Chapter 3

Impact of massive image noise on the extent of automated quantified emphysema using multidetector-row computed tomography

Hester Gietema
Arnold Schilham
Bram van Ginneken
Jan-Willem Lammers
Mathias Prokop

Submitted

ABSTRACT

PURPOSE

To demonstrate the impact of massive image noise on the automated quantified extent of low-attenuated areas representing small extents of emphysema using multidetector-row computed tomography, before and after applying a dedicated noise reduction filter.

MATERIAL AND METHODS

Between March 2003 and May 2004, we enrolled 31 patients (16 men, 15 women; mean age 54y, range 19-74y) from the outpatient department of pulmonology referred for a non-contrast-enhanced chest CT. All patients underwent a standard dose CT-scan (SCT) (120kVp, 130mAs, 16 x 0.75mm collimation) followed by a low dose CT (LDCT) (90kVp, 20mAs). Emphysema was quantified for all scans using a fully automated program by calculating emphysema scores (ES) as the extent of low-attenuated areas using three prefixed thresholds: -910HU, -930HU and -950HU, expressed as percentage of total lung volume. Finally, ES for LDCTs was assessed after applying a dedicated noise reduction filter. ES for SCT and LDCT, before and after applying the filter, were compared by paired-samples t-tests.

RESULTS

The extent of emphysema was overestimated for LDCT compared to SCT for all thresholds (all $p<0.05$). Results for both CTs became similar after applying a dedicated noise reduction filter (all $p>0.05$).

CONCLUSION

For low extents of emphysema, massive image noise leads to overestimation of emphysema when automated quantified. Application of a dedicated noise reduction filter can prevent this overestimation.

INTRODUCTION

Smoking-related emphysema is a common disease with high morbidity and mortality [1] and with a well-described population at-risk. Early detection of emphysema may prevent the occurrence of severe airflow obstruction by smoking cessation or medical interventions [2]. Currently, chronic obstructive pulmonary disease (COPD) is staged according to the guidelines provided by the Global initiative on Obstructive Lung diseases (GOLD), which are mainly based on the forced expiratory volume in one second (FEV_1) [3], but emphysema and airflow obstruction have been shown to be only loosely correlated [4]. Moreover, FEV_1 has been shown to be a bad predictor of emphysema mortality [5].

Although the anatomical definition of emphysema as a permanent abnormal enlargement of the airspace distal to the terminal bronchioles without obvious fibrosis [6] actually requires histology for diagnosis, in clinical practice computed tomography (CT) is used to detect emphysema. In 1988, Müller et al have described a technique to quantify emphysema on CT by highlighting pixels with an attenuation below a prefixed threshold [7] and quantifying their area as percentage of the total investigated area in a range from 0% to 100%. The results were shown to have a good correlation with pathology. Müller and co-workers used a single 10mm thick slice, but in 1995 Gevenois validated the technique for high-resolution CTs performing thin slices (1.0 mm) at 10.0 mm intervals [8] and in 2006 together with Madani for multislice scans [9]. Nowadays, the method is automated and provided by many manufacturers, resulting in a technique which is widely available, quick and easy to apply.

Presently, there are several ongoing lung cancer screening trials [10-13]. Since lung cancer and emphysema share smoking as the main risk factor, CTs performed in these trials may provide suitable data for studying the prevalence and natural course of smoking-related emphysema in relatively healthy subjects [14]. Since only a subgroup of heavy smokers develop COPD [15], these data could be used to select groups of smokers in whom more aggressive risk-modifying treatment is necessary to prevent development of severe lung destruction and airflow limitation.

Lung cancer screening trials are being performed using low-dose protocols. Lowering the dose, however, increases image noise. Quantification of the extent of low-attenuated areas in patients suffering from severe emphysema will not be effected by the extent of image noise as shown by Shaker *et al.* [16] except for very low doses. Image noise is mainly limiting diagnostic information when there is a small contrast between the structure of interest and the surrounding tissue as in low extents of emphysema.

The aim of the present study was to demonstrate that for low extents of emphysema, the extent of emphysema is overestimated. Secondly, we aimed to show that this effect can be cancelled out by the application of a dedicated noise reduction filter.

