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Effects of CT Section Thickness and Reconstruction Kernel on Emphysema Quantification: Relationship to the Magnitude of the **CT Emphysema Index**

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Abstract

Rationale and Objectives—CT section thickness and reconstruction kernel each influence CT measurements of emphysema. This study was performed to assess whether their effects are related to the magnitude of the measurement.

Materials and Methods—Low-radiation-dose multidetector CT was performed in 21 subjects representing a wide range of emphysema severity. Images were reconstructed using 20 different combinations of section thickness and reconstruction kernel. Emphysema index values were determined as the percentage of lung pixels having attenuation lower than multiple thresholds ranging from -960 HU to -890 HU. The index values obtained from the different thickness-kernel combinations were compared by repeated measures ANOVA and Bland-Altman plots of mean vs. difference, and correlated with quantitative histology (mean linear intercept, Lm) in a subset of resected lung specimens.

Results—The effects of section thickness and reconstruction kernel on the emphysema index were significant (p < 0.001) and diminished as the index threshold was raised. The changes in index values due to changing the thickness-kernel combination were largest for subjects with intermediate index values (10–30%), and became progressively smaller for those with lower and higher index values. This pattern was consistent regardless of the thickness-kernel combinations compared and the HU threshold used. Correlations between the emphysema index values obtained with each thicknesskernel combination and Lm ranged from r=0.55-0.68 (p=0.007-0.03).

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Keywords

Emphysema; computed tomography; histology

INTRODUCTION

Quantitative CT analysis of lung attenuation increasingly has been used in clinical research on chronic obstructive pulmonary disease (COPD) for the objective measurement of emphysema. Emphysema has been quantified from CT data obtained in clinical trials to identify associations between emphysema and demographic factors (1–3), genetic factors (4), and body habitus (5); to assess drug treatment effects (6,7); to distinguish COPD phenotypes with and without emphysema (8); and to evaluate the contribution of emphysema to airflow obstruction (9). Studies supporting the validity of measurements obtained using low-radiation-dose CT technique (10,11) may further expand applications in clinical research.

As the use of CT for emphysema quantification has grown, the potential for measurement variability related to certain CT technical parameters has been recognized (12–14). It has been reported that CT estimates of emphysema severity increase as section thickness decreases (11,15), and that higher resolution (edge-enhancing, sharper) image reconstruction kernels (also referred to as algorithms or filters) result in higher CT measurements of emphysema than lower resolution (smoothing) kernels (16). These effects may impact the ability to combine or compare CT measurements of emphysema in cross-sectional or longitudinal studies in which section thickness and reconstruction kernel are not held constant. This is particularly relevant to retrospective studies in which these parameters can no longer be changed, to prospective multicenter studies using multiple CT scanner models with different section thickness and kernel options, and to longitudinal studies during which scanners are replaced with new models.

Ideally, if technical parameter settings were not or cannot be held constant, those that provide equivalent measurements should be identified and used. In determining whether one measurement technique may substitute for another, it is important to know by how much the measurements differ, and whether the difference between the two measurements shows any bias related to the magnitude of the measurement (17). To our knowledge, these features have not been fully characterized for quantification of emphysema from multidetector CT scans reconstructed using different combinations of CT section thickness and reconstruction kernel.

We performed this study to assess the effects of both CT section thickness and reconstruction kernel on the CT quantification of emphysema in relation to the magnitude of the measurement. Because emphysema is defined histologically by airspace enlargement and alveolar wall destruction, imaging-pathology correlation is also important for validating the different technical approaches available with CT. Therefore, a secondary aim was to correlate CT emphysema measurements obtained using different section thicknesses and reconstruction kernels with quantitative histology.

MATERIALS AND METHODS

Subjects

The 21 subjects enrolled in this prospective study (Table 1) included 9 patients scheduled for lobectomy due to lung cancer and 12 patients scheduled for lung transplant surgery due to chronic obstructive pulmonary disease. Subjects with these diagnoses were chosen to capture

a wide range of emphysema severity as determined by quantitative CT analysis and pulmonary function impairment. There was no clinical evidence of active lung infection, no history of asthma or diffuse lung disease other than emphysema, and no CT evidence of infiltrative lung disease or more than subsegmental atelectasis.

