expressed by a linear combination of some features to separate data into two groups.¹³ As shown in Figure 3, when data of the well-controlled and non well-controlled groups are plotted in a 2-dimensional diagram of CWI and TRI, the linear discriminant function is determined as ' $z = a \times \text{CWI} + b \times \text{TRI} + c$ ' by conducting discriminant analysis (a , b , and c are the discriminant coefficients; ' z ' is the discriminant score). The discriminant score ' z ' corresponds to line ' z ' in Figure 3. By calculation of the linear discriminant function, each piece of data is mapped to line ' z ' (arrowed line in Fig. 3). The borderline to distinguish data can be drawn as a dashed line of ' $z = 0$ ' in Figure 3. This borderline is drawn at equal Mahalanobis generalized distances from the centroid of each group.¹⁴ By this method, the discriminant scores of the well-controlled group are negative, and those of the not-well-controlled group are positive. This discriminant score is called BSI.

STATISTICAL ANALYSES

Variables of breath sounds between the two study groups, that is, the well-controlled and not-well-controlled groups, were compared by the unpaired t-test. The correlation coefficients between the patient characteristics and variables of breath sounds were determined using Spearman's rank correlation coefficient. The correlation coefficients among variables of breath sounds were determined using Pearson's product-moment correlation coefficient. Values of $p < 0.05$ were considered statistically significant.

RESULTS

DEDUCTION OF THE INFLUENCE OF BODY SIZE AND AIRFLOW IN CWI AND TRI

CWI and TRI were not affected by body size and airflow. CWI did not correlate with body size (age: $r_s = -0.137$, body height: $r_s = -0.071$, body weight: $r_s = -0.071$, body mass index: $r_s = -0.047$). TRI did not correlate with body size (age: $r_s = -0.059$, body height: $r_s = -0.161$, body weight: $r_s = -0.199$, body mass index: $r_s = -0.365$). There was no correlation between TRI and the power of tracheal sounds ($r = 0.032$). Thus, CWI and TRI in this study were not affected by body size and airflow.

DIFFERENCE IN CWI AND TRI BETWEEN THE NON-ASTHMA AND ASTHMA GROUPS

Figure 4 shows the distributions of CWI and TRI for the non-asthma and asthma groups. The mean CWI was -17.0 ± 2.8 dB for non-asthma and -16.4 ± 4.1 dB for asthma. There was no significant difference in CWI between these two groups. The mean TRI was

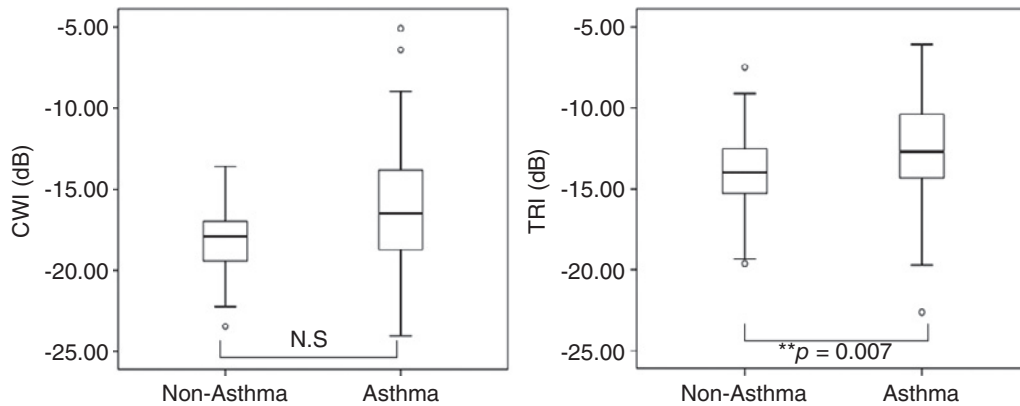


Fig. 4 Difference in CWI and TRI between the non-asthma and asthma groups. There was no significant difference in CWI between these two groups. There was a significant difference in TRI between these two groups ($p = 0.007$). CWI, chest wall sound index; TRI, tracheal sound index.

