J. Tokyo Med. Univ., **61**(5) : 433-440, 2003

Evaluation of chronic pulmonary emphysema by ultrafast computed tomography

Fumihiro TSUCHIDA[1], Hisanaga YAGYU[1], Shuji OHISHI[1], Hiroyuki NAKAMURA[1], Toshio KIGUCHI[2], Misako YAMAGUCHI[2], Takeshi MATSUOKA[1]

[1]Fifth Department of Internal Medicine, Tokyo Medical University, 3-20-1, Chuo, Ami, Inashiki 300-0395 Ibaraki, Japan
[2]Internal Medicine, Tachikawa Hospital, Niigata, Japan

Abstract

Objective : We compared pulmonary ventilation dynamics between 41 patients with pulmonary emphysema and 11 healthy subjects with normal pulmonary function using ultrafast computed tomography (CT).
Methodology : Regions of interest (ROIs) for multislice scanning were selected from the anatomical levels of the carina in the right upper lung field. Several identical slices were selected from the inspiratory and expiratory scans. The average CT values in the ROIs (AvROI) were obtained during the inspiratory phase (inAvROI) and the expiratory phase (exAvROI. The ratio of change from inAvROI to exAvROI ((I−E)/E ratio) was also used for image analysis. Furthermore, possible correlations between the CT image parameters and pulmonary function test parameters were examined.
Results : The results showed that the exAvROI and inAvROI values and (I−E)/E ratio were lower in the emphysema group than in the normal pulmonary function group. Among the image data parameters, the exAvROI value correlated most closely with pulmonary function parameters, in particular, with the pulmonary diffusing capacity.
Conclusions : These findings suggest that image data parameters of ventilation dynamics may be useful for evaluating the severity of pulmonary emphysema.

Introduction

Qualitative and quantitative computed tomography (CT) image analysis of obstructive pulmonary disease, in particular pulmonary emphysema, has been performed in recent studies. Correlations between parameters obtained by such analysis and parameters of pulmonary function test have often been described using high-resolution computed tomography (HRCT. HRCT, however, requires patients to hold their breath for several tens of seconds. However, breath-holding for even such short periods may be difficult for patients with severe obstructive pulmonary disease, thus HRCT may not always be useful for an accurate assessment of severity in these patients.

In contrast, resting ultrafast CT does not necessitate breath-holding during scanning. This modality might therefore allow physicians to perform a dynamic pulmonary image analysis. In the current study, we examined the correlation between ultrafast CT image parameters and parameters of pulmonary function tests, to determine whether or not this type of CT is useful for patients with obstructive pulmonary disease.

Subjects and Methods

A total of 52 subjects were included in this study.

Received April 5, 2003, Accepted June 23, 2003
Key words : Key words : Ultrafast computed tomography (CT), Pulmonary function test, Ventilation dynamics, Pulmonary emphysema
Fifth Department of Internal Medicine, Tokyo Medical University, 3-20-1, Chuo, Ami, Inashiki 300-0395 Ibaraki, Japan

Forty-one male patients with a history of smoking and given a diagnosis pulmonary emphysema, were assigned to the emphysema group, and 11 subjects with normal plain chest X-ray findings, whose percent forced expiratory volume in the first second ($FEV_{1.0}$%) was more than 70%, were assigned to the normal pulmonary function group. The normal pulmonary function group was volunteer group. There was no significant difference in mean age between the emphysema group and the normal pulmonary function group (Table 1). Informed consent was obtained from each patient before entry into the study.

Pulmonary function tests were carried out using a Fudac 70 (Fukuda Co. Ltd., Tokyo, Japan). The parameters examined in this study were vital capacity (%VC), FEV_1% of the predicted FEV_1 (FEV_1% predicted), the ratio of the residual volume to the total lung capacity (RV/TLC), pulmonary carbon monoxide diffusing capacity (%DLco/VA), and $\dot{V}_{50}$.

