Three-dimensional airway lumen volumetry: comparison with bronchial wall area and parenchymal densitometry in assessment of airway obstruction in pulmonary emphysema

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Objectives: The purpose of this study was to compare three-dimensional airway lumen volumetry with bronchial wall area and parenchymal densitometry in the assessment of airway obstruction in pulmonary emphysema.

Methods: 56 patients, who were smokers, underwent CT examination and pulmonary function tests (PFTs). For quantitative assessments, the following parameters were computationally calculated: (1) percentage of voxels –950, –960 and –970 HU in the lung (%LAA_{–950}, %LAA_{–960} and %LAA_{–970}, respectively); (2) percentage of partial bronchi luminal volumes per total luminal volumes (LV_{main}, main and distal bronchial volume/total luminal volume; LV_{lobe}, lobar and distal bronchial volume/total luminal volume); and (3) mean wall area percentages of segmental bronchi of the right apical and left apicoposterior segment (WA%_{seg}) and of subsegmental bronchi (WA%_{sub}) in the upper lobes. These parameters were correlated with PFTs and statistically compared between a chronic obstructive pulmonary disease (COPD) group [forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC)<70] and a non-COPD group.

Results: FEV1, maximum mid-expiratory flow rate and forced expiratory flow at 25% vital capacity had significant correlation with LV_{main} ($r>0.53$, $p<0.0001$), LV_{lobe} ($r>0.52$, $p<0.0001$), WA%_{seg} ($|r|>0.29$, $p<0.05$) and WA%_{sub} ($|r|>0.31$, $p<0.05$). FEV1/FVC had significant correlation with all parameters ($0.27<|r|<0.52$, $p<0.05$). LV_{main} and LV_{lobe} and WA%_{seg} and WA%_{sub} were significantly different between the two groups (LV_{main} and LV_{lobe}: $p<0.0001$, WA%_{seg} and WA%_{sub}: $p<0.05$).

Conclusions: Bronchial luminal volumetric assessment better reflected the airflow limitation parameters.

Advances in knowledge: Bronchial luminal volumetric assessment can potentially be used to gauge airflow limitation in pulmonary emphysema.

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Worldwide, chronic obstructive pulmonary disease (COPD) is currently the fourth leading cause of mortality and the twelfth leading cause of disability, and by 2020 it is expected to be the third leading cause of death and the fifth leading cause of disability [1]. COPD is a slowly progressive disease characterised by airflow limitation, cough, sputum production and, at the later stages, dyspnoea. It is assessed using whole-lung pulmonary function tests (PFTs) and is characterised by increased airway obstruction and diffusional abnormalities detected in routine clinical practice. Recently, assessments of the extent and severity of pulmonary emphysema based on

morphological findings in CT have become a popular method [2, 3]. There are two main CT-based methods of assessing morphological change caused by COPD. One assesses destruction of lung parenchyma; the other assesses bronchial wall thickening and decreasing of the bronchial lumen.

Destruction of lung parenchyma corresponds to the low attenuation areas (LAAs) detected through CT imagery. CT has been used to quantify emphysema by detecting LAAs and to assess disease severity quantitatively and qualitatively [4, 5]. However, airflow limitation in COPD is a complicated phenomenon related only in part to emphysematous lung destruction; therefore, the extent of emphysema does not always correlate with the severity of airflow limitation [6, 7]. On the other hand, regarding bronchial wall thickening and decreasing of the bronchial lumen, many investigators qualitatively and quantitatively evaluated the relationship between the CT findings and increased airflow limitation [8–10]. In CT-based quantitative analyses of these

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findings, the standard parameters are the area of the bronchial wall as a percentage and the ratio of the total bronchial cross-sectional area to the airway's inner luminal area. In recent studies, airway dimensions have been obtained using volumetric CT, which allows for measurement in a plane orthogonal to the long axis of the airways [9, 10]. However, evaluations of lung destruction are limited when two-dimensional (2D) measurements are made to only one or a few parts of the bronchi. This occurs because PFTs reflect the function of the whole [10]. Airflow obstruction can also be in different lobes or in different orders of bronchi, depending on the type and distribution of emphysema [10]. In addition, in patients with COPD, potential heterogeneity in the distribution of pathological bronchi has not yet been clarified [10].

