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主論文

Longitudinal shape irregularity of airway lumen assessed by computed tomography in patients with bronchial asthma and COPD

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Abstract

Background

Airway remodeling in bronchial asthma (BA) and chronic obstructive lung disease (COPD) has been quantitatively assessed by analyzing the percentage of wall area to luminal area on cross-sectional computed tomography (CT) images. To date, there have been no reports on assessment of the longitudinal structure of the airway lumen.

Methods

Quantitative airway analysis using CT was performed on 3 groups consisting of 29 BA patients, 58 COPD patients, and 59 healthy controls. To assess the longitudinal shape irregularity of the airway lumen, new quantitative CT parameters, validated by a phantom study, were established. The internal radii of imaginary inscribed spheres in the airway lumen were measured as a function of distance from the level of carina to the fifth-order branches of the right posterior basal bronchus. The gaps of these radii from the regression line were calculated as parameters to reflect the longitudinal airway lumen shape irregularity. These new parameters were compared among the study groups as well as with the conventional parameters of airway wall thickening and luminal area.

Results

The longitudinal airway lumen shape irregularity was significantly greater in COPD patients than in BA patients and controls. Wall thickening was significantly greater and luminal area was smaller in BA patients than in COPD patients and controls. These results were consistent even among the BA and COPD subgroups with similar airflow limitation.

Conclusions

The combination of cross-sectional and longitudinal airway structure analyses using CT

images may suggest differences in the characteristics of airway remodeling between COPD and asthma.

Key messages

What is the key question?

Is there any difference between bronchial asthma and chronic obstructive lung disease (COPD) with regard to the longitudinal shape irregularity of the airway lumen?

What is the bottom line?

The longitudinal shape irregularity of the airway lumen was significantly greater in COPD patients than in bronchial asthma patients and controls, whereas wall thickening was significantly greater in bronchial asthma patients than in patients with COPD and controls.

Why read on?

This is the first report to investigate the longitudinal structure of the airway lumen using quantitative CT analysis to assess airway remodeling in obstructive pulmonary diseases.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by persistent airflow limitation due to a combination of airway disease and parenchymal destruction (emphysema).[1] Chest computed tomography (CT) is a useful technique for assessing these structural changes in vivo. Pulmonary emphysema is recognized on CT images as an area with low attenuation. Numerous studies have used the ratio of low attenuation area (LAA) to total lung area as a useful parameter to quantitatively evaluate the extent of emphysema.[2-4] Moreover, developments in CT and techniques of image analysis have been applied in the assessment of airway lesions. However, accurate quantitative evaluation of small airways, which are key sites of airway inflammation and airflow limitation in COPD, is not possible with these techniques.[5, 6] Hence, CT evaluation of airway remodeling usually entails measurement of airway dimensions from the proximal airways up to approximately subsubsegmental airways.[7-10] CT indices such as the ratio of airway wall area (WA) to total airway wall area (WA%) as well as luminal area (Ai) have been used for the quantitative analysis of airway wall thickening and airway narrowing. These parameters have also been applied for clinical studies on bronchial asthma (BA), which is another common obstructive pulmonary disease.[11-13] A recent study that compared multidetector-row CT (MDCT) airway dimensions among COPD patients, asthma patients, and healthy controls has reported that WA% was significantly larger and Ai was smaller in BA patients than in COPD patients and controls; there were no differences in WA% and Ai between COPD patients and healthy controls.[14] However, these CT parameters were basically derived from an evaluation that focused on airway wall thickness at a specific cross-sectional

slice. There are no reports to establish CT parameters that cover a wide range of airways in the longitudinal plane. This perspective is also an advantage for 3-dimensional CT image analysis compared with a pathological approach, by which quantitative analysis of longitudinal airway dimensions is difficult to evaluate.

Thus, we hypothesized that the analysis of the longitudinal structure of airways using CT images could further characterize airway remodeling in COPD patients, asthma patients, and healthy controls. In the present study, we focused on the longitudinal structure of the airway lumen, a feature closely related to airflow limitation. We established new parameters to reflect the shape irregularity of the airway lumen by measuring changes in the internal radii of imaginary inscribed spheres in the airway lumen from the level of the proximal carina to the peripheral bronchial subsegments on CT images. These new CT parameters, as well as WA% and Ai, were compared among COPD patients, asthma patients, and healthy controls to investigate the characteristics of airway remodeling in obstructive lung diseases.

METHODS

Subjects

A total of 29 patients with stable BA (BA group), 58 patients with stable COPD (COPD group), and 59 healthy controls (control group) were studied. BA was diagnosed according to the American Thoracic Society criteria,[15] whereas COPD was diagnosed according the Global Initiative for Chronic Obstructive Lung Disease Workshop Report.[1] All patients in the BA and COPD groups were studied at Kyoto University Hospital (Kyoto, Japan). Seventeen healthy controls visited the hospital for

further examination of chest X-ray abnormalities and underwent CT scanning, whereas 42 healthy controls visited Kitano Hospital (Osaka, Japan) for receiving lung health screening, including spirometry and chest CT scan. No abnormal findings on CT were observed for all healthy controls. They had no respiratory symptoms and no history of respiratory disease, and had a forced vital capacity (FVC) of ≥80% predicted and forced expiratory volume in one second (FEV_1)/FVC of ≥70% on spirometry.