Table 1 Subject characteristics and pulmonary function tests

	NORMAL (n=11)	EMPHYSEMA (n=41)
Age (yr)	68±8	70±7
B.I.**	1,028±324	1,326±422
%VC (%)	107±16	91±23
FEV_1% (%)	78±5	50±13*
FEV_1%pred (%)	108±15	61±22*
$\dot{V}_{50}$ (l/sec)	3.08±1.16	0.76±0.46*
RV/TLC (%)	38±10	53±11*
DLco/VA (%)	102±16	57±33*

Values are expressed as mean±SD
*$p < 0.0001$
**B.I.=Brinkmann index for cigarette smoking (cigarettes per day×years smoking)

Multislice CT scanning was performed using an Imatron C-150L (Imatron Inc, South San Francisco, USA), which generated eight 7-mm-thick slices from the anatomical level of the carina in the right upper lung field in 0.1 seconds. The subject was asked to wear a mouthpiece and to breathe easily (almost functional residual capacity level) through the device. According to the manufacturer's instruction manual, CT scanning was performed at the expiratory and inspiratory peak determined on a flow-volume recorder (Fig. 1). Hard-copy images were photographed using a window setting appropriate for the lungs (level : −700HU ; width : 1,000 HU).

Image analysis

Regions of interest (ROIs) were selected from the anatomical levels of carina in the right upper lung field. Several identical slices were chosen from 8 slices each obtained during the inspiratory and expiratory phases. We calculated the CT values in the ROIs with 8 slices each (Fig. 2). The average of 8 slice's CT values in the ROIs (AvROI) were obtained during the inspiratory phase (inAvROI) and the expiratory phase (exAvROI). The parameters were read by three expert physicians. Their readings agreed well and the data were expressed as means±SD. In this study, we selected the right upper lung field for scanning, taking into consideration that pulmonary emphysema is most commonly of the centrilobular type, and that emphysematous lesions are

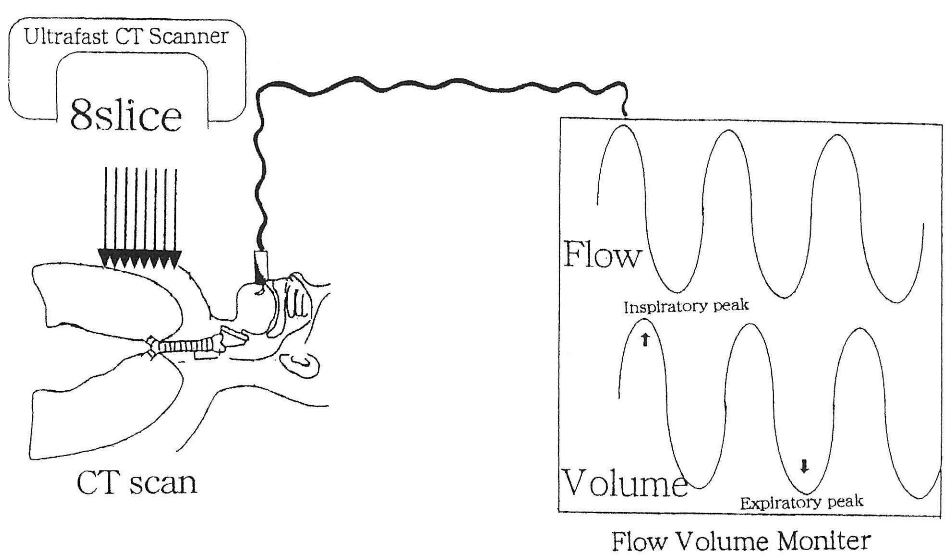

Fig. 1 Multislice CT scanning was performed using an Imatron C-150L, which generated eight 7-mm-thick slices from the anatomic level of the carina in the right upper lung field in 0.1 seconds. The subject was asked to wear a mouthpiece and to breathe easily (almost functional residual capacity level) through the device. In order to acquire peak expiratory and respiratory CT images, the operator performed CT scanning according to the manufacturer's instruction manual, watching the subject's respiration at inspiratory and expiratory phases on a flow-volume recorder