MATERIAL AND METHODS

PATIENTS AND SCANNING PROTOCOL

Between March 2003 and May 2004, we enrolled 31 patients (17 men, 14 women; mean age 54y, range 19-74y) from the outpatient department of pulmonology referred for a non-contrast-enhanced chest CT. Three patients were current smokers, 6 patients were ex-smokers and 22 patients were never smokers. The study was approved by our institutional review board and written informed consent was obtained from all patients.

Indications for referral were sarcoidosis (n=6), interstitial lung diseases (n=8), emphysema (n=6), follow-up of infectious diseases (n=7), pneumothorax (n=2, both turned out to be recovered at the time the CT was performed), chest pain (n=1) and dyspnoea (n=1).

All scans were acquired on a 16-slice CT scanner (Mx8000 IDT, Philips Medical Systems, Cleveland, OH) using a spiral mode with 16x0.75mm collimation and 15mm table feed per rotation (pitch = 1.3). CT scans for clinical purposes were realized in full inspiration using 120kVp, 130mAs ($CTDI_{vol}$ = 8.7mGy), without contrast injection. The standard-dose chest CT (SCT) was followed by a low-dose CT (LDCT) realized with identical parameters except for the radiation dose (90kVp, 20mAs, $CTDI_{vol}$ = 0.6mGy). Axial images were reconstructed at 1.0mm thickness and 0.7mm increment, using a moderately soft kernel (Philips, filter "B") and the smallest field of view (FOV) that included the outer rib margins at the widest dimension of the thorax.

EMPHYSEMA QUANTIFICATION

Data were transferred to a digital workstation with in-house developed software. Total lung volume was calculated using the following steps. Segmentation of trachea, left and right lung was performed by a fully automated region growing program starting in the trachea, which included all connected areas below -500HU. In a second step, trachea and main bronchi were excluded from the lungs. The algorithm is similar to the one described by Hu [17]. A frequency distribution histogram of voxel attenuation in lung fields was calculated for each CT. Finally, the extent of low-attenuation areas was determined by highlighting voxels with attenuation below a prefixed threshold. Emphysema scores (ES) were calculated as volume of these low-attenuation areas and expressed as percentage of total lung volume in a range from 0% to 100% for three attenuation thresholds often mentioned in literature: -910HU, -930HU and -950HU. The discussion about the most optimal attenuation threshold to apply was beyond the scope of this study.

First of all, we calculated emphysema scores for all scans without reduction of image noise. Secondly, we applied the NOVA denoising filter as post-processing step to the reconstructed 1.0 mm slices of the low-dose scans before the

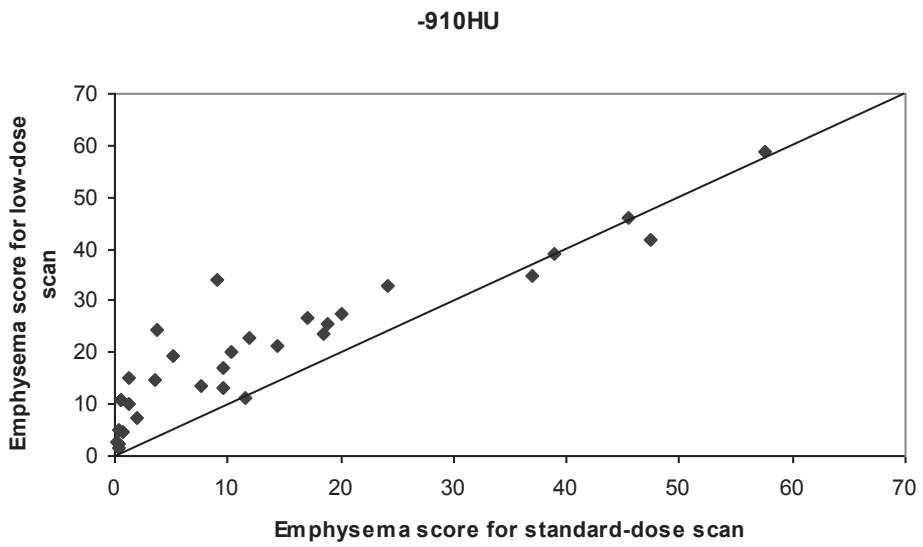
calculation of emphysema scores in order to reduce image noise as described by Schilham et al [18]. This filter was developed specifically for chest CT data, and uses prior knowledge about the noise and tissue distribution to determine at each spatial location the proper amount of local averaging. Emphysema scores of the filtered low-dose scans were compared to results from the unfiltered low-dose scans and the standard-dose scans.

