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Quantitative CT of the Lungs and Airways in Healthy Non-smoking Adults

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Abstract

Objectives—The purposes of this study are to evaluate the normal range of quantitative CT (QCT) measures of lung attenuation and airway parameters measurements in healthy non-smoking adults and to identify sources of variation in those measures and possible means to adjust for them.

Materials and Methods—Within the COPDGene® study, 92 healthy non-Hispanic White non-smokers [29 male, 63 female, mean age 62.7 (SD 9.0), BMI 28.1 (SD 5.1)] underwent volumetric CT at full inspiration and at the end of a normal expiration. On QCT analysis (Pulmonary Workstation 2, VIDA Diagnostics), inspiratory low attenuation areas were defined as lung tissue with attenuation values ≤ −950 Hounsfield Units (HU) on inspiratory CT ($LAA_{I\text{-}950}$). Expiratory low attenuation areas were defined as lung tissue ≤ −856 HU on expiratory CT ($LAA_{E\text{-}856}$). We used simple linear regression to determine the impact of age and gender on QCT parameters and multiple regression to assess the additional impact of total lung capacity and functional residual capacity measured by CT (TLC_{CT} and FRC_{CT}), scanner type, and mean tracheal air attenuation. Airways were evaluated using measures of airway wall thickness (AWT), inner luminal area (ILA), wall area percent (WA%) and standardized thickness of an airway with inner perimeter of 10mm (Pi10).

Results—Mean $\%LAA_{I\text{-}950}$ was 2.0 (SD 2.7), and mean $\%LAA_{E\text{-}856}$ was 9.2 (SD 6.8). Mean $\%LAA_{I\text{-}950}$ was 3.6 (SD 3.2) % in men, compared with 1.3 (SD 2.0) in women (P<0.001). The $\%LAA_{I\text{-}950}$ did not change significantly with age (P=0.08) or BMI (P=0.52). $\%LAA_{E\text{-}856}$ did not show any independent relationship with age (P=0.33), gender (P=0.70), or BMI (P=0.32). On multivariate analysis, $\%LAA_{I\text{-}950}$ showed a direct relationship to TLC_{CT} (P=0.002) and an inverse relationship to mean tracheal air attenuation (P=0.003), and $\%LAA_{E\text{-}856}$ was related to age (P=0.001), FRC_{CT} (P=0.007) and scanner type (P<0.001). Multivariate analysis of segmental airways showed that ILA and WA% were significantly related to TLC_{CT} (P<0.001) and age (0.006). WA% was also associated with gender (P=0.05), axial pixel size (P=0.03) and slice interval (P=0.04). Lastly, AWT is strongly influenced by axial pixel size (P<0.001).

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Conclusions—Although the attenuation characteristics of normal lung differ by age and gender, these differences do not persist on multivariate analysis. Potential sources of variation in measurement of attenuation-based quantitative CT parameters include depth of inspiration/expiration, and scanner type. Tracheal air attenuation may partially correct variation due to scanner type. Sources of variation in QCT airway measurements may include age, gender, BMI, depth of inspiration, and spatial resolution.

Keywords

Quantitative CT; Lungs; Airways; Non-smokers

Introduction

Quantitative measures of CT (QCT) are increasingly used in characterization of chronic obstructive pulmonary disease (COPD). Specifically, QCT permits accurate quantification of three distinct components of COPD: emphysema (1, 2), airway luminal diameter and airway wall thickness (3), and expiratory air trapping (4-6). Studies in patients with COPD and asthma have shown that extent of emphysema (7-11) and gas trapping (4-6) as quantified on CT provides strong but incomplete correlations with spirometry results. There is evidence that quantitative evaluation of segmental and subsegmental airway abnormalities correlates with physiologic severity of airway obstruction (2) and also with the frequency of COPD exacerbations (12).

Through sophisticated imaging techniques, along with genetic and physiological assessments, several subtypes within the COPD population with differing QCT characteristics in airways and lung parenchyma have begun to emerge. However, understanding of the quantitative CT phenotypes is impaired by the absence of a healthy group with which to compare these disease cohorts. There has been relatively little description of QCT parameters in healthy non-smokers (13-16). The purpose of the current study is to describe the range of QCT parameters within a normal population for comparison with cohorts of individuals with lung diseases. We also wished to review the sources of variation within the normal population.