Current CT techniques with three-dimensional (3D) post-processing allow quantitative volumetry of various anatomical subsets, in addition to providing volumetric measurements. Quantitative volumetry could potentially add information different from that produced by conventional 2D measurement analysis. A recent report on volumetric analysis using a 3D technique to assess pulmonary hypertension showed a high correlation between pulmonary artery volumes and mean pulmonary artery pressures in patients with and without pulmonary hypertension [11]. In addition, quantitative volumetric assessment of the bronchial lumen in emphysema patients was shown to be potentially useful for clinical evaluations of disease severity [12]. However, to the best of our knowledge, no major studies have yet been reported comparing volumetric assessment of the bronchial lumen with 2D bronchial measurement analysis and LAAs for assessing the relationship between pulmonary function loss and quantitative CT parameters. We hypothesised that 3D airway lumen volumetry reflects airflow limitation in comparison with bronchial wall area and parenchymal densitometry in the assessment of airway obstruction. The purpose of this study was therefore to compare bronchial luminal volumetric assessment with other quantitative CT parameters to assess airflow limitation in pulmonary emphysema.

Methods and materials

Subjects

The institutional review board of Kobe University Hospital, Kobe, Japan, approved this study, and informed

consent was obtained from every subject prior to his or her enrolment.

Between November 2009 and December 2010, a total of 129 consecutive patients (88 males, 41 females; mean age 65.5 years) who were suspected of having COPD underwent non-contrast CT with a 320-detector row CT scanner. Then, patients were selected according to the criterion that they had undergone both chest CT imaging and PFTs at approximately the same time. Of these 129 patients, 56 (40 men and 16 women; mean age 65.5 years; age range 32–85 years) met the criterion and were enrolled in the study. All patients were smokers and lifetime smoking exposure was quantified using pack years (range 10–90 pack years; mean 38.8 pack years). These patients were classified into two groups: a COPD group [forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) < 70, $n=29$] and a non-COPD group (FEV1/FVC > 70, $n=27$). The characteristics of the subjects are shown in Table 1.

Pulmonary function tests

PFTs were performed while the patients were at rest in a seated position. These tests consisted of spirometry and body plethysmography (System 21 device, Minato Ikagaku, Osaka, Japan). FVC, FEV1, FEV1/FVC, maximum mid-expiratory flow rate (MMF) and forced expiratory flow at 25% vital capacity (V25) were obtained following the American Thoracic Society standards [13–15]. FEV1, MMF and V25 were expressed as percentages of predicted values. The median of intervals between the thin-section multidetector CT and the PFT was 7 days.

CT scan protocols

The patients were scanned with a 320-detector row CT scanner (Aquilion ONE™; Toshiba Medical Systems, Ohtawara, Japan). Non-contrast CT images of the entire lung were obtained from the lung apex to the diaphragm during suspended respiration at the end of inhalation. All CT examinations were performed with volumetric scanning by wide volume scanning without helical scanning. The 320-row-wide volume scan is characterised by a long scan field (16 cm in length) using a single gantry rotation (step-and-shoot scanning), which makes it possible to obtain volumetric scan data for the entire lung with a few rotations during a single breath-hold. The scan parameters were as follow: (256–320) × 0.5 mm collimation, 120 kVp, 270 mA, a 0.5 s

Table 1. Characteristics of the subjects

Characteristics	Non-COPD group ($n=27$)	COPD group ($n=29$)
Male/female	16/11	24/5
Age (years)	60.4 ± 13.0 (32–82)	70.2 ± 8.0 (51–85)
FEV1 (% predicted)	101.9 ± 20.4 (68.7–131.8)	68.9 ± 19.6 (29.1–109.3)
FEV1/FVC (%)	79.5 ± 5.5 (79.4–89.1)	58.2 ± 8.8 (33.4–67.8)
MMF (% predicted)	81.6 ± 26.7 (81.6–26.7)	26.8 ± 10.8 (6.6–49.8)
V25 (% predicted)	60.8 ± 30.3 (60.8–30.3)	23.0 ± 12.3 (7.3–70.9)

COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; MMF, maximum mid-expiratory flow rate; V25, forced expiratory flow at 25% vital capacity.

Data are number or mean ± standard deviation (range).

gantry rotation time, a 512×512 matrix and a 300–350 mm field of view with 3–4 time scans.

