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Quantitative Assessment of Lung Volumes using Multi-detector Row Computed Tomography (MDCT) in Patients with Chronic Obstructive Pulmonary Disease (COPD)[1]

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Purpose: To evaluate the clinical value of the multi-detector row computed tomography (MDCT) in the quantitative assessment of lung volumes and to assess the relationship between the MDCT results and disease severity as determined by a pulmonary function test (PFT) in Chronic Obstructive Pulmonary Disease (COPD) patients.

Materials and Methods: We performed a PFT and MDCT on 39 COPD patients. Using the GOLD classification, we divided the patients into three groups according to disease severity; stage I (mild, $n=10$), stage II (moderate, $n=15$), and stage III (severe, $n=14$). Using the pulmo-CT software program, we measured the proportion of lung volumes with attenuation values below -910 and -950 HU.

Results: The mean FEV1 (% of predicted) and FEV1/FVC was 82.2±2% and 66.2±3% in stage I, 53.5±11% and 52±6% in stage II, and 32.3±7% and 44.2±13% in stage III, respectively. Differences in lung volume percentages at each of the thresholds (-910 and -950 HU) among the 3 stages were statistically significant ($p<0.01$, $p<0.01$) and correlated well with the FEV1 and FEV1/FVC (r= -0.803, r= -0.766, r= -0.817, and r= -0.795, respectively).

Conclusion: The volumetric measurement obtained by MDCT provides an accurate means of quantifying pulmonary emphysema.

Index words : Chronic obstructive pulmonary disease
Computed tomography (CT)
Lung volume measurements
Chest

With chronic obstructive pulmonary disease (COPD), the assessment of normal lung volume is important for monitoring the course and severity of the disease. In COPD, it is mainly destruction (or failure to repair) the lung parenchyma that leads to emphysema and it is important to detect structural alterations that occur to varying degrees in the small bronchi and membranous bronchioli (i.e., airways <2 mm in diameter) (1). The structural alterations in these two sites are considered to be the most important contributors to the airflow limitation and accelerated decline of FEV1 in COPD. Consequently, sequential measurements of FEV1 are mostly used for monitoring the progress of the disease. However, no single pulmonary function test exists to evaluate all the parameters necessary to diagnose and

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assess the severity, prognosis, and course of the disease.

High-resolution computed tomography (HRCT) is known to be a useful method for quantifying the extent of emphysema. Several reports have shown the relationship between the HRCT scan and the pulmonary function test (PFT) in the analysis of COPD (2 - 7). With the recent advances in multi-detector row computed tomography (MDCT) technology, volumetric data can be acquired more quickly and easily for use in the evaluation of lung volume (8). Because the range of CT values in the lung is strongly influenced by the content of air per voxel, the extent of emphysema can be accurately determined by a quantitative volumetric CT that analyzes the range, frequency, and distribution of CT values using MDCT at a certain threshold.

The purpose of this study was to evaluate the clinical usefulness of MDCT for the quantitative assessment of lung volumes and to assess the relationship between MDCT results and the severity of COPD disease as determined by the PFT.

Materials and Methods

Patients Selection

Between August 2004 and December 2006, 39 patients with COPD underwent a PFT and MDCT. The study patients included 32 men and 7 women, aged from 50 to 71 years (mean age, 62 years).

The diagnosis of COPD was made based on a clinical examination, chest radiographs, and lung function parameters from the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop Report (9). We excluded patients who had severe cardiac disease, diffuse or focal parenchymal abnormalities affecting more than one segment, or pleural effusion.

The study patients were divided into three groups according to disease severity based on the criteria set by the GOLD workshop report (9); stage I: ($n=10$, mild, FEV1/FVC < 70% of predicted, FEV1/predicted FEV1 > 0.8), stage II: ($n=15$, moderate, FEV1/FVC < 70% of predicted, 0.3 $\leq$FEV1/predicted FEV1 < 0.8) and stage III:($n=14$, severe, FEV1/FVC < 70% of predicted, FEV1/predicted FEV1 < 0.3 or FEV1/predicted FEV1 < 0.5 with respiratory failure or clinical signs of right heart failure).

This study was approved by the institutional review boards.