Materials and Methods

Subjects

108 healthy non-smokers, between the ages of 45 and 80 years, were recruited at multiple sites to participate in the COPDGene® study. These were subjects with a lifetime smoking history of fewer than 100 cigarettes, no history of lung disease, and with normal post-bronchodilator spirometry ($FEV_1 \geq 80\%$ predicted and $FEV_1/FVC \geq 0.7$). The complete cohort consisted of 100 non-Hispanic whites and 8 African Americans. We excluded 9 subjects (eight white and one African American) whose TLC_{CT} was less than 80% of the predicted physiologic TLC by standard reference calculations (17). For analysis of the QCT parameters, we focused primarily on the 92 non-Hispanic whites because only 7 African Americans were included in the cohort, and we felt that race might have a significant effect on some QCT parameters, since it influences physiologic measurements (18, 19). (QCT data for African Americans is included in Appendix 1) Table 1 provides age, height, body mass index (BMI) and physiologic information regarding the cohort. The 92 non-Hispanic whites evaluated here had mean FEV_1% predicted of 103.5 (SD 13.8). FEV_1 % predicted was slightly higher in men than in women (P=0.03) (18). For age comparisons in Table 2 the cohort was divided into two groups with a cutoff of 65 years. Because recruitment was stratified by age, exactly half of the cohort (n=46) were < 65 years and half were ≥ 65 years. All multivariate models were evaluated using age as a continuous variable. Subjects were

recruited from 11 clinical centers throughout the United States (Supplemental Materials: Appendix 4). IRB approved informed consent was obtained for every subject prior to enrollment. All data were collected and protected in accordance with HIPAA regulations.

Image Acquisition

All subjects underwent volumetric CT at full inspiration and at the end of a normal expiration using a standardized technique (20). All CT scans were performed with a tube potential of 120kVp with an effective mAs of 200 for inspiration and 50 for expiration. The images all consisted of thin section, contiguous slices. The reconstructed slice thicknesses were 0.625, 0.75 or 0.9mm depending on the scanner manufacturer: General Electric Medical Systems, Siemens and Philips, respectively. The slice intervals by manufacturer were 0.625, 0.5 and 0.45mm, respectively. The convolution kernels used for image reconstruction were Standard, B31f and B (20). Scan quality was assessed for motion artifacts, adequacy of inspiration/expiration and inclusion of all of the lung, as well as adherence to scanning protocol. A total of 8 different types of scanners were utilized to acquire these scans. Siemens scanners, used in 73 cases, included: Sensation 64-slice (n=2), Definition 64-slice (n=40), Definition AS+ 128-slice (n=5) and Definition Flash 128-slice (n=26). GE scanners, used in 17 cases, included: Lightspeed 16-slice (n=11), Discovery CT750HD (n=5) and Lightspeed Pro 16-slice (n=1). Last, the Philips Brilliance 64-slice scanner was used in 2 cases. Scanners were calibrated weekly and monthly scans were performed on a standard phantom to maintain and track consistency of CT attenuation.

