Kyung J. Park, MD
Colleen J. Bergin, MB, ChB
Jack L. Clausen, MD

Index terms:
Computed tomography (CT), three-dimensional, 60.12117
Emphysema, pulmonary, 60.751, 60.7511, 60.7512, 60.7513
Lung, CT, 60.751
Lung, density, 60.751

Radiology 1999; 211:541–547

Abbreviations:
D_{LCO} = diffusing capacity of the lungs for carbon monoxide
FEV_1 = forced expiratory volume in 1 second
FVC = forced vital capacity
TLC = total lung capacity
2D = two-dimensional
3D = three-dimensional

[1] From the Department of Diagnostic Radiology, Ajou University Medical Center, Suwon, South Korea (K.J.P.); and the Departments of Radiology (C.J.B.) and Pulmonary Medicine (J.L.C.), University of California Medical Center, San Diego. Received January 2, 1998; revision requested March 27; final revision received August 11; accepted November 5. Supported in part by National Institutes of Health grants R29-HL48854 and MO1 RR00827. **Address reprint requests to** C.J.B., Department of Radiology, Auckland Hospital, Park Road, Grafton, Auckland, New Zealand.

Author contributions:
Guarantor of integrity of entire study, C.J.B.; study concepts and design, C.J.B.; literature research, K.J.P.; clinical studies, K.J.P., J.L.C.; data acquisition, K.J.P., C.J.B., J.L.C.; data analysis, K.J.P., C.J.B.; statistical analysis, K.J.P.; manuscript preparation, K.J.P.; manuscript editing, K.J.P., C.J.B.; manuscript review, J.L.C.

Quantitation of Emphysema with Three-dimensional CT Densitometry: Comparison with Two-dimensional Analysis, Visual Emphysema Scores, and Pulmonary Function Test Results[1]

PURPOSE: To compare lung densitometric measurements that use a three-dimensional (3D) reconstruction of the lungs with those obtained from analysis of two-dimensional (2D) computed tomographic (CT) images, visual emphysema scores, and data from pulmonary function tests.

MATERIALS AND METHODS: Thoracic helical CT scans were obtained in 60 adult patients (35 with no visual evidence of emphysema and 25 with emphysema). The lungs were reconstructed as a 3D model on a commercial workstation, with a threshold of −600 HU. By analysis of histograms, the proportions of lung volumes with attenuation values below −950, −910, and −900 HU were measured, in addition to mean lung attenuation. These values were compared with lung densitometric results obtained from 2D CT images, visual emphysema scores, and data from pulmonary function tests.

RESULTS: Quantitation of emphysema with 3D reconstruction was efficient and accurate. Correlation was good among densitometric quantitation with 3D analysis, that obtained with 2D analysis (r = 0.98–0.99), and visual scoring (r = 0.74–0.82). Correlation was reasonable between 3D densitometric quantitation and the diffusing capacity of the lungs for carbon monoxide (D_{LCO}) (r = −0.57 to −0.64), total lung capacity (r = 0.62–0.71), forced expiratory volume in 1 second (FEV_1) (r = −0.57 to −0.60), and the ratio of FEV_1 to forced vital capacity (FVC) (r = −0.75 to −0.82). The visual CT quantitation of emphysema correlated best with D_{LCO} (r = −0.82) and FEV_1/FVC (r = −0.89).

CONCLUSION: Lung densitometry with 3D reconstruction of helical CT data is a fast and accurate method for quantifying emphysema.

Computed tomographic (CT) quantitation of emphysema has been correlated with pulmonary function (1–4) and has been used to predict postoperative function in patients with lung cancer (5); more recently, such quantitation has been used to demonstrate a decrease in emphysema after lung-volume reduction surgery (6–10). The two systems that are used for quantitation of emphysema are visual grading and more objective techniques that use CT software to distinguish pixels with abnormally low attenuation, representing emphysema, from those of normal lung.

First applied to two-dimensional (2D) CT sections, the ''density mask'' technique was shown to represent accurately the morphologic extent of emphysema (11), but this method is time-consuming to perform on multiple sections. Various automated and semiauto-

mated techniques subsequently have been developed to increase the speed with which emphysema in the whole lung can be quantitated (5–7,12–14), but such software has not been universally available.

With the advent of helical CT technology, volumetric data can now be acquired and manipulated with the use of three-dimensional (3D) lung reconstruction on software that is available on most commercial scanners. To our knowledge, measurements of lung attenuation obtained from 3D reconstruction have not been compared with those from 2D analysis or with visual assessment. The objectives of this study were to compare lung densitometric quantitation of emphysema obtained with the use of a 3D lung model reconstructed from helical CT data with densitometric measurements from analysis of 2D CT images, visual emphysema scores, and data from pulmonary function tests.

MATERIALS AND METHODS

Patients

Thoracic helical CT scans obtained without the use of intravascular contrast material from 60 patients older than 18 years between January and November 1997 were included for analysis. Patients were excluded if diffuse or focal parenchymal abnormalities affecting more than one pulmonary segment were identified, if there was bronchiectasis or pleural effusion, or if there was a clinical history of bronchial asthma, severe cardiac disease, or renal disease.

