



Inter-scan repeatability of CT-based lung densitometry in the surveillance of emphysema in a lung cancer screening setting

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ABSTRACT

Purpose: To investigate the inter-scan repeatability of CT-based lung densitometry protocols in the surveillance of emphysema in a lung cancer screening setting.

Materials and methods: Fifty-two healthy subjects who underwent low-dose chest CT and subsequent follow-up scan within a 16 month interval were retrospectively evaluated. Inter-scan repeatabilities were assessed for 9 different CT-based lung densitometry protocols with standard deviation (SD) of inter-scan differences. Susceptibility to inspiratory level was additionally assessed for each protocol, and volume adjustment (VA) was applied in order to evaluate the potential improvement of repeatability after compensating the influence of inspiratory level.

Results: A wide variation of inter-scan repeatability was observed among the evaluated protocols showing a difference of up to a factor of 9. Susceptibility of inspiratory level was found to be highly associated with the inter-scan repeatability of densitometric protocols. The application of VA could substantially reduce the influence of inspiratory level for all protocols, which results in an improvement of repeatability up to 51%.

The order of repeatability among the protocols remained unchanged after VA. The resulting two best protocols in terms of inter-scan repeatability were RA970 and Perc1 which showed SD of 0.8% and 5.5 HU, respectively.

Conclusions: Lung densitometry protocols produce different levels of repeatability for an asymptomatic population, each being influenced by inspiratory level to a different degree. For surveillance of emphysema in a lung cancer screening setting, RA970 and Perc1 may be the most suitable protocols, in which the application of VA needs to be included as a critical part.

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1. Introduction

The increasing use of low-dose computed tomography (CT) in a lung cancer screening provides an opportunity to apply CT-based lung densitometry for surveillance and early detection of emphysema in an asymptomatic population [1–5]. In surveillance of emphysema, variations of lung density due to different inspiratory level and natural loss of lung parenchyma during follow-up make it difficult to distinguish real emphysematous changes from those physiological noises. Thus, assessing the repeatability of CT-based lung densitometry, especially for healthy subjects, is an important necessary step for the application of emphysema surveillance in

a lung cancer screening setting. To the knowledge of the authors, however, still there is no comprehensive report on repeatability of various CT-based lung densitometry protocols and their robustness to inspiratory level for healthy subjects. Therefore, the purpose of this study was to investigate the inter-scan repeatability of various densitometry protocols (relative area below $-n$ HU, RA n ; the lowest n th percentile, Perc(n)) most often mentioned in the literature in an asymptomatic population in order to assess their potential for use in the quantitative monitoring of emphysema in a lung cancer screening setting.

2. Materials and methods

2.1. Patients

This single center retrospective study was approved by the institutional review board of our hospital, and informed consent

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Table 1
Clinical characteristics of subjects.

	Mean $\pm$ SD	Range
Age (year)	54.27 $\pm$ 9.07	34–71
Pack years	24 $\pm$ 13	5–60
FEV ₁ % predicted	99.0 $\pm$ 11.08	87–116
FVC % predicted	95.29 $\pm$ 6.99	88–109
FEV ₁ /FVC (%)	75.71 $\pm$ 3.30	72–80
TLV (mL)	4795 $\pm$ 943	3037–7148

Note: FEV₁ = forced expiratory volume in 1 s, FVC = forced expiratory vital capacity, TLV = total lung volume, SD = standard deviation.

was waived. Between February 2007 and March 2009, 52 subjects (39 men and 13 women; mean age, 54.5 years; age range, 34–71 years) who met the inclusion criteria on the day of CT examination (absence of severe tuberculosis sequelae, consolidation, bronchiolitis, congenital other abnormality, respiratory illness, and FEV₁/FVC <70%), underwent two low-dose chest CTs within mean follow-up period of 8 months (range, 12–480 days) in a lung cancer screening setting. On average, the subjects smoked 24 $\pm$ 13 pack-years (range, 5–60 pack-years). Pulmonary function tests (PFT) were performed on the day of baseline scanning and were not performed again on the day of repeat scanning. No subject received medical intervention. The extent of emphysematous lesions seen in all subjects was reviewed by two chest radiologists who were blinded to the clinical information. All subjects were in GOLD stage 0 (Table 1) [6].

2.2. Data acquisition

All scans were obtained using a 16-detector row CT (Sensation 16, Siemens Medical Systems, Erlangen, Germany) at suspended full inspiration with 1.0-mm section thickness and a pitch of 0.75. Spirometric gating was not applied in our lung cancer screening setting. No intravenous contrast media were injected. Exposure setting was fixed at 40 mAs at 120 kVp for all patients in both scans. Detector collimation of CT was 1.0 mm, and the rotation time was 0.5 s. All scans were reconstructed in a 512 $\times$ 512 matrix with a moderately soft B30f kernel.