All controls and asthmatic patients had a smoking history of ≤5 pack-years and did not smoke for ≥1 year prior to the CT examination. Eight patients in the COPD group were current smokers.

This study was approved by the ethics committees of all the institutions, and written informed consent was obtained from all subjects.

MDCT image acquisition

MDCT scans (Aquilion 64; Toshiba, Tokyo, Japan) were acquired at 0.5-mm collimation, with a scan time of 500 milliseconds, 120 kilovolts peak (kVp), and auto-exposure control. The images were reconstructed with lung algorithm FC56. Both lungs were scanned from top to bottom with the subjects holding their breath at deep inspiration in the supine position. No contrast media were used.

Airway analysis using CT Image

The measurements of cross-sectional airway dimensions were made using software described previously.[6] The WA and Ai of the right apical bronchus and right posterior basal bronchus were measured using a full-width at half-maximum method for defining airway walls. The ratio of WA to WA% was calculated as WA/(Ai + WA) ×

100; Ai was corrected by body surface area (BSA).

Next, we developed a new software by making modifications to our previous software to investigate the luminal structure of the right bronchus in the longitudinal direction by calculating the internal radii of imaginary inscribed spheres (see online Figure S1) in the airway lumen from the level of the carina to the fifth-order branches of the right posterior basal bronchus. The procedure of analysis using this software was as follows: first, a longitudinal line in the airway lumen was defined by connecting central points in the cross-sectional airway lumen from the carina to the fifth-order branch of the right posterior basal bronchus; second, a temporary radius was calculated by measuring the distance from the central longitudinal line to the airway wall in 128 directions, spanning 360 degrees. This procedure was repeated on different sections by tilting the image plane every 180/64 degrees. Thus, a total of 8192 values (128 × 64 = 8192) were obtained. The minimum value of these 8192 measurements was chosen as the first radius value. Next, we set another temporary center just near the initial temporary center and repeated the previous two steps, eventually obtaining the second radius value. This process was repeated to find the center point with a maximum radius value. The final value of the radius (*Ri*) was the maximum value of these radius values, and the temporary center point where this value was obtained was considered as the final center. This procedure was repeated from the carina to fifth-order branch of the right posterior basal bronchus by a pixel dimension (0.68 mm) (Figure 1). The values of *Ri* were expressed as a function of distance (l) from the carina. The *Ri* decreases with distance from the proximal carina to the periphery in a fluctuating manner (Figure 2). To evaluate this longitudinal fluctuation of *Ri*, standard deviation (SD_*Ri*) of gaps from the regression line was calculated from the relationship between *Ri* and l, and

coefficient of variation (CV_ *Ri*) was defined as SD_ *Ri* divided by mean values of *Ri*.

To validate our method for *Ri* measurements, an airway phantom (Kyoto Kagaku Co., Ltd., Kyoto, Japan) was scanned under the same conditions as those of the subjects. The measurements obtained by the software were compared with theoretical values. The correlation coefficient was high (r = 0.995) and slope of regression line was close to 1.0 (see online Appendix).

Spirometry

Subjects underwent spirometry using a Chestac-55V unit (Chest, Tokyo, Japan), according to ATS/ERS recommendations.[16] FVC and FEV_1 were examined, and their predicted values were calculated according to the guidelines of the Japanese Respiratory Society.[17]

Statistical analysis

All statistical analyses were performed using JMP 6.0.3 software (SAS Campus Drive, Cary, NC, USA). Differences among groups were analyzed using Tukey–Kramer honestly significant difference test. Student t-test was used to assess differences between 2 subgroups. Relationships among data obtained from CT were assessed by the Pearson product–moment correlation coefficient test. P values of <0.05 were considered significant.

RESULTS

Characteristics of subjects

Table 1 shows the characteristics of the subjects in the 3 groups. The COPD

group showed a preponderance of men and older patients, and it had lower FEV_1 and FEV_1/FVC than the other 2 groups. Among 58 COPD patients, 4 were classified as stage 1, 29 were stage 2, 23 were stage 3, and 2 were stage 4.[1] Although COPD patients were taller than BA patients, there were no significant differences in BSA among the 3 groups. The BA group showed a preponderance of women and had less FEV_1 compared with the control group.

Comparison of CT parameters among groups

With regard to airway wall thickness and luminal area at the apical and basal bronchi, the BA group had significantly lower Ai and higher WA% than the other 2 groups at both segmental bronchi; however, there were no significant differences between the COPD and control groups (Table 2).

On the other hand, measures of the longitudinal shape irregularity of the airway lumen showed that the COPD group had significantly higher SD_ *Ri*, SD_ $Ri/\sqrt{}$BSA, and CV_ *Ri* than the other 2 groups. Figure 3 shows representative images of more fluctuated internal diameter and the shape irregularity of the airway lumen in the longitudinal direction in a COPD patient in comparison with a control subject.

For further comparison of structural airway changes between the BA and COPD groups, subgroups of the BA group with percent predicted FEV_1 <80% and that of the COPD group with mild to moderate COPD with at ≥50% predicted FEV_1 were investigated (Table 3). Although there were no differences in age, height, and airflow limitation between these groups, the BA subgroup still had significantly smaller Ai and higher WA%, whereas the COPD subgroup had significantly larger SD_ *Ri*.