Patient data are summarized in Table 1. The patients included 37 men and 23 women whose ages ranged from 18 to 90 years (mean, 53.9 years). Clinical indications for the CT examinations were staging or metastatic work-up of malignant disease in 22 patients; further evaluation of a chest radiographic abnormality in 17 patients; assessment for pulmonary symptoms, including dyspnea and hemoptysis, in nine patients; evaluation of emphysema in eight patients; and suspected mediastinal abnormality in four patients.

At visual inspection of axial CT images, 25 patients had evidence of emphysema, and 35 had no evidence of emphysema. Twenty-three of the patients with emphysema were smokers, and six had panlobular emphysema (panacinar emphysema) associated with severe α_1-antitrypsin deficiency. The group with no clinical or CT evidence of emphysema included 10 smokers and 22 nonsmokers. Smoking histories were unavailable in five other patients.

TABLE 1
Patient Characteristics and Results of Pulmonary Function Tests, CT Densitometry, and Visual Assessment

Parameter	Patients with Visual Emphysema on CT Scan (n = 25)		Patients without Visual Emphysema on CT Scan (n = 35)	
	Mean ± SD	Range	Mean ± SD	Range
Age (y)	62.4 ± 11.8	33–80	47.8 ± 20.4	18–90
M/F ratio	18:7	NA	19:16	NA
No. of smokers	23	NA	10	NA
Pack-years	53.0 ± 39.0	5–150	29.2 ± 27.1	2–75
Pulmonary function				
D_{LCO} (% of predicted)	44.7 ± 23.6*	4–76*	79.6 ± 14.3†	57–98†
TLC (% of predicted)	119.7 ± 21.6‡	95–182‡	100.6 ± 18.6†	68–119†
FEV_1 (% of predicted)	46.8 ± 19.3§	15–79§	93.7 ± 26.2†	45–119†
FEV_1/FVC (%)	44.2 ± 15.0§	21–69§	78.4 ± 6.0†	70–86†
3D measurements				
Mean attenuation (HU)	−858 ± 26	−800 to −907	−809 ± 37	−715 to −870
Lower attenuation volume (%)				
−950 HU	8.3 ± 8.5	0.1–32.9	0.4 ± 0.5	0–1.9
−910 HU	27.5 ± 17.0	1.0–63.3	5.1 ± 10.4	0–30.3
−900 HU	34.0 ± 18.1	2.3–68.3	8.2 ± 10.4	0.1–41.9
2D measurements				
Mean attenuation (HU)	−864 ± 25	−813 to −905	−816 ± 38	−726 to −881
Lower attenuation area (%)				
−950 HU	9.4 ± 8.4	0.1–30.4	0.5 ± 0.6	0–2.4
−910 HU	30.4 ± 16.9	1.0–61.7	6.2 ± 8.5	0–36.1
−900 HU	36.6 ± 18.1	2.5–66.5	9.7 ± 12.2	0.1–48.6
Visual emphysema score	2.21 ± 1.07	0.25–4.00	0	0

Note.—NA = not applicable.
* Data from 17 patients.
† Data from seven patients.
‡ Data from 16 patients.
§ Data from 19 patients.

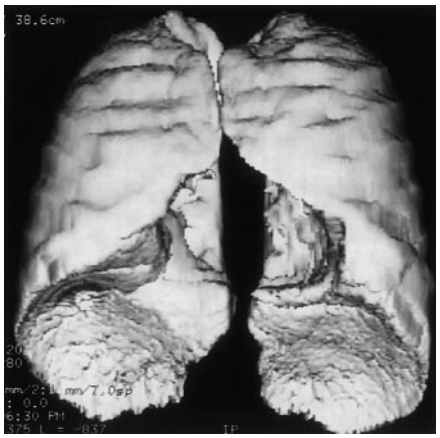
CT Technique

CT examinations were performed with a commercially available scanner (HiSpeed Advantage; GE Medical Systems, Milwaukee, Wis) in the helical mode without intravascular contrast material. With the patient in the supine position, scans were obtained during full inspiration, with the following parameters: 120 kVp, 250–280 mA, 7-mm (56 patients) or 5-mm (four patients) collimation, and a pitch of 1.5. At our institution, 7-mm collimation is used for most thoracic helical CT scans. Thinner collimation was used to investigate hemoptysis or for better evaluation of the tracheobronchial tree. Inspiratory scans were selected because of their reported greater accuracy in depicting anatomic emphysema (15). Scan volumes extended from the thoracic inlet to the lung base and were acquired in two breath-hold periods. Lung images were reconstructed with the lung algorithm.

