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Quantitative airway assessment on computed tomography in patients with α_1 -antitrypsin deficiency

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Abstract

Background—The relationship between quantitative airway measurements on computed tomography (CT) and airflow limitation in individuals with severe α_1 -antitrypsin deficiency (AATD) is undefined.

Objectives—To clarify the relationship between CT-based airway indices and airflow limitation in AATD.

Methods—52 patients with AATD underwent chest CT and pre-bronchodilator spirometry at three institutions. In the right upper (RUL) and lower (RLL) lobes, wall area percent (WA%) and luminal area (Ai) were measured in the third, fourth, and fifth generations of the bronchi. The severity of

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Conflicts of interest:

Dr. Yamashiro, Dr. Matsuoka, Dr. San Jose Estepar, Dr. Diaz, Dr. Murayama, Dr. Hatabu, and Dr. Washko have no conflicts of interest to disclose. Dr. Silverman received an honorarium for a talk on COPD genetics in 2006, and grant support and consulting fees from GlaxoSmithKline for two studies of COPD genetics. Dr. Silverman also received honoraria from Bayer in 2005, and from AstraZeneca in 2007 and 2008.

The information of other co-authors will be submitted to the Editorial Office personally.

*Special note for the name of Dr. San José Estépar

Please note that his first name is Raúl, and family name is San José Estépar. The authors would really appreciate it if the editors would pay attention to his first/family name and accents.

emphysema was also calculated in each lobe and expressed as low attenuation area percent (LAA %). Correlations between obtained measurements and FEV₁% predicted (FEV₁%P) were evaluated by the Spearman rank correlation test.

Results—In RUL, WA% of all generations was significantly correlated with FEV₁%P (3rd, R=−0.33, p=0.02; 4th, R=−0.39, p=0.004; 5th, R=−0.57, p<0.001; respectively). Ai also showed significant correlations (3rd, R=0.32, p=0.02; 4th, R=0.34, p=0.01; 5th, R=0.56, p<0.001; respectively). Measured correlation coefficients improved when the airway progressed distally from the third to fifth generations. LAA% also correlated with FEV₁%P (R=−0.51, p<0.001). In RLL, WA% showed weak correlations with FEV₁%P in all generations (3rd, R=−0.34, p=0.01; 4th, R=−0.30, p=0.03; 5th, R=−0.31, p=0.03; respectively). Only Ai from the fifth generation significantly correlated with FEV₁%P in this lobe (R=0.34, p=0.01). LAA% strongly correlated with FEV₁%P (R=−0.71, p<0.001).

Conclusions—Quantitative airway measurements are significantly correlated with airflow limitation in AATD, particularly in the distal airways of RUL. Emphysema of the lower lung is the predominant component; however, airway disease also has a significant impact on airflow limitation in AATD.

INTRODUCTION

α_1 -antitrypsin deficiency (AATD) is characterized by low serum concentrations of α_1 -antitrypsin protein, which is usually caused by homozygosity for the Z allele of the SERPINA1 gene on chromosome 14q31–32.3 [1]. Of the related conditions of AATD, pulmonary emphysema is the most frequently observed. A typical pattern of emphysema with AATD is panlobular with basal predominance, while centrilobular emphysema with apical dominance is more typically seen in emphysema without AATD [1,2]. Several previous reports have demonstrated the effectiveness of quantitative assessment on emphysematous lesions by using computed tomography (CT) to predict lung function in AATD [3–10]. In these reports, the extent of emphysema, particularly in the lower part of the lung, strongly correlates with airflow limitation on pulmonary function tests (PFT).

In chronic obstructive pulmonary disease (COPD) without AATD, it has been already acknowledged that airflow limitation can be caused not only by emphysema but also by small airway disease [11]. Several previous studies have demonstrated that quantitative CT indices of the airway, including wall area percent (WA%) and luminal area (Ai), are useful to evaluate airflow limitation [11–13]. In addition, these airway parameters from the distal airways are more closely correlated with FEV₁ percent predicted (FEV₁%P) than those from the proximal airways [11,14].

