

# Multi-detector CT of the Chest: Influence of Dose Onto Quantitative Evaluation of Severe Emphysema A Simulation Study

Julia Zaporozhan, MD,\* Sebastian Ley, MD,\*† Oliver Weinheimer,‡ Ralf Eberhardt, MD,§ Ioannis Tsakiris,\* Yasuhiro Noshi,|| Felix Herth, MD, PhD,§ and Hans-Ulrich Kauczor MD, PhD\*

**Purpose:** Quantitative evaluation of the lung parenchyma might be impaired or unreliable by use of reduced-dose CT protocols. Aim of the study was to define the threshold where reduced dose has significant impact on quantitative emphysema parameters.

**Materials and Methods:** Thirty patients with severe centrilobular emphysema underwent multidetector computed tomography (120 kV, 150 mAs). Original CT raw data were simulated using 10 mAs settings (10–100 SIMmAs). Quantitative analysis provided lung volume, emphysema volume, emphysema index, mean lung density, and 4 emphysema volume classes. Simulated low-dose results were compared with original acquisition.

**Results:** Emphysema index showed no clinical relevant variation down to 30 SIMmAs. The large emphysema volume class was significantly different below 50 SIMmAs. The intermediate and small classes showed an overproportional variation below 50 SIMmAs.

**Conclusions:** Dose reduction down to 30 SIMmAs is possible for clinical routine. Settings below 50 SIMmAs significantly alter the in-detailed 3-dimensional emphysema quantification.

**Key Words:** 3-dimensional quantitative volumetric analysis, dose simulation, multidetector computed tomography, low dose, emphysema

(*J Comput Assist Tomogr* 2006;30:460–468)

Pulmonary emphysema is defined by the American Thoracic Society as an abnormal permanent enlargement of the air spaces distal to the terminal bronchiole, accompanied by the destruction of their walls, most often caused by COPD or  $\alpha_1$ -antitrypsin deficiency.<sup>1</sup> High-resolution computed tomography (HRCT) is currently the method of choice for noninvasive and sensitive assessment of pathologic

changes in emphysema and has been shown to correlate well with pathological grading.<sup>2,3</sup> The introduction of multi-detector computed tomography (MDCT) provided a powerful advantage of 3-dimensional imaging of the lungs. However, the new protocols with thin collimation resulted in a potential increase in radiation dose. To counteract the noise inherent to thin sections, high exposure factors (120–140 kV and 240–300 mA) were originally recommended for high-resolution protocols with MDCT<sup>4</sup> but lower dose techniques have since been investigated. The kV and mAs used in high-resolution protocols with MDCT vary between 140 kV/70 mAs,<sup>5</sup> 120–140 kV/90–120 mAs,<sup>6</sup> and 140 kV/140 mAs.<sup>7</sup> The image quality is usual assessed by visual, subjective grading. The quality and diagnostic accuracy of low dose scans are not significantly different from standard dose scans.<sup>8–10</sup> Comparing HRCT images at two-dose levels it was found that some case failed to demonstrate subtle ground glass opacity and emphysema despite satisfactory visualization of the lung parenchyma.<sup>11</sup>

Objective quantification of emphysema can be obtained by measuring the relative lung area occupied by pixels with attenuation values below a predetermined threshold. One example is the so called emphysema index (EI).<sup>12</sup> Objective methods are preferable over those based on visual scoring because they reflect the extent of macroscopic emphysema more precisely and are less operator dependent.<sup>13</sup> Low-attenuation areas on CT represent macroscopic and microscopic emphysematous changes of the lung.<sup>14</sup>

Beside pure analysis of EI, CT data can be approached by more sophisticated analysis tools. Contiguous emphysema areas can be clustered to obtain the volumes for small-, medium-, and large-sized emphysematous areas.<sup>15</sup> The cluster distribution was reported to be useful in revealing the pattern of progression of emphysema. However, such advanced analysis tools were only applied to thick slice CT scans.<sup>16</sup> If low-dose protocols associated with higher noise levels were used, quantitative evaluation could be impaired or unreliable.

Because no systematic analyses of the influence of reduced dose onto quantitative results are known, the aim of this study was to investigate the effects of reduced-dose 3-dimensional HRCT protocols onto quantitative evaluation of emphysema and characterization using a raw data simulator. The first endpoint was to look at the influence of reduced-dose protocols onto conventional quantitative

From the \*Department of Radiology (E 010), German Cancer Research Center, Heidelberg, Germany; †Department of Pediatric Radiology, Ruprecht-Karls-University, Heidelberg, Germany; ‡Department of Radiology, Johannes Gutenberg University Hospital, Mainz, Germany; §Department of Pulmology, Thoraxklinik, Heidelberg, Germany; and ||CT Application and Research Group, CT Systems Development Department, Toshiba Medical Systems Corporation, Tochigi, Japan.

Received for publication October 25, 2005; accepted October 25, 2005.

Reprints: Julia Zaporozhan, MD, Department of Radiology E010, German Cancer Research Center, Im Neuenheimer Feld 280, 69120 Heidelberg, Germany (e-mail: juliazapo@web.de).

Copyright © 2006 by Lippincott Williams & Wilkins

**TABLE 1.** Mean Values for LV, MLD, EV, EI, and 4 EC

Original 150 mAs	LV (L)	MLD (HU)	EV (L)	EI (%)
	7.08 ± 1.44	−897 ± 18	3.81 ± 1.39	52.28 ± 10.31
	Volume of EC classes (L)			
	Class 4	Class 3	Class 2	Class 1
	3.60 ± 1.43	0.02 ± 0.01	0.12 ± 0.04	0.03 ± 0.01

parameters such as EI. For this, the clinical relevance of dose reduction was proofed. The second endpoint was to evaluate the influence of noise onto quantitative evaluation on a more subtle structural level. Therefore, dedicated volumetric emphysema classification analysis was used.

### MATERIALS AND METHODS

Ten female and 20 male patients (mean [±SD] age 61 ± 8 years, range 41–76) were included in this study. All patients were suffering clinically from COPD and radiological evaluation revealed severe emphysema (no patient presented with  $\alpha_1$ -antitrypsin deficiency). Patients had a smoking history of 42 ± 21 packyears (range 10–120 packyears).