ANALYSIS

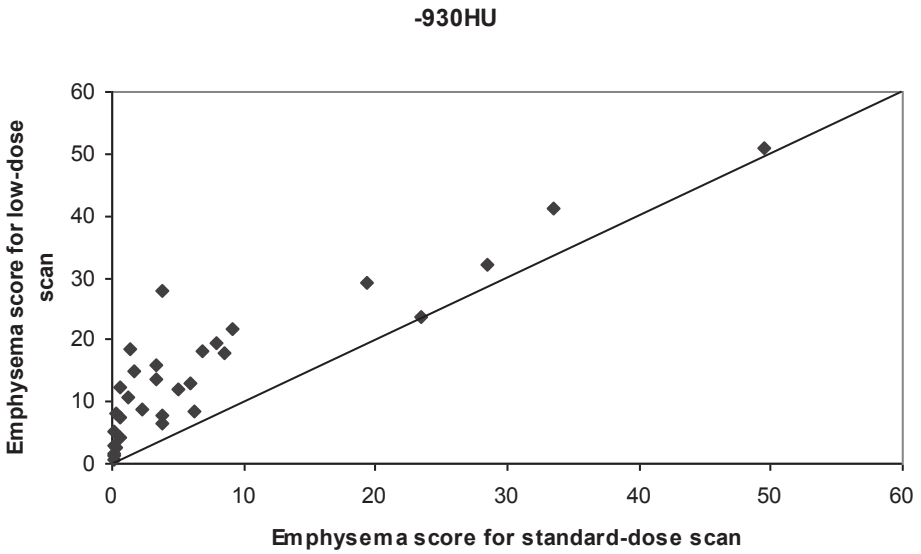
All statistical calculations were performed using SPSS statistical software release 12.0 (SPSS Inc, Chicago, Ill.). Results were shown as median and 25%-75% interquartile ranges for non-normal distributed emphysema scores and lung volumes. Lung volumes of both scans were compared for each patient using paired-samples t-tests in order to make differences in emphysema scores between both techniques caused by variation in inspirational levels less probable. Emphysema scores of the standard-dose scans were compared to emphysema scores of the low-dose scans, before and after the application of the NOVA-filter, with Spearman's correlation coefficients and with paired-samples t-tests. P-values <0.05 were considered significant.

RESULTS

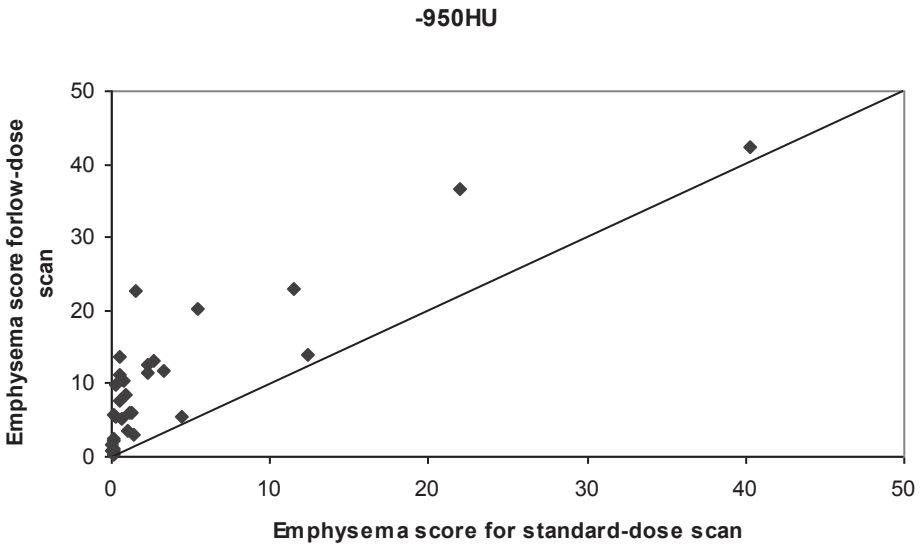
All patients completed both scans and all scans were eligible for analysis. Median lung volume was 6660 ml (interquartile range 5088ml-7822ml) for standard-dose scans (SCT) and 6845 ml (interquartile range 4930ml-8169ml) for low-dose scans (LDCT; p=0.28). Spearman's correlation coefficients for emphysema scores (ES) calculated for LDCTs and SCTs without noise reduction showed good to excellent correlations with coefficients of 0.91, 0.86 and 0.80 for extent of low-attenuation areas below -910HU, -930HU and -950HU, respectively. However, ES for LDCT were significantly higher compared to ES for scans performed at standard radiation dose (p<0.0001 for all thresholds). As shown in Figure 1, emphysema scores raised significantly after dose reduction for low to moderate extents of emphysema, while for severe emphysema (ES>30) scores were similar.