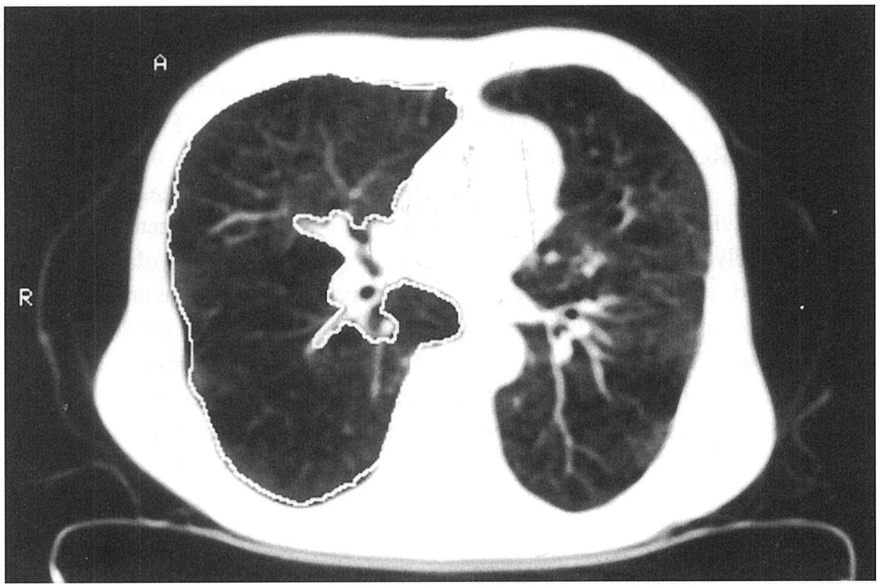

Fig. 2 Regions of interest (ROIs) for multislice scanning were selected from the anatomic levels of the carina in the right upper lung field.
Several identical slices were taken from 8 slices each from the inspiratory and expiratory phases. We calculated CT values in the ROIs with 8 slices each. The average CT values in the ROIs (AvROI) were obtained during the inspiratory phase (inAvROI) and the expiratory phase (exAvROI.

found mainly in the upper lobe. In fact, it has been reported that CT image analysis revealed that the percentage of low attenuation area (LAA%) was significantly higher in the upper lobe than in the lower lobe[1,2,3,4]. Wright et al.[5] indicated that either lower lobe or upper lobe scanning may provide information for global pulmonary assessment. Therefore, the anatomical levels of the carina in the right upper lung field was chosen, since the limited vertical motion in this region was expected to allow acquisition of several identical slices from among 8 slices each obtained during the inspiratory and expiratory phases with the patient on a stable table on a single scan.

The image data indicators used in this study were inAvROI, exAVROI, and I−E/E ratio ((defined as (inAvROI-exAvROI)/exAvROI×100)) to examine changes in CT values from inspiratory to expiratory phase. Correlations among these image data parameters and pulmonary function test parameters were tested using Spearman's coefficient of rank correlation. A p-value of less than 0.05 was considered to denote a statistically significant difference.

Results

As shown in Table 2, the inAvROI, exAvROI and (I−E)/E ratio values were expressed as means±SD. There were significant differences in all of these image parameters between the emphysema group and the normal pulmonary function group. Table 3 shows the correlation coefficients (r) between the image parameters and the pulmonary function test parameters in individual cases. There were weak positive correlations between the %VC and the image parameters, inAvROI, exAVROI, and (I−E)/E ratio.