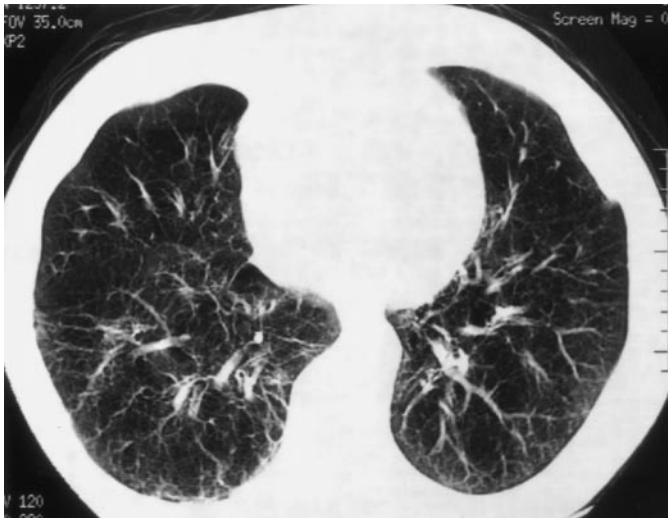
Densitometry

The 3D models of the lungs were reconstructed with the Advantage Windows 3D Analysis Package (GE Medical Systems). The time for reconstruction of the 3D model was reduced considerably by not using the high-resolution mode that manipulates a voxel matrix of 512 × 512 pixels. Threshold limits of −600 to −1,024 HU were applied to exclude soft tissue surrounding the lung and large vessels within the lung. The 3D model was viewed as a shaded surface display at multiple angles to ensure that the model was valid (Fig 1). The trachea, main-stem bronchi, and gastrointestinal structures were selectively removed from the model.

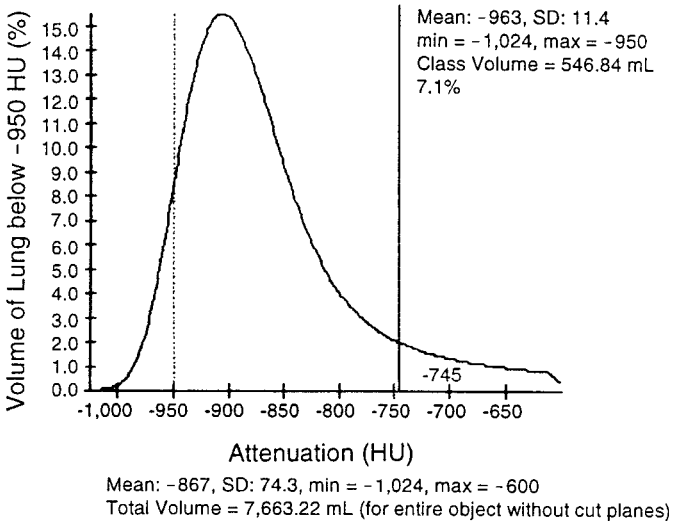
A histogram display of the model showed the volume, attenuation distribution, mean attenuation, and SD of attenuation of the whole lung. The histogram provided a frequency distribution of voxels with specific attenuation numbers (in Hounsfield units) in the lung. The percentage of voxels with attenuation values below a specified level is defined as the lower attenuation volume at that threshold. Values for the lower attenuation volume at thresholds of −950, −910, and −900 HU were measured by moving the boundary line on the histogram (Fig 1).



a.



b.



c.

Figure 1. Images and graph of data from a 53-year-old man with panlobular emphysema. **(a)** Three-dimensional shaded surface display of the lungs reconstructed from helical CT data is the type of model from which both 2D and 3D attenuation measurements are obtained. **(b)** Axial CT image demonstrates lower lobar emphysema, as shown by areas of hypoattenuation and splaying of pulmonary vessels. **(c)** Graph obtained from the 3D data set indicates the percentage volume of the lung below −950 HU, the total lung volume, and mean lung attenuation.

With this program, 2D axial images can also be analyzed with the same pixel attenuation range as that chosen for the voxel attenuation values on the 3D lung model. We measured the cross-sectional area of the lung, the mean lung attenuation, and the percentage of the cross-sectional area with lower attenuation (lower attenuation area) at thresholds of −950, −910, and −900 HU. The 2D densitometry was performed on axial images selected from three levels: the top of the aortic arch, through the carina, and at the level of the left atrium. The mean values for the lower attenuation area for these three sections were calculated for each patient to provide the mean 2D estimate of the extent of emphysema.

Visual Emphysema Score

On hard-copy CT images photographed at a window width of 1,500 HU and centered at a level of −600 HU, visual emphysema scores for all axial sections were determined for each patient. Emphysema was identified as areas of hypovascular low attenuation and was graded with a five-point scale based on the percentage of lung involved: 0, no emphysema; 1, up to 25% of lung parenchyma involved; 2, between 26% and 50% of lung parenchyma involved; 3, between 51% and 75% of lung parenchyma involved; and 4, between 76% and 100% of lung parenchyma involved. Grades for the axial images of each lung were added and divided by the number of images evaluated to yield emphysema scores that ranged from 0 to 4.