The mean FEV<sub>1</sub> percentage predicted was (33 ± 9)% (range 21–62%), and the body mass index of our study population was 24 ± 3 kg/m<sup>2</sup> (range 19–30 kg/m<sup>2</sup>).

The study was approved by the local ethics committee. All subjects were informed before the investigation. The CT examination was performed as part of routine standard workup of the patients for tentative surgical<sup>17</sup> or endobronchial treatment.<sup>18,19</sup> Inclusion criteria for the tentative treatment were a past smoking history, severe changes in lung function tests indicative for obstructive disease, and no  $\alpha_1$ -antitrypsin deficiency.

Computed tomography was performed using a 16-detector CT (Aquilion-16, Toshiba, Japan) as part of standard clinical investigation. The scanner was calibrated regularly

**TABLE 2.** Median and Quartile for the Distribution of LV, EV, EI, and Large (Class 4), Intermediate (Class 3), and Small (Class 2 and 1) EC

Simulated Dose (mAs)	Median and (Quartile) for Distribution of				Effective Dose (mSv)
	LV (L)	MLD (HU)	EV (L)	EI (%)	
150 (original)	6.85 (5.90–8.18)	−869 (−909.75; −880.25)	3.72 (2.78–4.78)	52.11 (43.3–60.39)	7.6
100	6.85 (5.90–8.18)	−896 (−909.75; −880.25)	3.72 (2.78–4.79)	52.14 (43.41–60.41)	5.0
90	6.85 (5.90–8.18)	−896 (−909.75; −880.25)	3.72 (2.78–4.79)	52.17 (43.44–60.43)	4.5
80	6.85 (5.90–8.18)	−896 (−909.75; −880.25)	3.73 (2.79–4.79)	52.19 (43.49–60.44)	4.0
70	6.85 (5.90–8.18)	−896 (−909.75; −880.25)	3.73 (2.79–4.79)	52.23 (43.56–60.46)	3.5
60	6.85 (5.90–8.18)	−896 (−909.75; −880.25)	3.74 (2.79–4.79)	52.28 (43.65–60.49)	3.0
50	6.85 (5.90–8.18)	−896 (−909.75; −880.25)	3.74 (2.8–4.8)	52.35 (43.78–60.54)	2.5
40	6.85 (5.90–8.18)	−896 (−909.75; −880.25)	3.75 (2.812–4.8)	52.47 (43.99–60.60)	2.0
30	6.85 (5.90–8.18)	−896 (−909.75; −880.25)	3.77 (2.83–4.8)	52.67 (44.33–60.68)	1.5
20	6.85 (5.90–8.18)	−896 (−909.75; −880.25)	3.8 (2.88–4.81)	52.91 (44.89–60.85)	1.0
10	6.86 (5.90–8.18)	−895 (−909.25; −879.75)	3.8 (2.92–4.83)	53.0 (45.62–61.19)	0.5
Simulated Dose (mAs)	Median and (Quartile) for Distribution of EC Classes				
	Class 4 (L)	Class 3 (L)	Class 2 (L)	Class 1 (L)	
150 (original)	3.46 (2.43–4.64)	0.02 (0.01–0.03)	0.12 (0.09–0.15)	0.03 (0.02–0.03)	
100	3.46 (2.43–4.64)	0.02 (0.01–0.03)	0.11 (0.09–0.15)	0.03 (0.02–0.03)	
90	3.46 (2.43–4.64)	0.02 (0.01–0.03)	0.12 (0.09–0.15)	0.03 (0.02–0.03)	
80	3.46 (2.43–4.64)	0.02 (0.01–0.03)	0.12 (0.09–0.15)	0.03 (0.02–0.03)	
70	3.46 (2.43–4.64)	0.02 (0.01–0.03)	0.12 (0.09–0.15)	0.03 (0.02–0.03)	
60	3.46 (2.43–4.64)	0.02 (0.01–0.03)	0.12 (0.098–0.16)	0.03 (0.02–0.04)	
50	3.46 (2.43–4.65)	0.02 (0.01–0.03)	0.12 (0.098–0.16)	0.03 (0.02–0.04)	
40	3.46 (2.43–4.65)	0.02 (0.01–0.03)	0.13 (0.09–0.16)	0.03 (0.02–0.04)	
30	3.46 (2.43–4.65)	0.02 (0.01–0.03)	0.13 (0.1–0.16)	0.03 (0.02–0.04)	
20	3.46 (2.45–4.65)	0.025 (0.018–0.04)	0.13 (0.1–0.17)	0.03 (0.02–0.05)	
10	3.46 (2.49–4.64)	0.03 (0.02–0.05)	0.15 (0.11–0.20)	0.04 (0.02–0.06)	

The effective dose was calculated for every protocol for a male patient with a thoracic length of 35 cm using CT Expo 1.4 D software.

using a water phantom to allow for reliable measurements and comparison between examinations. CT was done during deep inspiratory breath-hold in supine position. Every patient was carefully instructed how to breathe before the study and again right before the scan. The breath-hold period ranged between 9–13 s (mean 11 s), depending on the individual lung size. MDCT parameters were: collimation 1 mm, 120 kV, 150 mAs, gantry rotation time 0.5 s, pitch 1.5, and large scan field. No intravenous contrast medium was administered.

### Raw Data Simulation

After the CT scan, the original raw data were transferred to a dedicated PC for further processing. Using a noise simulation software (Raw Based Noise Simulator 1.0, Toshiba Medical Systems Corporation, Japan) the original CT raw data were further reconstructed with 10 different mAs settings ranging from 10 to 100 SIMmAs by adding noise to the original raw data acquired with 150 mAs. No additional scans were taken on the patients. All original and simulated images were reconstructed using a soft tissue reconstruction algorithm with a slice thickness of 1 mm and a reconstruction interval of 0.8 mm.