Pulmonary Function Test

A PFT was performed prior to the MDCT examinations in a dedicated pulmonary function laboratory, under the supervision of a certified pulmonary technologist. For all patients, the interval between the PFT and MDCT was less than 2 weeks.

The PFT indexes were measured using a spirometer (Vmax 229, Sensormedics, U.S.A.). The PFT parameters included the vital capacity (VC), forced expiratory volume in 1 sec (FEV1), ratio of the forced expiratory volume in 1 sec to the forced vital capacity (FEV1/FVC), and diffusing capacity of the lung for carbon monoxide (DLCO). The values for VC, FEV1, FEV1/FVC, and DLCO were expressed as percentages of the predicted values (percentage of predicted).

MDCT examination

A MDCT scan was performed using a sixteen-slice helical CT (Somatom Sensation 16, software version VA20, Siemens Medical Solutions, Forchheim, Germany) without intravascular contrast material administration. The CT scan was performed in the supine position, from the lung apices to the level of the adrenal gland during inspiration. To obtain thin-section CT images, we used the following parameters: 120 kVp, 180 mAs, 1 mm table feed/rotation, 1 mm collimation, and 0.5 mm interval. The image data were reconstructed with a 1.0 mm thickness using a bone algorithm.

Volumetric assessment technique (densitometry)

The MDCT scans were evaluated using the Pulmo-CT software (Pulmo, Wizard, Siemens Medical Solutions, Germany). The boundaries of each lung were automatically determined by a density-discriminating software program. The trachea, main-stem bronchi, mediastinal structures, and soft tissues were selectively removed by the pulmo-CT software. Manual corrections of lung contour tracing were usually needed at the carina level due to the irregular shape of the hilar bronchovascular structures. Furthermore, we manually removed the soft tissue structures, main bronchus, and vessels, which could not be done automatically using the pulmo-CT software. Lung density values were calculated according to the threshold values. The numeric analysis of lung attenuation was demonstrated in different forms including histograms, and tables (Fig. 1).

The threshold limits for total lung volume ranged from - 600 to - 1024 HU in order to exclude soft tissue surrounding the lung and large vessels within the lung

(10). The volume, attenuation distribution, mean attenuation, and SD of attenuation of the whole lung volume were demonstrated using a histogram display. The histogram provided a frequency distribution of voxels with specific attenuation numbers (in HU) in the lung. The percentage of voxels with attenuation values below a specific level was defined as the lower attenuation volume at that threshold. Using the pulmo-CT software program, we measured the proportion of lung volumes with attenuation values below the -910 and -950 HU thresholds. The thresholds for the assessment of abnormally low attenuation of the lung were made on the basis of previous studies (2 - 6).

The percentages of abnormally low attenuation of lung volumes were calculated using the following formula: percentage of low attenuation of lung volume = 100*[hypo-attenuating volume (l)/total lung volume (l)].

Table 1. Results from the Pulmonary Function Tests in 39 Patients with Chronic Obstructive Pulmonary Disease

Parameter	Stage I (n=10)	Stage II (n=15)	Stage III (n=14)
VC (% of predicted)	101.3 ± 4	85.4 ± 13	71.9 ± 15
FEV1(% of predicted)	82.2 ± 2	53.5 ± 11	32.3 ± 7
FEV1/FVC(% of predicted)	66.2 ± 3	52.0 ± 6	44.2 ± 13
DLCO(% of predicted)	72.5 ± 2	48.3 ± 10	36.7 ± 12

VC: Vital capacity, FEV1: forced expiratory volume in 1 second, FEV1/FVC: the ratio of the forced expiratory volume in 1 second to the forced vital capacity, DLCO: diffusing capacity of the lung for carbon monoxide.
Stage I: (FEV1/FVC <70% of predicted, FEV1/predicted FEV1 >0.8)
Stage II: (FEV1/FVC <70% of predicted, 0.3≤FEV1/predicted FEV1 <0.8)
Stage III: (FEV1/FVC <70% of predicted, FEV1/predicted FEV1 <0.3 or FEV1/predicted FEV1 <0.5 with respiratory failure or clinical signs of right heart failure)