Pulmonary Function Tests

The results of pulmonary function tests were available for 26 patients. The interval between pulmonary function tests and CT examinations was less than 8 months for all but two patients. In one patient with panlobular emphysema, the interval was 3½ years, and in a patient with centrilobular emphysema, the interval was 15 months. The measures of pulmonary function tested included the forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), total lung capacity (TLC), and diffusing capacity of the lung for carbon monoxide (D_{LCO}). Values for FEV_1, TLC, and D_{LCO} were expressed as the percentages of predicted values (percentage of predicted).

Spirometry was performed in accord with the 1987 American Thoracic Society standards (16), and single-breath D_{LCO} measurements were obtained in accord with the 1987 American Thoracic Society recommendations (17). D_{LCO} values were adjusted for the most recently measured hemoglobin concentration in accord with the American Thoracic Society standards (17). TLC values were measured with a variable-pressure body plethysmograph. All pulmonary function tests were per-

formed with a pneumotachograph-based system (Master Lab models; Erich Jaeger, Würzburg, Germany). The predicted normal values used were those of Crapo et al (18) for spirometric data, those of Miller et al (19) for DLCO, and those of Goldman and Becklake (20) for TLC.

Statistical Analysis

The Student *t* test was used to compare the two groups of patients (with and without visual evidence of emphysema) with regard to the mean values of (*a*) lung attenuation; (*b*) lower attenuation volumes at thresholds of −950, −910, and −900 HU; and (*c*) lower attenuation areas at thresholds of −950, −910, and −900 HU.

Pearson correlation was used to compare data from pulmonary function tests with densitometric values obtained from both 3D and 2D analyses that included mean attenuation and lower attenuation volume at −950, −910, and −900 HU. Pearson correlation was also used to compare measures of lower attenuation volume at −950, −910, and −900 HU obtained with 3D densitometry with those obtained with 2D densitometry. The relationships between visual emphysema scores and measurements of lung attenuation were evaluated with Spearman rank correlation. A commercially available computer program (PC!INFO; Retriever Data Systems, Seattle, Wash) was used for statistical analysis.

RESULTS

The 3D lung models took little time to reconstruct and were easily analyzed to generate histograms of attenuation in Hounsfield units for the lungs of each patient. The mean time for reconstruction of the lung model and 3D analysis for each patient was less than 10 minutes. The time to reconstruct the lung model would have been longer had a high-resolution algorithm been used.

Because the 2D sections were selected after postprocessing removal of the esophagus and tracheobronchial structures, 2D analysis also took approximately 10 minutes. The time for visual inspection of all sections in each patient varied from 10 to 15 minutes.

A summary of the densitometric data obtained from 3D models and 2D axial images, visual emphysema scores, and pulmonary function tests is shown in Table 1. Mean values of lung attenuation and of lower attenuation volume and lower attenuation area at thresholds of −950, −910, and −900 HU were significantly larger for patients with visual evidence of emphysema than for those in whom no visual evidence of emphysema was seen on the CT scans ($P < .01$ for all parameters).

Close correlation was observed between lung attenuation measurements obtained with the 3D model and those from the 2D axial images, with correlation coefficients (*r*) of 0.98 (−950 HU), 0.98 (−910 HU), and 0.99 (−900 HU). Attenuation measurements obtained from both the 3D model and from the 2D axial sections correlated well with visual emphysema scores, with the closest correlation demonstrated for lower attenuation volume at −950 HU and lower attenuation area at −950 HU (Table 2, Fig 2).

We found that the visual CT scoring system correlated better than either 2D or 3D densitometric measurements with DLCO (percentage of predicted) (r = −0.82) and FEV_1/FVC ($r = -0.89$). Correlation was reasonable between each of the lower attenuation volumes obtained from 3D models and DLCO (percentage of predicted), TLC (percentage of predicted), FEV_1 (percentage of predicted), and FEV_1/FVC. The lower attenuation volume at −950 HU correlated more closely with DLCO (percentage of predicted) and FEV_1 (percentage of predicted) than did either lower attenuation volume at −910 HU or lower attenuation volume at −900 HU.

TABLE 2
Correlation of Visual Emphysema Scores with Results of Densitometry and Pulmonary Function Tests (Spearman Rank Correlation)

Variable	Correlation Coefficient	No. of Data	*P* value
3D measurements			
Lower attenuation volume			
−950 HU	0.82	60	<.001
−910 HU	0.77	60	<.001
−900 HU	0.74	60	<.001
Mean attenuation	−0.70	60	<.001
2D measurements			
Lower attenuation area			
−950 HU	0.82	60	<.001
−910 HU	0.76	60	<.001
−900 HU	0.74	60	<.001
Mean attenuation	−0.70	60	<.001
Pulmonary function tests			
DLCO (% of predicted)	−0.82	24	<.001
TLC (% of predicted)	0.46	23	.028
FEV_1 (% of predicted)	−0.73	26	<.001
FEV_1/FVC (%)	−0.89	26	<.001