Image Analysis

All CT images were analyzed using the Pulmonary Workstation 2 software (VIDA Diagnostics, Inc, Coralville, IA). Automated segmentation of the right and left lungs from the chest wall and mediastinum allowed for measurements of lung attenuation. Lobar segmentation was also performed for individual evaluation of five lobes, right upper lobe (RUL), right middle lobe (RML), right lower lobe (RLL), left upper lobe (LUL) and left lower lobe (LLL). For further regional comparison, lobes were grouped into upper (RUL, RML and LUL) and lower (RLL and LLL) lobes. Thresholds for lung attenuation using the density mask technique were set at −950HU, −910HU and −856HU. Percent inspiratory low attenuation areas were defined as percent lung tissue ≤ −950HU on inspiration ($\%LAA_{I\text{-}950}$) (21). Percent expiratory low attenuation areas were defined as percent lung tissue ≤ −856HU on expiration ($\%LAA_{E\text{-}856}$) (22). Full data for all thresholds are provided in Appendix 1. The CT total lung capacity (TLC_{CT}) was defined as the segmented lung volume on inspiratory CT. The CT functional residual capacity (FRC_{CT}) was defined as the segmented lung volume on expiratory CT. These findings were compared to well-established prediction equations to determine % predicted values for TLC and FRC as a measure of adequacy of inspiration/expiration (18). The $\%LAA_{I\text{-}950}$ and $\%LAA_{E\text{-}856}$ values were adjusted for TLC_{CT} and FRC_{CT}, respectively, according to the method outlined by Dirksen (23). The airway tree was generated using an automated region-growing technique. Detailed airway analysis was completed to the segmental bronchi, as well as two generations distally, in six selected airway pathways (RB1, RB4, RB10, LB1, LB4 & LB10). In each subject an automated process was used to determine mean attenuation of voxels of tracheal air within a spherical region of 1cm diameter centered between the tracheal walls directly above the carina. This was used as a measure of scanner variability in attenuation measurement. Airway wall thickening was evaluated on inspiratory CT using measures of airway wall thickness (AWT), inner luminal area (ILA), wall area percent (WA%: % wall area/total bronchial area) and a standardized wall thickness measure of an airway with an inner perimeter of 10mm (Pi10) (24, 25). These were quantified in segmental bronchi, as well as two generations subsegmental. Airway measurements were obtained as averages across the middle third of each segment. Airway measures were averaged at each generation for all six

pathways, and whole lung averages were obtained at each generation, as well. (26) Every scan underwent thorough visual assessment for accuracy of lung/lobar segmentations, as well as completeness of the airway tree and accuracy of airway labels. Manual editing of automated segmentations was performed when necessary.

Statistical Analysis

Statistical analyses were performed using JMP 8 (copyright © 2008 SAS Institute Inc) or the SAS/STAT software package, Version 9.2 of the SAS System for Windows XP (copyright © 2002–2008 SAS Institute Inc). All descriptive parameters are described as mean (SD). Initial analyses were done using simple linear regression analysis to assess the impact of age and sex on $\%LAA_{I\text{-}950}$ and $\%LAA_{E\text{-}856}$. Multiple regression was done to evaluate the relative impact of TLC_{CT}, age, sex, BMI, scanner model and average tracheal air attenuation on $\%LAA_{I\text{-}950}$. The same analysis was done to evaluate these parameters against $\%LAA_{E\text{-}856}$ with FRC_{CT} in place of TLC_{CT}. Airway parameters were also evaluated using multiple regression with the additional variables of axial pixel size and slice interval. Associations were considered statistically significant at $p < 0.05$.

Results

Table 2 provides average QCT lung parameters for the entire cohort by whole lung and by lobe. Total volume of the upper lobes and right middle lobe measured by CT was similar to the volume of the lower lobes. However, on expiration, the % volume change was significantly less in the upper lobes (P<0.001) resulting in significantly higher FRC_{CT} in the upper lobes (P<0.001). There was also no significant difference in $\%LAA_{I\text{-}950}$ between the upper and lower lobes. However, $\%LAA_{E\text{-}856}$ was significantly higher in the upper lobes than in the lower lobes (P<0.001). Mean lung attenuation on both inspiration and expiration was significantly lower in the upper lobes (both P<0.001).

Table 3 shows the univariate analysis results from QCT analysis of inspiratory and expiratory CT scans, compared by sex and age group. The men had significantly higher TLC_{CT}, FRC_{CT} and change in lung volume than women (P<0.001). Mean lung attenuation on inspiration was significantly lower in men, −861 (SD 14) HU, than in women, −838 (SD 21) HU (P<0.001). There was no sex difference in mean lung attenuation on expiration. TLC_{CT} % predicted was the same in men and women, about 98.5%, but FRC_{CT} % predicted was significantly higher in women than in men, 88.8% and 79.9% respectively (P=0.001). Total mean $\%LAA_{I\text{-}950}$ was 2.0 (SD 2.7) %, and mean $\%LAA_{E\text{-}856}$ was 9.2 (SD 6.8) %. Mean $\%LAA_{I\text{-}950}$ was 3.6 (SD 3.2) % in men, compared with 1.3 (SD 2.0) % in women (P<0.001). Adjustment of $\%LAA_{I\text{-}950}$ by the TLC_{CT} and of $\%LAA_{E\text{-}856}$ by FRC_{CT} (23) had little effect on the data and no effect on the relationships found here. Thus, we excluded these adjustments from our analyses.