On the contrary, in AATD, the published information on CT-assessed airway disease has been limited in scope. Though a few previous papers have suggested a potential association between AATD and the presence of both bronchiectasis and bronchial wall thickening [15–18], the relationship between these airway abnormalities and lung function was undefined. In 2007, Parr and coworkers first reported that visual scoring of airway disease in AATD can reflect health status and airflow limitation. They suggested that visual scores of bronchial wall thickening were significantly correlated with FEV₁%P [19]. However, to our knowledge, no previous paper has done quantitative CT assessment of the airways in AATD.

Based on previous investigations, we hypothesized that airway parameters quantitatively measured by CT can be correlated with airflow limitation in AATD. Furthermore, similarly to COPD without AATD, the parameters of the more distal airways may show stronger correlations to airflow limitation. Thus, the aim of this study is: (i) to clarify the relationship between airflow limitation and quantitatively assessed airway abnormalities on CT in AATD;

and (ii) to verify the impact of bronchial generation on the association between airway measurements and airflow limitation in AATD.

METHODS

Subjects

This study was approved by the Institutional Review Board at each institution. 52 subjects (27 females and 25 males) with severe AATD, who underwent chest CT from August 1999 to February 2007, were selected. Among them, 50 subjects had the phenotype PI ZZ, with one known PI ZNull included. Another patient without information on the AATD phenotype was also included, whose serum level of α_1 -antitrypsin was 35 mg/dL and concordant with PI ZZ [1]. 36 subjects were enrolled from the National Jewish Medical and Research Center, 8 from the University of Florida, and 8 from Brigham and Women's Hospital. All subjects gave written informed consent. Chest CT and PFT were performed as part of routine clinical care. Patients who had severe cystic bronchiectasis or atelectasis in the targeted lobe were not included in the study.

Computed tomography

All subjects underwent chest CT at full inspiration and in the supine position. No subject received contrast material.

36 subjects from the National Jewish Medical and Research Center were scanned by 16-detector CT (LightSpeed 16; GE Medical Systems, Milwaukee, WI). The tube voltage was 120 kVp and the current varied using auto-regulation. Rotation time was 0.5 sec. For airway analysis, images were reconstructed with a slice thickness of 1.25mm and an interval of 10 mm, using the 'bone' algorithm. For the evaluation of emphysema, conventional CT scans, which were contiguously reconstructed with a 5mm-slice thickness using the 'lung' algorithm, were selected.

Eight subjects from the University of Florida underwent chest CT with 4-detector CT (LightSpeed QX/i; GE Medical Systems, Milwaukee, WI). The tube voltage and current were 120 kVp and 220 or 300 mA. Rotation time was 1 sec or less. For airway analysis, image reconstruction was performed using the 'bone' algorithm with a slice thickness of 1.25 mm (n = 6) or 1 mm (n = 2), with or without a 10mm-slice interval. For the emphysema study, images were contiguously reconstructed using the 'lung' algorithm with 5mm- (n = 6) or 7mm-slice thickness (n = 2).

Eight subjects from Brigham and Women's hospital were scanned by 16- or 4-detector CT (Sensation 16, Sensation 4, or Volume Zoom 4; Siemens, Erlangen, Germany). The voltage was 120 kVp and the current varied based on auto-regulation. Rotation time was 0.5 sec. Image reconstruction was done for airway analysis using the B60f (n = 5) or B50f (n = 3) algorithm, with a slice thickness of 1.25mm (n = 4) or 1mm (n = 4). An image interval of 10mm was applied to all subjects. For emphysema analysis, contiguous image reconstruction was performed with a 5-mm slice thickness using the B50f algorithm.

