

# Pulmonary Emphysema: Radiation Dose and Section Thickness at Multidetector CT Quantification—Comparison with Macroscopic and Microscopic Morphometry<sup>1</sup>

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## Purpose:

To prospectively investigate the effects of radiation dose and section thickness on quantitative multidetector computed tomographic (CT) indexes of pulmonary emphysema.

## Materials and Methods:

The institutional review board approved this protocol. Written informed consent was obtained from all patients. Seventy patients (49 men, 21 women; age range, 38–79 years) referred for surgical resection of a lung tumor underwent multidetector CT with  $4 \times 1$ -mm collimation, 120 kVp, and 20 and 120 effective mAs. At each radiation dose, 1.25-, 5.0-, and 10.0-mm-thick sections were reconstructed at 10-mm intervals. From scans of the lobe or whole lung to be resected, relative areas (RAs) of lung with attenuation coefficients lower than nine thresholds and eight percentiles of the distribution of attenuation coefficients were compared with the histopathologic extent of emphysema, which was measured microscopically—by using the corrected mean interwall distance (MIWD) and the corrected mean perimeter (MP)—and macroscopically. Correlations between the data obtained by using attenuation thresholds and percentiles and the parameters macroscopic extent of emphysema, MIWD, and MP were investigated by using Spearman coefficients.

## Results:

The 1st percentile ( $r$  range,  $-0.394$  to  $-0.675$ ;  $P < .001$ ) and attenuation coefficients of  $-980$ ,  $-970$ , and  $-960$  HU ( $r$  range,  $0.478$ – $0.664$ ;  $P < .001$ ) yielded the strongest correlations with macroscopic extent, MIWD, and MP, regardless of radiation dose or section thickness. The effects of radiation dose and section thickness on RAs of lung with attenuation coefficients lower than  $-960$  HU ( $P = .007$  and  $P < .001$ , respectively) and lower than  $-970$  HU ( $P = .001$  and  $P < .001$ , respectively) were significant. The effect of section thickness on the 1st percentile was significant ( $P < .001$ ), whereas the effect of dose was not ( $P = .910$ ).

## Conclusion:

At CT quantification of pulmonary emphysema, the tube current–time product can be reduced to 20 mAs, but both tube current–time product and section thickness should be kept constant in follow-up examinations.

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**P**ulmonary emphysema is a chronic obstructive pulmonary disease and worldwide the sixth and 12th most common cause of mortality and morbidity, respectively (1). Computed tomography (CT) yields densitometric measurements that are highly reproducible and that have been correlated with morphometric measurements of alveolar tissue. As a result, this technique has been recommended for follow-up examinations, particularly those to evaluate therapeutic interventions (2–5). Although multi-detector row CT is of interest for the quantification of heterogeneously distributed lung disorders such as pulmonary emphysema, the use of this technique increases the radiation dose by an additional 300% per examination compared with the dose required for incremental single-detector row CT, which yields thin sections in 1-cm intervals (6). This increased radiation dose is of special concern in patients with emphysema, because these individuals may be young and may have a favorable prognosis. The relatively high level of radiation that patients with emphysema are exposed to at multi-detector CT is compounded by the repeated follow-up examinations that they undergo throughout their life. Although reduced radiation doses have been successfully used in patients with various thoracic disorders (7–12), the effect of dose on densitometric measurements is not known.

#### Advances in Knowledge

- Reducing the radiation dose to 20 mAs is recommended for patients undergoing CT quantification of pulmonary emphysema.
- Comparisons between examinations require that both the radiation dose and the section thickness remain constant.
- The 1st percentile and relative areas of lung with attenuation coefficients lower than  $-960$  and  $-970$  HU best reflect the extent of pulmonary emphysema depicted on 1.25-, 5.0-, and 10.0-mm-thick CT sections obtained at 20 and 120 mAs.

Multi-detector row CT yields a large number of images—generally, 350 images with contiguous 1-mm-thick sections throughout the thorax. Quantifying the pulmonary emphysema on such an amount of images is very time consuming. By increasing the section thickness, one could reduce this number and still appreciate the lung parenchyma in its entirety on contiguous thicker sections. Nevertheless, to our knowledge, the effect of section thickness on densitometric measurements is also not known. Thus, the purpose of our study was to prospectively investigate the effects of radiation dose and section thickness on quantitative multidetector CT indexes of pulmonary emphysema.