The effective dose was calculated for every protocol for a male patient with a thoracic length of 35 cm using CT Expo 1.4 D software.<sup>20</sup>

### IMAGE ANALYSIS

All images were transferred via PACS to a PC (Intel Pentium 4, 2.7 GHz, 768 MB RAM, Windows XP Prof.). A self-written software (YACTA<sup>®</sup>, Mainz, Germany) was used for evaluation. The software was not used for diagnosis. Reading of the CT images was routinely performed by a radiologist on the original set of images. The software combines different techniques for semiautomatic segmentation like region growing, threshold- and expert-based methods, and morphological analysis.<sup>15,21,22</sup> A Gaussian filter was applied to all images. Important morphological landmarks (i.e. trachea, right and left lung) were automatically detected. The trachea and the bronchi down to the eighth generation were automatically segmented

and excluded from the evaluation of the lung parenchyma as they contain “respiratory dead space.” Without this segmentation, the airways would have been detected as emphysema as they contain air with a density below 950 HU.

On the basis of the pulmonary landmarks, the lung is detected by region growing with a N6 neighborhood system and an upper threshold of –500 HU. This resulted in a “safe” segmentation of the lung parenchyma without surrounding thoracic structures. However, areas within the lung parenchyma like vessels were not segmented. These areas were automatically included within the segmented lung area by a “closing” procedure. All voxels marked as lung parenchyma were analyzed. Voxels below –950 HU were segmented as emphysema.<sup>2,3,23</sup> This was followed by a correction factor which included all voxels from –950 to –910 HU if they were surrounded by emphysema voxels.

From this conventional analysis, we received the total lung volume (LV), emphysema volume (EV), EI, and mean lung density (MLD).

Thin slice MDCT allows for further 3-dimensional segmentation and in-depth volumetric evaluation of different compartments of the lung parenchyma. After having detected all emphysematous regions, it was possible to perform a volumetric classification of these regions (volumetric classification analysis). The 3-dimensional emphysematous areas were sorted by their volume: 2–8 mm<sup>3</sup> (class 1), 8–65 mm<sup>3</sup> (class 2), 65–120 mm<sup>3</sup> (class 3), and >120 mm<sup>3</sup> (class 4), modified from Blechschmidt et al.<sup>15,24</sup> Knowing the volumes of the different emphysema clusters it is possible to determine if there are shifts in class sizes because of reduced-dose CT scanning, whereas the gross EI may not be affected. For better visualization of the different lung regions and EV, those regions were color coded and displayed as overlays over the CT images. The software was applied to all MDCT datasets.

### STATISTICAL EVALUATION

For statistical evaluation between different mAs levels the, sign test was used (SPSS for Windows, Version 12.0, Chicago, IL). The primary purpose was to proof the variation of EI values of the simulated data on clinical relevance. On

**TABLE 3.** Variation and Standard Deviation of Different Dose Settings From the Original 150mAs Dataset for Mean LV, EV, EI, and Mean of Large (Class 4), Intermediate (Class 3), and Small (Class 2 and 1) EC

Simulated Dose (mAs)	Variation From Original 150mAs Data (%)							
	LV	MLD	EV	EI	Class 4	Class 3	Class 2	Class 1
100	0 ± 0.01	0.01 ± 0.03	0.12 ± 0.17*	0.12 ± 0.17*	0 ± 0.06	2.72 ± 6.22	1.04 ± 2.01	2.60 ± 3.93
90	0 ± 0.01	0.01 ± 0.03	0.17 ± 0.20*	0.17 ± 0.20*	0.01 ± 0.06	4.13 ± 8.61	1.31 ± 2.19	3.40 ± 4.53
80	0 ± 0.01	0.01 ± 0.03	0.23 ± 0.25*	0.23 ± 0.25*	0.01 ± 0.07	5.29 ± 8.19	1.81 ± 2.54	4.44 ± 4.96
70	0 ± 0.01	0.01 ± 0.04	0.30 ± 0.32*	0.30 ± 0.32*	0.02 ± 0.09	6.32 ± 8.38	2.36 ± 2.93*	5.79 ± 5.86*
60	0 ± 0.01	0.01 ± 0.04	0.41 ± 0.41*	0.41 ± 0.41*	0.05 ± 0.12	6.66 ± 9.45	2.99 ± 3.51*	7.48 ± 7.24*
50	0 ± 0.01	0.01 ± 0.04	0.55 ± 0.53*	0.55 ± 0.53*	0.07 ± 0.17	10.14 ± 8.73	4.00 ± 4.35*	9.54 ± 8.69*
40	0.01 ± 0.01	0.02 ± 0.05	0.78 ± 0.72*	0.77 ± 0.72*	0.11 ± 0.23*	13.58 ± 9.97	5.36 ± 5.84*	13.05 ± 10.69*
30	0.01 ± 0.01	0 ± 0.06	1.14 ± 1.03*	1.13 ± 1.03*	0.16 ± 0.38*	19.39 ± 15.31*	8.26 ± 7.88*	19.04 ± 13.88*
20	0.03 ± 0.04	–0.01 ± 0.07	1.84 ± 1.63*	1.81 ± 1.62*	0.25 ± 0.62	30.97 ± 22.18*	14.52 ± 12.17*	30.27 ± 18.15*
10	0.06 ± 0.11	–0.09 ± 0.14*	3.50 ± 3.23*	3.44 ± 3.18*	0.20 ± 1.18	71.50 ± 37.28*	32.84 ± 19.75*	59.30 ± 26.17*

\*A local level of  $P < 0.05$  was assumed to be significant (sign test).

the basis of the primary endpoint calculation of patients to be included was performed and resulted in  $n = 26$ . A variance less than 2% was defined as “not clinically relevant.”<sup>25</sup> The Bonferroni correction for multiple level analyses was applied (level of significance  $P < 0.005$ ).

For the secondary endpoint of the study, the sign test was applied for all parameters and a local level of significance  $P < 0.05$  was assumed to be significantly different. The dimension of variation was presented using median and quartile. Additionally, the simulated data were given as variation from the original acquired data, which were taken as 0%.