Airway analysis

Airway analysis was performed on transverse images using open-source software (AirwayInspector, Brigham and Women's Hospital, Boston, MA) [www.airwayinspector.org]. One radiologist (T.Y.) identified the three bronchi of three different generations (from third to fifth) both in the right upper (RUL) and lower lobes (RLL). In this study, a segmental bronchus was defined as the third generation. The upper apical segmental bronchus (B1) and the posterior basal segmental bronchus (B10) were mainly

selected. However, if the optimal bronchus was missing due to image intervals, an alternative bronchus of the same generation was measured in the same lobe. In order to determine which bronchi to measure, the following rules were applied: (i) the bronchial tree and generations were observed using both conventional and thin-section CT; (ii) if the third generation of B1 or B10 was missing on thin-section CT due to image intervals, the posterior apical segmental bronchus (B2) or the lateral basal segmental bronchus (B9) was selected (switched segmental bronchus); (iii) the fourth and fifth generations were selected on the distal trunk of the segmental bronchus finally selected; (iv) if the fourth generation was missing on thin-section CT, the fourth generation of the different segmental bronchus in the same lobe was selected (alternative fourth generation); and (v) the fifth generation could be measured on the same trunk of the third generation finally selected in all subjects. Following this procedure, 'switched segmental bronchus' was selected in 10 subjects in RUL (19%) and 1 subject in RLL (2%). 'Alternative fourth generation' was selected in 4 subjects in RUL (8%) and not applied in RLL.

Airway measurement was semi-automatically performed by the software and the two parameters, WA% and Ai, were obtained using the full-width at half-maximum (FWHM) method [11–13]. It was confirmed that the ratio of the long and short axes was within two in all measured bronchi. In brief, the following procedures were done in the analysis. (i) The airway lumen of the bronchus was identified initially to find the temporal centroid point of the lumen. (ii) 128 rays were fanned out over 360° from the centroid point of the lumen to determine the inner and outer border pixels of the airway wall. When an adjacent vessel obscured the outer boundary, sector measurements were made of the part of the airway wall that was clearly segmented. (iii) The adjacent inner and outer border pixels of the airway wall were connected by straight lines to determine the boundaries of the airway wall and wall thickness (WT). The area of the inner lumen was designated as Ai. Assuming that in a cross-sectional plane the airway lumen is a true circle and WT is constant throughout the wall, the total diameter (D) of the bronchus was calculated as $D = 2\sqrt{(A_i/\pi)} + 2WT$. The outer area of the bronchus (Ao) and wall area (WA) were calculated as follows: $A_o = \pi(D/2)^2$ and $WA = A_o - A_i$. The percentage of wall area (WA%) was calculated as follows: $WA\% = (WA/A_o) \times 100$.

Reproducibility of airway analysis

Intraobserver error was tested by having one observer (T.Y.) measure WA% and Ai of the three generations of RUL twice in 15 subjects, who were randomly selected from a total of 52 subjects. The second measurement was done four months after the first session. To evaluate interobserver error, two observers (T.Y. and S.M.) independently measured WA% and Ai from RUL in the 15 subjects. Analysis of intra- and interobserver reproducibility was conducted using the Bland-Altman analysis [20].

CT densitometry

Emphysema was evaluated by low attenuation areas (LAA) [<-950 Hounsfield unit (HU)]. The percentage of LAA (LAA%) was calculated using different open-source software (Image J, National Institutes of Health, Bethesda, MD) [<http://rsb.info.nih.gov/ij>]. The protocols were similar to what was described previously [21]. In brief, the lung parenchyma was automatically segmented from the chest wall and the hilum on each CT image. The lung field was adjusted by manually tracing the fissures when the major or the minor fissures were observed. The dimensions of the lung parenchyma and LAA were calculated on each image. Finally, LAA% was obtained by dividing the total LAA by the total parenchymal dimension both in RUL and RLL.

Pulmonary function test

Forced vital capacity (FVC), and forced expiratory volume in 1 second (FEV₁) were measured by pre-bronchodilator spirometry in all 52 subjects. These were expressed as the percentages of predicted values.

Statistical analysis

Statistical analyses were performed using JMP7.0 software (SAS Institute, Cary, NC). Data were expressed as mean $\pm$ standard deviation. Univariate linear regression analysis and the Spearman rank correlation analysis were used to estimate the relationship between measured CT parameters and FEV₁%P. Multivariate analysis using pre-bronchodilator FEV₁%P as the dependent outcome was also performed to evaluate measured CT values and patient's characteristics. P values less than 0.05 were considered statistically significant.