Effects of gender and age on CT indices in the control group

Table 4 shows that there were no significant differences in CT indices between the sexes. Moreover, SD_*Ri* and CV_*Ri* did not show significant correlation with age ($p = 0.23$ and $p = 0.61$, respectively) and height ($p = 0.25$ and. $p = 0.19$, respectively).

Relationships between CT indices and spirometry in COPD and BA group

Correlations between CT indices and spirometry in the COPD (Table 5) and BA groups (Table 6) are shown. In the COPD group, shape irregularity indices of the airway lumen revealed significant correlations with FEV_1/FVC, and CV_*Ri* significantly correlated with percent predicted FEV_1 and mean forced expiratory flow between 25% and 75% of FVC ($FEF_{25-75\%}$). In contrast, in the BA group, none of the shape irregularity indices showed significant correlation with spirometry, whereas Ai/BSA and WA% of the basal bronchus correlated with % predicted FVC, % predicted FEV_1, and $FEF_{25-75\%}$.

DISCUSSION

To the best of our knowledge, this is the first study to establish a new method, validated by a phantom study, to assess the longitudinal structural changes of the airway lumen on CT images by measuring longitudinal fluctuation of internal radius from the carina. This method could provide additional evaluation of airway remodeling in obstructive pulmonary diseases, in combination with the parameters for cross-sectional airway wall thickness and luminal area, as described previously. The BA group showed significantly larger WA% and smaller Ai at both apical and basal segmental bronchi than the COPD group and control group. On the other hand, the COPD group showed

significantly larger SD_*Ri* than the BA and control groups.

So far, the quantitative evaluation of airway remodeling using CT images has been performed by measuring airway wall thickness and luminal area using cross-sectional images of airways at specific sites, such as the right apical bronchus. Asthmatic patients have increased airway wall thickness that has been correlated with airflow limitation and airway hyperresponsiveness.[12, 13] In patients with COPD, WA% correlated with airflow limitation.[7, 9, 10] Pathologically, thickened reticular basement membrane, increased bronchial smooth muscle, especially at large airways, submucosal gland hypertrophy, and proliferation of bronchial vessels were reported in asthma; on the other hand, mucous metaplasia, increased bronchial smooth muscle, and airway wall fibrosis in small airways are features of COPD.[18, 19] Structural changes in airways on CT images are considered to reflect a combination of these pathological changes. Similar to a previous report,[14] our present study demonstrated that the BA group showed significantly larger WA% and smaller Ai, at both apical and basal segmental bronchi, than the COPD and control groups. In addition, we developed new parameters for the shape irregularity of the airway lumen, such as, SD_*Ri* and CV_*Ri*, to assess longitudinal fluctuation of the airway lumen from the trachea to the right basal bronchus. Although *Ri* is not always equal to the internal radius of the airway lumen, *Ri* can be measured even at the bifurcation of a bronchus; thus, *Ri* can be expressed as a continuous function that covers a wide range of the airway lumen in the longitudinal direction.

These parameters cannot be easily determined visually on CT images in the usual clinical setting, because they are derived from analysis of 3-dimensional reconstructed images. These are different from previous parameters for airway wall

thickening and WA% on cross-sectional images of airways. In this study, we found that the COPD group showed significantly larger SD_*Ri* than the BA and control groups. These results were still consistent with those in the subgroups of COPD and BA patients with similar level of airflow limitation. Moreover, comparing the relationship between CT indices and spirometry, the longitudinal shape irregularity of the airway lumen significantly correlated with airflow limitation in the COPD group, but not in the BA group. Thus, these results may reflect the differences in pathogenesis of airway remodeling between COPD and BA.

Figure 4 shows a bubble chart that uses a combination of 2 CT parameters for airway, i.e., the longitudinal shape irregularity of the airway lumen (SD_*Ri*) and cross-sectional airway wall thickening (WA%), among 3 groups. This chart suggests overlapping differences in airway structure among the 3 groups, probably because of disease severity and heterogeneity.

The limitations of this study are the relatively small number of subjects in the BA group, and the significant differences in sex and age among the 3 groups. However, there were no differences in SD_*Ri* between the sexes, and no correlation of SD_*Ri* with age in the control group. In addition, even in subgroup analysis, COPD patients showed significantly larger values of SD_*Ri,* and lower WA% and Ai than BA patients with a similar level of airflow limitation. Thus, SD_*Ri* may reflect disease-specific characteristics of airway remodeling. Another limitation is that new parameters in this study, SD_*Ri* and CV_*Ri*, cannot represent all changes in the longitudinal shape of the airway lumen. Further studies that define other useful CT indices will be warranted.

In conclusion, we developed new CT indices to reflect the longitudinal shape irregularity of the airway lumen to detect additional characteristics of airway structure

in COPD. The longitudinal fluctuation of airway internal radius was significantly larger in COPD patients than in BA patients and controls; wall thickening was significantly greater, and luminal area significantly smaller, in BA patients than in COPD patients and controls. The combination of cross-sectional and longitudinal airway analyses may suggest differences in the characteristics of airway remodeling between COPD and asthma.