#### Materials and Methods

##### Patients

This investigation was approved by the local ethics committee of Université Libre de Bruxelles-Hôpital Erasme, and written informed consent was obtained from all patients. This prospective study initially included 105 consecutive patients who were referred to the Department of Thoracic Surgery, Université Libre de Bruxelles-Hôpital Erasme, between November 2001 and June 2003 for surgical resection of a lung tumor. The majority of these patients were a part of our previous study (13), in which we prospectively compared both helical CT indexes and pulmonary function test findings with macroscopic and microscopic measurements as independent methods of reference. In the previous study, all CT parameters were kept constant (13).

Twenty-eight patients were not included in our research protocol because they had pneumonia ( $n = 4$ ), pulmonary atelectasis ( $n = 4$ ), or interstitial lung disease ( $n = 3$ ) at admission or because they were referred for tumorectomy (resection of tumor only rather than of entire lobe) ( $n = 17$ ). Two additional patients were excluded after undergoing multi-detector row CT owing to breathing artifacts ( $n = 1$ ) or evidence of interstitial lung disease in the nontumoral parenchyma ( $n = 1$ ). Five pa-

tients were excluded after undergoing thoracic surgery because they underwent segmentectomy, a procedure that would prevent us from appropriately fixing the lung specimen in preparation for morphometric measurements.

A total of 70 patients (49 men, 21 women) aged 38–79 years (mean, 63 years  $\pm 1$  [standard error of the mean]) were included in our current study. The mean time from CT to surgery was 3 days (range, 1–7 days). Sixty-four patients underwent lobe resection, and six underwent whole-lung resection. Thirteen patients were nonsmokers, 14 were ex-smokers, and 43 were current smokers. The current smokers and ex-smokers had smoked a mean of 38 pack-years  $\pm 2$  (range, 10–100 pack-years). The mean body mass index, calculated from data in the medical chart (14), was 25.1 kg/m<sup>2</sup>  $\pm 0.5$  (range, 15.6–37.6 kg/m<sup>2</sup>).

##### CT Examinations

CT scans were obtained by using a commercially available four-channel multi-detector row scanner (Somatom Volume Zoom; Siemens Medical Solutions, Forchheim, Germany). The scale of attenuation coefficients in this CT scanner ranges from  $-1024$  to  $3072$  HU. The scanner was calibrated periodically and after major maintenance work. Patients were

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##### Abbreviations:

MIWD = corrected mean interwall distance

MP = corrected mean perimeter

RA<sub>960</sub> = relative area of lung with attenuation coefficient lower than  $-960$  HU

RA<sub>970</sub> = relative area of lung with attenuation coefficient lower than  $-970$  HU

##### Author contributions:

Guarantors of integrity of entire study, A.M., P.A.G.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, A.M., P.A.G.; clinical studies, A.M., J.Z.; statistical analysis, V.D.M.; and manuscript editing, A.M., V.D.M., P.A.G.

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scanned craniocaudally during a full-inspiration breath hold. No spirometric controlling of lung volume was performed because this procedure has not been shown to substantially improve the repeatability of quantitative CT scanning in the assessment of the extent of emphysema (3). No patient received intravenous contrast material. CT was performed twice with  $4 \times 1$ -mm collimation, 120 kVp (constant), and 20 and 120 effective mAs. No tube current modulation was applied during the acquisitions. Effective milliamperesecond, as defined by Mahesh et al (15), refers to the milliamperesecond value divided by the pitch, where pitch is defined, according to Silverman et al (16), as the ratio between the table feed per rotation and the x-ray beam width. The table feed was 6 mm per 0.75-second rotation (8 mm/sec). These parameters resulted in a pitch of 1.5:1. The total absorbed doses—expressed as weighted CT dose indexes—were 2.66 and 15.96 mGy, respectively, at 20 and 120 mAs. The weighted CT dose index was calculated as the sum of two-thirds the peripheral dose and one-third the central dose measured in a plastic phantom (17). From the raw data derived with each radiation dose, 1.25-, 5.0-, and 10.0-mm-thick sections were reconstructed with a soft-tissue algorithm (20S; Siemens Medical Solutions) at 10-mm intervals. We used this interval because it has been widely used in CT studies of diffusely distributed lung disease.