RESULTS

Subjects characteristics

Subject characteristics are summarized in Table 1. Only two subjects were cigarette smokers at the time of evaluation and 29 were former smokers. Mean cigarette index of the smokers was 26.5 pack-years, while mean index of the overall study population was 15.6 pack-years. Smoking index was significantly correlated with pre-bronchodilator FEV₁%P ($R=-0.402$, $p=0.003$).

Reproducibility of airway analysis

The intra- and interobserver reproducibility of airway analysis is shown in Table 2. Plots of the average of and the difference between the measured values are shown in Fig. 1. The mean difference did not appreciably deviate from zero, and the limits of agreement were small.

Airway measurements

CT measurements of airway parameters and correlations with FEV₁%P are demonstrated in Table 3. In RUL, WA% of all generations showed significant correlations with pre-bronchodilator FEV₁%P (Fig. 2; Fig. 3rd, $R=-0.332$, $p=0.02$; 4th, $R=-0.392$, $p=0.004$; 5th, $R=-0.573$, $p<0.001$; respectively). Ai of all generations also significantly correlated (Fig. 3; Fig. 3rd, $R=0.317$, $p=0.02$; 4th, $R=0.339$, $p=0.01$; 5th, $R=0.564$, $p<0.001$; respectively). The correlation coefficients of both WA% and Ai improved as the generations progressed peripherally from the third to fifth generations.

In RLL, WA% demonstrated weak, negative correlations with pre-bronchodilator FEV₁%P in all generations (3rd, $R=-0.338$, $p=0.01$; 4th, $R=-0.296$, $p=0.03$; 5th, $R=-0.310$, $p=0.03$; respectively). Ai of only the fifth generation showed a weak, positive correlation ($R=0.340$, $p=0.01$).

Prevalence of emphysema

Mean values of LAA% were $24.2\% \pm 13.2$ in RUL and $28.0\% \pm 16.4$ in RLL. Significant negative correlation was observed between LAA% and FEV₁%P in each lobe (Table 4 and Fig. 4). The correlation coefficient of LAA% in RLL was the highest among overall CT indices in this study ($R=-0.705$, $p<0.001$).

Relative impact on airflow limitation

The relative contributions of airway disease, emphysema and other clinical factors were evaluated by a multivariate model. Based on the results from the univariate analyses, LAA%

of RLL, WA% of the fifth generation in RUL, and other patient's characteristics (gender, age, and smoking index) were selected as predictors for FEV₁%P. While these patient's characteristics were not significant, both WA% and LAA% were significant predictors of FEV₁%P (Table 5).

Airway and emphysema measurements in non-smoking subjects

A supplementary analysis was performed to confirm correlations between airway/emphysema measures and airflow limitation in lifelong non-smoking subjects (n=21). Significant correlations were found between FEV₁%P and airway measures of 5th generation in RUL (WA%, R=-0.712, p<0.001; Ai, R=0.595, p=0.004; respectively). Also, LAA% of RUL and RLL showed significant correlations with FEV₁%P (RUL, R=-0.642, p=0.002; RLL, R=-0.722, p<0.001; respectively) (Table 6).

Airway and emphysema measurements in subjects with a standardized CT protocol

Another supplementary analysis was completed for 36 subjects, who were scanned with a completely standardized CT protocol at a single institution. Similar observations were found between FEV₁%P and airway/emphysema measures; a higher correlation coefficient was obtained when the generation of the bronchi progressed peripherally in RUL, and emphysema measurements in RLL showed a higher correlation than in RUL (Table 7).

DISCUSSION

The current study found that the quantitatively measured airway parameters are significantly related to airflow limitation in severe AATD. Moreover, in RUL, these airway parameters from the distal airways are more closely correlated with FEV₁%P than those from the proximal airways. It is observed in our study that the severity of emphysema in the lower lobe is the strongest predictor for FEV₁%P; however, the results indicate that airway disease is also significant in determining the severity of airflow limitation in AATD. We think, therefore, that the airway component may also be a target in the future strategy for the treatment of AATD.

