—Original—

Evaluation of the Usefulness of Spectral Analysis of Inspiratory Lung Sounds Recorded with Phonopneumography in Patients with Interstitial Pneumonia

Hiroshi Ono, Yasuyuki Taniguchi, Kinya Shinoda,
Tetsu Sakamoto, Shoji Kudoh and Akihiko Gemma

Division of Pulmonary Medicine, Infection Diseases and Oncology, Graduate School of Medicine, Nippon Medical School

Abstract

Purpose: We investigated whether spectral analysis with fast Fourier transform (FFT) of inspiratory lung sounds is useful in the diagnosis and evaluation of the severity of interstitial pneumonia (IP).

Subjects and Methods: The study population included 10 healthy volunteers (healthy group) and 21 patients with IP (IP group). We generated inspiratory averaged linear intensities using FFT and determined frequency at maximum sound intensity (Fmax), and quartile frequencies (f25, f50, and f75), compared these values between the groups, generated receiver operating characteristic curves to compare the detectability of IP between the indices and auscultation in all cases, and tested for the correlation of these indices with pulmonary function tests and the fibrosis scores from high-resolution computed tomography images assessed by 3 observers.

Results: Both f50 and f75 were significantly higher in the IP group, but their ability to detect IP was inferior to that of auscultation. They had negative correlations with percent vital capacity and had positive correlations with the fibrosis scores calculated by the 3 different observers.

Discussion: These results were considered to reflect the presence of fine crackles and alterations in pulmonary sound-conduction characteristics caused by IP and indicate that spectral analysis of lung sounds is useful in the diagnosis and evaluation of the severity of IP, although future study is necessary to improve its utility.
(J Nippon Med Sch 2009; 76: 67–75)

Key words: lung sounds, phonopneumograph, interstitial pneumonia, fast Fourier transform

Introduction

Auscultatory findings are important for the diagnosis of interstitial pneumonia (IP). Auscultation is easy and noninvasive, but an objective evaluation of lung sounds is essential because auscultation often lacks objectivity. The spectral analysis of lung

Correspondence to Hiroshi Ono, Department of Pulmonary Medicine/Infection and Oncology, Nippon Medical School, 1–1–5 Sendagi, Bunkyo-ku, Tokyo 113–8603, Japan
E-mail: h-ono@nms.ac.jp
Journal Website (http://www.nms.ac.jp/jnms/)

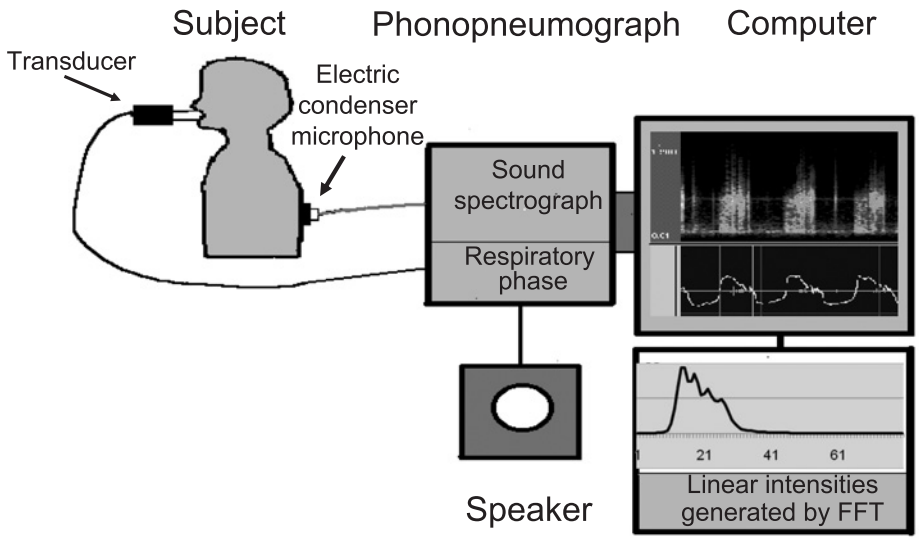


Fig. 1 Phonopneumograph setup
An electric condenser microphone was attached to the subject's back 5 cm below the lower margin of the right or left scapula. The subject held a transducer in his/her mouth, and a stethoscope-shaped electric condenser microphone was attached with double-stick tape to a position 3 finger-widths below the inferior angle of the right/left scapula on the subject's back. Under these conditions, each subject performed 10 spontaneous respirations while lung sounds were obtained with the microphone and the inspiratory and expiratory phases were detected with a transducer.

sounds with the fast Fourier transform (FFT) is a method that can provide objective and quantitative data. However, few studies have investigated the association between lung sounds analyzed with FFT and the diagnosis and evaluation of the severity of IP. Using a phonopneumograph developed by our group, we recorded the inspiratory lung sounds of healthy subjects and patients with IP, analyzed the data with FFT, and considered whether the results could be useful in the diagnosis and evaluation of the severity of IP.