The CT raw data were reconstructed to 1.0 mm section thicknesses using a standard kernel (*i.e.* FC13).

Image analysis

For our quantitative CT assessments, we transferred all images via a picture archiving and communication system to a personal computer (Windows® XP Professional; Microsoft, Redmond, WA) and analysed them using proprietary software developed for MATLAB (MathWorks® Inc., Natick, MA) with the density-masked CT technique [12, 16]. The software combined different techniques for semiautomatic segmentation, such as the region-growing and threshold-based methods, and a 3D airway tree was automatically reconstructed with a given threshold level expressed in Hounsfield units (HU). The threshold level was determined on an individual basis (–950 to –990 HU) to obtain airway images at the level of the subsegmental bronchus that was maximally distal.

Each extraction of the all-segmental and subsegmental bronchi by this software was judged using a two-point scale (Score 0: impossible extraction; Score 1: possible extraction) by a chest radiologist (HK) without access to any patient information, and the sites were recorded. On the level of subsegmental bronchi, Score 1 was defined when it was possible to extract at least one bronchus.

To acquire the percentage of low attenuation area (%LAA) of the whole lung, the 3D airway tree for each lung was automatically excluded from the total 3D lung, and %LAA was then automatically calculated from the

total lung volume. The lower threshold CT values varied from –950 HU (%LAA_{–950}) to –960 HU (%LAA_{–960}) to –970 HU (%LAA_{–970}). For this image segmentation, no user interventions were required. A representative case is shown in Figure 1.

To acquire the bronchial luminal volume, the assessment was performed according to published procedure [12]. A 3D map of the lumen of the major airways was computationally derived. The trachea and lobar bronchi were manually segmented from more peripheral airways by a chest radiologist (HK), without access to any patient information. Based on this, the following ratios were obtained: LV_{main} (main and distal bronchial volume/total luminal volume) and LV_{lobe} (lobar and distal bronchial volume/total luminal volume). A representative case is shown in Figure 2.

To acquire 2D quantitative data of the bronchus, the nearest point between the voxel of the surface of the airway and the voxel of the lung region—the threshold located by the peak of the histogram in the lung—was searched for computationally using the same software. The voxel of the lung region was searched for computationally over the whole lung region, which meant that the nearest point between the voxel of the surface of the airway and the voxel of the lung region was not necessarily in the same slice. The thickness of the airway wall (T) was defined as the average value of the full width at half the maximum of the profile curves at the two points. When it was thicker than 2.5 mm, it was defined as an error, and the voxel of the surface of the airway was excluded from the calculations. In this study, we selected two bronchi: one was the apical bronchus of the right upper lobe (RB1) and the other was the left apicoposterior bronchus (LB1+2). We selected those bronchi because they

(a)

(b)

Figure 1. Quantification of lung parenchymal densitometry (63-year-old female with pulmonary emphysema). (a) Coronal CT image shows low-attenuation area in both lungs and bronchial wall thickening. (b) Quantitative coronal CT images adopted –950 HU as the threshold CT value (%LAA_{–950}). Quantitative CT scan shows the destruction of lung parenchyma (red) due to emphysema. %LAA_{–950} is 28.5%.

Figure 2. Quantification of bronchial luminal volume (63-year-old female with pulmonary emphysema). (a) A reconstructed image shows the lumen of the bronchial tree, including intrathoracic trachea and bronchi, extracted from CT images. The voxels of this image corresponded to total luminal voxels, including the luminal voxels of the trachea and all bronchi. (b) A reconstructed image shows the lumen from the main bronchi to the distal bronchi extracted from the bronchial tree (a). The voxels of this image corresponded to the voxels of the main and distal bronchi. The ratio of the main and distal bronchi to total luminal voxels (LV_{main}) in this case was 56.6%. (c) A reconstructed image showing the lumen from lobar bronchi to the distal bronchi extracted from the bronchial tree (a). The voxels of this image corresponded to the voxels of the lobar and distal bronchi. The ratio of the lobar and distal bronchi to the total luminal voxels (LV_{lobe}) in this case was 32.6%.

are relatively free from transmitted cardiac motion artefacts and are relatively perpendicular in orientation to the scanning plane. At the level of subsegmental bronchi, we selected only one bronchus for evaluation.