FEV_1%predicted, FEV_1% and $\dot{V}_{50}$ showed positive

Table 2 The score of image parameters

	NORMAL (n=11)	EMPHYSEMA (n=41)
exAvROI	−746±34	−825±42*
inAvROI	−773±29	−837±38*
(I-E)/E ratio	3.98±1.51	1.99±1.60*

*p<0.0001

Table 3 Correlation coefficients between pulmonary function tests and score

	%VC	FEV_1 % predicted	FEV_1%	$\dot{V}_{50}$	RV/TLC	% DLco/VA
exAVROI	−0.351†	−0.641*	−0.965*	−0.668*	0.676*	−0.793*
inAvROI	−0.283†	−0.574*	−0.660*	−0.613*	0.611*	−0.770*
(I-E)/E ratio	0.295†	0.603*	0.625*	0.560*	−0.562*	0.619*

*p<0.0001, †p<0.05

correlations with the inAvROI, exAVROI, and the (I−E)/E ratio, while RV/TLC showed a negative correlation with inAvROI, exAVROI and the (I−E)/E ratio. The %DLco/VA showed a strong positive correlation with both inAvROI and exAvROI, and also with the (I−E)/E ratio.

The results revealed that inAvROI, exAvROI, and the (I−E)/E ratio all moderately correlated with the FEV_1% predicted, FEV_1% and $\dot{V}_{50}$, which are used as indicators for the assessment of obstructive pulmonary disease. The image parameters also moderately correlated with RV/TLC, an indicator of overinflation[6,7]. In addition, the three image parameters showed strong correlations with the %DLco/VA, which is used for assessing the extent of alveolar structure destruction. On the other hand, there was only a weak correlation between each image parameter and the %VC, consistent with the results of previous studies.

Among the image parameters, exAvROI showed a stronger correlation with each of the pulmonary function test parameters examined in this study, i.e., FEV_1% predicted, FEV_1%, $\dot{V}_{50}$, RV/TLC and %DLco/VA. In particular, there was a strong, positive correlation between exAvROI and the diffusion capacity parameter, %DLCo/VA ($r=0.793$) (Fig. 3).

Discussion

Qualitative and quantitative image data analysis of chronic obstructive pulmonary disease (COPD) using CT, has been become increasingly popular over the past few years. In this study, we employed ultrafast CT to evaluate local pulmonary ventilation in subjects during unrestrained breathing. Ultrafast CT on a 50-msec multislice scanner can provide contiguous, visually sharp images of the target area, allowing scanning of patients during unrestrained breathing. This is very advantageous in patients with respiratory disorders and young children who cannot manage to hold their breath during scanning. In addition, transmitted cardiac motion causes no artifacts in the pulmonary area adjacent to the heart during acquisition of images on ultrafast CT. Because of these advantages, we performed ultrafast CT scanning in patients with emphysema during unrestrained breathing and compared the current findings with those reported previously from studies conducted using conventional HRTC scans during breath-holding.

Quantitative image analysis of HRCT has been performed using parameters such as an average CT value in ROI[8], LAA%[3,9,10,11], histogram of CT numbers[12,13,14], and the change ratio ((I−E)/E ratio. The average CT value in a ROI is the average value of lung CT densities (CT number) in ROI. LAA%, the percentage of low attenuation areas having CT numbers that are at the prescribed level or lower, is used as an indicator of pathological emphysematous changes in the lung. A histogram of CT numbers depicts the distribution frequency of CT numbers in the lung, and the peak CT number or average CT number in the area that forms the lowest 5th percentile of the histogram is used as an indicator of emphysema.

Among these parameters, the average CT values in ROIs is the most easily obtained and therefore commonly applied in CT image analysis. However, the average CT value in a ROI is affected by the central airway and larger pulmonary vessels. If such influences were eliminated, the average CT value in a ROI might become a very good indicator of pulmonary lesions involving alveoli and small airways. On the other hand, the LAA% refers to the percentage of low attenuation areas in which the CT numbers are at a certain prescribed level or lower, reflecting the degree of destruction of the lung structure and air-trapping only. Therefore, the average CT value in a ROI is considered to be a better indicator of emphysematous changes.