1A



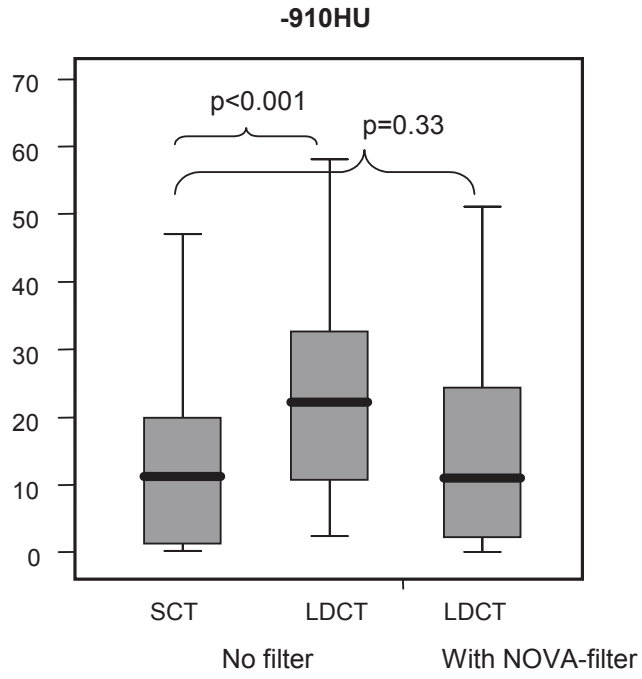
1B



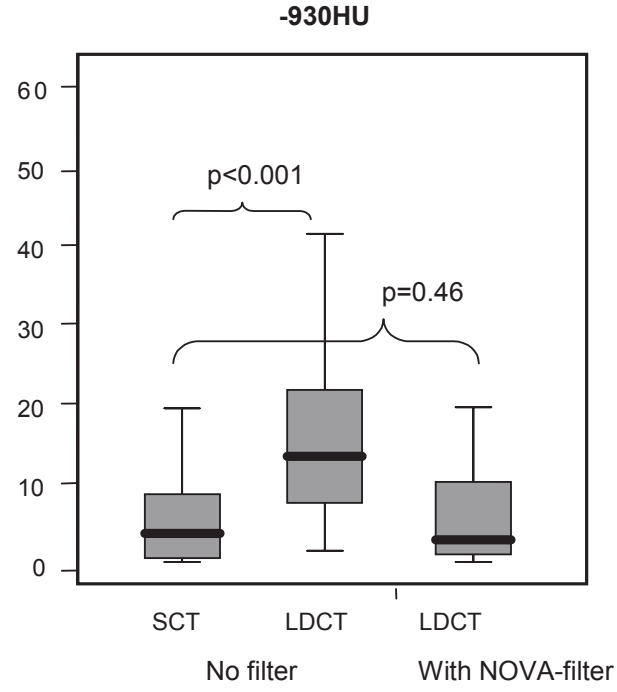
1C

Figure 1

Scatter plots showing emphysema scores performed on standard-dose scans correlated to emphysema scores performed on low-dose scans. The continuous line represents x=y. Note that emphysema scores for low-dose scans are higher than emphysema scores for standard dose scans from the same patients, except for scans with low-attenuation areas below -910HU comprising >30% of total lung volume.