The luminal area (A_i) and T of the RB1 segmental bronchus, the RB1 subsegmental bronchus, the LB1+2 segmental bronchus and the LB1+2 sub-segmental bronchus were computationally acquired from each one slice. The slices were chosen by the same chest radiologist (HK) without access to any patient information. After acquiring A_i and T , the total diameter (D) of the bronchus was calculated as $D = 2 \times \sqrt{(A_i/\pi) + 2T}$. We calculated the outer area of the bronchus (A_o) from D : $A_o = \pi (D/2)^2$. The airway wall area (WA) was calculated as $A_o - A_i$. We used, as 2D quantitative data from the bronchus, the percentage wall area [$WA\% = (WA/A_o) \times 100$]. By these methods, the mean $WA\%$ between the segmental bronchi of RB1 and LB1+2 ($WA\%_{seg}$) and the mean $WA\%$ between the subsegmental bronchi of RB1 and

LB1+2 ($WA\%_{sub}$) were acquired. A representative case is shown in Figure 3.

Statistical analysis

First, to determine the software's success at extracting the segmental and subsegmental bronchi, its ability to extract segmental and subsegmental bronchi were compared between the COPD group ($FEV1/FVC < 70$) and the non-COPD group, using a χ^2 test.

Second, to determine the ability of these quantitative CT parameters—that is $\%LAA$, LV and $WA\%$ —to predict airflow limitation, the parameters were correlated with the PFTs.

Finally, to determine their ability to predict a diagnosis of COPD, the parameters were statistically compared between the COPD group ($FEV1/FVC < 70$) and the non-COPD group using the Mann-Whitney U -test.

Figure 3. Quantification of bronchial wall area (63-year-old female with pulmonary emphysema). (a) CT images of lung and the bronchi, the image extracted lumen of the bronchi (red) and the thickness of the airway wall at the segmental bronchus of the apical bronchus (RB1) of the right upper lobe (left to right). The wall area's mean percent ($WA\%_{seg}$) was 58.0%. (b) CT images of lung and the bronchi, the image extracted lumen of the bronchi (red), and the RB1 of the right upper lobe (left to right). $WA\%_{sub}$ was 60.6%.

A p -value <0.05 was considered significant for all statistical analyses. All statistical analyses were performed with statistical software based on Excel 2003 (Microsoft Corporation, Redmond, WA) (StatMate III; ATOMS, Oita, Japan).

Results

The results for this software's success rate at extracting segmental and subsegmental bronchi are shown in Table 2. The overall success rates for segmental bronchi and subsegmental bronchi were 92.9% (936/1008) and 74.8% (754/1008), respectively. In the non-COPD group, the success rates for segmental and subsegmental bronchi were 93.4% (454/486) and 79.0% (384/486), respectively. On the other hand, in the COPD group, the success rates for segmental and subsegmental bronchi were 92.3% (482/522) and 70.9% (370/522), respectively. As to the assessment of segmental bronchi, there was no significant difference between the two groups ($p=0.51$). However, the assessment for subsegmental bronchi showed that the success rates for the COPD group were significantly lower than those for the non-COPD group ($p=0.003$). By comparison, the success rates for the B1 and LB1+2 segmental and subsegmental bronchi were both 100%.

The results of the correlations between the PFTs and the quantitative CT parameters are shown in Table 3. FEV1 had significant correlations with LV_{main} ($r=0.53$,

$p<0.001$), LV_{lobe} ($r=0.61$, $p<0.001$), $WA\%_{seg}$ ($r=-0.30$, $p<0.05$) and $WA\%_{sub}$ ($r=-0.31$, $p<0.05$). FEV1/FVC had significant correlations with all parameters ($0.27<|r|<0.52$, $p<0.05$). MMF had significant correlations with LV_{main} ($r=0.62$, $p<0.001$), LV_{lobe} ($r=0.65$, $p<0.001$), $WA\%_{seg}$ ($r=-0.34$, $p<0.05$) and $WA\%_{sub}$ ($r=-0.36$, $p<0.01$). V25 had significant correlations with LV_{main} ($r=0.53$, $p<0.001$), LV_{lobe} ($r=0.52$, $p<0.001$), $WA\%_{seg}$ ($r=-0.30$, $p<0.05$) and $WA\%_{sub}$ ($r=-0.33$, $p<0.01$). LV_{lobe} had the strongest correlations with FEV1, FEV1/FVC and MMF amongst the CT parameters, and LV_{main} had the strongest correlation with V25 out of the CT parameters.