The (I−E)/E ratio was also examined in this study. Eda et al.[15] investigated a possible relationship between respiratory functions and the ratio of deep expiratory CT number to deep inspiratory CT number (E/I ratio. The E/I ratio used by them is considered to be essentially the same parameter as the (I−E)/E ratio, even though the scanning procedures differ between the two. They reported that the E/I ratio strongly correlated with the FEV_1% and RV/TLC, while it showed a weak correlation with the %DLco/VA. Based on these results, they concluded that the E/I ratio reliably depicted air trapping, indicative of bronchiolar lesions. Therefore, the E/I ratio was considered to be a good indicator of airway lesions.

Taking the above into account, we used the average CT values in ROIs and the (I−E)/E ratio for the clinical evaluation of pulmonary ventilation.

In this study, the average CT values in ROIs were correlated with pulmonary function test parameters in both expiratory and inspiratory scans, and the exAvROI showed a stronger correlation with the %VC, FEV_1% predicted, FEV_1%, $\dot{V}_{50}$, RV/TLC, and %DLco/VA, than the inAvROI (Table 3).

Muller et al.[9], Knudson et al.[11] and Miniati et al.[16] reported that CT number during the expiratory phase correlated better with all respiratory function test parameters than those obtained during the inspiratory phase. Yamaguchi et al.[4] indicated that the average CT values in ROIs obtained during the expiratory phase were more sensitive to pulmonary abnormalities than those obtained during the inspiratory phase, whereas the LAA% obtained during the expiratory phase was less sensitive to pulmonary damage than that obtained during the inspiratory phase. Gevenois et al.[17] report-