Subjects and Methods

The present study included 21 patients with IP ("IP group") who visited the unit of respiratory medicine of Nippon Medical School Hospital (Tokyo, Japan) from April 2003 through August 2005 and were not treated with corticosteroids or immunosuppressive agents, and 10 healthy volunteers who served as controls ("healthy group"). The subjects of both groups were informed about the purpose of the study and consented to participate. Pulmonary function testing included measurements of percent vital capacity (%VC) and percent forced expiratory volume in 1 second ($FEV_{1.0}$%) for all subjects and percent diffusing lung capacity for carbon monoxide (%DLCO) in 17 subjects (2 in the healthy group and 15 in the IP group). In addition, high-resolution computed tomography (HRCT) of the chest was performed in all patients of the IP group. At baseline, we recorded the age, sex, height, body weight, body mass index (BMI), %VC, $FEV_{1.0}$%, %DLCO, and average inspiration time for all subjects.

Collection and Analysis of Lung Sounds with a Phonopneumograph

We used a phonopneumograph (LSA2000, Kenz Medico Co., Saitama, Japan) to record lung sounds in a sound-proof room. The subject held a transducer in his/her mouth, and a stethoscope-shaped electric condenser microphone was attached with double-stick tape to a position 3 finger-widths (about 5 cm) below the inferior angle of the right/left scapula on the subject's back (**Fig. 1**). Under these conditions, each subject performed 10 spontaneous respirations while lung sounds were obtained with the

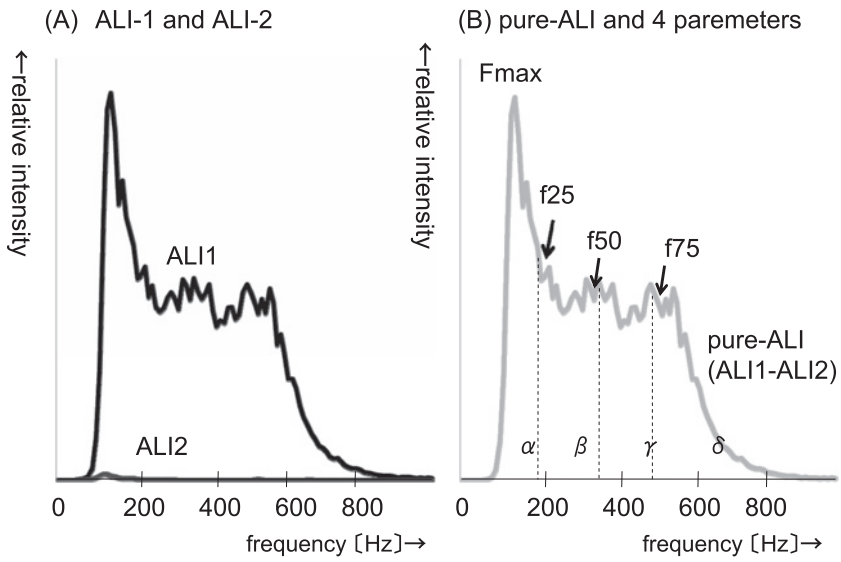


Fig. 2 ALIs
(A) ALI-1: ALI of inspiration; AHI-2: ALI of background noise; (B) all areas α, β, γ, and δ are aequalis.

microphone and the inspiratory and expiratory phases were detected with a transducer.

Linear Intensity of Inspiratory Lung Sounds and Calculation of 4 Indices

Recorded lung sounds were processed with the FFT using the phonopneumograph and a personal computer. All data were digitized through a 12-bit analog-digital converter at a sampling rate of 5 kHz. The linear intensities (LIs) were calculated with the FFT after application of a hanning window. Each sound sample consisted of 512 points, and the time window was 100 msec. The resulting LI was displayed on the monitor of a personal computer, with the x-axis representing frequency and the y-axis representing the intensity of sounds.