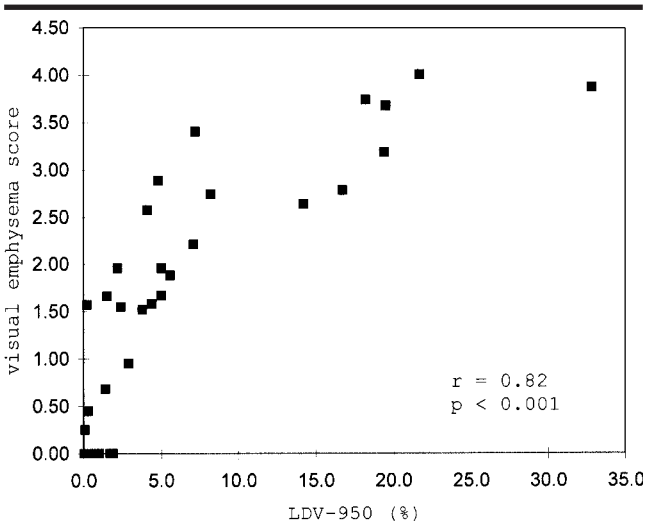


Figure 2. Graph shows correlation between lower attenuation volume below −950 HU (*LDV-950*) and visual emphysema score.

TABLE 3
Correlation Coefficients for Comparison between Data from Densitometry and Data from Pulmonary Function Tests (Pearson Correlation)

Parameter	D_{LCO} (n = 24)	TLC (n = 23)	FEV_1 (n = 26)	FEV_1/FVC (n = 26)
3D measurements				
Lower attenuation volume				
−950 HU	−0.64*	0.62*	−0.60*	−0.75†
−910 HU	−0.64*	0.70†	−0.59*	−0.83†
−900 HU	−0.57*	0.71†	−0.57*	−0.82†
Mean attenuation	0.54*	−0.65*	0.52*	0.75†
2D measurements				
Lower attenuation area				
−950 HU	−0.69†	0.61*	−0.62*	−0.76†
−910 HU	−0.63*	0.68†	−0.60*	−0.83†
−900 HU	−0.59*	0.68†	−0.55*	−0.80†
Mean attenuation	0.56*	−0.61*	0.51*	0.73†

Note.—TLC, D_{LCO}, and FEV_1 are the values in percentage of predicted.
* Significance: $P < .01$.
† Significance: $P < .001$.

Lower attenuation volumes at −900 and −910 HU correlated more closely with TLC (percentage of predicted) and with FEV_1/FVC, respectively (Table 3, Fig 3). Correlations between data from each of the pulmonary function tests and measurements of lower attenuation area obtained from the 2D axial images were very similar to those obtained from the 3D models.

DISCUSSION

Measurement of CT pixel attenuation values provides an objective method for quantitating emphysema, but analysis of multiple 2D sections is limited by time constraints. Various automated and semiautomated CT techniques have been designed to separate the lungs from other soft tissues and thereby reduce the time involved for this analysis, but these techniques have been limited by the availability of necessary hardware or by software requirements.

However, voxel attenuation values can now be measured without the need to transfer data to other computer systems. With software that is available on most modern commercial scanners, 3D lung models can be generated with volumetric data acquired in the helical mode. The lungs are easily separated from soft-tissue structures and from structures with lower attenuation, such as the trachea, mainstem bronchi, and esophagus, with minimal postprocessing on the shaded surface display. With this model, the proportion of voxels with attenuation values within the range of emphysema is readily determined by moving a boundary line to the defined threshold on a histogram of attenuation values that represent the whole lung.

Reproducibility of lung attenuation measurements is known to be affected by patient factors and by variation in CT scanning techniques (21,22). Enhancement with contrast media increases lung attenuation (23), and a change in section thickness may also affect measured Hounsfield numbers (23,24). Kilovoltage, positioning of the patient in the scanner, the reconstruction algorithm, and the type of scanner all have been described as affecting the reproducibility of CT densitometric measurements, although with modern scanners, these factors are considered to have minimal influence (24).

One of the most important factors that influence the reproducibility of lung attenuation measurements is the respiratory status of the patient. Spirometric gating has been used to control for depth of inspiration (14,25), but with helical CT, only one or two breath holds are necessary to scan the entire lungs, which greatly diminishes the problems of motion artifacts and respiratory misregistration.

We found that acquiring CT data in the helical mode and using the reconstructed 3D model improved our efficiency in quantitating emphysema and provided values that were very similar to those obtained from analysis of 2D images. Because of the well-known heterogeneous distribution of emphysema, we expected 3D analysis of the whole lung to reflect the extent of emphysema more accurately than evaluation of three axial sections but instead found very close correlation between the two techniques. Lung attenuation measurements obtained from voxels with the use of the 3D lung model correlated well with those obtained from 2D axial images and also with visual assessment.

In our study, visual inspection scores correlated more closely with D_{LCO} (percentage of predicted) and FEV_1/FVC than did either the 2D or 3D analyses. Müller et al (11) also found visual scoring of emphysema to be comparable in accuracy to the 2D density mask method correlated with pathologic scores. However, visual inspection is known to be affected by observer experience, by interobserver and intraobserver variability (26), and by technical factors such as window settings. Correlation between each of the lower attenuation volume thresholds and pulmonary function measurements was similar to lower attenuation areas measured by others with the density mask (2).