-910HU
70
60
50
40
30
20
10
0
p<0.001
p=0.33
SCT
LDCT
LDCT
No filter
With NOVA-filter

2A


-930HU
60
50
40
30
20
10
0
p<0.001
p=0.46
SCT
LDCT
LDCT
No filter
With NOVA-filter

2B

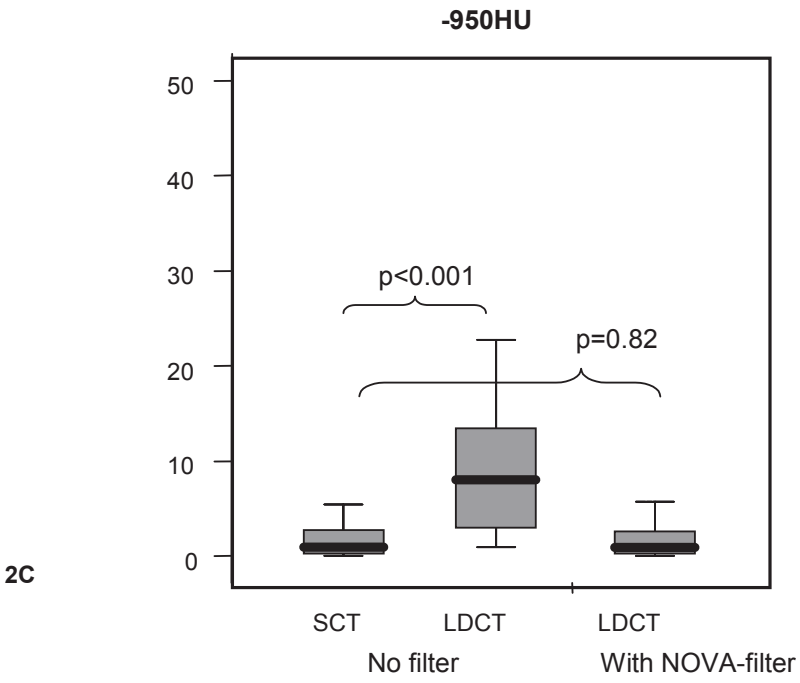


Figure 2

Box plots showing mean emphysema score and standard deviations at three attenuation thresholds for standard-dose and low-dose scans with and without noise reduction (NOVA-filter).

After filtering low-dose scans for image noise, emphysema scores dropped to the range of ES of standard-dose scans ($p>0.05$; Figure 2). This effect becomes more clear when looking at the shape of the histogram showing the number of voxels plotted against CT-values (Figure 3). This figure shows the histograms of a standard-dose CT and a low-dose CT performed for the same patient. The histogram of the low-dose CT is more flattened and shows far more voxels with a CT-number close to the attenuation of air than the standard dose scan, resulting in upraised emphysema scores. Moreover, this figure demonstrates the effect of applying a noise reduction filter, showing that the histogram of the low-dose CT after noise reduction becomes similar to that of the standard-dose CT.