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Contributors TO, TH and MM contributed to the study concept and design. TO, TH, MF, NT, SM, HN, HI, SS, AN, II, HM, and SM acquired the data. TO, TH, AN, HM, and SM contributed to the data interpretation. TO and TH analyzed the data and wrote the manuscript. MM supervised the study.

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Competing interests None.

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FIGURE LEGEND

Figure 1. Schema of the longitudinal central line in the airway lumen, from which different radius measurements were made from the carina (start) to the fifth-order branch of the right posterior basal bronchus (end). Right panel shows a reconstructed image to represent luminal structure, according to the longitudinal central line.

Figure 2. An example of continuous radius (*Ri*) measurements and regression line (dotted line) from the proximal carina to the distal bronchial segments.

Figure 3. Representative images of the airway lumen with (A) lower SD_*Ri* in a control subject, and (B) higher SD_*Ri* in a COPD patient. These images were reconstructed in the multiplanar plane along a central line in the right bronchial lumen from the carina to the fifth-order branch of the right posterior basal bronchus; the gray area with a white border represents the shape irregularity of the airway lumen, which was calculated from the radii of the inscribed sphere and was overlaid on the multiplanar reconstructed images. There were some black areas in the airway lumen at sites other than the bifurcation. This is because as the large cross-sectional area of the airway lumen (black) comes farther away from the circle, the more it deviates away from the cross section of the inscribed sphere (gray area with white border).

Figure 4. Comparison of longitudinal luminal structure (SD_*Ri*), and cross-sectional airway wall thickening (WA%, apical) among 3 groups. The center of each ellipse corresponds to the mean value, whereas the radius represents SD.

Table 1 Characteristics of subjects

Group	BA	COPD	control
N	29	58	59
Sex (M/F)	6 /23	54 / 4	23 / 36
Age (years)	66 (31-83)	73 (56–83) † ‡	66 (45–77)
Height (cm)	155.5 (9.0)	161.9 (7.0) ‡	158.5 (9.8)
BSA (m^2)	1.54 (0.19)	1.58 (0.14)	1.57 (0.18)
Smoking history (pack-years)	0 (0-3)	57 (21–168) † ‡	0 (0–5)
FVC (% predicted)	86.1 (22.4)	95.4 (16.8)	99.1 (13.5)
FEV_1 (L)	1.54 (0.66) †	1.39 (0.50) † ‡	2.30 (0.63)
FEV_1 (% predicted)	76.5 (20.7) †	53.2 (16.8) † ‡	100.5 (16.1)
FEV_1/FVC (%)	68.2 (10.8) †	44.2 (11.8) † ‡	78.4 (5.0)
Use of inhaled corticosteroids (%)	89.7	28.8	0
Use of long-acting beta agonists (%)	48.3	23.7	0
Use of long-acting muscarinic antagonist (%)	0	30.5	0
Use of oral corticosteroids (%)	6.9	6.6	0

In lines of age and smoking history, each value is shown as median (range).
In other lines, each value is shown as mean (standard deviation).
† significantly different from the control group
‡ significantly different from the BA group
BSA, body surface area; FVC, forced vital capacity; FEV_1, forced expiratory volume in one second.

Table 2 Comparisons of CT parameters between 3 groups

Group	BA	COPD	control
Ai/BSA (apical)	9.4 (3.4) † §	13.3 (5.5)	12.0 (3.9)
WA% (apical) (%)	65.6 (6.2) † §	61.1 (5.9)	58.0 (6.0)
Ai/BSA (basal)	10.7 (4.3) §	13.3 (4.2)	12.7 (3.7)
WA% (basal) (%)	62.1 (7.5) † §	58.9 (5.7)	56.7 (5.5)
Mean *Ri* (mm)	2.94 (0.64) † §	3.38 (0.46)	3.25 (0.46)
SD_*Ri* (mm)	0.16 (0.057)	0.22 (0.044) † ‡	0.17 (0.046)
SD_*Ri*/√BSA	0.13 (0.046)	0.17 (0.035) † ‡	0.14 (0.037)
CV_*Ri*	0.057 (0.021)	0.065 (0.017) †	0.054 (0.015)

Each value is shown as mean (standard deviation).
† significantly different from the control group
‡ significantly different from the BA group
§ significantly different from the COPD group
BSA, body surface area; Ai, luminal area; WA%, percentage ratio of wall area to total airway wall area; *Ri*, radius of inscribed sphere in the airway lumen (see text); SD_*Ri* and CV_*Ri*, parameters for shape irregularity of the airway lumen (see text).

Table 3 Comparisons of characteristics and CT indices between the BA group with airway obstruction (FEV_1 % predicted< 80) and mild and moderate COPD group (FEV_1 % predicted ≥50).