While it is widely accepted that AATD is mainly characterized by severe, panlobular emphysema, previous publications have called attention to clinical manifestations of airway disease in AATD [10,22–25]. However, only a limited number of studies have evaluated airway abnormalities by using CT in AATD [15–19]. Recent research by Parr and colleagues first clarified that airway abnormalities on CT were associated with health status and lung function. They successfully demonstrated that visual scores of bronchial wall thickening correlated with FEV₁%P, and were additive to measures of emphysema in multivariate regression analysis to predict airflow obstruction [19]. In the current study, we also demonstrate that airway wall thickening and narrowing of the airway lumen can be related to airflow limitation in AATD. Furthermore, WA% of RUL, as well as emphysema index, is a significant predictor for FEV₁%P in the multivariate analysis. These observations indicate that airway disease has a significant impact on airflow limitation in AATD.

In COPD without AATD, the role of the bronchial generations on airflow limitation has been gradually recognized by CT studies. Hasegawa and colleagues first reported three-dimensional CT assessment of each generation, from the third to sixth of the selected bronchi, in COPD [11]. They demonstrated that Ai and WA% were significantly correlated with FEV₁%P, and the correlation coefficients improved as the airways progressed distally. More recently, Matsuoka and colleagues similarly demonstrated that Ai from the distal airways significantly correlated with FEV₁%P, in particular on expiratory CT [14]. These studies follow previous clinicopathological investigations that have clarified that airway disease in the distal, small bronchi is important for the severity of COPD [26,27]. Though the impact of airway generation

has not been pathologically investigated in AATD, our current study suggests that AATD basically has similar tendencies to COPD without AATD, to the extent that the distal airways play an important role for airflow limitation.

In the current study, airway parameters in RUL have strong correlations with FEV₁%P, while those from RLL proved to be much weaker predictors of lung function. On the other hand, emphysema was more closely correlated with airflow limitation in RLL than in RUL, which is basically in agreement with previous studies [4–6]. Currently, the etiology of this lobar differential of airway parameters is unclear, but may in part be due to the potential basilar preponderance of bronchiectatic changes in AATD. Parr and colleagues pointed out that more airway changes, which include bronchiectasis and mirror the severity of emphysema, were observed in the lower lobe than in the upper or middle (lingula) lobes.[19] Such changes may artifactually influence objective measures of airway disease and their relationship to lung function. In patients with bronchiectasis not associated with AATD, some previous reports have already mentioned the importance of bronchial wall thickening on airflow limitation [28,29]. However, to the best of our knowledge, no previous paper has rigorously assessed bronchiectasis using quantitative airway parameters in evaluating lung function. Our study may indicate a potential difficulty in using quantitative airway measurement for conditions resulting in bronchiectasis. Further investigation is needed on the relationship between the severity or distribution of airway deformation and airflow limitation, not only in AATD but also in general COPD.

We should mention some of the limitations of this study. First, because three different institutions took part in the current study, the CT scanner and protocol were different at each institution. Although we think the difference in protocols among the institutions is acceptable, this may lead to a questioning of our original CT data and the reliability of measured parameters. We performed a supplementary analysis using the data of a subgroup (n=36) from a single institution, in which the scanning and reconstruction protocol was completely standardized (Table 7). We confirmed that, similar to the results for all 52 subjects, significant correlations existed between airway indices and FEV₁%P, and that more distal bronchi showed higher correlation coefficients in RUL. We believe, therefore, that the major observations in this study are robust and not amplified through the use of different protocols. However, standardization of imaging methods to compare different scanning/reconstruction protocols should be discussed for future research.

Second, the underlying pathological change of the airways in AATD remains ambiguous. It has been reported that although wall thickening of the small airways occurs in AATD, the ratio of wall area to basement membrane perimeter is not strongly correlated with FEV₁%P [30]. Because of the limited number of previous pathological reports on airway abnormalities in AATD, a detailed study is recommended from the perspective of pathological changes in affected airways.

Third, the impact of smoking on airway abnormalities was not fully investigated. In a subgroup of non-smoking subjects, WA% and Ai of the distal airway in RUL showed significant correlations with FEV₁%P (Table 6). Further, another supplementary study showed that there was no significant difference on any airway parameter or on emphysema value between two groups of smoking and non-smoking subjects (data not shown). However, further study would be needed to evaluate the differences in those CT measures between smoking and non-smoking subjects, and to exclude the impact of smoking on airway abnormalities in AATD.