By using the Pulmo CT program (Siemens Medical Solutions), which automatically recognizes the lungs and traces the lung contours, the attenuation coefficients of each lung CT section were measured by a radiologist (A.M.) with 11 years experience in chest CT. The interlobar limits were traced manually in the cases of patients who underwent lobe resection. From these coefficients, we calculated for each lobe or whole lung to be resected relative areas of lung (expressed as percentages) with attenuation coefficients lower than thresholds ranging from  $-900$  to  $-980$  HU ( $-900$ ,  $-910$ ,  $-920$ ,  $-930$ ,  $-940$ ,  $-950$ ,  $-960$ ,  $-970$ , and  $-980$  HU) and eight percentiles (1st, 3rd, 5th, 7th, 10th, 12th, 15th, and 18th percentiles) of the distribution of attenuation coefficients, at each radiation dose and each section thickness.

#### Macroscopic Quantification of Emphysema

The resected lung samples were prepared for macroscopic quantification as extensively described elsewhere (13): The resected lobes and whole lungs were inflated and were immersed in a formalin solution for 48 hours immediately after surgery. By using a modified Gough-Wentworth technique, two 1-mm-thick vertical whole-lung sections were obtained from the fixed specimens (18). The sections were cut by a pathologist who was blinded to the quantitative CT results about the remaining nontumoral

lung parenchyma and were mounted (A.M.) between two transparency films for plain paper copiers (3M, St Paul, Minn), digitized (Hewlett Packard Scan JET 6100C/T; Hewlett Packard, Palo Alto, Calif), and stored on a personal computer by a physicist (J.Z.) with more than 10 years of experience regarding lung pathology measurements and who was blinded to the quantitative CT results. The area macroscopically shown to be occupied by emphysema was measured on these sections by using a previously validated computer-assisted method (19). The relative area (expressed as a percentage) with a low densitometric reading corresponded to the pathologic extent of emphysema seen macroscopically.

#### Microscopic Quantification of Emphysema

The resected lung samples were prepared for microscopic quantification as extensively described elsewhere (13): For each patient, the material to be used for microscopic quantification consisted of 18 samples from the nontumoral lung parenchyma, which the pathologist obtained from each of nine regions in the lung specimen that were selected by dividing the specimen along the cephalocaudal direction in the upper, middle, and lower zones and along the horizontal direction in the centropulmonary, middle, and peripheral zones. Lung sections were observed at  $\times 25$  magnification by using a microscope

**Table 1**

#### Correlation Coefficients for Relationships between Macroscopic Extent of Emphysema and Relative Area Measured with Various Attenuation Thresholds, Tube Current–Time Products, and Section Thicknesses

Attenuation Coefficient Threshold (HU)	20 mAs						120 mAs					
	1.25 mm		5.0 mm		10.0 mm		1.25 mm		5.0 mm		10.0 mm	
	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value
−900	0.156	.200	0.172	.159	0.190	.118	0.211	.082	0.134	.271	0.222	.067
−910	0.194	.110	0.211	.081	0.224	.065	0.246	.042	0.168	.169	0.267	.026
−920	0.237	.050	0.263	.029	0.283	.019	0.295	.014	0.220	.069	0.332	.005
−930	0.294	.014	0.334	.005	0.344	.004	0.358	.003	0.274	.022	0.360	.002
−940	0.360	.002	0.387	.001	0.379	.001	0.407	.001	0.331	.005	0.397	.001
−950	0.401	.001	0.434	<.001	0.419	<.001	0.438	<.001	0.370	.002	0.434	<.001
−960	0.447	<.001	0.485	<.001	0.452	<.001	0.462	<.001	0.410	<.001	0.473	<.001
−970	0.488	<.001	0.509	<.001	0.478	<.001	0.493	<.001	0.455	<.001	0.510	<.001
−980	0.510	<.001	0.537	<.001	0.498	<.001	0.522	<.001	0.478	<.001	0.510	<.001

Note.—Relative areas were measured by using tube current–time products of 20 and 120 mAs and section thicknesses of 1.25, 5.0, and 10.0 mm. *r* = Spearman correlation coefficient.

connected to a high-resolution video camera. From each lung section, two microscopic fields were digitized (J.Z.), and after the image threshold was established, the total perimeter of the alveoli and alveolar ducts in the field was measured with an image analyzer system (model KS400; Carl Zeiss Vision, Hallbergmaas, Germany).