Age related variations in lung parameters are also displayed in Table 3. There was no difference between the younger and older groups for TLC_{CT}. There was a significantly higher FRC_{CT} (P=0.02) in the older group and significantly less volume change in the older group (P=0.02). TLC_{CT} and FRC_{CT} % predicted values did not differ between the groups. Mean inspiratory lung attenuation was the same between the groups and $\%LAA_{I\text{-}950}$ was also similar (P=0.11). Mean expiratory lung attenuation was significantly lower in the older group (P=0.0022), but the $\%LAA_{E\text{-}856}$ was no different (P=0.30).

Using simple linear regression, $\%LAA_{I\text{-}950}$ did not change significantly with age (P=0.08) or BMI (P=0.52). $\%LAA_{E\text{-}856}$ did not show any relationship with age (P=0.33), sex (P=0.70), or BMI (P=0.32). Using multiple regression (Table 4a), $\%LAA_{I\text{-}950}$ was significantly related to TLC_{CT} (P<0.001) and scanner model (P<0.001). When tracheal air

attenuation (P=0.003) was added to the model the scanner variation became statistically insignificant (P=0.18) but the relationship with TLC_{CT} remained statistically significant (P=0.002) (Table 4b). $\%LAA_{E-856}$ was related to FRC_{CT}, age and scanner model (all P<0.001) (Table 5a); adjusting for tracheal air attenuation (P=0.08, Table 5b) had no significant impact on these relationships.

Table 6 shows results of multivariate analysis of whole lung average airway parameters at the segmental level. WA% and ILA were strongly related to TLC_{CT} (P<0.001) and age (P=0.006) WA% was also influenced by sex (P=0.05), axial pixel size (P=0.03) and slice interval (P=0.04). The only significant association for AWT was with axial pixel size (P<0.001). This multivariate model showed no significant associations with Pi10. ILA decreases roughly 40% through each generation. AWT decreases about 7% from the segmental to subsegmental level, and remains relatively constant beyond. Appendix 1 of the supplemental materials contains detailed data of lung attenuation and airway parameters for this cohort.

Discussion

Quantitative CT is quickly gaining relevance and importance in the study of lung disease. Barriers to widespread implementation of QCT in the past have included cumbersome software, inter-scanner variation, and lack of knowledge of the normal range of QCT measurements. With rapid advances in scanning technology and analytic software platforms, the evaluation of lung parenchyma and small airways is becoming an efficient technique for characterization and determining severity of obstructive lung diseases like COPD. The current study has provided normal values for comparing against extents of emphysema and gas trapping in disease cohorts. Normal airway parameters are also presented with analysis of multiple contributing variables. Previous smaller studies have evaluated non-smoking cohorts, but they lack the full volumetric QCT approach utilized here, as well as expiratory QCT evaluation, and airway measurements.

Prior research has produced varied results for $\%LAA_{I-950}$ in non-smokers. Gevenois et al. showed much higher scores for $\%LAA_{I-950}$ in a group of 42 non-smokers, around 8% (13). This may be related, at least in part, to high inspiratory lung volumes (average TLC_{CT} about 110% of predicted values). In contrast, Irion et al. identified average $\%LAA_{I-950}$ scores less than 1% in a group of 30 normal subjects (14). However, their cohort consisted of much younger subjects with an average age of 26 years. The cohort of 185 individuals evaluated by Marsh et al. is quite similar to the one presented here (15). The proportion of males there was higher, 47.6% compared with 31.5%. However, the relationship of sex with $\%LAA_{I-950}$ is in accordance with the data presented here, showing that men have slightly higher scores than women. The median $\%LAA_{I-950}$ value obtained, 1.4%, was also comparable to the current study at 0.9%. That study, though, opted for evaluation of just three images per subject, as opposed to the volumetric approach utilized here (15).