The results from using the quantitative parameters to predict diagnoses of COPD are shown in Table 4. LV_{main} and LV_{lobe} and $WA\%_{seg}$ and $WA\%_{sub}$ were significantly different between the non-COPD group and COPD group (LV_{main} and LV_{lobe} , $p<0.0001$; $WA\%_{seg}$ and $WA\%_{sub}$, $p<0.05$). However, $\%LAA_{-950}$, $\%LAA_{-960}$ and $\%LAA_{-970}$ were not significantly different between the two groups ($p>0.05$).

Discussion

Our study demonstrated that all the quantitative CT parameters had significant correlations with FEV1/FVC, and that the volumetric assessment of the bronchial lumen and of the airway wall area significantly correlated with FEV1, MMF and V25. Meanwhile,

Table 2. Success rate of extraction of segmental and subsegmental bronchi

	<i>n</i>	Segmental bronchi	Subsegmental bronchi
Overall	56	92.9% (936/1008)	74.8% (754/1008)
Non-COPD group	27	93.4% (454/486)	79.0% (384/486)
COPD group	29	92.3% (482/522)	70.9% ^a (370/522)

^aSignificant difference with non-COPD group by χ^2 test ($p<0.005$).

Table 3. Correlation between pulmonary function tests and quantitative CT parameters

Quantitative CT parameters	Mean $\pm$ SD (range)	FEV1		FEV1/FVC		MMF		V25	
		<i>r</i> -value	<i>p</i> -value	<i>r</i> -value	<i>p</i> -value	<i>r</i> -value	<i>p</i> -value	<i>r</i> -value	<i>p</i> -value
$\%LAA_{-950}$	18.1 ± 13.2 (0.3–47.2)	–0.11	NS (0.39)	–0.27	0.04	–0.1	NS (0.49)	0.02	NS (0.86)
$\%LAA_{-960}$	12.6 ± 10.8 (0.1–41.5)	–0.17	NS (0.21)	–0.34	0.01	–0.15	NS (0.28)	–0.02	NS (0.90)
$\%LAA_{-970}$	8.4 ± 8.5 (6.7–35.7)	–0.24	NS (0.08)	–0.41	<0.005	–0.21	NS (0.13)	–0.07	NS (0.61)
LV_{main} (%)	53.3 ± 8.1 (37.2–70.8)	0.53	<0.0001	0.52	<0.0001	0.62	<0.0001	0.53	<0.0001
LV_{lobe} (%)	29.3 ± 8.7 (14.1–54.1)	0.61	<0.0001	0.51	<0.0001	0.65	<0.0001	0.52	<0.0001
$WA\%_{seg}$	53.0 ± 8.6 (24.9–69.2)	–0.30	0.03	–0.33	0.01	–0.34	0.01	–0.29	0.03
$WA\%_{sub}$	52.0 ± 10.5 (23.7–73.0)	–0.31	0.02	–0.35	0.008	–0.36	0.007	–0.33	0.01

FEV1, forced expiratory volume in 1s; FVC, forced vital capacity; $\%LAA_{-950}$, percentage of voxels –950 HU; $\%LAA_{-960}$, percentage of voxels –960 HU; $\%LAA_{-970}$, percentage of voxels –970 HU; LV_{lobe} , lobar and distal bronchial volume/total luminal volume; LV_{main} , main and distal bronchial volume/total luminal volume; MMF, maximum mid-expiratory flow rate; NS, not significant; SD, standard deviation; V25, forced expiratory flow at 25% vital capacity; $WA\%_{seg}$, mean wall area percentages of segmental bronchi of the right apical and left apicoposterior segment in the upper lobes; $WA\%_{sub}$, mean wall area percentages of subsegmental bronchi of the right apical and left apicoposterior segment in the upper lobes.