Statistical analysis

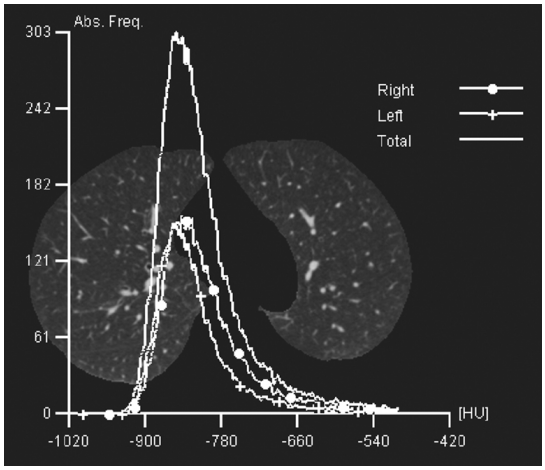
The percentages of the abnormally low attenuation lung volumes were compared among the three COPD groups using a one-way ANOVA via the Student-Newman-Keuls method. Further, the percentages of the abnormally low attenuation lung volumes were tested for a possible relationship with the PFT results using a Pearson's correlation. *P*-values less than 0.05 were considered statistically significant.

The SPSS software (Version 10.0 Statistical Package for the Social Sciences, Chicago, IL) was used for the statistical evaluations.

Results

The PFT results of 39 COPD patients are summarized in Table 1. A total of 10 patients in stage I, 15 in stage II, and 14 in stage III had mean FEV1 (% of predicted) and FEV1/FVC of 82.2 ± 2% and 66.2 ± 3%, 53.5 ± 11% and 52 ± 6%, and 32.3 ± 7% and 44.2 ± 13%, respectively.

Table 2 shows the CT densitometry results of the 39 patients with COPD. The values for the lower attenuation volume at the -910 and -950 HU thresholds at inspiration were 22.5 ± 5% and 11.2 ± 3% in stage I, 37.7 ± 10% and 21.6 ± 8% in stage II, and 51.6 ± 11% and 39.3 ± 12% in stage III, respectively. The differences in lung volume percentages at a threshold of -910 HU among the three stages were statistically significant (22.5 ± 5%, 37.7 ± 10%, and 51.6 ± 11%, for stage I, II and III, respectively, p<0.01). The differences in the



A

Evaluation Range (*) : -1024 HU to -600 HU (*) = FWHM within full H

Statistics		Left	Right	Total
Mean	[HU]	-805.5	-798.2	**-802.1**
Stand. Dev	[HU]	66.8	70.7	**68.8**
Area	[cm2]	17543.2	15623.0	**33166.1**
FWHM	[HU]	142	142	**142**
Volume	[cm3]	1754.0	1560.2	**3314.3**
Height	[cm]	23.2	23.2	**23.2**

B

Fig. 1. Demonstration of pulmo-CT results with a histogram (**A**) and table (**B**).

percentage of lung volume at a threshold of -950 HU among the three stages were statistically significant (11.2 ± 3%, 21.6 ± 8%, and 39.3 ± 12%, for stage I, II and III, respectively, $p < 0.01$).

The percentage of lung volumes at a threshold of -910 HU showed a strong correlation with the FEV1 (% of predicted) and FEV1/FVC (% of predicted) (r = -0.803 and r = -0.766, respectively (Fig. 2). The percentage of lung volumes at a threshold of -950 HU correlated well with the FEV1 (% of predicted) and FEV1/FVC (% of predicted) (r = -0.817 and r = -0.795, respectively) (Fig. 3).

Table 2. Results from CT Densitometry in 39 Patients with Chronic Obstructive Pulmonary Disease