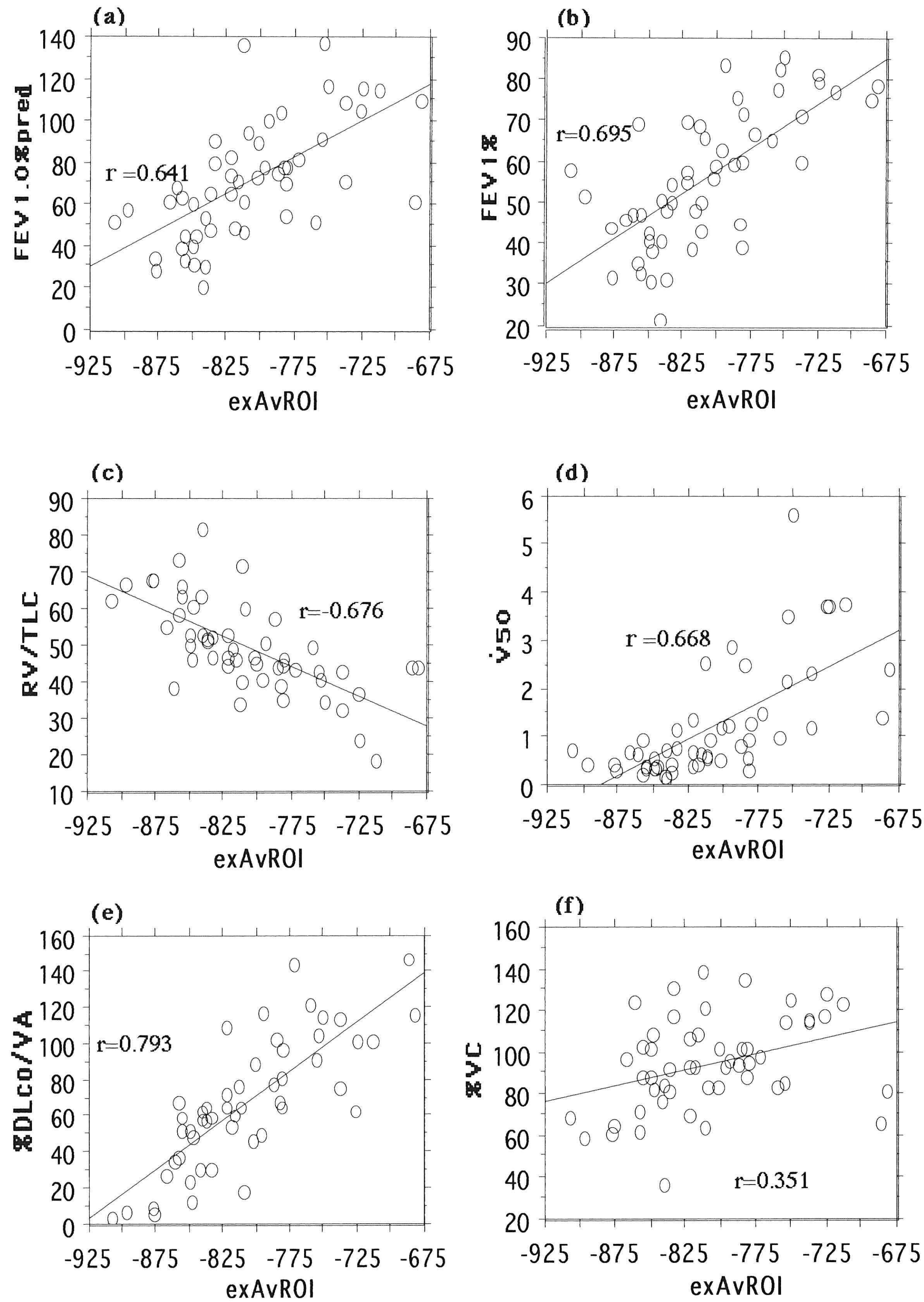

Fig. 3 Relationship of exAvROI to (a) FEV$_1$%predicted (b) FEV$_1$% (c) RV/TLC (d) $\dot{V}_{50}$ (e) %Dlco/VA (f) %VC
Among the image parameters, exAvROI showed a stronger correlation with each of the respiratory function test parameters examined in this study, i.e., FEV$_1$% predicted, FEV$_1$%, $\dot{V}_{50}$, RV/TLC and %DLco/VA.

ed that the results of quantitative analysis of expiratory LAA% were not more accurate than that of inspiratory LAA% to determine the severity of pathological pulmonary emphysema. They concluded that inspiratory LAA% was a better parameter to determine the severity of emphysema, reasoning that expiratory LAA% might more reliably represent air trapping than emphysematous changes in the lung.

In this study, the results showed that the exAvROI correlated better with lung function test parameters than inAvROI. This is probably because resting ultrafast scanning depicts visually sharp images of emphysematous lesions without the influence of air trapping.

In addition, the results of this study showed similar correlations between the (I−E)/E ratio and each pulmonary function test parameter, including %VC, FEV_1% predicted, FEV_1% and RV/TLC, as Eda et al.[15] described previously. However, the (I−E)/E ratio more closely correlated with the %DLco/VA in this study. The difference between the results of the two studies may be explained by assuming that the CT scanning during resting ventilation and CT scanning during deep breathing created different CT images, depicting emphysematous changes such as acinar bronchiolar lesions, and microscopic tissue fibrosis, and changes in blood flow in conjunction with respiration.

In this study, the most noteworthy finding was that the image parameters used for resting CT correlated well with the diffusion capacity. A close correlation between the diffusion capacity and pathological emphysematous alterations has already been reported[18,19,20,21,22], and the correlation between the diffusion capacity and the degree of emphysema depicted on CT views has also been described[3,11,14,19,20,22]. The correlation coefficient between DLCO and CT image parameters in those studies ranged from 0.53 to 0.80[2,3,10,23]. The correlation coefficient in our study was as great as these reported figures. We presume that the resting AvROI might capture emphysematous degeneration complicated by acinar bronchiolar lesions and microscopic tissue fibrosis without the influence of air trapping, which were not acquired by CT scanning during deep breathing in previous studies.