When Mahagnah and Gavriery examined the repeatability of the LIs of respiratory sounds in 6 healthy persons in 1994, they used 3 techniques to minimize the contribution of heart sounds and background noises. The techniques consisted of the following: 1) sounds were high-pass filtered at 75 Hz; 2) intensities from each respiratory phase were averaged; and 3) intensities from the surrounding noise were measured during a breath hold and subtracted from the intensities of lung sounds[1]. In our study, in an attempt to incorporate these techniques, we used LI that had been averaged during 10 cycles of inspiratory phases (averaged LI-1; ALI-1 in **(Fig. 2A)** and used a section greater than 140 Hz. However, we did not ask the subjects to hold their breath because patients with IP might not be able to temporarily stop their breathing, as instructed, without triggering respiratory symptoms. Therefore, we considered a brief time (0.16 second) between inspiration and expiration to represent a respiratory pause. We performed FFT of the sound during this period, which was calculated to cover a total of 3.04 seconds (0.16 second × 19 pauses) during 10 respirations, and averaged the LI (ALI-2 in **(Fig. 2 A)**. In addition, we generated an averaged LI of pure inspiratory lung sounds (pure-ALI in **(Fig. 2B)** by subtracting the intensity of ALI-2 from that of ALI-1, at every frequency.

For the pure-ALI, we determined 4 indices: the frequency with the maximum intensity (Fmax), and the first, second, and third quartile frequencies in the linear intensities (f25, f50, and f75 in **(Fig. 1B)**. For the configuration of pursued ALI and the 4 indices, we reviewed the following.

1) Four indices: We compared the 4 indices between the IP group and the normal group.

2) Receiver operating characteristic curve analysis: We generated receiver operating characteristic (ROC) curves and determined the area under the ROC curve (AUC) for the indices among the 4 that

Table 1 Thin-section CT scoring system for idiopathic pulmonary fibrosis (Kazerooni EA, et al. AJR: 1997; 169: 977－983)

Ground-glass score
0: No ground-glass opacity
1: Ground-glass opacity involving ≤ 5% of the lobe
2: Ground-glass opacity involving 5－<25% of the lobe
3: Ground-glass opacity involving 25－49% of the lobe
4: Ground-glass opacity involving 50－75% of the lobe
5: Ground-glass opacity involving >75% of the lobe
Fibrosis score
0: No fibrosis
1: Interlobular septal thickening; no discrete honeycombing
2: Honeycombing involving <25% of the lung
3: Honeycombing involving 25－49% of the lung
4: Honeycombing involving 50－75% of the lung
5: Honeycombing involving >75% of the lung

Table 2 The background of the subjects

	IP (N=21)	healthy (N=10)	p (t-test)
Age (years)	65.7 ± 11.0	54.5 ± 14.3	0.014*
Sex, n (male)	11	5	0.905
Height (cm)	157.0 ± 7.7	160.4 ± 7.8	0.257
Weight (kg)	57.0 ± 9.7	61.8 ± 8.9	0.202
BMI (kg/m^2)	23.1 ± 3.2	27.2 ± 12.3	0.158
%VC	71.7 ± 26.4	108.7 ± 19.4	<0.001**
$FEV_{1.0\%}$	83.1 ± 15.8	80.0 ± 7.0	0.535
%DLCO†	56.2 ± 21.0	110.3 ± 4.5	<0.001**
Duration of inspiration (s)	1.3 ± 0.4	1.7 ± 0.5	0.006**

Most data are presented as mean ± SD.
*p<0.05, **p<0.01 (statistically significant between-group differences).
†%DLCO was determined in 17 cases: 2 in the healthy group and 15 in IP group.

differed significantly between groups, and the presence of fine crackles by auscultation of two experienced respiratory physicians (B and D) who were blinded to clinical information except lung sounds.

3) Representative subjects: As representative subjects, we selected 1 subject from the healthy group, 1 subject with fine crackles from the IP group, and 1 subject without fine crackles from the IP group. Their data were then analyzed for the presence of a difference in configuration of the pure-ALI.

4) Correlations: Data from the IP group were analyzed for the presence of correlation between the four indices, and the results of pulmonary function tests which included %VC, $FEV_{1.0}$% and %DLCO, or the extent of pulmonary fibrotic lesions identified in the chest HRCT images on the same side from which lung sounds were collected. We used 2 HRCT slices located 4 and 5 cm beneath the scapular inferior angle. The extent of lesions was calculated as a total of the scores from the 2 slices, using the pulmonary fibrosis scoring of HRCT images proposed by Kazerooni and colleagues (**Table 1**)[2]. The interpretation of HRCT images and the calculation of scores were performed by 3 experienced respiratory physicians (A, B, and C). Two of these physicians (A and B) were blinded to all clinical information except HRCT. One of the physicians (C) was involved in the analysis of lung sounds but performed the CT interpretation and scoring before the analysis of pulmonary sounds, to prevent the possibility of bias.