Age Relationship

The lack of change in lung attenuation values with increasing age on univariate and multivariate analysis may at first glance appear to contradict previous studies which showed that lung attenuation decreased with age (13, 15, 16). Seojima et al. performed a longitudinal study evaluating the same non-smokers at baseline and with 5-year follow-up. That study showed up to 1% increase per year of inspiratory %LAA and significant correlation with age. However, that study used a cutoff of −912HU for classifying LAA which would lead to higher estimates (16). The difference between previous normal studies and our study may also be related to the fact that our study group did not include individuals less than 45 years old. Gevenois et al. had a study cohort age range of 23-71 years, with an average age of 42

years (13). Marsh et al. had a study cohort age range of 25-75 years, with an average age of 54 years (15). Our data suggest that CT attenuation remains relatively similar within the age range of 45 to 80.

We also examined the relationship between age and $\%LAA_{E-856}$. On univariate analysis there were no significant findings. Simple linear regression showed no direct correlation between age and $\%LAA_{E-856}$. The lack of correlation held up when we divided the cohort into two age groups. However, upon multivariate analysis, gas trapping measured by $\%LAA_{E-856}$ appeared to increase significantly with age ($P<0.001$). This remained true even when the model was adjusted for tracheal air ($P=0.001$). The apparent increase in gas trapping with age may represent a phenomenon of normal aging evident by the lower change in volume from TLC to FRC in the older subjects.

Influence of Scanner Model and Correcting for Tracheal Air

Because it has previously been shown that scanner make and model may result in significant variation in CT attenuation values of lung tissue (18, 19, 27, 28), we evaluated the role of scanner model and tracheal air attenuation as predictors of $\%LAA_{I-950}$ and $\%LAA_{E-856}$. The models also included TLC_{CT}/FRC_{CT}, age, sex and BMI. While $\%LAA_{I-950}$ was significantly different between males and females on univariate analysis, sex was not a significant contributor to any of the multivariate models. The sex difference was most likely accounted for by the relatively higher TLC_{CT} in males.

Our initial multivariate model indicated a significant influence of scanner model for $\%LAA_{I-950}$ and $\%LAA_{E-856}$. When we placed average tracheal air attenuation in the model, scanner model was eliminated as an independent predictor of $\%LAA_{I-950}$, but remained a significant predictor for $\%LAA_{E-856}$. In both models the GE Lightspeed 16 scanner was the main contributor to the variation, but there were several scanners associated with variation in the model for $\%LAA_{E-856}$. For large multi-center studies differing scanner models will always be a substantial source of variation when measuring lung density. It seems that correcting for average tracheal air attenuation may alleviate some of these concerns for $\%LAA_{I-950}$. However, $\%LAA_{E-856}$ may be more sensitive to scanner variations and may not benefit from the tracheal air correction. This might be due to the lower CT dose used for the expiratory scans, with consequent increase in image noise, which may exaggerate inter-scanner differences. Further study should investigate the use of tracheal air attenuation as a possible correction that may be applied when evaluating lung density by CT, as well as possible correction by phantom scanning.

Lobar Variation

Lobar segmentation offers novel insights into the study of lungs in health and disease. The current study shows distinct regional differences in the normal functioning of healthy adult lungs. The upper lobes show markedly less volume change between inspiration and expiration. This leads to significantly higher $\%LAA_{E-856}$ in the upper lobes when compared with the lower lobes. These differences might be accounted for by the relatively more posterior position of the lower lobes, and also by the effectiveness of diaphragmatic movement in promoting expiratory evacuation of air from the lower lobes. These normal lobar variations should be taken into account when evaluating lung attenuation parameters in disease cohorts. They may be important for calibrating future QCT findings to a range of normal in individual lobes.

Airway Parameters

TLC_{CT} seems to be most strongly associated with many airway parameters in non-smokers. This is probably because TLC_{CT} functions as a composite variable accounting for all other

body size variables. In cigarette smokers, women have been shown to have a higher WA% than men even after adjusting for other modifiers (29), leading to speculation that sex affects the airway response to cigarette smoke. However, since we have shown this relationship exists even in non-smokers, sex, along with age may need to be considered as a covariate in studies of airway diameters. In our study, WA% showed slight decrease with increasing age, while ILA showed a slight increase with age. Airway wall parameters are greatly influenced by CT scanner resolution which needs to be accounted for when evaluating these measures in future cohorts. Our multivariate model showed no strong associations with Pi10, so this may be a good independent measure for evaluating small airway disease.