## RESULTS

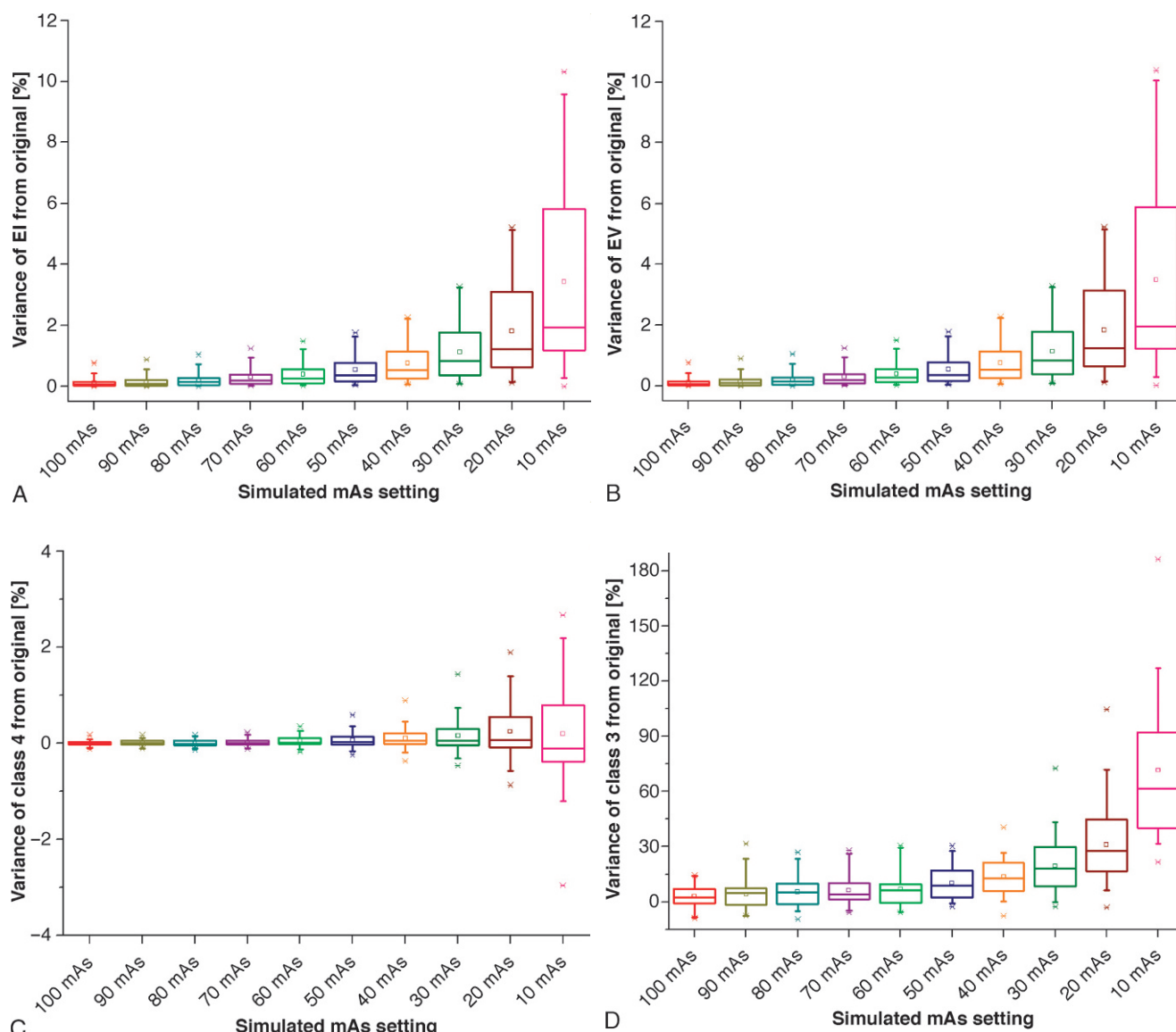
In all cases, the leading CT diagnosis was severe centrilobular emphysema with architectural destruction. No

single large emphysema bullae or area of ground glass opacity was detected.

All 330 data sets were eligible for evaluation (whole lung assessed, no breathing artifacts). The mean absolute values for LV, MLD, EV, EI, and volumes for the 4 emphysema classes are given in Table 1. The medians and quartiles of distribution of all parameters for all mAs levels are presented in Table 2.

## CONVENTIONAL ANALYSIS

Mean LV was  $7.1 \pm 1.4$  L and were similar for all dose settings. Mean MLD was  $-897 \pm 18$  HU and showed no significant difference ( $P > 0.05$ ) for all dose levels till 10 SIMmAs, where the data for MLD was significantly different ( $P < 0.001$ ) compared with the original data set. Mean EV was



**FIGURE 1.** Box-plots showing the variance [%] of emphysema index (A), emphysema volume (B), volume of emphysema clusters class 4 (C), class 3 (D), class 2 (E) and class 1 (F) from the original 150 mAs protocol which was taken as 0%.