We used the paired t-test for comparison of the groups, Spearman's coefficient for evaluation of correlation, and Dr. SPSS II software (SPSS Japan Inc., Tokyo, Japan) for statistical analysis. P-values <0.05 were considered to indicate statistical significance. This present study was approved by the Ethical Review Board of Nippon Medical School.

Results

Characteristics of Subjects

The background characteristics of the subjects are shown in **Table 2**. The mean age ± standard deviation (SD) was significantly higher in the IP group (65.7 ± 11.0 years) than in the healthy group (54.5 ± 14.3 years, p=0.014). However, sex, height, body weight, and BMI, did not differ significantly between the groups. The average duration of inspiration, which is the mean inspiration time per breath, was significantly shorter in the IP group (1.3 ± 0.4 seconds) than in the healthy group (1.7 ± 0.5 seconds, p=0.006). In the IP group both the %VC (71.7% ± 26.4%) and the %DLCO (56.2% ± 21.0%) were significantly lower than those in the healthy group (108.7% ± 19.4% and 110.3% ± 4.5%,

(A)

	IP (n=21)	healthy (n=10)	p value
Fmax	168.1±99.8	143±48.3	0.264
f25	153.8±42.8	139±87.6	0.142
f50	231.9±104.7	167±14.9	**0.011***
f75	335.2±142.7	218±21.0	**0.001****

(B)

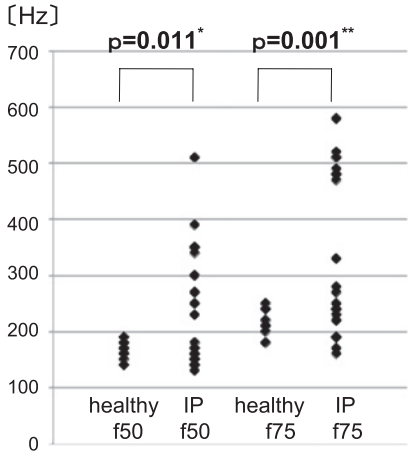


Fig. 3 Comparison of Fmax, f25, f50, and f75 between the groups

respectively; both p<0.001). However, $FEV_{1.0}$% did not differ between the groups.

1) Four indices

In **Figure 3A**, in the IP group, the f50 value (231.9 ± 104.7 Hz) and the f75 value (335.4 ± 142.7 Hz) were significantly higher than those in the healthy group (167.0 ± 149.4 Hz, p=0.011, and 246.0 ± 42.5 Hz, p=0.001, respectively). However, the Fmax and the f25 did not differ between the IP group (168.1 ± 134.4 Hz and 153.9 ± 42.8 Hz, respectively) and the healthy group (143.0 ± 48.3 Hz, p=0.264, and 139.0 ± 87.6 Hz, p=0.142, respectively). The scatter diagram of f50 and f75 in both groups is shown in **Figure 3B**.

2) ROC analysis

In the healthy group, fine crackles were heard in 2 of 10 subjects by observer B and in 1 subject by observer D, but fine crackles were not heard by both observers in any single patient. In the IP group, fine crackles were heard in 17 of 21 subjects by observer B and in 14 subjects by observer D, and in 1 subject fine crackles were not heard by either observer. ROC curves and AUCs of f50 and f75 and the presence of fine crackles during inspiration heard by 2 observers, B and D (FC-B and FC-D), are shown in **Figure 4**. The AUC was 0.612 in f50, 0.750 in f75, 0.805 in FC-B, and 0.783 in FC-D, and the ability to detect IP, in descending order, was FC-B, FC-D, f75, and f50.