In a second step, the distances between intersections of the alveolar and duct walls and seven horizontal lines arbitrarily drawn by the computer were automatically measured with the image analyzer. These interwall distance values re-

flected the diameters of the alveoli and alveolar ducts combined. Perimeters and interwall distances were measured in 36 fields, 35 of which having been recommended by Gould et al (20). From the measurements obtained from one lung specimen, the mean perimeter per field and the mean interwall distance were calculated. These values, originally expressed in pixels, were converted to micrometers: With the optical system used, 1 pixel corresponded to 3.205  $\mu\text{m}$ .

The mean perimeter per field and the mean interwall distance calculated from the histologic slides were cor-

rected for shrinkage and distortion (mainly due to dehydration) caused by processing and cutting the tissue (21).

### Statistical Analyses

Quantitative variables were expressed as means  $\pm$  standard errors of the mean. Relative areas of lung with attenuation coefficients lower than each considered threshold and all eight percentiles were compared with the macroscopic and microscopic quantitative indexes.

For each radiation dose and each section thickness, we calculated Spearman correlation coefficients for the relationships between each set of CT data obtained with the nine tested attenuation thresholds and the eight percentiles and the corrected mean interwall distance (MIWD) and between each set of CT data and the corrected mean perimeter (MP). The higher the coefficient (for a given set of data), the more appropriate was the threshold for quantifying emphysema.

Three analyses of variance for repeated measurements were performed to investigate the most appropriate threshold and percentile as functions of (a) the potential effect of radiation dose—that is, the tube current-time product (factor at two levels), (b) the potential effect of section thickness (factor at three levels), and (c) the potential effect of the interaction of these two

**Table 2**

**Correlation Coefficients for Relationships between MIWD and Relative Area Measured with Various Attenuation Thresholds, Tube Current-Time Products, and Section Thicknesses**

Attenuation Coefficient Threshold (HU)	20 mAs			120 mAs		
	1.25 mm	5.0 mm	10.0 mm	1.25 mm	5.0 mm	10.0 mm
-900	0.458	0.431	0.465	0.461	0.367	0.459
-910	0.498	0.474	0.502	0.517	0.424	0.519
-920	0.535	0.507	0.545	0.568	0.469	0.576
-930	0.577	0.556	0.587	0.613	0.510	0.592
-940	0.608	0.600	0.620	0.639	0.531	0.617
-950	0.622	0.613	0.641	0.652	0.564	0.646
-960	0.638	0.633	0.654	0.657	0.577	0.664
-970	0.648	0.635	0.641	0.653	0.572	0.657
-980	0.645	0.626	0.627	0.628	0.554	0.626

Note.—Data are Spearman correlation coefficients. Relative areas were measured by using tube current-time products of 20 and 120 mAs and section thicknesses of 1.25, 5.0, and 10.0 mm.  $P < .001$  for all comparisons except that between MIWD and relative area measured by using -900 HU, 120 mAs, and 5.0-mm section thickness ( $P = .002$ ).