To distinguish patients with emphysema from those with no emphysema, we used visual inspection of CT images; this was based on the recognized superiority of CT scans, compared with pulmonary function tests, for use in identifying emphysema (3,21,27–29). Differences in mean pulmonary function data between these groups helped to confirm the visual impression that patients in the group with emphysema were physiologically different from those with no visual evidence of emphysema. The six patients with α_1-antitrypsin deficiency likely contribute to the marked difference in mean values for lower attenuation volume, lower attenuation area, and pulmonary function data between these two groups; however, an additional 19 patients in the group with emphysema had visual CT evidence of centrilobular emphysema (centriacinar emphysema).

Some overlap in pulmonary function existed between the group with and the group without emphysema, particularly in measurements of TLC (percentage of predicted) and FEV_1 (percentage of predicted). The broad range noted in patients with no visual CT evidence of emphysema is likely caused by airways disease not detected on CT images and emphasizes the limitations of pulmonary function tests in quantitating emphysema (3,27,28).

The low attenuation thresholds that have been used most widely to identify emphysema on conventional 10-mm-thick CT sections are −900 or −910 HU (2,5,6,11,13). In some studies, CT scans were obtained after intravenous administration of contrast material. Using thin-

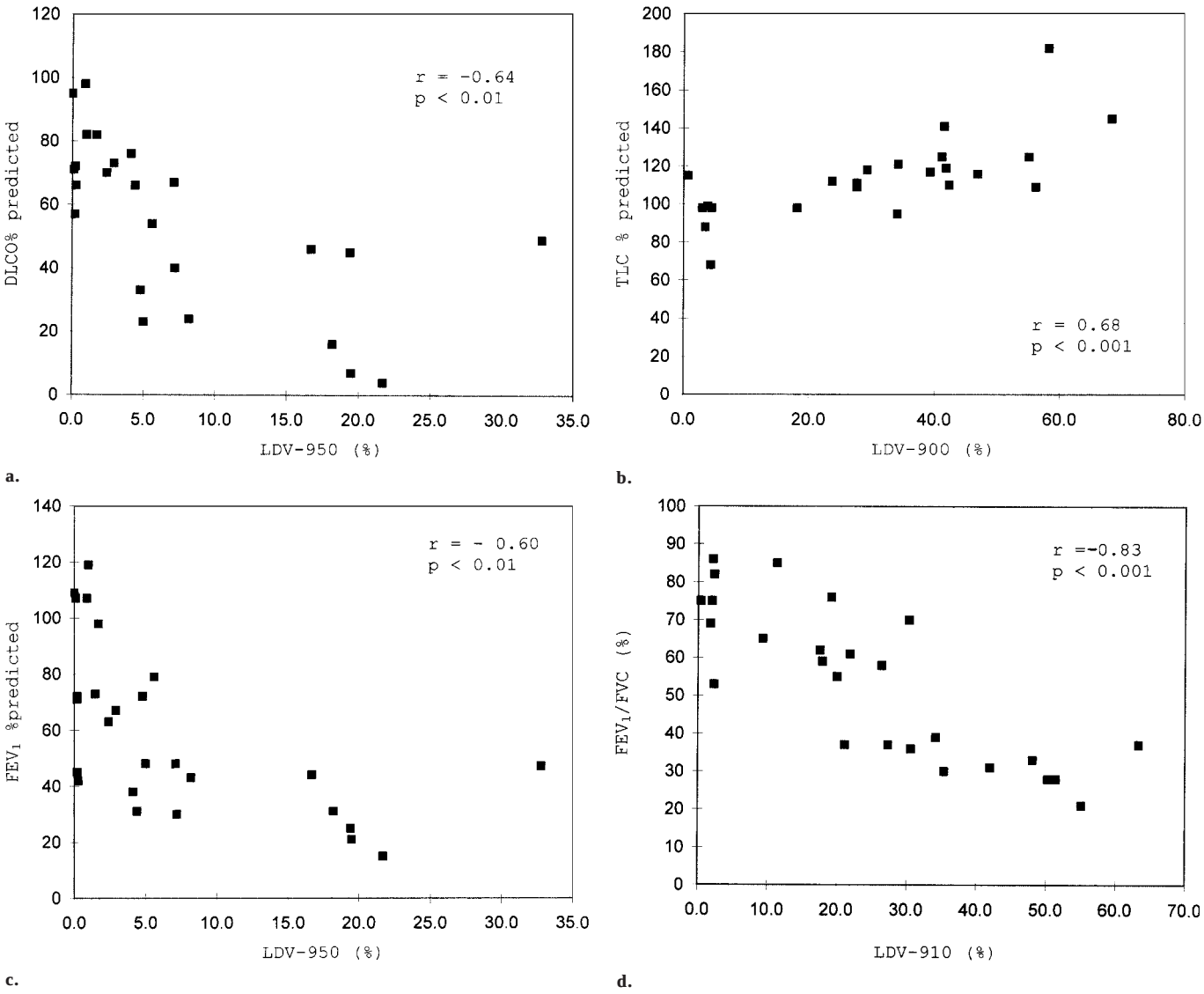


Figure 3. Graphs show closest correlations between attenuation measurements and pulmonary function. **(a)** Relationship between lower attenuation volume below −950 HU (*LDV-950*) and DLCO (percentage of predicted). **(b)** Relationship between lower attenuation volume below −900 HU (*LDV-900*) and TLC (percentage of predicted). **(c)** Relationship between lower attenuation volume below −950 HU (*LDV-950*) and FEV_1 (percentage of predicted). **(d)** Relationship between lower attenuation volume below −910 HU (*LDV-910*) and FEV_1/FVC.