3) Representative cases

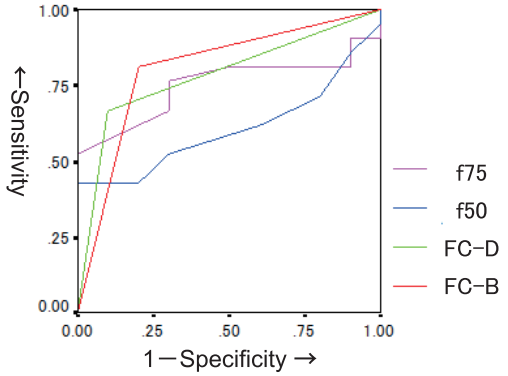
The ALI of a representative subject with IP with FC is shown in **Figure 5A**, that of the only subject with IP in whom fine crackles were not heard by either observer is shown in **Figure 5B**, and that of a representative subject of the healthy group is shown in **Figure 5C**. We had the impression that the relative intensity of sounds in the range of frequencies from 300 to 600 Hz of the ALI in the subject having IP with FC is higher than that of the healthy subject or the subject having IP without FC. The configuration of ALI of the subject having IP without FC resembled that of a healthy subject rather than that of subject having IP with FC.

4) Correlation

The results are shown in **Table 3**. Negative correlations were found between %VC and f25 (r=−0.602, p=0.004), f50 (r=−0.601, p=0.004), and f75 (r=−0.533, p=0.013). The scatter diagram of the correlations between %VC and f25, f50, and f75 is shown in **Figure 6**.

The ground glass score (GGS) by observer A was negatively correlated with Fmax (r=−0.464; p=0.034) and f25 (r=−0.453, p=0.039).

Significant positive correlations were found between the fibrosis score (FS) by observer A and f50 (r=0.448, p=0.041) and f75 (r=0.47, p=0.032); between the FS by observer B and Fmax (r=0.577, p=0.006), f25 (r=0.636, p=0.002), f50 (r=0.651, p=0.001),



	AUC	SE	p	95 % CI
f75	0.75	0.087	0.027*	0.579–0.921
f50	0.612	0.099	0.321	0.418–0.806
FC–D	0.783	0.086	0.012*	0.614–0.953
FC–B	0.805	0.090	0.007**	0.629–0.980

Fig. 4 The ROC curves and the areas under the curves of f75, f50, and auscultation of fine crackles by two different observers
p: significant probability when we assumed "AUC=0.5" null hypothesis; 95%CI: 95% confidence interval; FC-D: presence of fine crackles during inspiration in auscultation by observer D; FC-B: presence of fine crackles during inspiration in auscultation by observer B.

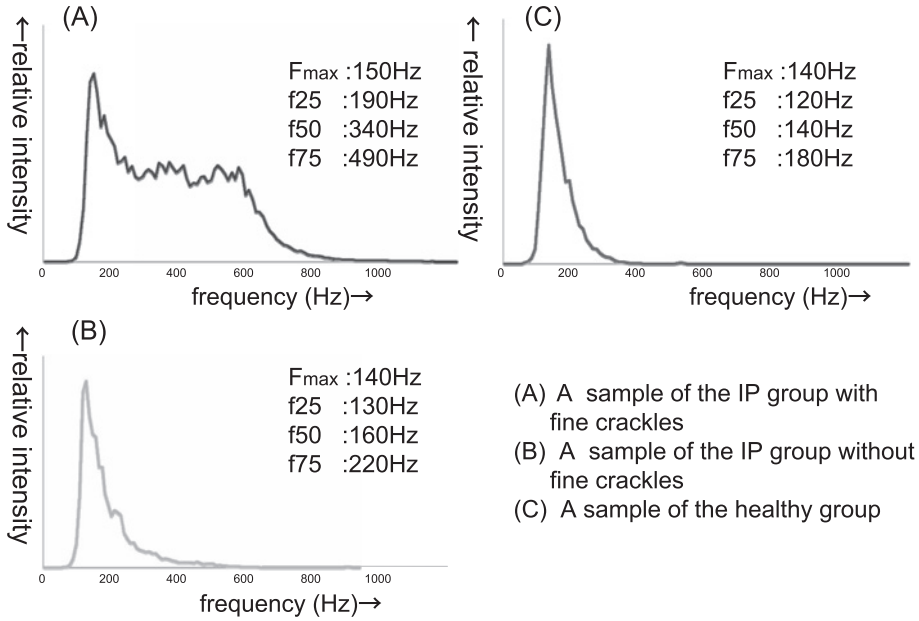


Fig. 5 Representative ALIs of the healthy group and of the IP group with and without fine crackles

and f75 (r=0.537, p=0.012); between the FS by observer C and Fmax (r=0.612, p=0.003), f25 (r=0.643, p=0.002), f50 (r=0.675, p<0.001), f75 (r=0.69, p<0.001); between the sum of FS by 3 observers and Fmax (r=0.588, p=0.005), f25 (r=0.725, p<0.002), f50 (r=0.783, p<0.001) and and f75 (r=0.759, p<0.001). The scatter diagrams of the correlations between the sum of FS by 3 observers and f50 or f75 are shown in **Figure 7**.