Group	BA	COPD
N	13	29
Age (years)	68 (43–83)	72 (58–83)
Height (cm)	158.7 (11.0)	160.6 (7.3)
BSA (m^2)	1.59 (0.20)	1.58 (0.11)
FEV_1 (% predicted)	75.8 (22.7)	65.2 (13.8)
FEV_1/FVC (%)	68.1 (13.0)	52.3 (8.9)
Ai/BSA (apical)	8.7 (3.6) §	13.6 (4.6)
WA% (apical) (%)	66.6 (4.6) §	60.5 (5.1)
Ai/BSA (basal)	10.0 (4.9) §	14.1 (3.6)
WA% (basal) (%)	62.8 (7.1) §	57.9 (5.1)
Mean *Ri* (mm)	3.14 (0.14) §	3.35 (0.09)
SD_ *Ri* (mm)	0.16 (0.054) §	0.20 (0.042)
SD_ *Ri* /√BSA	0.13 (0.043) §	0.16 (0.035)
CV_*Ri*	0.053 (0.018)	0.058 (0.015)

In line of age, each value is shown as median (range).
In other lines, each value is shown as mean (standard deviation).
§ significantly different from the COPD group
BSA, body surface area; FVC, forced vital capacity; FEV_1, forced expiratory volume in one second; Ai, luminal area; WA%, percentage ratio of wall area to total airway wall area; *Ri*, radius of inscribed sphere in the airway lumen (see text); SD_*Ri* and CV_*Ri*, parameters for shape irregularity of the airway lumen (see text).

Table 4 Comparisons of CT indices between male and female subjects in control group

	male	female
N	23	36
Age (years)	64 (47–77)	67 (50–77)
Height (cm)	167.2 (6.7)	152.4 (6.6)
BSA (m^2)	1.74 (0.14)	1.46 (0.10)
Ai/BSA (apical)	12.5 (4.1)	11.6 (3.8)
WA% (apical) (%)	57.0 (5.8)	58.8 (6.2)
Ai/BSA (basal)	12.5 (2.9)	12.7 (4.3)
WA% (basal) (%)	55.7 (3.9)	57.2 (6.2)
SD_*Ri* (mm)	0.18 (0.0043)	0.17 (0.047)
SD_*Ri*/√BSA	0.14 (0.034)	0.14 (0.040)
CV_*Ri*	0.052 (0.013)	0.055 (0.016)

In line of age, each value is shown as median (range).
In other lines, each value is shown as mean (standard deviation).
No parameter showed significant difference.
BSA, body surface area; Ai, luminal area; WA%, percentage ratio of wall area to total airway wall area; SD_*Ri* and CV_*Ri*, parameters for shape irregularity of the airway lumen (see text).

Table 5 Correlation between CT indices and spirometry in the COPD group

	FVC (% predicted)	FEV_1 (% predicted)	FEV_1/FVC	$FEF_{25-75\%}$
Ai/BSA (apical)	-	-	-	-
WA% (apical) (%)	-0.32†	-0.32†	-	-
Ai/BSA (basal)	-	0.26†	-	-
WA% (basal) (%)	-	-	-	-
Mean *Ri* (mm)	0.28†	0.39‡	0.29†	0.36‡
SD_*Ri* (mm)	-	-	-0.35‡	-
SD_*Ri*/√BSA	-	-	-0.34‡	-
CV_*Ri*	-	-0.40‡	-0.42‡	-0.29†

- not significant, †:$p< 0.05$, ‡:$p<0.01$

FVC, forced vital capacity; FEV_1, forced expiratory volume in one second; $FEF_{25-75\%}$, mean forced expiratory flow between 25% and 75% of FVC; BSA, body surface area; Ai, luminal area; WA%, percentage ratio of wall area to total airway wall area; *Ri*, radius of inscribed sphere in the airway lumen (see text); SD_*Ri* and CV_*Ri*, parameters for shape irregularity of the airway lumen (see text).

Table 6 Correlation between CT indices and spirometry in the BA group

	FVC (% predicted)	FEV_1 (% predicted)	FEV_1/FVC	$FEF_{25-75\%}$
Ai/BSA (apical)	-	-	-	-
WA% (apical) (%)	-	-	-	-
Ai/BSA (basal)	0.51‡	0.55‡	-	0.49‡
WA% (basal) (%)	-0.50‡	-0.57‡	-	-0.46†
Mean *Ri* (mm)	-	-	-	-
SD_*Ri* (mm)	-	-	-	-
SD_*Ri*/√BSA	-	-	-	-
CV_*Ri*	-	-	-	-

- not significant, ‡:$p<0.01$

FVC, forced vital capacity; FEV_1, forced expiratory volume in one second; $FEF_{25-75\%}$, mean forced expiratory flow between 25% and 75% of FVC; BSA, body surface area; Ai, luminal area; WA%, percentage ratio of wall area to total airway wall area; *Ri*, radius of inscribed sphere in the airway lumen (see text); SD_*Ri* and CV_*Ri*, parameters for shape irregularity of the airway lumen (see text).