section CT scans at 1-mm collimation without intravenous administration of contrast material, Gevenois et al (30,31) found that a lower attenuation threshold of −950 HU correlated best with morphologic emphysema. No intravascular administration of contrast material was used in our study, in which we also found that the lower attenuation volume threshold of −950 HU obtained with both 3D and 2D analysis correlated marginally better with visual grades, DLCO (percentage of predicted), and FEV_1 (percentage of predicted) than did either −910 or −900 HU but correlated less closely with TLC (percentage of predicted) and FEV_1/FVC.

With the recent development of surgical and pharmacologic methods for treating patients with emphysema, accurate quantification of lung destruction in this disease is becoming increasingly relevant. Lung-volume reduction surgery is being performed more frequently to improve pulmonary function and exercise tolerance in patients with severe emphysema, and CT quantification of emphysema has been used both for patient selection and to evaluate surgical outcome in these patients (6–10). For purposes of patient selection or surgical planning, the distribution of emphysema is better appreciated by viewing the axial CT images; however, emphysema distribution can be quantitated by reconstructing the upper and lower halves of the lungs separately in three dimensions (9,10,32).

Antielastolytic agents are being evaluated for potential roles in preventing progressive lung destruction in patients with panlobular emphysema caused by α_1-antitrypsin deficiency (33), but the feasibility of studies to assess the efficacy of these new therapeutic options is markedly limited by the relative insensitivity of tools for assessing outcome (34). Efficient quantitation of emphysema in these patients may help both in the selection of patients for drug therapy and in the assessment of the therapeutic results.

In conclusion, we found that lung attenuation measurements obtained from

3D lung models that were reconstructed from volumetric helical CT data accurately distinguished patients with emphysema from those with normal lungs, correlated closely with both 2D analysis and visual quantitation, and showed significant correlation with measurements of D_{LCO} (percentage of predicted), TLC (percentage of predicted), FEV_1 (percentage of predicted), and FEV_1/FVC. Lung densitometry derived from 3D lung models was easily and efficiently performed and provides a widely available alternative to 2D methods for quantifying emphysema.