2.3. Quality control

For quality control, the scanner used in our study was calibrated every 2 months with an AAPM (The American Association of Physicists in Medicine) CT performance phantom (model 76-410, Fluke Biomedical, Cleveland, OH), [7]. Then, to confirm the CT quality control, changes in mean CT numbers between baseline and repeat scans by using 4 circular regions of interest (ROI) placed on the images of 22 randomly selected patients were evaluated. Mean densities and standard deviations (SD) of ROIs in vessels, fat, lung parenchyma, and liver were calculated using freely available software (ImageJ 1.38x, NIH, Bethesda, MD).

In order to evaluate the consistency of inspiratory level between the two scans, we obtained the Pearson correlation coefficient between inspiratory levels of baseline and repeat scans. Total lung volume (TLV) was used as a surrogate for inspiratory level. Truncation effect of RA_n protocols was monitored so that any case with a relative area of 0% below the cut-off value in either scan could be found and excluded.

2.4. Volume adjustment

It is well known that lung densities measured by CT are significantly influenced by the inspiratory level of the patient at the particular examination [8]. As our subjects were of an asymptomatic population and were scanned without spirometric gating, it was expected that the lung densities of our subjects would be

highly susceptible to variation of inspiratory level between the two scans. Therefore, to standardize the influence of variation in inspiratory level to lung densitometry, we applied a volume adjustment (VA) technique as described previously in another study [9].

2.5. Densitometry

Our PC-based in-house software was used for fully automated quantification of lung density using the various protocols examined in this study [10]. The resulting CT data of the lung parenchyma were used to calculate TLVs and densitometric results according to the nine different protocols: RA910, RA930, RA950, RA960, RA970, Perc1, Perc5, Perc10, and Perc15. Example images are shown in Fig. 1.

2.6. Inter-scan repeatability

Inter-scan repeatability was evaluated using SD of differences in densitometric measurements between baseline and repeat scans for each protocol. Mean of differences was also evaluated to examine if there was a bias of measurements caused by technical factors or disease progression. In addition, we assessed the susceptibility of each densitometric protocol to inspiratory level. In this study, we defined the susceptibility to inspiratory level as the magnitude of the correlation coefficient between the inter-scan changes in lung densities and the inter-scan changes in inspiratory level. We used the magnitude of correlation coefficient because the Perc(*n*) protocols gives an opposite sign of correlation to RA_n protocols.

2.7. Statistical analysis

All statistical analyses were performed using a commercially available software program (SPSS 13.0 for Windows, SPSS, Chicago, Ill). The Student *t* test was used to determine the statistical significance of differences between ROI measurements, TLVs, and densitometric results in baseline and repeat scans. All densitometric results are given as mean $\pm$ SD (Table 2). To evaluate the effect of VA, the Pearson correlation coefficient of densitometric results between the two scans and limits of agreement based-on Bland–Altman plots were compared before and after applying VA for selected protocols. A *P* value of less than 0.05 was considered to indicate a statistical significance.

3. Results

3.1. Quality control

CT numbers measured at four different ROIs in baseline vs. repeat scans were: 44.0 $\pm$ 6.9 HU vs. 45.6 $\pm$ 6.7 HU for vessels (*P*=0.38), –106.8 $\pm$ 4.0 HU vs. –106.1 $\pm$ 5.9 HU for fat (*P*=0.50), –898.9 $\pm$ 18.0 HU vs. –903.6 $\pm$ 21.8 HU for lung parenchyma (*P*=0.34), and 59.5 $\pm$ 3.9 HU vs. 57.3 $\pm$ 6.1 HU for the liver (*P*=0.13). No significant differences were observed in measured CT values between baseline and repeat scans, thus the CT values were deemed to be consistent between the two scans.

Measurements of TLV for our study population were 4784 $\pm$ 908 mL at baseline scan, and 4806 $\pm$ 978 mL at repeat scan. Although we were unable to control the inspiratory levels of the patients to be exactly the same during our lung cancer screening trial, their inspiratory levels showed a similar distribution between the two scans (*r*=0.87), and no statistically significant difference (*P*=0.74; Fig. 2). The truncation effect was observed in 3 subjects in the RA970 protocol and 2 subjects in the RA950 protocol after VA which resulted in negative percentage values. Those cases were excluded in subsequent analysis for all protocols in order to avoid a bias in evaluation results due to the truncation

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