Positive correlations were found between the sum of GGS and FS by observer B and Fmax (0.649, p=

Table 3 The correlation between 4 variables and results of pulmonary function test and FS on chest HRCT in the IP group

	(Fmax) r	p	(f25) r	p	(f50) r	p	(f75) r	p
%VC	− 0.222	0.333	− 0.602	0.004**	− 0.601	0.004**	− 0.533	0.013*
FEV1.0%	0.092	0.690	− 0.147	0.526	− 0.058	0.804	− 0.051	0.825
DLCO	− 0.303	0.237	− 0.131	0.617	− 0.219	0.398	− 0.206	0.427
GGS-A	− 0.464	0.034*	− 0.453	0.039*	− 0.391	0.079	− 0.340	0.131
GGS-B	0.250	0.275	0.029	0.902	− 0.062	0.788	− 0.093	0.690
GGS-C	− 0.098	0.672	− 0.065	0.778	0.002	0.992	− 0.055	0.812
total-GGS	− 0.147	0.524	− 0.306	0.177	− 0.268	0.241	− 0.276	0.227
FS-A	0.080	0.730	0.343	0.128	0.448	0.041*	0.47	0.032
FS-B	0.577	0.006**	0.636	0.002**	0.651	0.001**	0.537	0.012
FS-C	0.612	0.003**	0.643	0.002**	0.675	<0.001**	0.69	<0.001**
total-FS	0.588	0.005**	0.725	<0.001**	0.783	<0.001**	0.759	<0.001**
GF-A	− 0.268	0.240	− 0.102	0.659	− 0.012	0.959	0.045	0.847
GF-B	0.649	0.001**	0.400	0.072	0.315	0.164	0.211	0.359
GF-C	0.408	0.066	0.543	0.011*	0.599	0.004**	0.522	0.015*
total GF	0.452	0.04*	0.422	0.057	0.475	0.029*	0.411	0.065

GF: the sum of GGS and FS

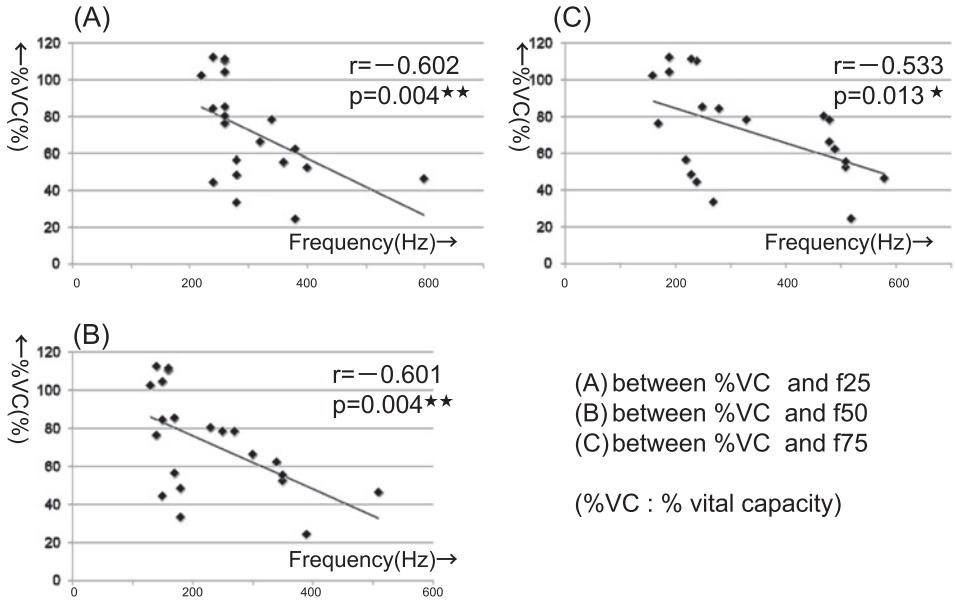


Fig. 6 The correlations between %VC and f25, f50, or f75 in the IP group

0.001), that by observer C and f25 (r=0.543, p=0.011), f50 (r=0.599, p=0.004), and f75 (r=0.522, p=0.015), that by the 3 observers and Fmax (r=0.452, p=0.04) and f50 (r=0.475, p=0.029).