References

1. Sakai F, Gamsu G, Im JG, Ray CS. Pulmonary function abnormalities in patients with CT-determined emphysema. J Comput Assist Tomogr 1987; 11:963–968.
2. Kinsella M, Müller NL, Staples C, Abboud RT, Morrison NJ, DyBuncio A. Quantitation of emphysema by computed tomography using a ''density mask'' program and correlation with pulmonary function test. Chest 1990; 97:315–321.
3. Gurney JW, Jones KK, Robbins RA, et al. Regional distribution of emphysema: correlation of high-resolution CT with pulmonary function tests in unselected smokers. Radiology 1992; 183:457–463.
4. Sakai N, Mishima M, Nishimura K, Itch H, Kuno K. An automated method to assess the distribution of low attenuation areas on chest CT scans in chronic pulmonary emphysema patients. Chest 1994; 106: 1319–1325.
5. Wu MT, Chang JM, Chiang AA, et al. Use of quantitative CT to predict postoperative lung function in patients with lung cancer. Radiology 1994; 191:257–262.
6. Bae KT, Slone RM, Gierada DS, Yusen RD, Cooper JD. Patients with emphysema: quantitative CT analysis before and after lung volume reduction surgery. Radiology 1997; 203:705–714.
7. Gierada DS, Slone RM, Bae KT, Yusen RD, Lefrak SS, Cooper JD. Pulmonary emphysema: comparison of preoperative quantitative CT and physiologic index values with clinical outcome after lung-volume reduction surgery. Radiology 1997; 205: 235–242.
8. Holbert JM, Brown ML, Sciurba FC, Keenan RJ, Landreneau RJ, Holzer AD. Changes in lung volume and volume of emphysema after unilateral lung reduction surgery: analysis with CT lung densitometry. Radiology 1996; 201:793–797.
9. Kazerooni EA, Martinez FJ, Quint LE, Whyte RI. Quantitative helical CT indexes of emphysema as predictors of outcome after lung volume reduction surgery (abstr). Radiology 1996; 201(P):298.
10. Kazerooni EA, Whyte RI, Flint A, Martinez FJ. Imaging of emphysema and lung volume reduction surgery. RadioGraphics 1997; 17:1023–1036.
11. Müller NL, Staples CA, Miller RR, Abboud RT. ''Density mask'': an objective method to quantitate emphysema using computed tomography. Chest 1988; 94:782–787.
12. Kalender WA, Fichte H, Bautz W, Skalej M. Semiautomatic evaluation procedures for quantitative CT of the lung. J Comput Assist Tomogr 1991; 15:248–255.
13. Archer DC, Coblentz CL, deKemp RA, Nahmias C, Norman G. Automated in vivo quantification of emphysema. Radiology 1993; 188:835–838.
14. Zagers R, Vrooman HA, Aarts NJ, et al. Quantitative analysis of computed tomography scans of the lungs for the diagnosis of pulmonary emphysema: a validation study of a semiautomated contour detection technique. Invest Radiol 1995; 9:552–562.
15. Genevois PA, De Vuyst P, Sy M, et al. Pulmonary emphysema: quantitative CT during expiration. Radiology 1996; 199: 825–829.
16. Standardization of spirometry: 1987 update—statement of the American Thoracic Society. Am Rev Respir Dis 1987; 136:1285–1298.
17. Single breath carbon monoxide diffusing capacity (transfer factor): recommendation for a standard technique. Am Rev Respir Dis 1987; 136:1299–1307.
18. Crapo RO, Morris AH, Gardner RM. Reference spirometric values using techniques and equipment that meet ATS recommendations. Am Rev Respir Dis 1981; 123:659–664.
19. Miller A, Thornton JC, Warshaw R, Anderson H, Teirstein AS, Selikoff IJ. Single breath diffusing capacity in a representative sample of the population of Michigan, a large industrial state: predicted values, lower limits of normal, and frequencies of abnormality by smoking history. Am Rev Respir Dis 1983; 127:270–277.
20. Goldman HI, Becklake MR. Respiratory function tests: normal values at median altitudes and the prediction of normal results. Am Rev Tuberc 1959; 79:457–467.
21. Stern EJ, Frank MS. CT of the lung in patients with pulmonary emphysema: diagnosis, quantification, and correlation with pathologic and physiologic findings. AJR 1994; 162:791–798.
22. Thurlbeck WM, Müller NL. Emphysema: definition, imaging, quantification. AJR 1994; 163:1017–1025.
23. Adams H, Bernard MS, McConnochie K. An appraisal of CT pulmonary density mapping in normal subjects. Clin Radiol 1991; 43:238–242.
24. Kemerink GJ, Lamers RJS, Thelissen GRP, van Engelshoven JMA. Scanner conformity in CT densitometry of the lungs. Radiology 1995; 197:749–752.
25. Lamers RJ, Thelissen GR, Kessels AG, Wouters EF, Engelshoven JM. Chronic obstructive pulmonary disease: evaluation with spirometrically controlled CT lung densitometry. Radiology 1994; 193:109–113.
26. Bergin CJ, Müller NL, Nichols DM, et al. The diagnosis of emphysema: a computed tomographic-pathologic condition. Am Rev Respir Dis 1986; 133:541–546.
27. Klein JS, Gamsu G, Webb WR, Golden JA, Müller NL. High-resolution CT diagnosis of emphysema in symptomatic patients with normal chest radiographs and isolated low diffusing capacity. Radiology 1992; 182:817–821.
28. Sanders C, Nath PH, Bailey WC. Detection of emphysema with computed tomography: correlation with pulmonary function tests and chest radiography. Invest Radiol 1988; 23:262–266.
29. Miniati M, Filippi E, Falaschi F, et al. Radiologic evaluation of emphysema in patients with chronic obstructive pulmonary disease: chest radiography versus high resolution computed tomography. Am J Respir Crit Care Med 1995; 151: 1359–1367.
30. Gevenois PA, de Maertelaer V, De Vuyst P, Zanen J, Yernault JC. Comparison of computed density and macroscopic morphometry in pulmonary emphysema. Am J Respir Crit Care Med 1995; 152:653–657.
31. Gevenois PA, De Vuyst P, de Maertelaer V, et al. Comparison of computed density and microscopic morphometry in pulmonary emphysema. Am J Respir Crit Care Med 1996; 154:187–192.
32. Hartman TE, Tazelaar HD, Swensen SJ, Müller NL. Cigarette smoking: CT and pathologic findings of associated pulmonary diseases. RadioGraphics 1997; 17: 377–390.
33. Schwaiblmair M, Vogelmeier C, Fruhmann G. Long-term augmentation therapy in 20 patients with severe alpha-l-antitrypsin deficiency: three-year follow-up. Respiration 1997; 64:10–15.
34. Hutchison DCS, Hughes MD. Alpha-l-antitrypsin replacement therapy: will its efficacy ever be proved? Eur Respir J 1997; 10:2191–2193.