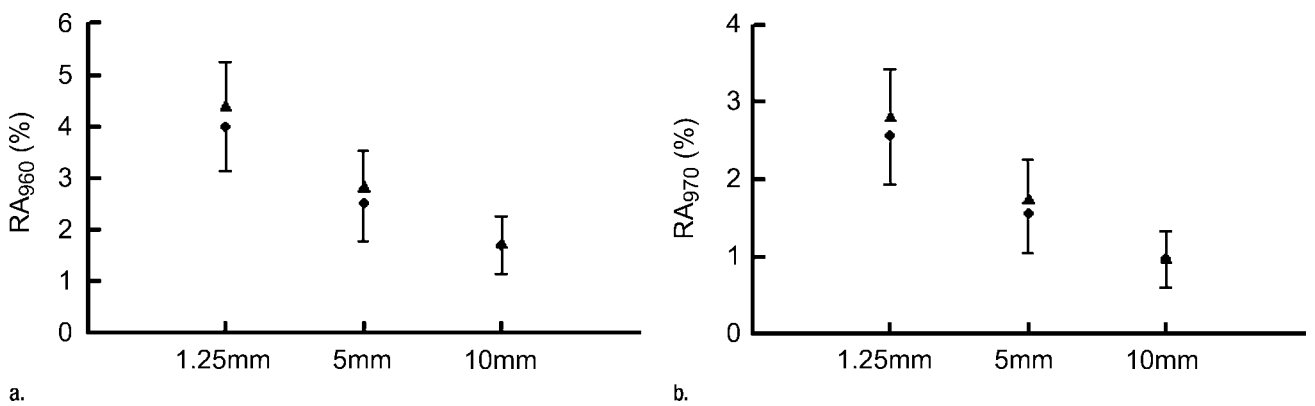
**Table 3**

**Correlation Coefficients for Relationships between MP and Relative Area Measured with Various Attenuation Thresholds, Tube Current-Time Products, and Section Thicknesses**

Attenuation Coefficient Threshold (HU)	20 mAs						120 mAs					
	1.25 mm		5.0 mm		10.0 mm		1.25 mm		5.0 mm		10.0 mm	
	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value
-900	-0.379	.001	-0.378	.001	-0.395	.001	-0.400	.001	-0.294	.014	-0.377	.001
-910	-0.412	<.001	-0.414	<.001	-0.427	<.001	-0.448	<.001	-0.343	.004	-0.436	<.001
-920	-0.447	<.001	-0.443	<.001	-0.460	<.001	-0.496	<.001	-0.381	.001	-0.491	<.001
-930	-0.483	<.001	-0.486	<.001	-0.496	<.001	-0.534	<.001	-0.421	<.001	-0.506	<.001
-940	-0.509	<.001	-0.524	<.001	-0.525	<.001	-0.561	<.001	-0.444	<.001	-0.533	<.001
-950	-0.523	<.001	-0.538	<.001	-0.549	<.001	-0.575	<.001	-0.479	<.001	-0.561	<.001
-960	-0.542	<.001	-0.564	<.001	-0.566	<.001	-0.584	<.001	-0.492	<.001	-0.581	<.001
-970	-0.559	<.001	-0.569	<.001	-0.557	<.001	-0.586	<.001	-0.493	<.001	-0.577	<.001
-980	-0.560	<.001	-0.566	<.001	-0.550	<.001	-0.573	<.001	-0.485	<.001	-0.561	<.001

Note.—Relative areas were obtained by using tube current-time products of 20 and 120 mAs and section thicknesses of 1.25, 5.0, and 10.0 mm. *r* = Spearman correlation coefficient.

**Figure 1**



**Figure 1:** Mean (a) RA<sub>960</sub> and (b) RA<sub>970</sub> values (with standard errors of the mean) measured at 20 effective mAs (▲) and 120 effective mAs (◆) on 1.25-, 5.0-, and 10.0-mm-thick CT sections. Dose ( $P = .007$  and  $P = .001$ , respectively), section thickness ( $P < .001$  for both), and the interaction between dose and thickness ( $P = .036$  and  $P = .005$ , respectively) were found to have significant effects on RA<sub>960</sub> and RA<sub>970</sub>.

**Table 4**

**Correlation Coefficients for Relationships between Macroscopic Extent of Emphysema and Percentile Derived with Various Tube Current–Time Products and Section Thicknesses**

Percentile	20 mAs						120 mAs					
	1.25 mm		5.0 mm		10.0 mm		1.25 mm		5.0 mm		10.0 mm	
	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value
1st	−0.453	<.001	−0.464	<.001	−0.394	.001	−0.450	<.001	−0.456	<.001	−0.434	<.001
3rd	−0.410	<.001	−0.384	.001	−0.330	.006	−0.430	<.001	−0.280	.020	−0.347	.003
5th	−0.375	.002	−0.351	.003	−0.322	.007	−0.397	.001	−0.250	.038	−0.334	.005
7th	−0.347	.003	−0.337	.005	−0.308	.010	−0.381	.001	−0.252	.037	−0.329	.006
10th	−0.325	.006	−0.316	.008	−0.292	.015	−0.362	.002	−0.246	.041	−0.324	.007
12th	−0.311	.009	−0.312	.009	−0.278	.021	−0.354	.003	−0.235	.052	−0.315	.008
15th	−0.291	.015	−0.286	.017	−0.255	.034	−0.349	.003	−0.233	.054	−0.300	.012
18th	−0.277	.021	−0.265	.028	−0.234	.53	−0.332	.005	−0.215	.076	−0.288	.016