Discussion

In the present study the mean age of the IP group was 11 years greater than that of the healthy group. According to a study of the lung sounds of healthy subjects by Gross and colleagues[3], in a frequency spectra of inspiratory lung sounds generated by FFT, the ratio (Q%) of the sound intensity of 330 to 600 Hz (frequency "Band 2") to that of 60 to 330 Hz ("Band 1") showed a positive correlation with age, but the Q ratio of all subjects was less than 50%. In the present study, the age difference between the groups may have affected the difference in the

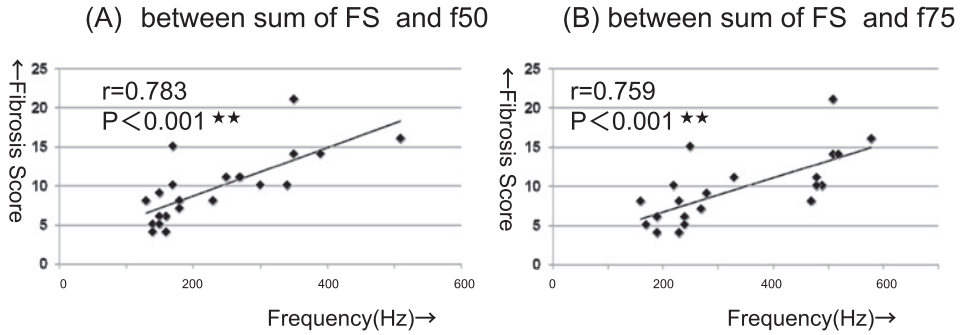


Fig. 7 The correlations between fibrosis score in chest HRCT and f50 or f75 in the IP group

configuration of ALI. However, when we measured Q with the procedure of Gross et al., Q was greater than 50% in 7 subjects of the IP group; in addition, although Gross et al. predicted a 10% increase in Q with an 11-year increase in age, in the present study the mean Q value in the IP group (43.8% ± 50.7%) was 7 times that in the healthy group (6.3% ± 3.7%). Therefore, we believe that a factor other than age affecting the configuration and quartile frequencies of ALI is present in the IP group.

In the IP group, the f50 and f75 were significantly higher than in the healthy group. The most important auscultatory finding in IP is the presence of fine crackles upon inspiration. Munakata and colleagues analyzed fine crackles with FFT and reported that the mean peak frequency of fine crackles was 443 ± 146 Hz[4], and Vyshedskiy and coworkers reported that the average frequency of crackles heard in patients with idiopathic pulmonary fibrosis was 462 ± 50 Hz[5]. Both reports agree with our result that the ALI of the IP group tend to have a higher sound intensity in the range of 300 to 600 Hz than did the healthy group. The presence of fine crackles affects the configurations of ALI and is a factor increasing f50 and f75 higher in the IP group, a conclusion supported by the configuration of ALI in subjects who have IP without fine crackles is similar to that in healthy subjects. According to the scatter diagram of f50 and f75, most of the subjects in whom f50 was greater than 200 Hz or in whom f75 was greater than 300 Hz were members of the IP group, a distinction that would be helpful for detecting IP. However, the sensitivity of f50 and f75 for detecting IP was poor because their AUCs were smaller than those of auscultation by 2 observers. To improve the detectability of IP, it would be necessary to perform studies with larger numbers of subjects and to establish new indices or the criteria instead of the indices used about spectrum analysis of lung sounds in conventional studies.

Furthermore, when we assessed the correlation of f50 or f75 with the HRCT findings of the 3 observers, we found that the 2 indices usually correlated significantly with the FSs of each observer and with the sum of the observers' FSs. In 2000, Piirilä and colleagues performed FFT of the inspiratory sounds of patients with asbestos-related lung disease and reported a positive correlation between the FS score from HRCT and the upper quartile frequency of the power spectrum[6]. However, we are not aware of any studies that have examined the correlation between FFT of lung sounds and HRCT findings in pure IP; therefore, the results of the present study appear to be the first such data relevant to IP. FS is the score showing the extent of honeycomb lung in a HRCT image. The preceding results suggest that lung sounds of high frequency become more easily conducted as honeycombing spreads.