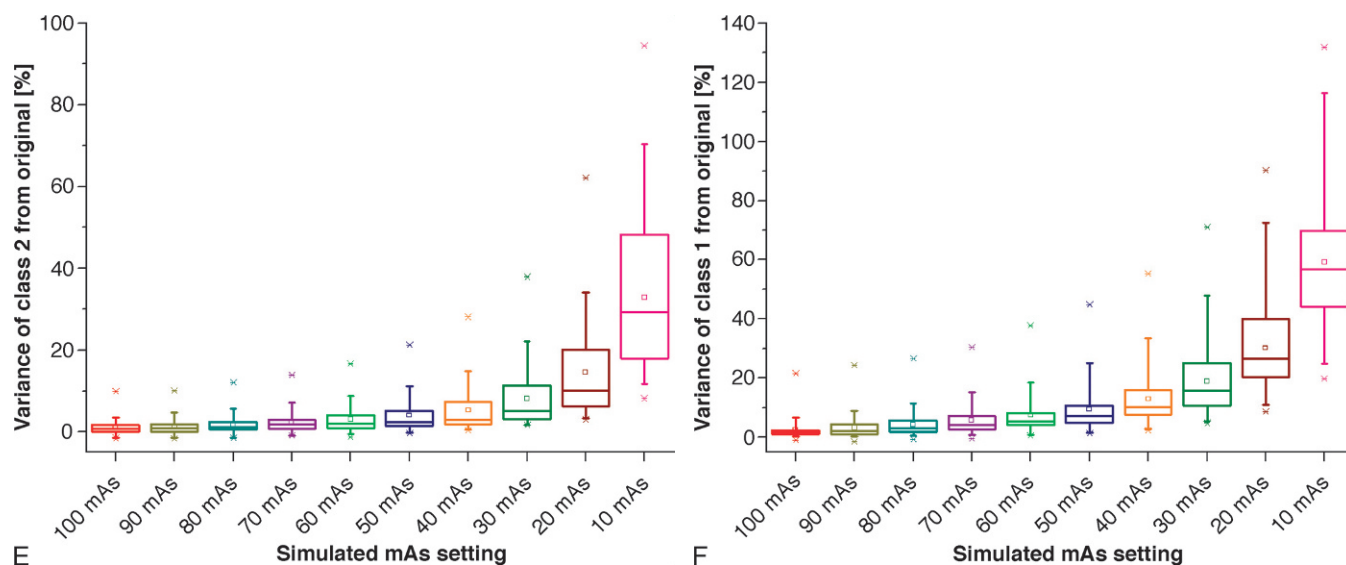
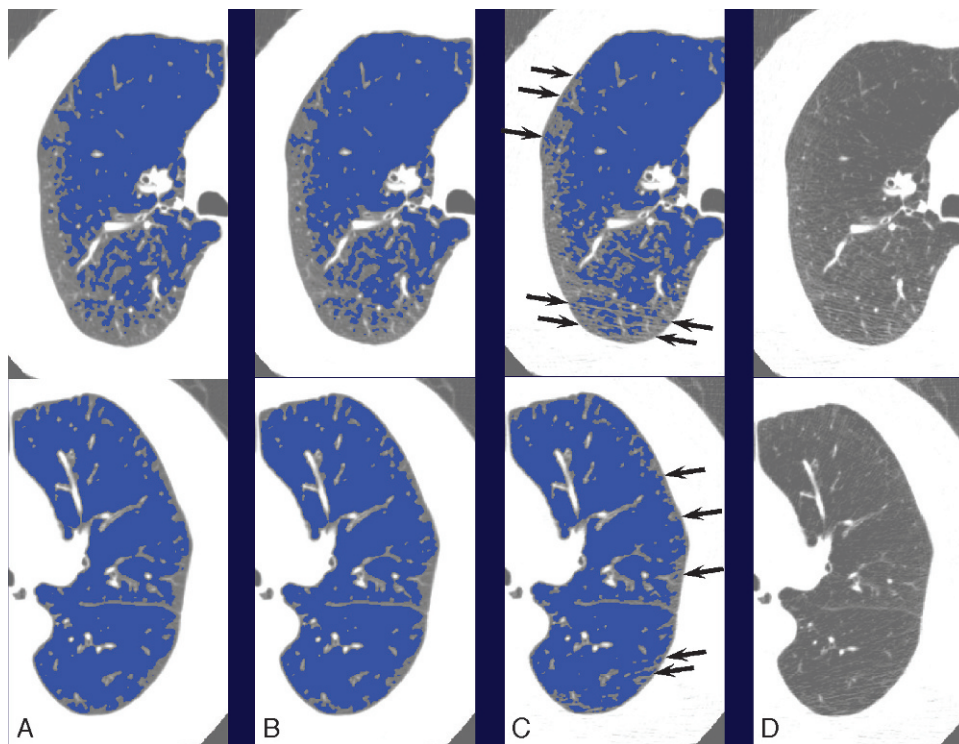


FIGURE 1. (continued)

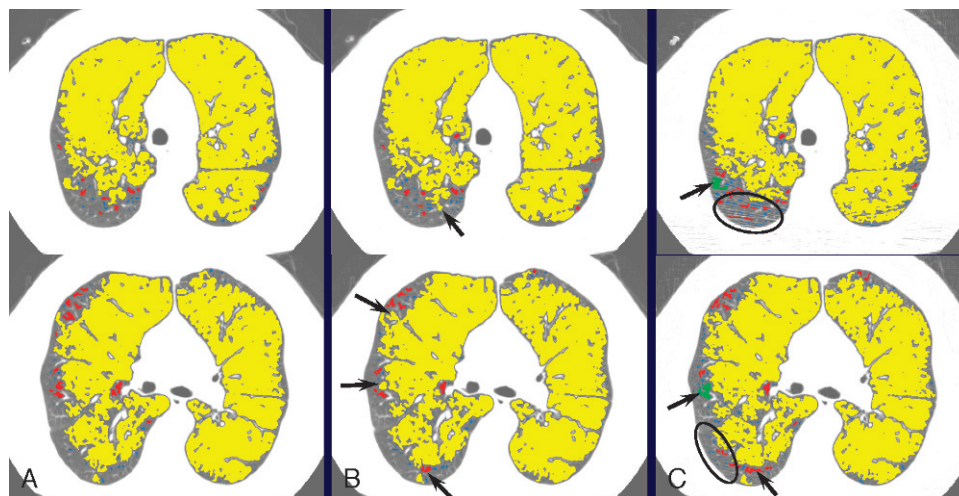
$3.81 \pm 1.39$  L and differ up to  $3.5\% \pm 3.2\%$  (Table 3). Mean EI was  $52.3\% \pm 10.3\%$  and showed a variation of  $3.4\% \pm 3.2\%$ . All EV and EI values for 10–100 SIMmAs were significantly different ( $P < 0.001$ ) from the original data set. Looking onto clinical relevance of EI data, only 10 and 20 SIMmAs showed more than 2% variance from the original data set ( $P < 0.005$ ).