Limitations

Some limitations of the current research will need to be studied for their effects on the data presented. As in most multicenter studies, spirometrically gated CT scanning was not feasible, and indeed we were obliged to eliminate 8 subjects who failed to attain an adequate inspiration. With a fixed mAs, different noise levels likely occurred related to patient size. The relatively small number of subjects, though larger than prior cohorts, limits statistical precision. Variations due to image analysis software cannot be determined, but are likely to be small. Further large scale studies in non-smokers would be difficult to achieve, but they may be necessary to fully understand QCT of healthy lungs as it relates to disease cohorts. The predominance of females may have led to some differences in the measured QCT parameters. The relatively narrow age range of the subjects has already been discussed. Also, the low level of recruitment of African-Americans indicates that no conclusions can be drawn regarding racial differences in QCT parameters.

CT scanner variation is a major factor when quantifying parameters of the lungs and airways. The utilization of numerous different types of scanners introduces more error into the measurements. Similarly, the lower mAs used in expiratory scanning in our subjects likely increased the noise and variability in those scans. Scanner manufacturers utilize different algorithms when compiling the raw data from the scans. The assorted reconstruction kernels lead to varying measures of tissue attenuation values, which in turn affect all of the QCT parameters. Further detailed study will need to be performed in order to establish a standard method of correcting for scanner related variation, perhaps based on phantom or tracheal air measurements. Also, the accuracy of the airway wall thickness, and similar variables, is limited by voxel resolution, particularly at the subsegmental level. Because of variations in slice thickness and interval available on different scanner models, we were unable to prescribe uniform voxel dimensions in this study, although submillimeter thickness and interval was achieved in all cases. We have shown that this variability in voxel dimensions affects the measures of airway wall parameters.

Conclusions

Although the attenuation characteristics of normal lung differ by age and gender, these associations do not persist on multivariate analysis. Potential sources of variation in measurement of attenuation-based quantitative CT parameters include depth of inspiration, CT resolution and scanner model. Adjustment for tracheal air attenuation may help alleviate some of the scanner-related variation present in QCT analysis. Since QCT parameters also vary by lobe, understanding of normal lobar values may improve regional QCT assessment of diffuse lung diseases. Sources of variation in QCT airway measurements include age, sex, BMI, depth of inspiration, and voxel resolution. Future studies will need to address these variations in order to gain the most precision from QCT techniques.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Demographics

	Male (n=29)	Female (n=63)	Total (n=92)
Age, years	63.4 (7.7)	62.3 (9.5)	62.7 (9.0)
BMI	28.1 (3.5)	28.1 (5.8)	28.1 (5.1)
Height, cm	175.3 (6.5)	161.8 (6.8)	166.0 (9.2)
FEV_1 , % pred	108.2 (13.8)	101.4 (13.4)	103.5 (13.8)
FVC, % pred	101.7 (11.8)	99.0 (12.6)	99.8 (12.4)
FEV_1/FVC	0.80 (0.05)	0.79 (0.04)	0.79 (0.04)

Table entries are means and standard deviations (in parentheses).

Table 2

Average Values for Lobar Attenuation Parameters

Parameter	Total Lung	RUL	RML	RLL	LUL	LLL	Upper Lobes and RML	Lower Lobes	P
Total Lung Capacity (L)	5.46 (1.18)	1.02 (0.23)	0.46 (0.13)	1.43 (0.35)	1.25 (0.29)	1.29 (0.35)	2.74 (0.59)	2.72 (0.68)	0.88
Functional Residual Capacity (L)	2.56 (0.46)	0.54 (0.11)	0.26 (0.08)	0.59 (0.12)	0.64 (0.14)	0.52 (0.12)	1.44 (0.30)	1.12 (0.22)	***<0.001****
% Volume Change	52.2 (8.2)	46.4 (9.2)	42.0 (10.9)	57.4 (7.9)	48.1 (9.5)	58.4 (8.2)	46.4 (9.0)	57.9 (7.9)	***<0.001****
%LAAI-950†	2.0 (2.7)	1.6 (2.4)	3.0 (3.7)	1.7 (2.3)	2.5 (3.5)	1.9 (2.4)	2.4 (3.2)	1.8 (2.3)	0.17
%LAAE-856†	9.2 (6.8)	10.6 (8.9)	20.9 (12.2)	4.1 (4.3)	12.0 (9.6)	3.6 (3.1)	14.5 (9.8)	3.8 (3.5)	***<0.001****
Mean inspiratory attenuation (HU)	−846 (22)	−847 (21)	−859 (19)	−840 (25)	−852 (21)	−838 (26)	−853 (19.8)	−839 (24.9)	<0.001*
Mean expiratory attenuation (HU)	−701 (33)	−726 (34)	-762 (30)	−660 (39)	−726 (38)	−654 (39)	−738 (31.6)	−657 (37.8)	<0.001*