Fourth, in order to minimize the influence of the asthmatic component on airflow limitation, PFT values of post-bronchodilator spirometry should have been used in this study. In the 45 subjects whose PFT data with post-bronchodilator spirometry were available, airway CT

indices demonstrated similar, significant correlations with EFV₁%P (data not shown). Although we believe that this result implies that our PFT data with pre-bronchodilator spirometry can also be used to evaluate COPD in our study, future study is recommended to exclude the impact of bronchial asthma on airflow limitation in AATD.

Fifth, the influence of lung volume on airway or emphysema measurements were not investigated in the current study. It can be predicted that these measurements are sensitive to the level of inspiration, which can be a confounder of CT analysis for COPD. Deep inspiration probably causes an increase in airway size (Ai), which leads to a decrease in WA% and would be interpreted as a less severe airway disease. On the contrary, it can also be predicted that the same deep inspiration can decrease lung density, which increases LAA%. To the best of our knowledge, no previous paper rigorously assessed these two opposing phenomena in a single study model. Further, it is still unclear whether or not over-inflation of the lung, caused by panlobular emphysema, directly affects airway size in AATD. Spirometry-gated CT and/or lobar segmentation technique would be of interest for future CT-based studies for AATD.

In summary, we first reported the quantitative CT assessment of the airways in subjects with AATD. Measured airway indices are significantly correlated with airflow limitation, particularly in RUL. In addition, in RUL, the correlation coefficients improved in more distal generations. Emphysema in the lower lung is the predominant component of COPD, but these results suggest that small airway disease is also significant for airflow limitation in AATD, which is similar to COPD without AATD.

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Figure 1. Intra- and interobserver error for measurement of wall area percent (WA%) and luminal area (Ai)

Plots show intraobserver (A, B) and interobserver (C, D) error for measurement of WA% and Ai according to the Bland-Altman analysis. The mean of the two measurements and the difference between them are plotted. The mean difference does not appreciably deviate from zero, and limits of agreement are small. There is no obvious relationship between the measurement error and these parameters.

Figure 2. Correlation between wall area percent (WA%) and FEV₁%P in the right upper lobe
 The correlation between WA% and FEV₁%P of the third (A), fourth (B), and fifth (C) generations in the right upper lobe is demonstrated. WA% from all three generations shows significant correlations with FEV₁%P. Interestingly, the correlation coefficients improve when the generations of the bronchi become distal from the third to fifth. WA% from the fifth generation has the highest correlation coefficient in overall airway measurements in this study.

Figure 3. Correlation between luminal area (Ai) and FEV₁%P in the right upper lobe
 Ai from all three generations demonstrates significant correlations with FEV₁%P (A, B, C).
 Note that correlation coefficients improve when the airway progressed peripherally, which is
 similar to WA%.

Figure 4. Correlation between the percentage of low attenuation area (LAA%) and FEV₁%P in the right upper and lower lobes

LAA% in the right lower lobe (**B**) is more closely correlated with FEV₁%P than that in the right upper lobe (**A**). Correlation coefficient of LAA% in the right lower lobe is the highest among overall measurements in this study.

Table 1

Summary of clinical parameters and pulmonary function tests

	Mean $\pm$ SD	Range
Age (years)	52.8 $\pm$ 9.4	36 – 76
Smoking index (pack-years)	15.6 $\pm$ 21.9	0 – 105
FVC% predicted (%)	81.6 $\pm$ 25.2	35.0 – 141.0
FEV ₁ % predicted (%)	57.2 $\pm$ 28.3	14.0 – 117.0

Table 2

Reproducibility of airway measurements

	Mean difference $\pm$ SD	Limit of agreement
Intraobserver error		
WA% (%)	-0.09 ± 0.63	$-1.34 - 1.17$
Ai (mm ²)	-0.06 ± 1.26	$-2.58 - 2.45$
Interobserver error		
WA% (%)	-0.19 ± 1.35	$-2.88 - 2.51$
Ai (mm ²)	-0.39 ± 1.34	$-3.06 - 2.29$

Definition of abbreviations: WA% = wall area percent; Ai = luminal area.