### VOLUMETRIC CLASSIFICATION ANALYSIS

The measured volume of large EC class 4 was  $3.6 \pm 1.4$  L. For large volumes, all simulations showed no significant difference from the original data except 40 and 30 SIMmAs. However, 20 and 10 SIMmAs showed a mean variation of  $0.25\% \pm 0.6\%$  and  $0.2\% \pm 1.2\%$ , with the range of  $-0.9$ – $1.9\%$



**FIGURE 2.** Emphysema voxels colored in blue for original 150 mAs (A), 50 SIMmAs (B), and 10 SIMmAs (C) magnified for right (top) and left lung (bottom). The source images with 10 SIMmAs (D) show the influence of the increased noise on the detection of the emphysema areas (arrows).

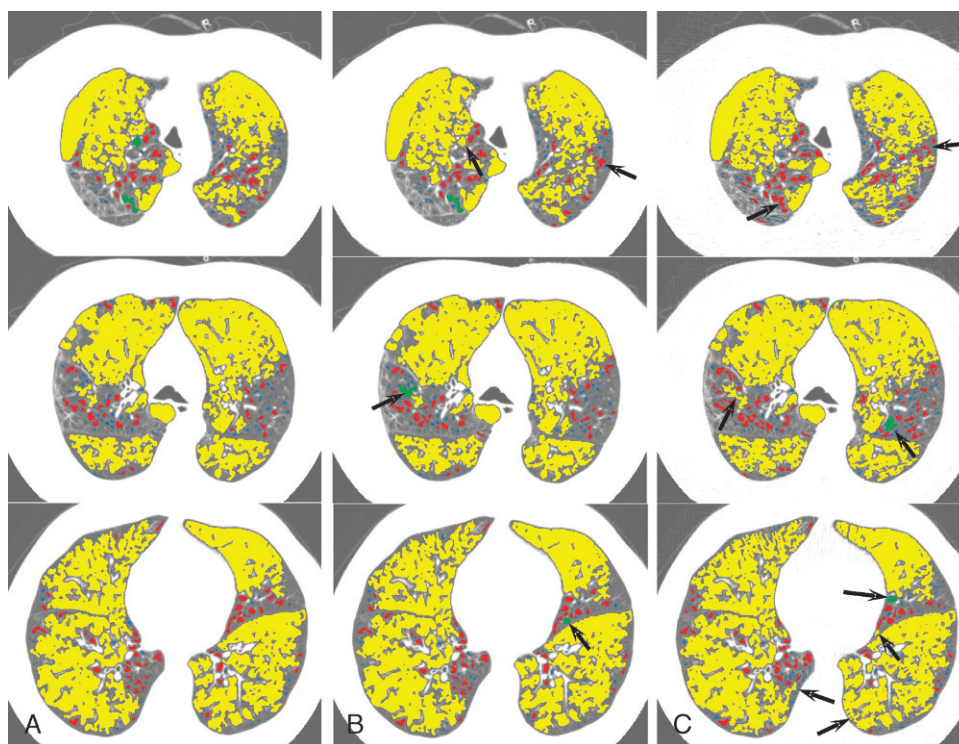


**FIGURE 3.** Color-coded map of original CT images with 150 mAs (A) and images with 50 SIMmAs (B) and 10 SIMmAs (C) settings on the level of the upper lobes and the carina: EC 4 (yellow), class 3 (green), class 2 (red), and class 1 (blue). The arrows point to the differences in the detection of the EC. The circles show the influence of the increased noise on the detection of the small EC.

and  $-3$ – $2.7\%$  (for 20 and 10 SIMmAs, respectively) from the original data (Fig. 1). The volume of intermediate EC class 3 was equal for 70–100 SIMmAs, 40–60 SIMmAs showed no significant difference, and 10–30 SIMmAs were significantly different. Although the absolute volumes were

very small (Table 1), the values of small EC classes 1 and 2 were significantly different from the original data for 10–70 SIMmAs.

The box plot chart (Fig. 1A–F) illustrates the median values and the 25 and 75 quartile and the minima and maxima



**FIGURE 4.** Color-coded map of original CT images with 150 mAs (A) and images with 50 SIMmAs (B) and 10 SIMmAs (C) settings at the level of the upper lobes, carina and middle/lower lobes: EC class 4 (yellow), class 3 (green), class 2 (red), and class 1 (blue). The arrows point to the differences in the detection of the EC.

of all parameters. A major increase in variation below 50 SIMmAs can be seen. The variation of mean EI and EV on 50 SIMmAs level was  $0.4\% \pm 0.9\%$  and  $0.6\% \pm 0.5\%$ , respectively. Because EI and EV results were significantly different on all dose levels in comparison with the original dataset, the in-depth analyses of EV subdivided in 4 EV classes were analyzed. The large EV class 4 showed no significant difference down to 50 SIMmAs with a variation of  $0.07\% \pm 0.2\%$  from the original data set. However, looking onto the volumes of the intermediate and small clusters, the variation was  $10.1\% \pm 8.7\%$ ,  $4\% \pm 4.4\%$ , and  $9.5\% \pm 8.7\%$  for 50 SIMmAs levels, respectively (Table 3). The variation increased overproportional below 50 SIMmAs. Looking at the intraindividual variation, the values of EV, EI, and all EC classes showed a broad spectrum (Fig. 1).

The increase of noise had an effect on the detection and evaluation of emphysema (Fig. 2). The color-coded maps illustrate the difference in the detection of the EC classes using different dose levels (Figs. 3 and 4).

The effective dose was calculated for every protocol (Table 2). The calculated effective dose of the original scan was 7.6 mSv. Using 50 SIMmAs, the dose was 2.5 mSv (33% of original dose).

## DISCUSSION

Quantitative analysis of simulated low dose MDCT protocols for the conventional emphysema parameters, such as EI and EV, were significantly different on all simulated dose levels from the original data set, although the absolute differences were small. Down to 30 SIMmAs, the variation of EI was below 2% and therefore assumed to be not clinically relevant. The MLD was equal for 20–100 SIMmAs. The in-depth emphysema analysis showed that the volume of emphysema class 4 was not significantly different down to 50 SIMmAs. The quantitative evaluation of intermediate and small EV classes remains below 10% variance from the original data down to the 50 SIMmAs level and increased overproportional below this level. In comparison with original 150 mAs acquisition, the radiation exposure can be decreased by 67% using 50-SIMmAs dose level.