Table 4. Capabilities for predicting diagnosis of emphysema using quantitative parameters

Quantitative CT parameters	Non-COPD group (n=27)	COPD group (n=29)	p-value
%LAA ₋₉₅₀	16.2 ± 11.6	19.9 ± 14.5	NS (0.38)
%LAA ₋₉₆₀	10.3 ± 8.7	14.8 ± 12.2	NS (0.21)
%LAA ₋₉₇₀	6.1 ± 5.9	10.6 ± 10.0	NS (0.10)
LV _{main} (%)	57.6 ± 7.7	49.3 ^a ± 6.2	<0.0001
LV _{lobe} (%)	33.7 ± 9.2	25.3 ^a ± 5.9	<0.0001
WA% _{seg}	50.6 ± 7.5	55.3 ^a ± 9.0	0.01
WA% _{sub}	49.8 ± 9.2	54.0 ^a ± 11.4	0.045

COPD, chronic obstructive pulmonary disease; %LAA₋₉₅₀, percentage of voxels -950 HU; %LAA₋₉₆₀, percentage of voxels -960 HU; %LAA₋₉₇₀, percentage of voxels -970 HU; LV_{lobe}, lobar and distal bronchial volume/total luminal volume; LV_{main}, main and distal bronchial volume/total luminal volume; NS, not significant; WA%_{seg}, mean wall area percentages of segmental bronchi of the right apical and left apicoposterior segment in the upper lobes; WA%_{sub}, mean wall area percentages of subsegmental bronchi of the right apical and left apicoposterior segment in the upper lobes.

Data are mean ± standard deviation unless otherwise indicated.

^aSignificant difference with non-COPD group using the Mann-Whitney U-test.

volumetric assessments of the bronchial lumen correlated better with PFTs than volumetric assessments of the airway wall area. These findings suggest that the luminal volumetric assessment better indicated the airflow limitation. In addition, in the comparison between the COPD group (FEV1/FVC < 70) and the non-COPD group, the luminal volumetric assessment corresponded better to the groups' respective diagnoses than the other assessments. The clear implication is that quantitative bronchial luminal volumetric assessments have the potential to serve as reliable indicators of disease development in patients with emphysema.

In this study, the overall success rates for the extraction of segmental and subsegmental bronchi by this software were 92.9% (936/1008) and 74.8% (754/1008), respectively (Table 2). One study has shown that 80.8% of third-generation bronchi and 72.5% of fourth-generation bronchi were successfully identified in this way, *in vivo* [17]. Although it was not possible to perform an accurate comparison, owing to the differences among subjects and evaluation methods, it seemed that there was no large difference between these results. Regarding this study's comparison between the non-COPD group and the COPD group, the success rates for the COPD group were lower than those for the non-COPD group in the assessment of segmental bronchi (Table 2). One of the reasons for this might be that the luminal area/volume of emphysema patients tends to decrease. In fact, Montaudon et al [17] showed that the number of bronchi reconstructed by their software package decreased dramatically beyond the fifth generation (third-generation bronchi 80.8%; fourth generation 72.5%; fifth generation 37.7%; sixth generation 10.7%). Considering these findings, it seems that luminal area/volume is influenced by the extraction of bronchi.

Regarding %LAA (the proportion of the lung affected by emphysema), numerous studies have demonstrated a significant correlation between the %LAA and PFT results [4, 5, 18]. Meanwhile, it has been shown that CT provides a better depiction of early-stage disease than of airflow obstruction or changes in diffusion capacity [19]. Moreover, the correlation between the extent of emphysema determined by CT and by global airflow limitation is weakened by coexistent intrinsic diseases of the small airways [20]. Conversely, some patients with severe emphysematous changes show no evidence of

clinical COPD. Airflow limitation in COPD is a complicated phenomenon that is related only in part to emphysematous lung destruction, and therefore the extent of emphysema does not always correlate with the severity of airflow limitation [6, 7]. In this study, %LAA had no significant correlation with PFT parameters, aside from FEV1/FVC (Table 3). Our results are compatible with these speculations.

On the other hand, many investigators quantitatively evaluated the relationship between the CT findings and increased airflow limitation [8–10]. Nakano et al [8] reported that wall thickening in the apical bronchus of the right upper lobe had a significant correlation with decreased FEV1 in patients with COPD. In recent studies, airway dimensions were obtained using volumetric CT, which allows for measurement in a plane orthogonal to the long axis of the airways. It was found that correlations of airway measurements with lung function varied according to the order of bronchial generation [9, 10]. In our study, the WA% of segmental bronchi corresponding to third-order bronchi and that of subsegmental bronchi corresponding to fourth-order bronchi were significantly correlated with FEV1 (Table 3). These results are compatible with those in the previous report [9], and the measurements of the bronchial wall area reflected the airflow limitations.