Figure 1

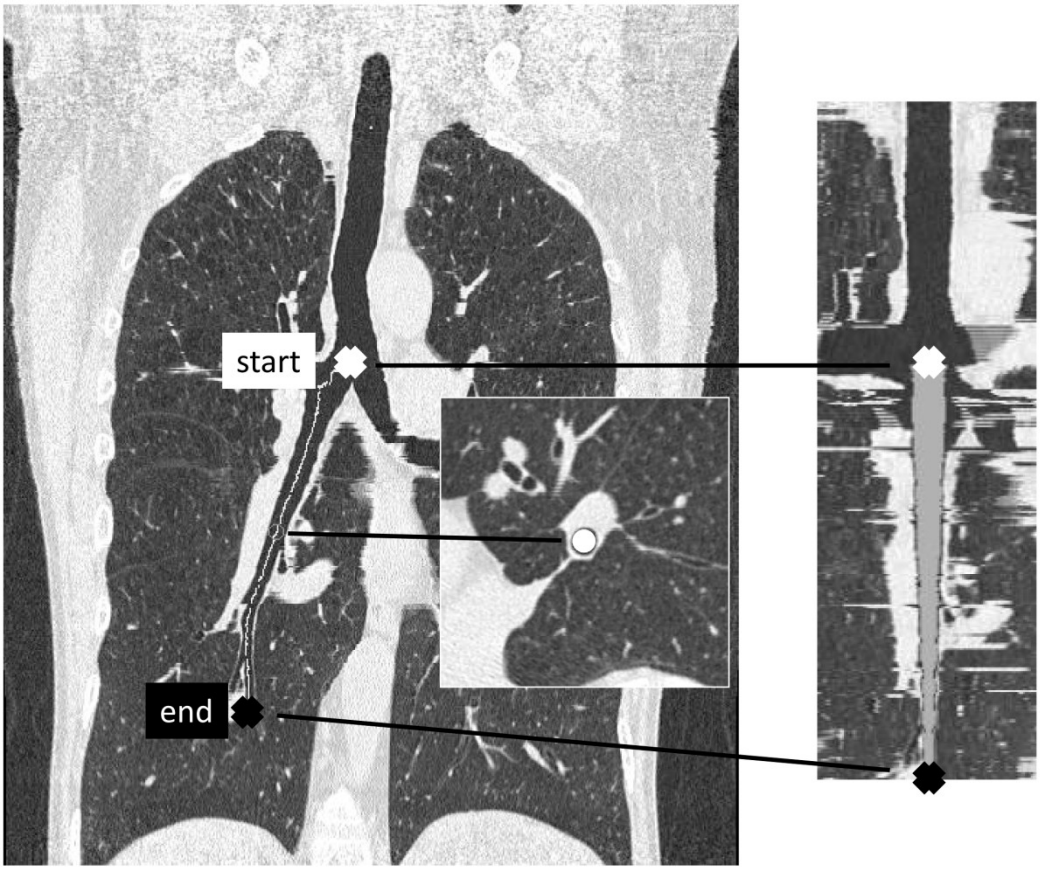


Figure 2

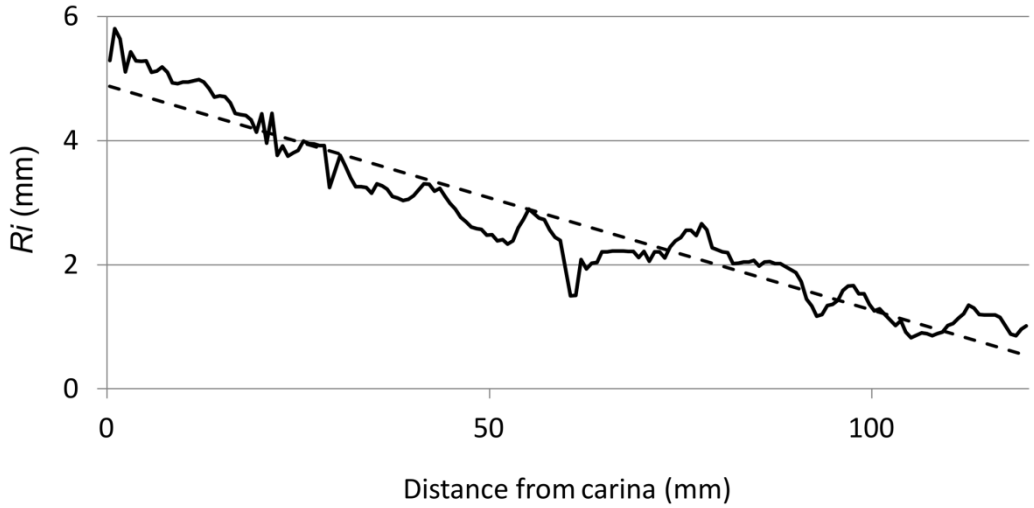


Figure 3

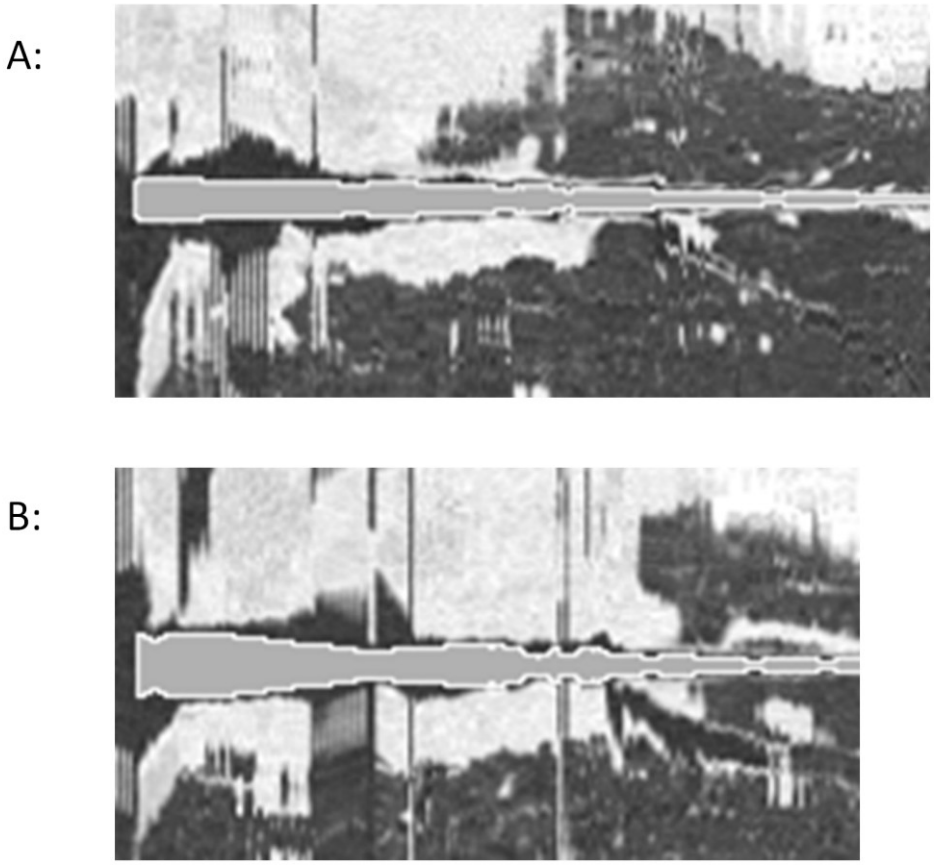
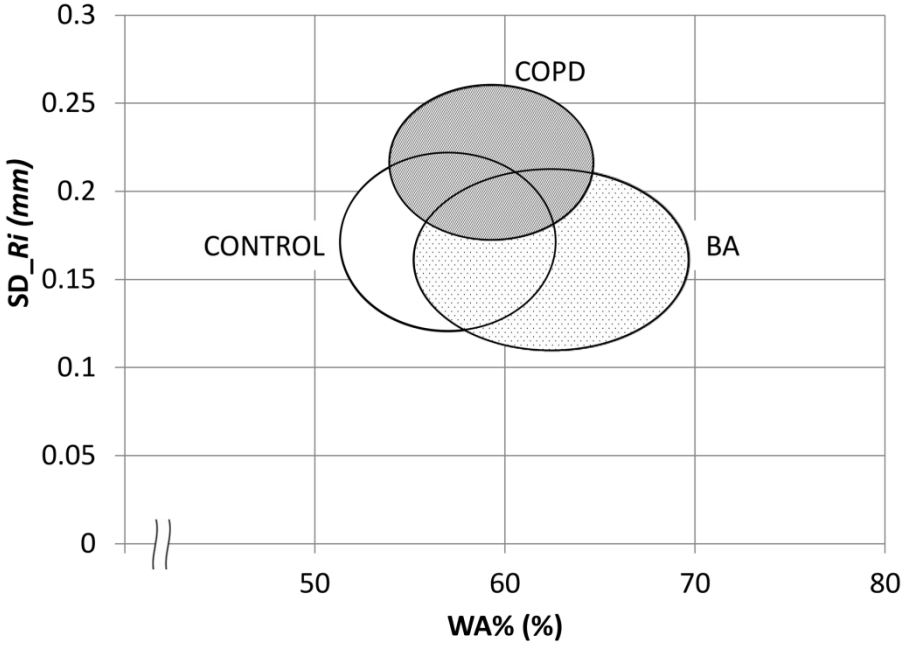


Figure 4



ONLINE APPENDIX

Validation of airway analysis using a phantom

The validity of our method for measurement of longitudinal structure of the airway lumen was examined using an airway phantom (Kyoto Kagaku Co., Ltd., Kyoto, Japan) (Fig. S1). The phantom consisted of eight acryl tubes with varying diameters (Fig. S1A). This phantom was scanned with the same conditions as those for the subjects (Fig. S1B). The measurements using our software were compared with theoretical values. Figure S2 shows the correlation between measured values and theoretical values from the phantoms. The correlation coefficient was high ($r = 0.995$) and the slope of regression line was close to 1.0 (Fig. S2).

FIGURE LEGEND

Figure S1.

A: Schema of airway phantom, in longitudinal section, for validation study. This phantom consists of 8 tubes, and each tube has dents (Y) on the internal surface of the baseline radius (X), simulating a varying internal diameter along the longitudinal direction. There were some variations in the X and Y values among the tubes, as shown in the table.

B: An axial slice CT image of airway phantom (left panel), and a reconstructed sagittal section of the phantom CT image showing the lumen of tube no. 2 (right panel).