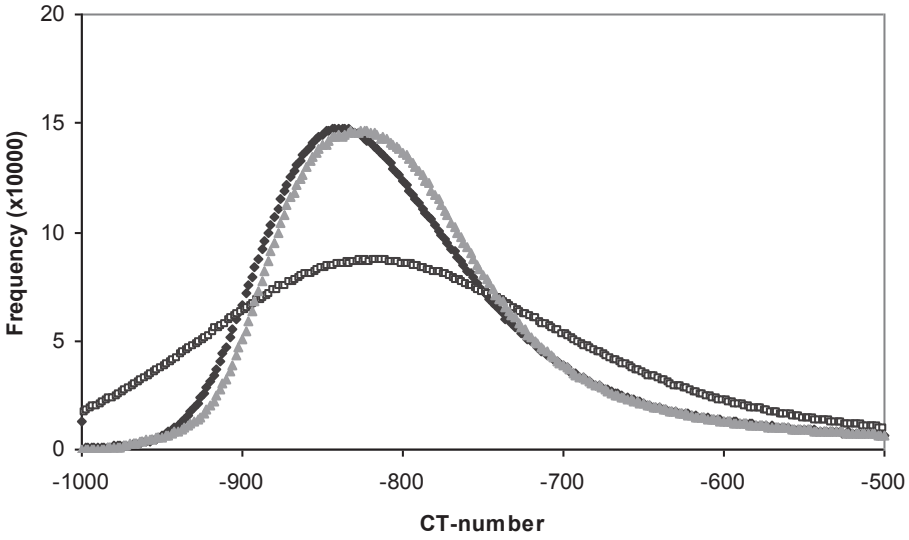


Figure 3

Histograms of the standard-dose (black diamonds) and the low-dose scan (white squares with black line) of one patient. Although the CT-numbers of the peaks of both histograms are similar, the slope of the low-dose scan is much less steep. The area under the curve of the low-dose scan includes obviously more voxels with CT-values close to -1000HU. The grey triangles represent the histogram of the low-dose scan after applying a noise reduction (NOVA) filter. Note that both histograms are almost but not completely similar. Lung volumes were 4782 ml for standard dose scan and 4882 ml for the low-dose scan.

DISCUSSION

Many factors influencing emphysema scores have been described in literature, as inspirational level [19], scanner calibration [20] and CT scanners [21], but to the best of our knowledge the impact of massive image noise on automatically obtained emphysema scores has not been reported yet.

Today, a standard method for emphysema quantification is not yet available [22]. Several studies have been performed to compare extent of emphysema detected at macroscopic and microscopic specimens and these studies recommend different attenuation thresholds as optimal threshold to use for emphysema quantification [7-9], mainly due to differences in applied scan protocols. Although the method of highlighting and quantifying low-attenuated areas has been described and validated against pathology almost twenty years ago [7], advancing technical developments have directed scan protocols applied in clinical practice to thinner collimations and reconstructed slices, and increasing applications for CT. This latter development has also increased the sense of radiation risk and subsequent temptations to decrease radiation dose to the dose "as low as reasonably achievable" (ALARA-principle) without losing diagnostic information. The high contrast in the chest between low-attenuated normal air and high-attenuated abnormal tissue makes large reduction of radiation dose in the chest possible [23;24]. Such low dose scans are already being performed in lung cancer screening studies [11;12;25;26], where the risk of dying from lung cancer highly exceeds the risk of developing cancer from the applied radiation dose [27].

COPD is a common and disabling disease. Nowadays, staging is based on the severity of airflow limitation according to the guidelines provided by the GOLD [3]. However, airflow limitation is a sign of advanced disease [28], while detection of early lung destruction can enable a more aggressive risk-modifying approach in order to slow down the progression to advanced disease or maybe even prevent the stage of airflow obstruction. Since lung cancer and COPD share smoking as the main risk factor and lung cancer screening is performed in healthy smokers, the smoking population participating in lung cancer screening trials is also the population at risk for suffering from early stages of emphysema. Therefore, routine emphysema quantification on CTs performed for lung cancer screening can be an attractive way to detect early emphysema in this high-risk population without applying additional radiation dose. Lung cancer screening trials are performed using low-dose protocols (120 or 140kVp and 20-50mAs), which are sufficient to detect and measure intrapulmonary nodules [10-13]. But for diseased areas with a low contrast to healthy tissue, such as in mild lung destruction, noise hampers the detection and especially the automated quantification of the diseased areas. Our study shows that automated emphysema quantification on low-dose chest CTs is feasible, also for low extents of lung destruction, but only after applying a denoising filter. Most vendors of CT post-processing software provide an automated emphysema quantification program, which is comparable

to the “density mask” method released by GE Healthcare and validated by Müller et al [7]. However, we showed that these programs can not be applied to patients with low extents of lung destruction without an additional filtering step. We used a noise filtering method developed by Schilham et al [18] as post-processing step before calculation of emphysema scores. This NOVA-filter was an in-house developed filter and is not commercially available. But the filter is well-described before [18] and can be reproduced by other manufacturers. Emphysema scores for low-dose scans filtered for image noise with this method were demonstrated to be similar to emphysema scores obtained from standard dose scans showing that, using this NOVA-filter, obtaining reliable emphysema scores from on low-dose scans becomes feasible. The NOVA-filter was developed especially to reduce noise in chest CT-scans performed with low radiation doses and it therefore not surprising that we obtained good results applying this filter on another group of patients, but scanned with the same protocol as the patient group Schilham and co-workers used for testing his NOVA-filter.