However, the assessments obtained using these techniques might have at least two limitations. One was that only a limited part of the airway was evaluated. The PFT reflects the function of the whole lung, and the airflow obstruction could have been in different lobes or different-order bronchi, depending on the type and distribution of emphysema [10]. In fact, the correlation was different between RB1 and RB8 in the third-order and fourth-order bronchi [9]. The other limitation was the presence of the pulmonary artery's adjacent bronchi. These arteries sometimes discourage impeccable measurement of bronchial wall thickness.

In this study, the volumetric assessment of the bronchial lumen had a better correlation with airflow limitation in the PFTs than in the 2D measurement (Table 3). It seems that there were three reasons for this result. First, more accurate comparisons regarding the assessment of wall area percentages may have been possible because there was no obstacle from an adjacent pulmonary artery. Regarding the assessment of bronchial

luminal areas, Hesegawa et al [9] reported that the airway luminal area had a correlation greater than that for the bronchial wall area. Second, the volumetric assessment used in this study may have better reflected the function of the whole lung than the 2D measurement, because all parts of the bronchial luminal volumes were measured. Meanwhile, regarding the volumetric assessment, there has been a report that volumetric assessments are significantly correlated with FEV1 [12]. Third, the structure of the airway changes in emphysema patients. In emphysema patients, the luminal area/volume of peripheral airways decreased owing to inflammation, and it has been reported that tracheal volume shows moderate positive correlations with lung volume [21], suggesting that emphysema patients have a tendency towards increased tracheal volume. In addition, there was a tendency in this study for the extraction of the peripheral airway in emphysema patients to be more difficult, probably because of the decreasing bronchial volume/area. These factors explain the relatively decreased volume of peripheral airways in emphysema patients. The efficacy of volumetric assessment of the bronchial lumen was found to be superior to that of 2D measurement.

There are certain limitations to this study. First, the number of cases was small and patient selection was biased by the entry criteria, which might limit comparison of the measurements. Further, we did not perform the comparisons using classified clinical stages, such as the clinical stages of the Global Initiative for Chronic Obstructive Lung Disease.

Second, airway segmentation was performed using a range of thresholds on an individual basis. This might have the potential to influence both results on success of segmentation and the segmented volumes, making comparison between cases using different thresholds difficult. This was an important issue; therefore, further improvement is necessary in the future.

Third, the extraction judgements, the divisions among the trachea, main bronchus and lobe bronchi, and the choice of slice for measuring the wall area percentages were made by a single chest radiologist. In addition, the divisions were not fully automated quantifications. However, it is likely that other radiologists would perform similarly, because the radiologist's role was limited, as just described.

Fourth, we did not use respiratory gating or electrocardiographic (ECG) gating in the scans in this study. Bronchial luminal volumes are changed by the level of inspiration, and this measure is likely to be highly dependent on respiratory effort. Meanwhile, it is assumed that LAAs are influenced by cardiac motion, and that the problem of artefacts from cardiac motion must sometimes occur in analyses of bronchial luminal volumes. Therefore, scans with respiratory gating and ECG gating might be needed for more accurate assessments.

Fifth, only a single CT machine, set of scan settings and software package were used to provide CT data. The effects of these variables should be assessed in future studies, because CT images are greatly influenced by scan settings such as tube potential, tube current and beam pitch, as well by as the differences in the reconstruction algorithms used by different software packages [22].

In summary, we compared bronchial luminal volumetric assessment with other quantitative CT parameters to assess airway obstruction in pulmonary emphysema. The assessment of bronchial luminal volume had a better correlation with pulmonary function loss than the other methods: it better indicated the quantitative bronchial luminal volume, and hence the degree of airflow limitation. The bronchial luminal volume method also found a significant difference between the non-COPD group and the COPD group. Thus, quantitative bronchial volumetric assessment has the potential to be a useful indicator of pulmonary function loss in emphysema patients.

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