Research into the complex relationship between radiation exposure, image quality, and diagnostic accuracy should be encouraged to establish the minimum radiation dose necessary to provide adequate diagnostic information for standard clinical questions.<sup>26,27</sup> However, missing important diagnostic information has to be avoided. As repeated scans at varying tube current-time products within one CT examination are ethically unacceptable, the use of dose-simulation software is essential to provide images with different reduced-dose levels. Because the radiation dose varies linearly with tube current at a fixed tube voltage and scan time, the addition of noise to the original raw data allows for reconstructing images with different low dose settings without the need to perform additional scanning.

In a previous study, it was shown that the addition of noise provides realistic reduced-dose images without patient radiation exposure and with identical image registration and motion artifact.<sup>28</sup> Simulated raw data on the level of 100 and 40 mAs

were reported to be visually indistinguishable from the real scans.<sup>28</sup> No significant difference in noise was observed between the real mAs and corresponding simulated mAs levels (96, 80, 64, 48, and 32 mAs, 140 kV, 0.8 s gantry rotation time, pitch 1, collimation and slice thickness of 2.5 mm) of a water phantom.<sup>29</sup>

The visual assessment of low-dose techniques has been investigated previously. Using 150, 100, 70, and 40 mAs (120 kV, pitch 2, no gantry rotation parameters were published, 3-mm collimation, 2-mm slice thickness) evaluation of 3 patients for each dose protocol showed no difference in image quality by visual assessment.<sup>9</sup> Comparing HRCT images acquired at 40 and 400 mAs it was found that the low-dose technique provided satisfactory visualization of the lung parenchyma in the majority of cases (97%). However, it failed to demonstrate subtle ground glass opacity in 20% and for emphysema in 11%.<sup>11</sup> No difference in diagnostic accuracy was found in 50 patients with chronic diffuse infiltrative lung disease comparing conventional dose (340 mAs, 120 kV) and low-dose (80 mAs) HRCT technique using a single slice CT.<sup>8</sup> In animal experiments, low-dose MDCT scanning with 20 mAs (140 kV, pitch 1.7) did not impair the diagnostic accuracy in acute lung injury in comparison with a standard protocol using 100 mAs.<sup>10</sup> In a recently published simulation study, the reduced-tube current affected evaluation of structures and lung findings and reduced the reader's subjective visual assessment of image quality.<sup>30</sup>

Quantitative evaluation of MLD of low-dose protocols was suitable for 43 mAs (140 kV, pitch 1.5) with 10 mm collimation<sup>31</sup> down to 16 mAs (140 kV, pitch 1.5) with 5 mm collimation.<sup>32</sup> In animal experiments of acute lung injury model, no statistical difference regarding density distribution of lung opacities was found.<sup>10</sup>

As presented earlier, there are no systematic analyses published so far of the influence of low dose onto quantitative results. Thus, we decided to evaluate the broad spectrum of simulated low-dose protocols from 100 to 10 SIMmAs to determine and not to miss the exact dose threshold value. Furthermore, this enabled us to follow all parameters and there variance to detect secondary influence parameters. The evaluation of low-dose 3-dimensional HRCT protocols onto quantitative evaluation of emphysema and characterization using a raw data simulator is unique in the literature. Using an advanced dedicated semiautomatic analysis tool the EV and emphysema classes were quantified for original and simulated low dose settings.

The first endpoint was to look at the influence of reduced-dose protocols onto conventional quantitative parameters such as EI and EV. Facilitated by the volumetric 3-dimensional approach, it is possible to determine the EI and EV of the whole lung. The intraindividual variation of EI on repeated scans was reported to be below 2%.<sup>25</sup> Thus, the variation of <2% was taken to be not relevant in clinical routine. We could demonstrate that using this approach the dose can be reduced down to 30 mAs for conventional analyses. The second endpoint was to evaluate the influence on the dedicated EC classes. A new classification and morphological emphysema analysis approach was introduced by Blechschmidt et al.<sup>15</sup> We adopted this approach and applied it to volumetric data sets with our software.<sup>24</sup> Therefore, the already determined EV was



classified by 4 different volumetric size classes. Because of the dedicated volumetric classification analysis, it was possible to assess the increase in noise not only on a global level but also on small regions of beginning emphysema. The EC of large classes was not significantly different down to 50 SIMmAs whereas the pure total EC was different on all dose levels. Because of the severity of lung destruction of the study population, the intermediate and small classes contributed less to the emphysema volume. The influence of noise became more obvious depending on volume size, thus the small classes showed the largest variation compared to the original dataset.

Some limitations of this study have to be noted. CT was only performed in patients with severe centrilobular emphysema who might undergo further surgical or interventional therapy. Looking at patients with mild or moderate emphysema will result in a higher number of small and intermediate EC classes which might have an impact on the results. The accurate detection of small clusters is important especially for the early detection of mild emphysematous changes. Therefore, the effect of low dose in patient population with mild and moderate emphysema should be further investigated. However, the prevalence of CT imaging in this patient population is very rare.

## CONCLUSIONS

The addition of noise to the raw data acquired by the MDCT scanner allows for reconstructing the images with different low-dose settings without the need to perform additional scanning. Quantitative analysis of severe emphysema from simulated low-dose MDCT protocols showed no clinical relevant variation for EI down to 30 SIMmAs, however being significantly different from original for all dose setting. Using additional emphysema characterization by volumetric size classes, down to 50 SIMmAs the quantification would not alter the results for large classes and showed a variation less than 10% for the smaller classes.

## ACKNOWLEDGMENTS

The authors are very grateful to Prof. Frank Krummenauer from the Department of Clinical Epidemiology, Rehabilitation and Sport Medicine, Carl Gustav Carus University Dresden for statistical support. Many thanks to Mr. Wolfram Stiller for physical support. The data are part of the doctoral thesis of Mr. Ioannis Tsakiris.