Fifteen resected lung specimens were obtained from 11 of the 21 subjects and used for quantitative histology as a reference standard for emphysema severity. Both resected lungs were obtained from 4 of the patients who underwent lung transplantation, one lung was obtained from 3 of the transplant patients, and one lobe was obtained from each of the 4 patients who underwent lobectomy for lung cancer.

Imaging and Image Analysis

CT scans were performed within one week prior to surgery on a multi-detector scanner (Siemens Sensation 16 in 20 subjects and Sensation 64 in 1 subject) (Siemens Medical Solutions, Erlangen, Germany) that underwent daily calibration checks. The scans were done at full inspiration, without intravenous contrast, at 120 kVp using a low-radiation-dose technique of 45 mAs and a pitch of 1.5 for an effective tube current of 30 mAs. Transverse images were reconstructed contiguously at 1 mm, 2 mm, 5 mm, and 10 mm section thicknesses, using five different reconstruction kernels of increasing resolution (edge enhancement) from smooth (Siemens B20f, B30f, and B40f) to sharp (Siemens B50f and B60f) for each section thickness. Thus, 20 complete CT data sets with a unique section thickness-kernel combination were reconstructed for each subject.

The CT images were analyzed using the Pulmonary Analysis Software Suite and Emphysema Profiler (VIDA Diagnostics, Iowa City, IA) computer program (18). The program automatically isolates the lungs and determines lung volumes and the histogram statistics of all lung pixel attenuation values. For emphysema quantification, a CT emphysema index was defined as the percentage of all pixels within the lungs having attenuation lower than a given Hounsfield unit (HU) attenuation threshold. Measurements at thresholds from -960 to -890 HU were obtained in 10 HU increments, a range which includes thresholds validated by previous studies (19–21).

The CT data from both lungs were used to evaluate the effects of section thickness and reconstruction kernel on emphysema index calculations in all 21 subjects. For the CT comparisons with quantitative histology, the automatically segmented single lung CT data were used for the transplant patients, and were modified manually to include only the resected lobe for the patients who underwent lung cancer surgery.

Lung Fixation and Quantitative Histology

Based on previously reported methods (22,23), the 15 resected specimens were ventilated under positive pressure of 12–25 cm H₂O for 4–10 hours with 50% formalin vapor heated to 46°C, using a diaphragm pump with an electronically controlled circuit that provided a brief exhalation (< 1 sec) every 6–8 sec. The inflation-fixed specimens were cut into 1–2 cm-thick transverse slices, and 20 paraffin-embedded tissue blocks per resected lobe and 40 per whole lung were obtained in a random manner (avoiding any tumor tissue). A histologic slide of 3 µm thickness from each tissue block was prepared and stained with hematoxylin and eosin. Shrinkage of the vapor-fixed tissue during histologic slide preparation, measured by comparing the cross-sectional area of tissue blocks and the cross-sectional area of the prepared and stained slides, was minimal (<5%).

Emphysema was quantified histologically as the mean linear intercept (Lm), i.e., the average distance between alveolar walls. Five random fields per histologic slide were digitally

photographed at $4 \times$ magnification. A computer program (Image Pro Plus, Media Cybernetics) was used to overlay a grid of parallel line segments on each field, automatically count the number of intersections of line segments and airspace walls, and divide the total length of the line segments by the number of intersections, to obtain the Lm for each field (24). These Lm values were averaged to determine a single Lm value for each specimen. For fields comprised of pure airspace, the diameter of the field (1.9 mm) was used as the Lm value.

Statistical Analysis

The emphysema index measurements obtained with the 20 combinations of section thickness and reconstruction kernel at each HU threshold were compared in a multivariable mixed model by repeated measures analysis of variance using JMP 6.0 (SAS Institute, Cary, NC), with subjects identified as a random effect and the two image reconstruction parameters identified as fixed effects. The relationship of the emphysema index magnitude to the effects of section thickness and reconstruction kernel was assessed by the method of Bland and Altman (25), plotting the emphysema index mean vs. difference of each pair of thickness-kernel combinations for each subject. The emphysema index mean was calculated according to the formula:

Emphysema index mean=[(Index from thickness-kernel combination a)+ (Index from thickness-kernel combination b)]÷2

The emphysema index difference was calculated according to the formula:

Emphysema index difference=(Index from thickness-kernel combination a)-(Index from thickness-kernal combination b)

The emphysema index mean vs. difference was examined at all HU thresholds. Curves were fit to these plots using linear and polynomial models with JMP 6.0 (SAS Institute, Cary, NC). Models having both the highest R^2 and F ratio were considered the best empirical fit.