Based on these findings, it is suggested that resting ultrafast CT scanning is as at least useful as conventional CT scans. ExAvROI may be more useful in the assessment of pulmonary emphysema, reflecting respiratory function. Further studies are required to establish an objective respiratory function evaluation based on self-evaluation of dyspnea, pulmonary function test parameters and CT images making use of the advantages of ultrafast CT.

References

1) Hitsuda Y, Kawasaki Y, Igishi T, Yasuda K, Mikami M, Kato K, Matsumoto S, Sasaki T: Utilization of NIH image for quantification of emphysema by computed tomography. Jpn respir soc **37**: 380–387, 1999
2) Sakai N, Mishima M, Nishimura K, Itoh H, Kuno K: An automated method to assess the distribution of low attenuation areas on chest CT scans in chronic pulmonary emphysema patients. Chest **106**: 1319–1325, 1994
3) Gurney JW, Jones KK, Robbins RA, Gossman GL, Nelson KJ, Daughton D, Spurzem JR, Rennard SI: Regional distribution of emphysema; correlation of high resolution CT with pulmonary function tests in unselected smokers. Radiology **183**: 457–463, 1992
4) Yamaguti K, Soejima K, Matsubara H, Oguma T, Imoue T, Shimada H, Mori M, Suzuki K, Koda E: Nomal predicted values of CT indices reflect emphysematous alterations in the lung. Jap J Thorac Dis **35**: 1060–1866, 1997
5) Wright JL, Barry W, Pare PD, Hogg JC: Ranking the severity of emphysema on whole lung slices: concordance of upper lobe, lower lobe, and entier lung ranks. Am Rev Respir Dis **133**: 930–931, 1986
6) Thurlbeck WM: Chronic airflow obstruction, correlation of structure and function. Baisil, New York, 129–188, 1985
7) West WW, Nagai A, Hodgkin JE, Thurlbeck WM: The national institutes of health intermittent positive pressure breathing trial-pathology studies. III the diagnosis of emphysema. Am Rev Respir Dis **135**: 123–129, 1987
8) Guenard H, Diallo MHH, Laurent F, Vergeret J: Lung density and lung mass in emphysema. Chest **102**: 198–203, 1992
9) Muller NL, Staples CA, Miller RR, Abboud RT: "Density Mask. an objective method to quantitative emphysema using computed tomography. Chest **94**: 782–787, 1988
10) Kinsella M, Muller NL, Abboud RT, Morrison NJ, DyBuncio A: Quantitation of emphysema by computed tomography using a "Density Mask" program and correlation with pulmonary function test. Chest **947**: 315–321, 1990
11) Knudson RJ, Standen JR, Kaltenborn WT, Knudson DE, Rehm K, Habib MP, Newell JD: Expiratory computed tomography for assessment of suspected pulmonary emphysema. Chest **99**: 1357–1366, 1991
12) Hayhurst MD, MacNee W, Flenley DC, Wright D, McLean A, Lamb D, Wightman AJA, Best J: Diagnosis of pulmonary emphysema by computerised tomography. Lancet **2**: 320–322, 1984
13) Gould GA, Redpath AT, Ryan M, Warren PM, Best JJK, Flenley DC, MacNee W: Lung CT density correlates with measurements of airflow limitation and the diffusing capacity. Eur Respir J **4**: 141–146, 1991
14) MacNee W, Gould GA, Lamb D: Quantifying emphysema by CT scanning. clinicopathologic