† Arc sine transformations of the actual percentages were analyzed using a mixed-model analysis of variance with subject as a random effect (30). Probabilities refer to the comparison of upper lobe averages versus lower lobe averages.

Table 3

Univariate Analysis for Lung Attenuation Parameters: By Sex and Age

Parameter	Male (n=29)	Female (n=63)	P	Under 65 (n=46)	65 and Over (n=46)	P
Total Lung Capacity (L)	6.81 (0.83)	4.83 (0.69)	***<0.001****	5.48 (1.13)	5.44 (1.23)	0.88
Functional Residual Capacity (L)	2.91 (0.47)	2.39 (0.35)	***<0.001****	2.45 (0.40)	2.67 (0.50)	***0.02****
% Volume Change	57.1 (5.4)	49.8 (8.3)	***<0.001****	54.2 (8.3)	50.1 (7.7)	***0.02****
TLC % Predicted	98.5 (10.2)	98.8 (10.0)	0.88	99.2 (11.0)	98.2 (9.0)	0.63
FRC % Predicted	79.9 (11.8)	88.8 (11.5)	***0.001****	83.5 (12.8)	88.5 (11.2)	0.053
$\%LAA_{I\text{-}950}$ †	3.6 (3.2)	1.3 (2.0)	***<0.001****	2.6 (3.4)	1.5 (1.4)	0.11
$\%LAA_{E\text{-}856}$ †	9.6 (5.4)	9.0 (7.4)	0.35	8.7 (6.9)	9.8 (6.7)	0.30
Mean Inspiratory HU	−861 (14)	−838 (21)	***<0.001****	−847 (24)	−844 (19)	0.41
Mean Expiratory HU	−701 (26)	−701 (36)	0.97	−691 (36)	−711 (25)	***0.0022****

† Entries for these values represent actual percentages, but the arc sine transformations of the actual percentages were analyzed —this transformation is useful for percentages less than 30% or greater than 70%— (30).

Table 4a

Multiple regression analysis for % Inspiratory $LAA_{I\text{-}950}$

Source	b_{SD} *	95% CI†	P
TLC_{CT}	2.15	0.96, 3.33	***<0.001*** *
Age	0.15	−0.73, 1.02	0.74
Sex ‡	−1.21	−3.65, 1.23	0.33
BMI	−0.01	−0.72, 0.70	0.98
Scanner model	NA	NA	***<0.001*** *

The arc sine transformations of the actual percentages for % Inspiratory $LAA_{I\text{-}950}$ were analyzed (30).

Residual plots demonstrated that the regression model using the transformed values was appropriate.

* First-order coefficient that represents the change per SD change in predictor variable.

† 95% confidence interval.

‡ Females compared to males.

For a 1 SD increase in TLC_{CT}, % inspiratory $LAA_{I\text{-}950}$ increases 2.15; this change differs from zero (P<0.001). In women (compared to men), % inspiratory $LAA_{I\text{-}950}$ decreases by 1.21, but this change is consistent with zero (P=0.33).

Table 4b

Multiple regression analysis for % Inspiratory $LAA_{I\text{-}950}$: Tracheal Air Correction

Source	b_{SD} *	95% CI †	P
Mean Tracheal Air Attenuation	−1.75	−2.87, −0.62	***0.003*** *
TLC_{CT}	1.83	0.68, 2.97	***0.002*** *
Age	0.05	−0.78, 0.89	0.90
Sex ‡	−0.76	−3.12, 1.61	0.53
BMI	0.42	−0.32, 1.15	0.26
Scanner model	NA	NA	0.18

The arc sine transformations of the actual percentages for % Inspiratory $LAA_{I\text{-}950}$ were analyzed (30).