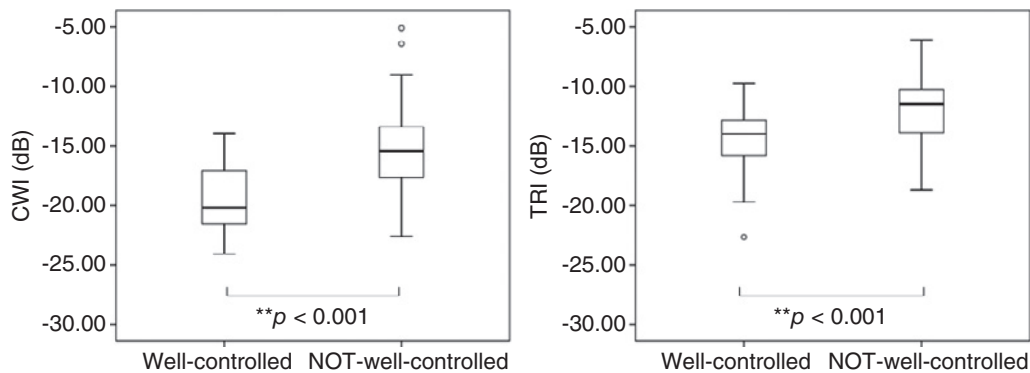


Fig. 5 Difference in CWI and TRI between the well-controlled and not-well-controlled groups. There was a significant difference in CWI between the well-controlled and not-well-controlled groups ($p < 0.001$). There was also a significant difference in TRI between the well-controlled and not-well-controlled groups ($p < 0.001$). CWI, chest wall sound index; TRI, tracheal sound index.

-14.0 $\pm$ 2.9 dB for non-asthma and -12.6 $\pm$ 3.0 dB for asthma. There was a significant difference in TRI between these two groups ($p = 0.007$).

DIFFERENCE IN CWI AND TRI BETWEEN THE WELL-CONTROLLED AND NOT-WELL-CONTROLLED GROUPS

Figure 5 shows the distributions of CWI and TRI for the well-controlled and not-well-controlled groups. The mean CWI was -19.5 $\pm$ 3.1 dB for the well-controlled group and -15.3 $\pm$ 3.7 dB for the not-well-controlled group. There was a significant difference in CWI between these two groups ($p < 0.001$). The mean TRI was -14.8 $\pm$ 3.1 dB for the well-controlled group and -12.0 $\pm$ 2.6 dB for the not-well-controlled group. There was a significant difference in TRI between these two groups ($p < 0.001$).

DIFFERENCE IN BSI BETWEEN THE NON-ASTHMA AND ASTHMA GROUPS

Figure 6 shows the distribution of BSI for the non-asthma and asthma groups. The mean BSI was -1.1 $\pm$ 1.0 for non-asthma and 0.0 $\pm$ 1.3 for asthma. There was a significant difference between these two groups ($p < 0.001$).

IDENTIFICATION OF THE WELL-CONTROLLED AND NOT-WELL-CONTROLLED GROUPS BY BSI

Figure 7 shows the well-controlled and not-well-controlled groups plotted on a 2-dimensional diagram of CWI and TRI. Circles and pluses are for the well-controlled and not-well-controlled groups, respectively. The solid line is the borderline to distinguish between the two groups. The sensitivity and specificity were 83.6% and 84.2%, respectively. AUC of the ROC curve was 0.90.

Figure 8 shows the distribution of BSI for the well-

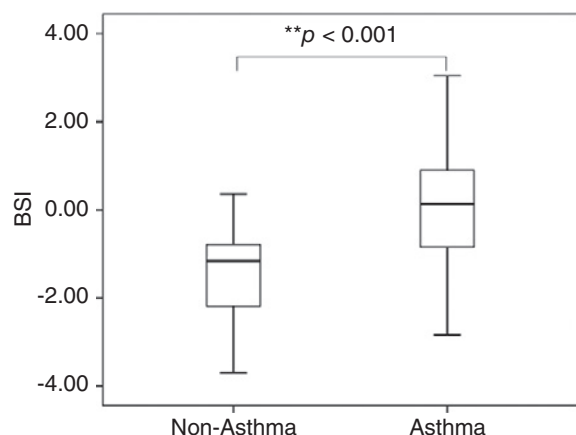


Fig. 6 Difference in BSI between the non-asthma and asthma groups. There was a significant difference between these two groups ($p < 0.001$). BSI, breath sound index.

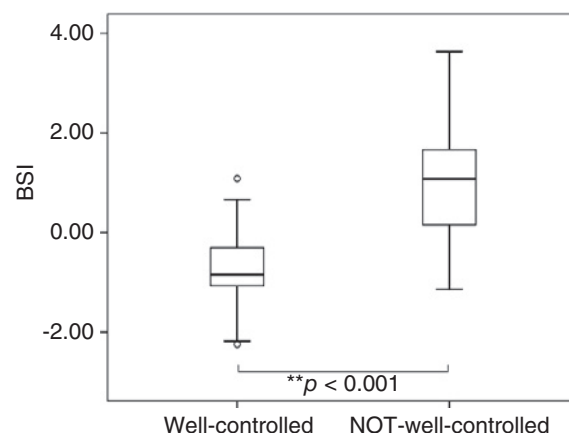


Fig. 8 Difference in BSI between the well-controlled and not-well-controlled groups. There was a significant difference in BSI between the well-controlled and not-well-controlled groups ($p < 0.001$). BSI, breath sound index.