Note.—Percentiles of the distribution of attenuation coefficients were derived by using tube current–time products of 20 and 120 mAs and section thicknesses of 1.25, 5.0, and 10.0 mm. *r* = Spearman correlation coefficient.

factors. For all tests,  $P < .05$  indicated statistical significance. The statistical software used was SPSS for Windows, release 13.0 (SPSS, Chicago, Ill).

**Results**

The mean percentage area of lung macroscopically seen to be occupied by emphysema ( $\pm$  standard error of the mean) was 7.34%  $\pm$  0.98 (range, 0.17%–30.94%). The MIWD was 233  $\mu\text{m} \pm 7$  (range, 164–472  $\mu\text{m}$ ). The MP was 20  $\mu\text{m}/\text{mm}^2 \pm 1$  (range, 10–29  $\mu\text{m}/\text{mm}^2$ ). Spearman correlation coeffi-

cients for the relationships between macroscopic extent of emphysema and MIWD and between macroscopic extent and MP were 0.667 and 0.689, respectively ( $P < .001$ ). The Spearman correlation coefficient for the relationship between the two microscopic indexes (MIWD and MP) was  $-0.947$  ( $P < .001$ ).

**Attenuation Coefficient Thresholds**

The highest correlation coefficients for the relationship between macroscopic extent of emphysema and relative area of lung with an attenuation coefficient lower than a given tested threshold ( $n =$

9), derived at each radiation dose and each section thickness, were obtained for an attenuation coefficient of  $-980$  HU, regardless of radiation dose or section thickness (Table 1).

With MIWD (Table 2) as the reference standard, the highest correlations between microscopic measurement and relative area of lung with an attenuation coefficient lower than a given tested threshold were obtained for attenuation coefficients of  $-960$  and  $-970$  HU, depending on radiation dose and section thickness. The highest correlation coefficients in each condition ranged from 0.657 to 0.664. With MP (Table 3) as

the reference standard, however, the highest correlations were obtained for attenuation coefficients of  $-980$ ,  $-970$ , and  $-960$  HU, depending on radiation dose and section thickness. The highest correlation coefficients in each condition ranged from  $-0.573$  to  $-0.586$ .

For relative area of lung with an attenuation coefficient lower than  $-960$  HU ( $RA_{960}$ ) and relative area of lung with an attenuation coefficient lower than  $-970$  HU ( $RA_{970}$ ) (Fig 1), we found dose ( $P = .007$  and  $P = .001$ , respectively), section thickness ( $P < .001$  for both), and the interaction between dose and thickness ( $P = .036$  and  $P = .005$ , respectively) to have significant effects.

### Percentiles

The highest correlations between percentile ( $n = 8$ ) of the distribution of attenuation coefficients and macroscopic extent of emphysema, at each radiation dose and each section thickness, were obtained for the 1st percentile, regardless of radiation dose or section thickness (Table 4). The highest correlations between percentile and microscopic measurement (MIWD or MP) also were obtained for the 1st percentile, regardless of dose or section thickness (Tables 5 and 6). Section thickness ( $P < .001$ )—but not dose ( $P = .910$ ) or interaction between dose and thickness ( $P = .215$ )—was found to have a significant effect on the 1st percentile (Fig 2).

### Discussion

The findings of this study are as follows: (a)  $RA_{960}$ ,  $RA_{970}$ , and the 1st percentile of the distribution of attenuation coefficients best reflected the extent of pulmonary emphysema depicted on 1.25-, 5.0-, and 10.0-mm-thick CT sections obtained at 20 and 120 mAs, regardless of radiation dose or section thickness; (b) all attenuation coefficient thresholds except the cutoff values of  $-910$  and  $-900$  HU had significant correlations with the histopathologic indexes; (c) radiation dose had a significant effect on  $RA_{960}$  and  $RA_{970}$  but not on the 1st percentile; and (d) section thickness had a significant effect on  $RA_{960}$ ,  $RA_{970}$ , and the 1st percentile.