The results of our study may also be an explanation for the results recently published by Madani et al, who showed that -960HU and -970HU showed better correlations to macroscopic emphysema for multi-slice scans than -950HU [9], recommended by Gevenois et al for single slice scanners [8]. They applied different radiation doses (140kVp; 80mAs versus 137kVp; 255mAs) which can have resulted in the reported difference in recommended attenuation threshold.

Several other factors than radiation dose influencing emphysema scores have been mentioned in literature [22], but we could exclude crucial factors like changes in inspirational level, sampling bias and scanner calibration, to cause the reported differences in ES between standard-dose and low-dose scans. Although lung volume is shown to influence emphysema scores [19], lung volumes in both scans were similar, which makes changes in lung volume as a explanation of the systematic higher emphysema scores on low-dose CTs less probable. Since we used continuous data sets, sampling error, which turned out the most important error in the study by Stoel et al [29], was also not applicable. Finally, the scans were performed in the same session, excluding a calibration error which can influence the scoring results [20].

Our study also has some limitations. First of all, we demonstrated the effect of massive image noise on emphysema scores, but we did not investigate several radiation doses. Such a study design would provide information about the correlation between radiation dose and emphysema scores. However, performing series of scans in the same patient would lead to massive increases of applied radiation doses for this patient and is therefore unethical. A series of several radiation dose reduction steps could also be performed using dose reduction simulation programs, but it is difficult to reproduce the real clinical situation with simulation programs.

A second limitation of the study was the absence of pathologic specimens that are crucial in the diagnosis of emphysema, by which we did not compare our results

to emphysema quantified at macroscopy. Although we proved that emphysema scores performed after noise reduction produces results that are similar to scores performed with standard-dose scans, no judgment can be done about the accuracy to detect the real extent of emphysema.
A third limitation is that only three patients in this study population were current smokers and 6 patients were former smokers. Since referral for standard dose chest CT was the only inclusion criterion to be included in our study investigating the applications of low-dose scans, the majority of participants turned out to be never smokers. But since the study population showed low extents of lung destruction, like many healthy smokers [14], these patients constituted a appropriate study group to demonstrate the effect of massive image noise in patients with low extents of lung destruction.

CONCLUSION

Radiation dose reduction has a significant effect on the results of emphysema quantification with the technique of highlighting and quantifying low-attenuated areas. Emphysema scoring is feasible for low-dose scans, but only when a dedicated noise reduction filter is applied before quantifying the extent of low-attenuation areas.

REFERENCE LIST

(1) Feenstra TL, van Genugten ML, Hoogenveen RT et al. The impact of aging and smoking on the future burden of chronic obstructive pulmonary disease: a model analysis in the Netherlands. Am J Respir Crit Care Med 2001; 164(4):590-596.

(2) Bankier AA, Madani A, Gevenois PA. CT quantification of pulmonary emphysema: assessment of lung structure and function. Crit Rev Comput Tomogr 2002; 43(6):399-417.

(3) www.goldcopd.com 2005.

(4) Clark KD, Wardrobe-Wong N, Elliott JJ et al. Patterns of Lung Disease in a "Normal" Smoking Population : Are Emphysema and Airflow Obstruction Found Together? Chest 2001; 120(3):743-747.

(5) Martinez FJ, Foster G, Curtis JL et al. Predictors of Mortality in Patients with Emphysema and Severe Airflow Obstruction. Am J Respir Crit Care Med 2006;200510-1677OC.

(6) The definition of emphysema. Report of a National Heart, Lung, and Blood Institute, Division of Lung Diseases workshop. Am Rev Respir Dis 1985; 132(1):182-185.