## REFERENCES

- Snider G, Kleinerman J, Thurlbeck WM, et al. The definition of emphysema. Report of a National Heart, Lung, and Blood Institute, Division of Lung Diseases workshop. *Am Rev Respir Dis*. 1985;132:182–185.
- Gevenois PA, de Maertelaer V, De Vuyst P, et al. Comparison of computed density and macroscopic morphometry in pulmonary emphysema. *Am J Respir Crit Care Med*. 1995;152:653–657.
- 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.
- Aziz ZA, Padley SP, Hansell DM. CT techniques for imaging the lung: recommendations for multislice and single slice computed tomography. *Eur J Radiol*. 2004;52:119–136.
- Cohnen M, Poll LJ, Puettmann C, et al. Effective doses in standard protocols for multi-slice CT scanning. *Eur Radiol*. 2003;13:1148–1153.
- Chooi WK, Morcos SK. High resolution volume imaging of airways and lung parenchyma with multislice CT. *Br J Radiol*. 2004;77 Spec No 1:S98–105.
- Schoepf UJ, Bruening RD, Hong C, et al. Multislice helical CT of focal and diffuse lung disease: comprehensive diagnosis with reconstruction of contiguous and high-resolution CT sections from a single thin-collimation scan. *AJR Am J Roentgenol*. 2001;177:179–184.
- Lee KS, Primack SL, Staples CA, et al. Chronic infiltrative lung disease: comparison of diagnostic accuracies of radiography and low- and conventional-dose thin-section CT. *Radiology*. 1994;191:669–673.
- Jung KJ, Lee KS, Kim SY, et al. Low-dose, volumetric helical CT: image quality, radiation dose, and usefulness for evaluation of bronchiectasis. *Invest Radiol*. 2000;35:557–563.
- Wildberger JE, Max M, Wein BB, et al. Low-dose multislice spiral computed tomography in acute lung injury: animal experience. *Invest Radiol*. 2003;38:9–16.
- Zwirewich CV, Mayo JR, Muller NL. Low-dose high-resolution CT of lung parenchyma. *Radiology*. 1991;180:413–417.
- Sakai N, Mishima M, Nishimura K, et al. 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.
- Bankier AA, De Maertelaer V, Keyzer C, et al. Pulmonary emphysema: subjective visual grading versus objective quantification with macroscopic morphometry and thin-section CT densitometry. *Radiology*. 1999;211:851–858.
- Nakano Y, Muro S, Sakai H, et al. Computed tomographic measurements of airway dimensions and emphysema in smokers. Correlation with lung function. *Am J Respir Crit Care Med*. 2000;162:1102–1108.
- Blehschmidt RA, Werthschützky R, Lorcher U. Automated CT image evaluation of the lung: a morphology-based concept. *IEEE Trans Med Imaging*. 2001;20:434–442.
- Mishima M, Hirai T, Itoh H, et al. Complexity of terminal airspace geometry assessed by lung computed tomography in normal subjects and patients with chronic obstructive pulmonary disease. *Proc Natl Acad Sci U S A*. 1999;96:8829–8834.
- McKenna RJ Jr, Gelb A, Brenner M. Lung volume reduction surgery for chronic obstructive pulmonary disease: where do we stand? *World J Surg*. 2001;25:231–237.
- Toma TP, Hopkinson NS, Hillier J, et al. Bronchoscopic volume reduction with valve implants in patients with severe emphysema. *Lancet*. 2003;361:931–933.
- Yim AP, Hwang TM, Lee TW, et al. Early results of endoscopic lung volume reduction for emphysema. *J Thorac Cardiovasc Surg*. 2004;127:1564–1573.
- Stamm G, Nagel HD. CT-expo-a novel program for dose evaluation in CT. *Fortschr Röntgenstr*. 2002;174:1570–1576.
- Mayer D, Bartz D, Fischer J, et al. Hybrid segmentation and virtual bronchoscopy based on CT images. *Acad Radiol*. 2004;11:551–565.
- Achenbach T, Weinheimer O, Buschsieweke C, et al. Fully automatic detection and quantification of emphysema on thin section MD-CT of the chest by a new and dedicated software. *Fortschr Röntgenstr*. 2004;176:1409–1415.
- Baldi S, Miniati M, Bellina CR, et al. Relationship between extent of pulmonary emphysema by high-resolution computed tomography and lung elastic recoil in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2001;164:585–589.
- Zaporożhan J, Ley S, Eberhardt R, et al. Paired inspiratory/expiratory volumetric thin-slice CT for emphysema analysis: comparison of different quantitative evaluations and pulmonary function test. *Chest*. 2005;128:3212–3220.
- Stolk J, Dirksen A, van der Lugt AA, et al. Repeatability of lung density measurements with low-dose computed tomography in subjects with alpha-1-antitrypsin deficiency-associated emphysema. *Invest Radiol*. 2001;36:648–651.
- ICRP. 1990 recommendations of the international commission on radiological protection. *Ann ICRP*. 1991;21:1–201.
- Mayo JR, Aldrich J, Muller NL. Radiation exposure at chest CT: a statement of the fleischner society. *Radiology*. 2003;228:15–21.



28. Mayo JR, Whittall KP, Leung AN, et al. Simulated dose reduction in conventional chest CT: validation study. *Radiology*. 1997;202:453–457.
29. Frush DP, Slack CC, Hollingsworth CL, et al. Computer-simulated radiation dose reduction for abdominal multidetector CT of pediatric patients. *AJR Am J Roentgenol*. 2002;179:1107–1113.
30. Mayo JR, Kim KI, MacDonald SL, et al. Reduced radiation dose helical chest CT: effect on reader evaluation of structures and lung findings. *Radiology*. 2004;232:749–756.
31. Orlandi I, Moroni C, Camiciottoli G, et al. Spirometric-gated computed tomography quantitative evaluation of lung emphysema in chronic obstructive pulmonary disease: a comparison of 3 techniques. *J Comput Assist Tomogr*. 2004;28:437–442.
32. Shaker SB, Dirksen A, Laursen LC, et al. Short-term reproducibility of computed tomography-based lung density measurements in alpha-1 antitrypsin deficiency and smokers with emphysema. *Acta Radiol*. 2004;45:424–430.