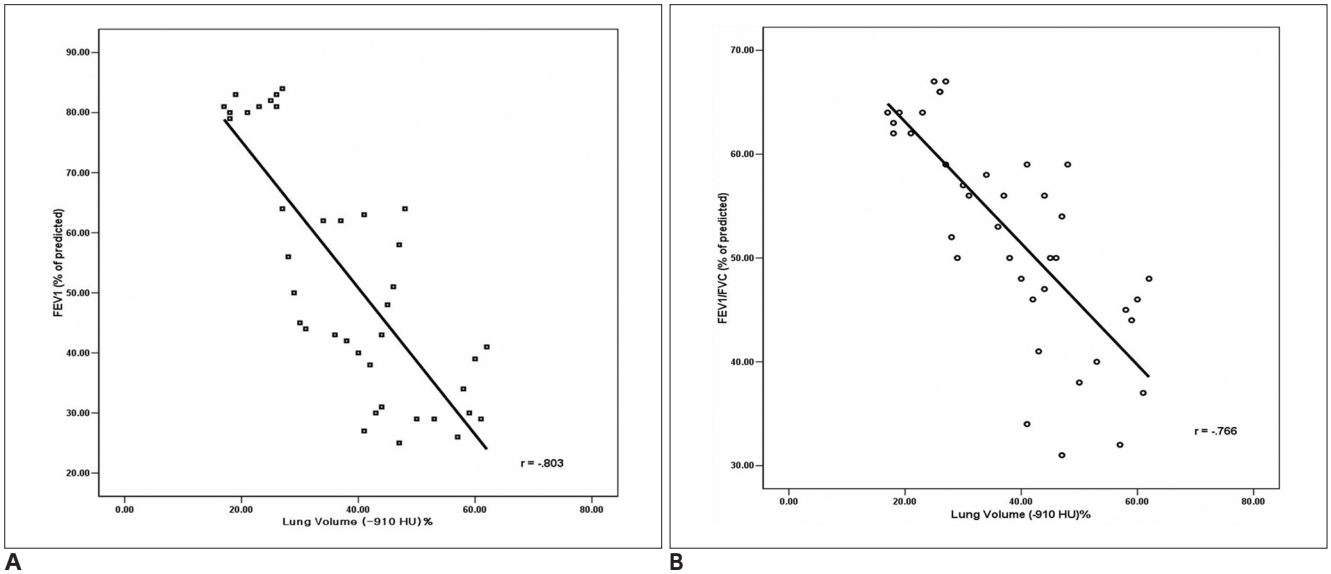
Parameter	Stage I (n=10)	Stage II (n=15)	Stage III (n=14)
Mean inspiratory attenuation (HU)	-879 ± 5	-886 ± 13	-891 ± 21
Total lung volume (cm^3)	5018 ± 1469	4857 ± 1446	4338 ± 1687
Percentage of lung volume (%)*			
-950 HU	11.2 ± 3	21.6 ± 8	39.3 ± 12
-910 HU	22.5 ± 5	37.7 ± 10	51.6 ± 11

Stage I: (FEV1/FVC < 70% of predicted, FEV1/predicted FEV1 > 0.8)
Stage II: (FEV1/FVC < 70% of predicted, 0.3≤FEV1/predicted FEV1 < 0.8)
Stage III: (FEV1/FVC < 70% of predicted, FEV1/predicted FEV1 < 0.3 or FEV1/predicted FEV1 < 0.5 with respiratory failure or clinical signs of right heart failure)
N = number of patients
Note: Mean values ± standard deviation (SD) are indicated.
*Percentages of abnormally low attenuation of lung volumes were calculated using the following formulas: percentage of low attenuation of lung volume = 100 * [hypo-attenuating volume (l)/total lung volume (l)].