Residual plots demonstrated that the regression model using the transformed values was appropriate.

* First-order coefficient that represents the change per SD change in predictor variable.

† 95% confidence interval.

‡ Females compared to males.

For a 1 SD increase in mean tracheal air attenuation, % inspiratory $LAA_{I\text{-}950}$ decreases 1.75; this change differs from zero (P=0.003). For a 1 SD increase in TLC_{CT}, % inspiratory $LAA_{I\text{-}950}$ increases 1.83; this change differs from zero (P=0.002).

Table 5a

Multiple regression analysis for % Expiratory LAA_{E-856}

Source	b_{SD} *	95% CI†	P
FRC $_{CT}$	2.50	1.16, 3.84	***<0.001*** *
Age	2.67	1.33, 4.01	***<0.001*** *
Sex ‡	1.12	−1.58, 3.83	0.41
BMI	−0.09	−1.22, 1.03	0.87
Scanner model	NA	NA	***<0.001*** *

The arc sine transformations of the actual percentages for % Expiratory LAA_{E-856} were analyzed (30).

Residual plots demonstrated that the regression model using the transformed values was appropriate.

*First-order coefficient that represents the change per SD change in predictor variable.

†95% confidence interval.

‡Females compared to males.

Table 5b

Multiple regression analysis for % Expiratory LAA_{E-856}: Tracheal Air Correction

Source	b_{SD} *	95% CI †	P
Mean Tracheal Air Attenuation	−1.76	−3.75, 0.22	0.08
FRC_{CT}	2.00	0.57, 3.42	***0.007*** *
Age	2.45	1.02, 3.89	***0.001*** *
Sex ≠	0.89	−1.85, 3.63	0.52
BMI	0.18	−1.21, 1.58	0.80
Scanner model	NA	NA	***<0.001*** *

The arc sine transformations of the actual percentages for % Expiratory LAA_{E-856} were analyzed (30).

Residual plots demonstrated that the regression model using the transformed values was appropriate.

* First-order coefficient that represents the change per SD change in predictor variable.

† 95% confidence interval.

≠ Females compared to males.

Table 6

Multivariate Analysis for Segmental Airway Parameters

	AWT			ILA		
Source	**b_{SD}***	**95% CI†**	**P**	**b_{SD}***	**95% CI†**	**P**
TLC_{CT}	0.02	−0.03, 0.08	0.42	3.60	2.18, 5.01	***<0.001*** *
Age	0.00	−0.04, 0.03	0.85	1.30	0.39, 2.21	***0.006*** *
Sex	0.01	−0.11, 0.12	0.90	1.31	−1.56, 4.17	0.37
BMI	−0.01	−0.04, 0.03	0.72	0.13	−0.75, 1.01	0.77
Axial pixel size	0.11	0.05, 0.16	***<0.001*** *	1.05	−0.25, 2.35	0.11
Slice interval	0.01	−0.02, 0.05	0.45	0.45	−0.47, 1.36	0.33
	WA %			**Pi10**		
Source	b_{SD}*	95% CI†	P	b_{SD}*	95% CI†	P
TLC_{CT}	−1.90	−2.49, −1.30	***<0.001*** *	−0.02	−0.04, 0.01	0.25
Age	−0.54	−0.92, −0.16	***0.006*** *	0.01	−0.01, 0.02	0.53
Sex	−1.22	−2.42, −0.01	***0.05*** *	0.04	−0.01, 0.09	0.14
BMI	0.00	−0.37, 0.37	0.99	−0.005	−0.02, 0.01	0.58
Axial pixel size	0.61	0.06, 1.15	***0.03*** *	0.001	−0.02, 0.03	0.94
Slice interval	−0.41	−0.79, −0.03	***0.04*** *	0.003	−0.01, 0.02	0.76

*First-order coefficient that represents the change per SD change in predictor variable after the other predictor variables have been accounted for.

†95% confidence interval.

‡Females compared to males.

Residual plots demonstrated that these regression models were appropriate.