Figure S2. Relationship between theoretical radius measurements (horizontal axis) and

measured radius measurements (vertical axis) in the phantom study. ($y = 0.990x + 0.219$; $r = 0.995$)

Figure S1

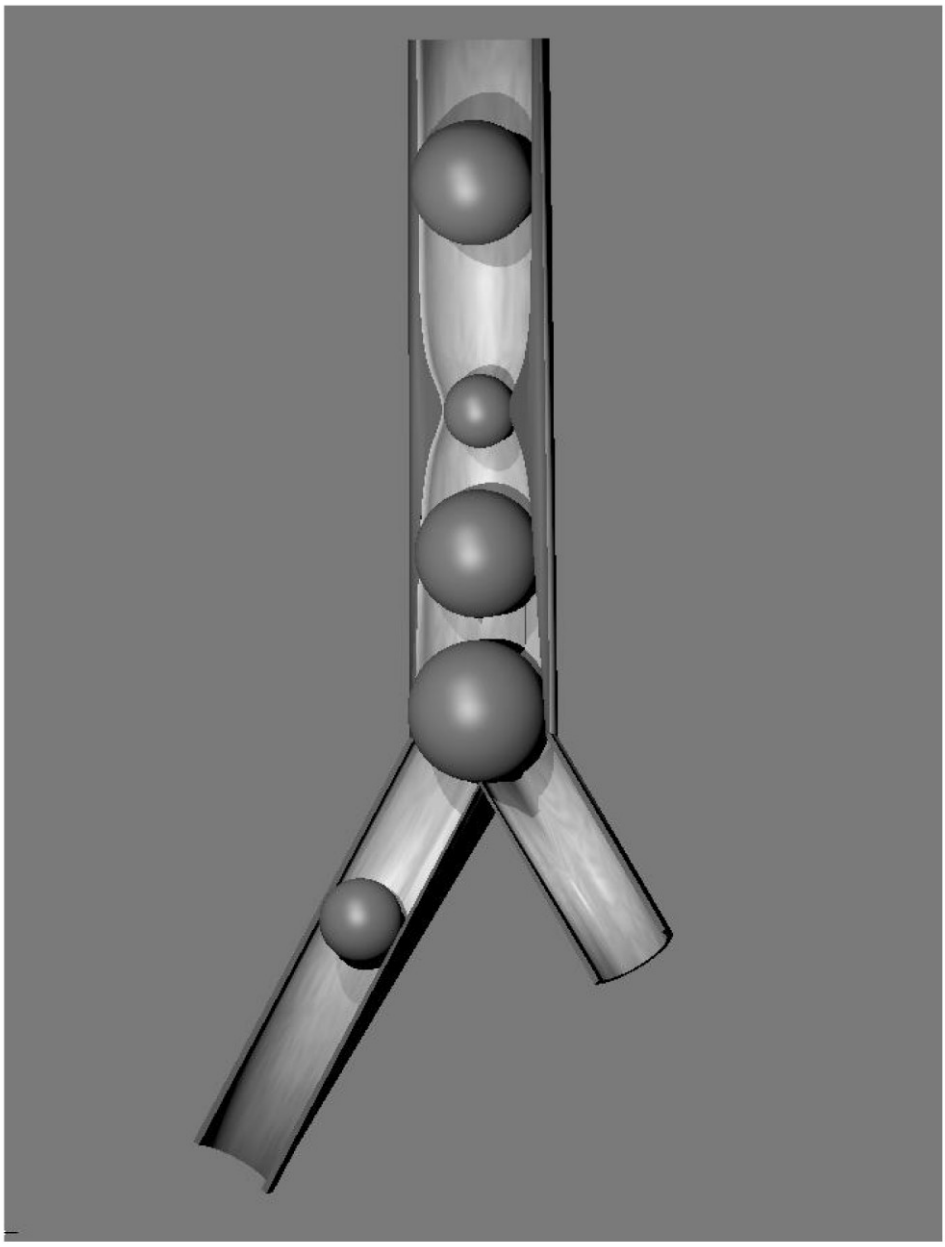
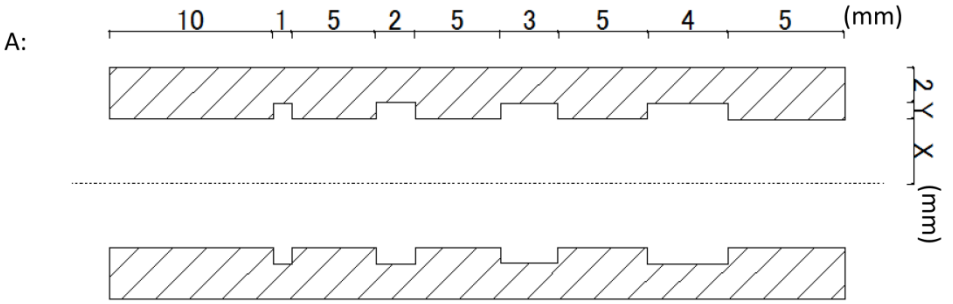


Figure S2



Tube No.	1	2	3	4	5	6	7	8
X (mm)	4	4	3	3	2	2	1.5	1
Y (mm)	0.5	1	0.5	1	0.5	1	0.5	0.5

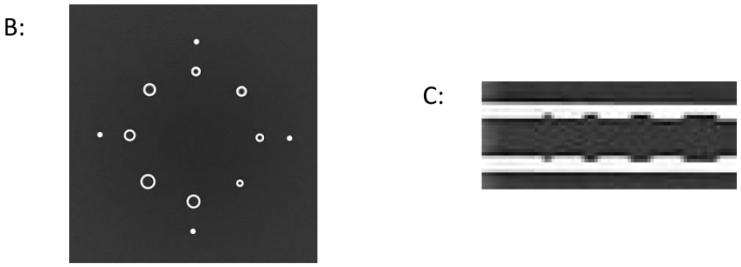


Figure S3