(7) Muller NL, Staples CA, Miller RR et al. "Density mask". An objective method to quantitate emphysema using computed tomography. Chest 1988; 94(4):782-787.

(8) Gevenois PA, De M, V, De VP et al. Comparison of computed density and macroscopic morphometry in pulmonary emphysema. Am J Respir Crit Care Med 1995; 152(2):653-657.

(9) Madani A, Zanen J, de Maertelaer V et al. Pulmonary Emphysema: Objective Quantification at Multi-Detector Row CT--Comparison with Macroscopic and Microscopic Morphometry. Radiology 2006;2382042196.

(10) Church TR. Chest radiography as the comparison for spiral CT in the National Lung Screening Trial. Acad Radiol 2003; 10(6):713-715.

(11) Henschke CI, McCauley DI, Yankelevitz DF et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. Lancet 1999; 354(9173):99-105.

(12) Sone S, Takashima S, Li F et al. Mass screening for lung cancer with mobile spiral computed tomography scanner. Lancet 1998; 351(9111):1242-1245.

(13) van Klaveren RJ, Habbema JD, de Koning HJ et al. [Screening for lung cancer in the Netherlands: the role of spiral CT scan]. Ned Tijdschr Geneeskd 2001; 145(11):521-526.

(14) Omori H, Nakashima R, Otsuka N et al. Emphysema detected by lung cancer screening with low-dose spiral CT: prevalence, and correlation with smoking habits and pulmonary function in Japanese male subjects. Respirology 2006; 11(2):205-210.

(15) Viegi G, Scognamiglio A, Baldacci S et al. Epidemiology of chronic obstructive pulmonary disease (COPD). Respiration 2001; 68(1):4-19.

(16) 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(4):424-430.

(17) Hu S, Hoffman EA, Reinhardt JM. Automatic lung segmentation for accurate quantitation of volumetric X-ray CT images. IEEE Trans Med Imaging 2001; 20(6):490-498.

(18) Schilham A, Van Ginneken B, Gietema H et al. Local Noise Weighted Filtering for Emphysema Scoring of Low-dose CT Images. IEEE Transactions on Medical Imaging 2006; 25(4):451-463.

(19) Shaker SB, Dirksen A, Laursen LC et al. Volume adjustment of lung density by computed tomography scans in patients with emphysema. Acta Radiol 2004; 45(4):417-423.

(20) Parr DG, Stoel BC, Stolk J et al. Influence of calibration on densitometric studies of emphysema progression using computed tomography. Am J Respir Crit Care Med 2004; 170(8):883-890.

(21)`Bakker ME, Stolk J, Putter H et al. Variability in Densitometric Assessment of Pulmonary Emphysema With Computed Tomography. Invest Radiol 2005; 40(12):777-783.

(22) Stoel BC, Stolk J. Optimization and standardization of lung densitometry in the assessment of pulmonary emphysema. Invest Radiol 2004; 39(11):681-688.
(23) Mayo JR, Hartman TE, Lee KS et al. CT of the chest: minimal tube current required for good image quality with the least radiation dose. AJR Am J Roentgenol 1995; 164 (3):603-607.
(24) Mayo JR, Kim KI, MacDonald SLS et al. Reduced Radiation Dose Helical Chest CT: Effect on Reader Evaluation of Structures and Lung Findings. Radiology 2004; 232 (3):749-756.
(25) Diederich S, Wormanns D, Heindel W. Lung cancer screening with low-dose CT. Eur J Radiol 2003; 45(1):2-7.
(26) Swensen SJ, Jett JR, Hartman TE et al. Lung cancer screening with CT: Mayo Clinic experience. Radiology 2003; 226(3):756-761.
(27) Brenner DJ. Radiation risks potentially associated with low-dose CT screening of adult smokers for lung cancer. Radiology 2004; 231(2):440-445.
(28) Madani A, Keyzer C, Gevenois PA. Quantitative computed tomography assessment of lung structure and function in pulmonary emphysema. Eur Respir J 2001; 18(4):720-730.
(29) Stoel BC, Vrooman HA, Stolk J et al. Sources of error in lung densitometry with CT. Invest Radiol 1999; 34(4):303-309.