Table 3

CT measurements of the airways and correlations with FEV₁%P

WA % (%)		Ai (mm ²)						
	Mean ± SD	Range	R	p	Mean ± SD	Range	R	p
RUL								
3 rd	58.3 ± 6.7	48.0 – 78.1	−0.332	0.02	23.7 ± 10.0	6.5 – 57.2	0.317	0.02
4 th	64.9 ± 6.6	53.8 – 83.8	−0.392	0.004	11.1 ± 5.0	2.5 – 23.9	0.339	0.01
5 th	71.1 ± 7.5	54.5 – 84.2	−0.573	<0.001	5.8 ± 3.0	1.2 – 14.6	0.564	<0.001
RLL								
3 rd	56.3 ± 8.4	41.1 – 75.8	−0.338	0.01	19.5 ± 10.9	3.9 – 70.9	0.240	NS
4 th	64.7 ± 8.2	46.2 – 87.1	−0.296	0.03	9.2 ± 5.8	0.7 – 27.4	0.241	NS
5 th	70.2 ± 8.7	51.8 – 92.5	−0.310	0.03	6.3 ± 3.9	0.5 – 17.6	0.340	0.01

Definition of abbreviations: RUL = right upper lobe; RLL = right lower lobe; WA% = wall area percent; Ai = luminal area
Ordinal numbers show the generation of the bronchus.

Table 4CT measurements of emphysema and correlations with FEV₁%P

	LAA% (%)			
	Mean $\pm$ SD	Range	R	p
RUL	24.2 $\pm$ 13.2	5.6 – 54.9	–0.514	<0.001
RLL	28.0 $\pm$ 16.4	4.2 – 70.7	–0.705	<0.001

Definition of abbreviations: LAA% = percentage of low attenuation area (< –950 HU); RUL = right upper lobe; RLL = right lower lobe

Table 5Predictors of FEV₁%P from multivariate analysis

	Standardized coefficient B	t value	p
WA%-RUL5 th (%)	−0.444	−5.45	<0.001
LAA%-RLL (%)	−0.631	−6.72	<0.001
Gender*	−0.017	−0.20	0.841
Age (years)	0.112	1.32	0.192
Smoking (pack-years)	−0.046	−0.50	0.618

Definition of abbreviations: WA%-RUL5th = wall area percent of the fifth generation in the right upper lobe; LAA%-RLL = percentage of low attenuation area (< −950 HU) in the right lower lobe.

* Gender is expressed as follows: 0 for females and 1 for males

Table 6
Correlations between CT measurements and FEV₁%P in non-smoking subjects (n=21)

	WA%		Ai		LAA%	
	R	p	R	p	R	p
RUL					-0.642	0.002
3 rd	-0.041	NS	0.072	NS		
4 th	-0.389	NS	0.438	0.04		
5 th	-0.712	<0.001	0.595	0.004		
RLL					-0.722	<0.001
3 rd	-0.155	NS	0.070	NS		
4 th	-0.298	NS	0.262	NS		
5 th	-0.124	NS	0.234	NS		

Definition of abbreviations: RUL = right upper lobe; RLL = right lower lobe; WA% = wall area percent; Ai = luminal area; LAA% = percentage of low attenuation area (< -950 HU)
Ordinal numbers show the generation of the bronchus.

Table 7

Correlations between CT measurements and FEV₁%P in a subgroup of subjects with a standardized scanning protocol (n=36)

	WA%		Ai		LAA%	
	R	p	R	p	R	p
RUL					-0.449	0.006
3 rd	-0.391	0.02	0.238	NS		
4 th	-0.448	0.006	0.400	0.02		
5 th	-0.623	<0.001	0.578	<0.001		
RLL					-0.698	<0.001
3 rd	-0.363	0.03	0.269	NS		
4 th	-0.320	NS	0.333	0.04		
5 th	-0.307	NS	0.405	0.01		

Definition of abbreviations: RUL = right upper lobe; RLL = right lower lobe; WA% = wall area percent; Ai = luminal area; LAA% = percentage of low attenuation area (< -950 HU)
Ordinal numbers show the generation of the bronchus.