Discussion

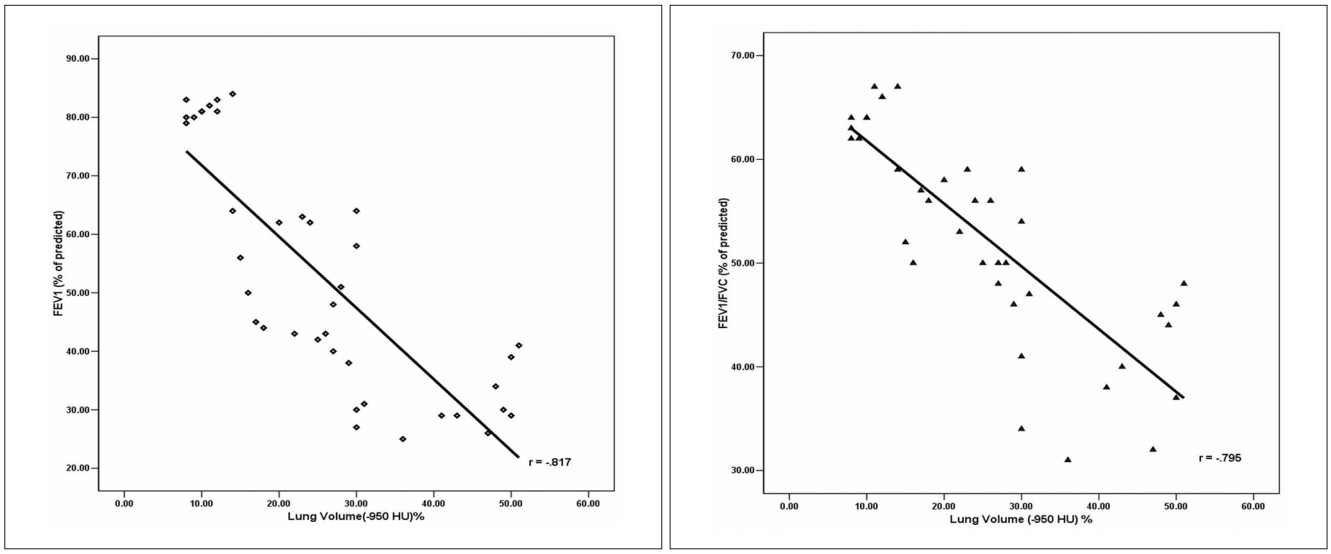
In the present study, we found that quantitative measurements of lung volumes by MDCT correlated well with disease severity as determined by a PFT. This finding suggests that the volumetric measurements obtained by MDCT provides an accurate means of quantifying lung volume and could be used for the diagnosis and monitoring of the progression of emphysema in COPD patients.

Many studies have assessed the use of CT for the quantitative analysis of structural abnormalities caused by airway obstruction and emphysema in COPD patients (2-6). Inspiration CT shows the extent of emphysema (4, 5), while the expiratory CT reflects the expiratory airflow limitation and the subsequent air trapping (6). In previous studies, it has been shown that the severity of anatomical emphysematous changes in the HRCT correlate well with a PFT (2, 3), According to Arakawa A et al. (3), a good correlation exists between the inspiratory and expiratory volumetric measurements of abnormally low attenuated lung volume and the percentage of FEV1, FEV1/FVC, and DLCO. Several



A B

Fig. 2. The relationship between the lung volume percentage at a threshold of -910 HU and the pulmonary function tests (PFT) in 39 patients with COPD.
A. Correlation between the lung volume percentages at a threshold of -910 HU and FEV1 (% of predicted), (r = -0.803).
B. Correlation between the lung volume percentages at a threshold of -910 HU and FEV1/FVC (% of predicted), (r = -0.766).



A B

Fig. 3. The relationship between the lung volume percentage at a threshold of -950 HU and the pulmonary function tests (PFT) in 39 patients with COPD.
A. Correlation between the lung volume percentages at a threshold of -950 HU and FEV1 (% of predicted), (r = -0.817).
B. Correlation between the lung volume percentages at a threshold of -950 HU and FEV1/FVC (% of predicted), (r = -0.795).

studies have demonstrated that expiratory CT assessments correlate more closely with the peripheral airway obstruction in COPD (11-13). However, one recent report (14) demonstrated that the inspiratory CT was equal to the expiratory CT with respect to its ability to quantify an abnormally low attenuation of the lungs caused by pulmonary emphysema. Our results also revealed a good correlation between inspiratory volumetric measurements of abnormally low attenuated lung volume and PFT parameters.

The low attenuation thresholds that have been most widely used to identify emphysema on conventional 10-mm-thick CT sections are -900 or -910 HU (7). Using thin section CT scans at 1-mm collimation without intravenous administration of contrast material, Gevenois et al. (4, 5) found that a lower attenuation threshold of -950 HU correlated best with morphologic emphysema. The low attenuation thresholds that were used in our study were -910 and -950 HU, because we used thin section CT scans at 1-mm collimation without intravenous administration of contrast material.