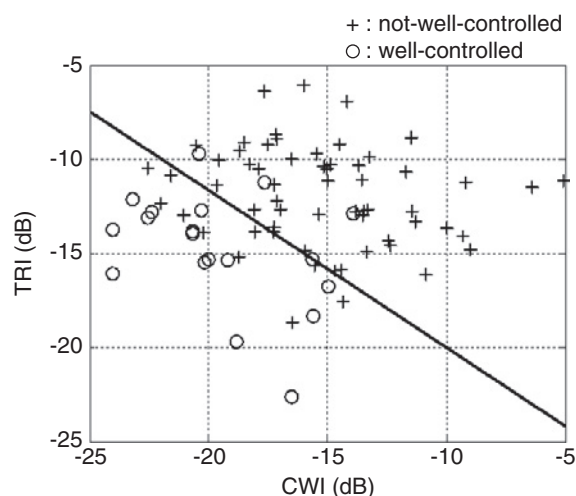


Fig. 7 Classification of asthma control by CWI and TRI. The sensitivity and specificity were 83.6% and 84.2%, respectively, by the linear discriminant function. Circles and pluses are data for the well-controlled and not-well-controlled groups, respectively. The solid line, drawn to distinguish between the not-well-controlled and well-controlled groups, was determined by the linear discriminant function. CWI, chest wall sound index; TRI, tracheal sound index.

controlled and not-well-controlled groups. The mean BSI was -0.7 ± 0.9 for the well-controlled group and 1.0 ± 1.0 for the not-well-controlled group. There was a significant difference between these two groups ($p < 0.001$).

DISCUSSION

The present study demonstrated that the analysis of breath sounds can be used to monitor the control of childhood asthma. We investigated changes of the transfer characteristics in the transition region of the

pulmonary system and the spectral shape of tracheal sounds according to the control level of asthma, and we evaluated the control level of asthma using new indices. The influences of body size and airflow were removed by our previously reported method; thus, these assessments were carried out by analyzing breath sounds alone.¹²

The sound transfer characteristics of the pulmonary system are similar to a low-pass filter because the higher-frequency components of breath sounds are largely attenuated through the lungs. Generally, the characteristics of a low-pass filter are divided into three frequency bands.¹⁵ One is a passband at which a signal can be transferred. Another is a stopband at which the signal transfer is disrupted. The third is a transition region at which a higher-frequency signal is largely attenuated.

When the management of asthma is not well-controlled, either CWI or TRI or both become large. When higher-frequency components of breath sounds are transferred to the chest wall, CWI becomes larger. The characteristics of breath sound attenuation in the propagation pathway are considered to vary according to the level of control of asthma. Donnerberg *et al.* previously studied the alteration of sound transmission of the lung in pre-congested and congested states in a canine model.¹⁶ They reported that an increased fluid content in tissue resulted in an increase of sound transmission at high frequency and that sound transmission through the lung was significantly dependent on the lung density. In bronchial asthma, airway narrowing is characterized by inflammatory changes, that is, mucus hypersecretion and airway edema. Matsumoto *et al.* had quantitatively assessed airway wall thickening and its clinical implication in asthma using CT.¹⁷ Airway wall thickening is accompanied by airway structural changes, such as

subbasement membrane thickening, mucous gland and goblet-cell hyperplasia, increased vascularity, and smooth-muscle hypertrophy and hyperplasia, as well as with chronic inflammation, such as mucosal edema and inflammatory cell infiltration. These inflammatory changes are assumed to increase the density and elasticity of the airway; thus, sound transmission at higher frequency can be increased when the airways are inflamed.

TRI becomes larger when the high-frequency power of tracheal sounds increases more than the low-frequency power. The spectral shape of generated breath sounds is affected by airway narrowing. Breath sounds are primarily generated by the turbulence within large airways. Inflammatory changes according to asthma reduce the caliber of these airways. This results in an increase of local airflow velocity when airflow at the mouth is the same before and after airway narrowing. Reduction of airway caliber as well as increase of the local airflow velocity leads to an increase of the frequency of breath sounds.¹⁸ Schreur *et al.* reported that the frequency of breath sounds of methacholine-induced acute airway narrowing was higher than that in a normal state.¹⁹ Their findings are largely in agreement with the our reported in this study.

Many studies on the changes of breath sounds in asthmatic conditions that are caused by changes of breath sound generation or transmission have been reported.³⁻⁶ In this study, we showed that CWI, TRI, and BSI will be useful in evaluating the control of asthma in children.

Even in children treated with inhaled corticosteroid (ICS), C-ACT and ACT are reported to show good correlation with the forced expiratory volume in the 1st second and/or the percent of predicted forced expiratory volume in 1 s.^{20,21} Further studies will be needed to elucidate the correlation between breath sounds and lung function and between breath sounds and the parameters of airway inflammation in these subjects.

We analyzed tracheal and chest breath sounds and developed novel indices, CWI, TRI, and BSI. We found that BSI was effective to evaluate the control of asthma in children. We conclude that we can assess the control of asthma non-invasively by analyzing breath sounds alone without measuring body size and airflow.

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