### Effect of Radiation Dose

Radiation dose does not substantially influence the strength of correlations between histopathologic indexes and either relative areas or percentiles. This finding suggests that reducing the dose to 20 mAs should be recommended for the CT quantification of pulmonary emphysema, especially in patients who will undergo repeated follow-up examinations. However, because radiation dose does affect  $RA_{960}$  and  $RA_{970}$ , it should be kept constant in comparative and follow-up examinations based on relative area. Our study results complement those of Stolk et al (22), who found that

measurements of both the relative area of lung with an attenuation coefficient lower than  $-910$  HU and the 15th percentile on 2.5-mm-thick CT sections obtained at 20 mAs are as repeatable as pulmonary function tests in individuals who have  $\alpha_1$ -antitrypsin deficiency-associated emphysema. However, our study revealed, on the basis of comparisons with macroscopic and microscopic indexes, that  $RA_{960}$ ,  $RA_{970}$ , and the 1st percentile are more appropriate for emphysema quantification than are relative area of lung with an attenuation coefficient lower than  $-910$  HU and the 15th percentile.

Other studies of the objective CT quantification of pulmonary emphysema have been based on tube current-time products ranging from 88 to 255 mAs (5,17,18,23–27). Results of numerous studies in which the effect of dose reduction on chest CT examinations was investigated by means of subjective assessment of image quality or diagnostic performance have suggested that the tube current-time product could be dramatically reduced for certain applications (28,29). These applications include pulmonary angiography (12) and the detection of lung nodules (7), bronchiectasis (8), ground-glass opacity (9), chronic infiltrative lung disease (10), and pleural and pulmonary asbestos-related abnormalities (11). Our study results show that radiation dose reduction could be extended to the objective CT quantification of pulmonary emphysema.

### Effect of Section Thickness

Section thickness does not substantially influence the strength of correlations between histopathologic indexes and either relative areas or percentiles. This finding suggests that increased section thickness has no advantage over thin sections obtained in 1-cm intervals. Nevertheless, section thickness does affect  $RA_{960}$ ,  $RA_{970}$ , and the 1st percentile. There is an average difference of 2% among  $RA_{960}$  and  $RA_{970}$  values measured on CT sections of different thicknesses ranging from 1.25 to 10.0 mm. For the 1st percentile, this represents a difference of 25 HU, indicating that the attenuation coefficient corresponding to

**Table 5**

#### Correlation Coefficients for Relationships between MIWD and Percentile Derived with Various Tube Current-Time Products and Section Thicknesses

Percentile	20 mAs			120 mAs		
	1.25 mm	5.0 mm	10.0 mm	1.25 mm	5.0 mm	10.0 mm
1st	-0.636	-0.653	-0.631	-0.627	-0.659	-0.675
3rd	-0.636	-0.579	-0.577	-0.646	-0.500	-0.582
5th	-0.615	-0.558	-0.566	-0.632	-0.474	-0.565
7th	-0.599	-0.554	-0.552	-0.617	-0.482	-0.555
10th	-0.581	-0.539	-0.543	-0.599	-0.473	-0.549
12th	-0.570	-0.536	-0.538	-0.594	-0.467	-0.544
15th	-0.560	-0.517	-0.522	-0.590	-0.457	-0.535
18th	-0.555	-0.508	-0.508	-0.579	-0.449	-0.521

Note.—Data are Spearman correlation coefficients. Percentiles of the distribution of attenuation coefficients were derived by using tube current-time products of 20 and 120 mAs and section thicknesses of 1.25, 5.0, and 10.0 mm.  $P < .001$  for all comparisons.