Advances with MDCT and the workstation made it possible to obtain and analyze the lung volume data in order to generate histograms of attenuation in Hounsfield units for the lung (8). The measurement of CT pixel attenuation values provides an objective method for quantifying the severity of emphysema. Various techniques have been performed to separate the lung from other soft tissues in order to reduce the time involved in this analysis, but with techniques available on most modern workstations, 3D lung models can be generated with volumetric data acquired by MDCT. The lungs are easily separated from the soft-tissue structures including the trachea, main stem bronchi, and esophagus, with minimal post-processing. With this model, 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. CT densitometry shows the difference in lung density between the dependent and nondependent portion. The differences are smallest for lung volumes near the total lung capacity (15).

In clinical practice, the severity and progression of emphysema are usually assessed on the basis of clinical symptoms and spirometric findings, which indicate global airflow obstruction. However, both of these parameters are relatively insensitive to small changes in the amount of emphysematous tissue in the lung. A variety of pharmacologic and endobronchial treatments of patients with smoking-related emphysema also are under development (16-19). With the advent of these new treatments, it is important to have a sensitive and accurate test to assess the degree of pulmonary emphysema for the early detection of the disease, monitoring the response to treatment, and initial drug validation. As a result, a quantitative chest CT has been proposed as a sen-

sitive test for quantifying emphysematous changes within the lung (20, 21). Our results showed a good correlation between abnormally low attenuated lung volume measurements and disease severity, which is reflected by the physiologic values from the pulmonary function test. Therefore, we believe that volumetric scanning of the entire lung via the MDCT is useful and representative of underlying pulmonary function.

Our study had the following limitations. Firstly, the study population was too small to generalize the results. Secondly, we did not include normal control subjects. Thirdly, the MDCT scans were performed during inspiration. Although several studies have demonstrated that expiratory parameters correlate more closely with airflow obstruction and air trapping than inspiratory parameters, in our study, the quantitative lung volumes obtained during inspiration correlated well with the PFT parameters. Fourthly, CT densitometry is influenced by the level of inspiration during CT. We did not use spirometric gating to control for lung volume during CT acquisition. Hence, we cannot exclude the possibility that an inadequate inspiratory effort by the patient could lead to an increase in lung attenuation, potentially simulating the histogram metric changes correlated to lung fibrosis. These limitations will need to be addressed in future studies.

In conclusion, the volumetric measurements obtained by MDCT can provide accurate quantification of lung volume in COPD patients. In addition, the measurements with MDCT correlate well with disease severity, as determined by a PFT. Therefore, we believe that volumetric scanning of the entire lung by MDCT is a promising tool for the diagnosis and monitoring of the progression of emphysema in COPD patients.

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만성 폐쇄성 폐질환 환자에서 MDCT를 사용한 폐용적의 정량분석[1]

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목적: 만성폐쇄성 폐질환 환자에서 MDCT를 이용한 폐 용적 정량분석의 임상적 유용성과, 측정된 폐 용적과 폐 기능 검사에 의한 질환의 중증도와의 관계를 알아보는 것을 목적으로 하였다.

대상과 방법: MDCT와 폐 기능 검사를 시행한 39명의 만성폐쇄성 폐질환 환자를 대상으로 하였다. GOLD 분류법을 사용하여 환자들을 질환의 중증도에 따라 stage I(경증, 10명), stage II(중등증, 15명) 그리고 stage III(중증, 14명)로 분류하였다. Pulmo - CT 프로그램 분석을 이용하여 MDCT에서 역치가 HU값이 - 910 이하 와 - 950 이하인 경우에서 폐 용적을 측정하였다.

결과: FEV1(% of predicted) 과 FEV1/FVC는 각 Stage에 따라서 82.2 ± 2%, 66.2 ± 3%(stage I), 53.5 ± 11%, 52 ± 6%(stage II) 그리고 32.3 ± 7%, 44.2 ± 13%(stage III)로 측정되었다. 각 역치값(- 910와 - 950 HU)에서 측정한 폐 용적은 질환의 중증도에 따라 통계학적으로 유의한 차이가 있었다($p < 0.01$, $p < 0.01$). 두 역치값(- 910와 - 950HU)에서 측정한 폐 용적률은 FEV1과 FEV1/FVC와 잘 일치하였다(r= - 0.803, r= - 0.766, r= - 0.817, r= - 0.795).

결론: MDCT를 이용한 폐 용적의 측정법은 폐기종을 정량화할 수 있는 유용한 방법이다.