correlates. Ann NY Acad Sci **624**: 179-194, 1991

15) Eda S, Kubo K, Fujimoto K, Matsuzawa Y, Sekiguchi M, Sakai F: The relations between expiratory chest CT and pulmonary function tests in emphysema. Am J Respir Crit Care Med **155**: 1290-1294, 1997
16) Miniati M, Filippi E, Falaschi F, Carrozzi L, Milne ENC, Sostman HD, Pistolesi M: Radiologic evaluation of emphysema in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med **151**: 1359-1367, 1995
17) Gevenoise PA, Vuyst PD, Sy M, Scillia P, Chaminade L, Maertelaer V, Zanen J, Yernault JC: Pulmonary emphysema. quantitative CT during expiration. Radiology **199**: 825-829, 1996
18) Bergin C, Muller N, Nichols DM, Lillington G, Hogg JC, Mullen B, Grymaloski MR, Osborne S, Pare PD: The diagnosis of emphysema. A computed tomographic-pathologic correlation. Am Rev Respir Dis **133**: 541-546, 1986
19) Gould GA, MacNee W, McLean A, Warren PM, Redpath A, Best JJK, Lamb D, Flenley DC: CT meansurements of lung density in life can quantitate distal airspace enlargement-An essential defining feature of human emphysema. Am Rev Respir Dis **137**: 380-392, 1988
20) Kuwano K, Matsuba K, Ikeda T, Murakami J, Araki A, Nishitani H, Ishida T, Yasumoto K, Shigematsu N: The diagnosis of mild emphysema. correlation of computedtomography and pathology scores. Am Rev Respir Dis **141**: 169-178, 1990
21) Ikeda T, Inuzuka T, Kuwano K, Murakami J, Araki T, Matsuba K, Shigematsu N: Evalution of pulmonary emphysema with high resolution computed tomography and the effect of smoking. Jap J Thorac Dis **29**: 202-205, 1991
22) Matsuba K, Kuwano K, Ikeda T, Murakami J, Ishida T, Yasumoto K, Shigemitsu N: The CT diagnosis of emphysema and correlation with pathologic findings. Jap J Thorac Dis **29**: 858-865, 1991
23) Gevenois PA, De Vuyst PD Maertelear V, Zanen J, Jacobovitz D, Cosio MG, Yernault JC: Comparison of computed density and microscopic morphometry in pulmonary emphysema. Am J Respir Crit Care Med **154**: 187-192, 1996

超高速 CT を用いた慢性肺気腫の検討

土田文宏　柳生久永　大石修司
中村博幸　木口俊郎　山口美沙子[2)]
松岡健

東京医科大学内科学第五講座
[2)]立川綜合病院

【要旨】 閉塞性肺疾患とくに肺気腫患者におけるこれまでの画像評価は、呼吸停止下で撮影されている。超高速 CT は、呼吸停止することなく安静換気下において撮影可能であるため動的状態における肺の画像評価が可能である。動的状態における肺の画像評価を試みた。

肺気腫患者 41 名と肺機能正常者 11 名を対象として超高速 CT を用いた換気動態画像を撮影した．関心領域を気管分岐部を中心とした右上肺野としマルチスライス法で撮影し吸気時、呼気時で同一スライスを数スライス選択した．その肺野平均 CT 値 (ROI) を計測しその平均値 (AvROI) を吸気時肺野平均 CT 値 (inAvROI)、呼気時肺野平均 CT 値 (exAvROI) として算出した．また吸気と呼気での CT 値の変化をみるための画像指標として変化率を用いた．これらの画像指標と呼吸機能検査につき比較検討した．肺機能正常群に比較して肺気腫群は、exAvROI、inAvROI とも低く変化率も有意に少なかった．画像指標の中では exAvROI が各肺機能と相関がよく、特に一秒率、拡散能との相関が強かった．我々の用いた画像指標の中では exAvROI が最も肺気腫の病態を反映していた。

安静換気下においてもこれまでの呼吸停止下における画像指標と同様に肺気腫の重症度評価が可能であると考えられた。超高速 CT を用いる事により動態換気時における画像指標が肺気腫評価の客観的指標の一つとなる事が示唆された．

〈**Key words**〉 超高速 CT、呼吸機能検査、換気動態、慢性肺気腫