Table 6

## Correlation Coefficients for Relationships between MP and Percentile Derived with Various Tube Current–Time Products and Section Thicknesses

Percentile	20 mAs						120 mAs					
	1.25 mm		5.0 mm		10.0 mm		1.25 mm		5.0 mm		10.0 mm	
	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value	<i>r</i>	<i>P</i> Value
1st	0.537	<.001	0.557	<.001	0.519	<.001	0.532	<.001	0.560	<.001	0.569	<.001
3rd	0.529	<.001	0.498	<.001	0.474	<.001	0.564	<.001	0.394	.001	0.485	<.001
5th	0.507	<.001	0.477	<.001	0.463	<.001	0.545	<.001	0.370	.002	0.468	<.001
7th	0.488	<.001	0.469	<.001	0.450	<.001	0.531	<.001	0.382	.001	0.459	<.001
10th	0.471	<.001	0.456	<.001	0.447	<.001	0.510	<.001	0.375	.001	0.453	<.001
12th	0.461	<.001	0.453	<.001	0.448	<.001	0.505	<.001	0.366	.002	0.448	<.001
15th	0.456	<.001	0.439	<.001	0.440	<.001	0.501	<.001	0.360	.002	0.447	<.001
18th	0.452	<.001	0.436	<.001	0.431	<.001	0.492	<.001	0.360	.002	0.440	<.001

Note.—Percentiles of the distribution of attenuation coefficients were derived by using tube current–time products of 20 and 120 mAs and section thicknesses of 1.25, 5.0, and 10.0 mm. *r* = Spearman correlation coefficient.

Figure 2

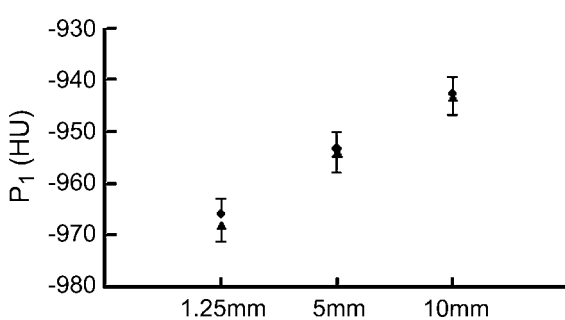


Figure 2: Mean 1st percentile ( $P_1$ ) values (with standard errors of the mean) measured at 20 effective mAs (▲) and 120 effective mAs (◆) on 1.25-, 5.0-, and 10.0-mm-thick CT sections. Section thickness ( $P < .001$ )—but not radiation dose ( $P = .910$ ) or the interaction between dose and thickness ( $P = .215$ )—was found to have a significant effect on 1st percentile values.

the 1st percentile increases slightly when the section thickness increases—for example, from  $-968$  HU at 1.25 mm to  $-943$  HU at 10.0 mm in our current study group. These differences prevent comparisons of values measured at different section thicknesses and suggest that the section thickness should be kept constant in follow-up examinations.

Thin-section incremental CT has been proposed for the quantification of pulmonary emphysema (24,25,27). Spiral CT has the major advantage of enabling coverage of the entire thorax during one breath hold. Our analyses were based on two-dimensional image findings because macroscopic and microscopic quantifications are also based on two-dimensional measurements. A very strong correlation between two-dimensional and three-dimensional image findings has been shown and suggests that the

results of our study could be applied to three-dimensional models (30).

Our study had limitations. First, only a few patients had severe emphysema; the majority of patients had moderate emphysema. This factor was inherent in the recruitment process, in which only those patients referred for thoracic surgery were accepted. It is not known whether the correlations between the CT measurements and the morphometric data would have been strengthened if a higher proportion of patients with severe emphysema had been included. Another limitation was related to the macroscopic sampling. We analyzed two macroscopic sections that were obtained mainly on the basis of the available nontumoral lung parenchyma and therefore might not have been perfectly representative of the entire lung parenchyma. However, to

consider the cephalocaudal gradient in the distribution of pulmonary emphysema, these sections were obtained vertically (22). A third limitation may have stemmed from the fact that analysis of variance procedures require the variables to be normally distributed. Nevertheless, according to the central limit theorem (31), the number of patients in our study ( $n = 70$ ) was sufficiently high such that we could be reasonably confident in the results obtained at these analyses.

In conclusion, we believe that reducing the radiation dose to 20 mAs should be recommended for patients undergoing CT quantification of pulmonary emphysema and that comparisons of findings between examinations, such as in follow-up studies, require that both the dose and the section thickness be kept constant.

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