We are considering 2 hypotheses for our results. One hypothesis is that the amount of fine crackles increases as a pulmonary fibrosis lesion spreads. If amount of fine crackles increases, the sound intensity of a range of frequency of fine crackles would increase, thereby increasing f50 and f75. However, arguing against this hypothesis is the finding of negative correlations between those indices and %VC in the present study, which suggests that another factor, in addition to fine crackles, that increases the indices is present.

Another hypothesis is an alteration of sound conduction characteristics of lung tissue by the spread of pulmonary fibrosis. The lung acts as a low-pass filter, allowing transmission of sounds of only low frequency through the lung parenchyma and intraalveolar air[7]. Donnerberg and coworkers examined the sound-conduction characteristics in a canine lung at autopsy and found that a sound of 180 to 230 Hz was conducted best; however, when they created lung congestion artificially, the conduction range rose as intrapulmonary liquids accumulated[8]. We have developed the hypothesis that, in IP, the mechanism by which the lung acts as a low-pass filter would be lost due to interstitial fibrosis and pneumatic decrease in the lungs, along with a decrease in lung volume caused by honeycombing; therefore, high-frequency sounds would be more easily heard.

In contrast to FS, the GGS of observer A was negatively correlated with Fmax and f25. Further studies will be necessary to determine whether this finding had a specific cause or was accidental. Both alveolar space and an interalveolar dissepiment can be the main locus of ground-glass opacity in HRCT images[9,10]. Therefore, we think that it would be difficult to establish a clear association between ground-glass opacity and lung sound findings, that is, the characteristics of pulmonary sound conduction, because the pathological characteristics of a patient showing ground-glass opacity upon CT imaging may vary.

There are several limitations of the present study. First, the number of subjects was small. Second, the mean patient age in the IP group was significantly higher than that in the healthy group, and we did not consider the effect of age on lung sounds. Third, we did not perform wave-form analysis and, in particular, we did not adequately assess how fine crackles contributed to the results because the phonopneumograph used does not perform numerical quantification of fine crackles. Fourth, we had subjects perform spontaneous respiration and did not control their respiratory speed or volume of ventilation. Fifth, we compared healthy subjects and patients with IP but did not perform comparisons between patients with IP and those with other lung diseases, such as bacterial pneumonia and pulmonary edema. However, the results of the present study suggest that spectral analysis by FFT of inspiratory lung sounds would be useful for diagnosis and for the evaluation of the severity and the effects of therapies, such as corticosteroids, of IP, although future study is necessary to improve its utility.

Acknowledgement: We are grateful to Mr. Torakazu Muratake of Kenz Medico Co., which cooperated in the preparation of this report.

References

1. Mahagnah M, Gavriely N: Repeatability of measurement of normal lung sounds. Am J Respir Crit Care Med 1994; 149 (Pt 1): 477–481.
2. Kazerooni EA, Martinez FJ, Flint A, et al.: Thin-section CT obtained at 10-mm increments versus limited three-level thin-section CT for idiopathic pulmonary fibrosis: correlation with pathologic scoring. AJR 1997; 169: 977–983.
3. Gross V, Dittmar A, Penzel T, et al.: The Relationship between Normal Lung Sounds, Age, and Gender. AJRCCM 2000; 162: 905–909.
4. Munakata M, Ukita H, Doi I, et al.: Spectral and waveform characteristics of fine and coarse crackles. Thorax 1991; 46: 651–657.
5. Vyshedskiy A, Bezares F, Pacicj R, et al.: Transmission of Crackles in Patients With Interstitial pulmonary Fibrosis, Congestive Heart failure, and Pneumonia. Chest 2005; 128: 1468–1474.
6. Piirilä P, Lehtola H, Zitting A, et al.: Lung sounds in asbestos induced pulmonary disorders. Eur Respir J 2000; 16: 901–908.
7. Bergstresser T, Ofengeim A, Vyshedskiy A, et al.: Sound transmission in the lung as a function of lung volume. J Appl Physiol 2002; 93: 667–674.
8. Donnerberg RL, Druzgalski CK, Hamlin RL, et al.: Sound transfer function of the congested canine lung. Br J Dis Chest 1980; 74: 23–31.
9. Noma K, Kubo T, Kazawa N, et al.: HRCT-pathologic correlation of ground glass density [article in Japanese]. Nichidoku-Ihou 1996; 41: 498–506.
10. Miller WT Jr, Shah RM: Isolated diffuse ground glass opacity in thoracic CT: cause and clinical presentations. AJR 2005; 184: 613–622.

(Received, November 7, 2008)
(Accepted, January 6, 2009)