For CT-histology correlation, each resected lung or lobe had been fixed and processed independently, and was used as an individual data point. Scatter plots of the Lm values and CT emphysema index for each combination of technical parameters were inspected, and Pearson correlation was performed using Excel (Microsoft). *P* values <0.05 were considered statistically significant.

The study was approved by the local Institutional Review Board, and informed consent was obtained from all subjects.

RESULTS

Effects of section thickness and reconstruction kernel

Section thickness had a statistically significant effect (p<0.001) on the CT emphysema index at all index attenuation thresholds. Reconstruction kernel had a statistically significant effect (p<0.001) on the index at all thresholds except for -910 HU (p=0.11). Although the main trend was for the emphysema index to increase with thinner sections and sharper kernels, the size of the effect decreased as the attenuation threshold was raised (Table 2). At the highest thresholds examined (-900 and -890 HU), the mean index of the entire cohort with the sharp kernels (B50f and B60f) was the same as or lower than the index with the smooth kernels.

The CT index values obtained with the 20 combinations of section thickness and kernel were highly correlated to each other at all HU thresholds (r=0.90–0.99).

Section thickness and reconstruction kernel had statistically significant effects on the CTmeasured lung volume (p<0.001 for section thickness, p=0.01 for kernel). The CT-measured lung volumes ranged from 6586 ± 1859 ml (10 mm-B20f) to 6606 ± 1848 ml (1 mm-B60f). The largest lung volume measured in any subject from the 20 different thickness-kernel combinations was 0.2% to 1.7% (mean 0.7%) greater than the smallest lung volume measured in the same subject.

Influence of emphysema index magnitude

The effects of section thickness and reconstruction kernel on the index values of individual subjects varied with the magnitude of the emphysema index in a systematic manner. This is shown in Fig. 1 and Fig. 2 comparing the emphysema index at different representative section thicknesses (Fig. 1) and reconstruction kernels (Fig. 2), for HU thresholds commonly used in clinical research studies. The peak difference between index values produced by any two thickness-kernel combinations (up to nearly 20 index percentage points in Fig. 1 and Fig. 2) occurred for subjects in whom the mean of the index values resulting from those two thicknesskernel combinations was in the range of approximately 10-30%. This difference became progressively smaller for subjects with lower and higher means, and became negative at the highest mean index values for some of the comparisons. The greatest difference between index values (the height of the peak) varied depending on the two thickness-kernel combinations compared and the HU threshold used, but the same pattern was seen for all of the comparisons, including those not shown. The best empiric fit for each mean vs. difference comparison was either a linear or a polynomial function, depending on the range of mean emphysema index values resulting from the specific thickness-kernel combinations compared and the HU threshold used (Fig. 1 and Fig. 2).

Quantitative CT and histology

The emphysema index values in the subset of 15 resected specimens from 11 subjects, and the effects of section thickness and kernel, were similar to those in the whole group of 21 subjects (Fig. 3). The average Lm for the 15 resected specimens was 0.71 mm, and ranged from 0.29 mm to 1.04 mm (Fig. 4). Correlation coefficients comparing the CT emphysema index values for the various CT section thickness-kernel combinations at multiple HU thresholds with the Lm ranged from r = 0.55 (p=0.03) to r = 0.68 (p=0.007) (Table 3). The correlations tended to be slightly stronger with the smoother (B20f, B30f, and B40f) kernels, particularly with 1 mm and 2 mm sections, but were similar at all section thicknesses.

DISCUSSION

The main finding of our study is that the effects of section thickness and reconstruction kernel on CT measurements of emphysema varied in a systematic manner related to the emphysema index magnitude. This was seen as a peak effect in which the difference in the emphysema index produced by two different thickness-kernel combinations was greatest for those subjects in whom the mean emphysema index produced by the same two combinations was in the intermediate range of approximately 10–30%. These differences were progressively smaller for those with lower and higher mean index values. The magnitude of each emphysema index measurement is determined in part by the specific combination of thickness, kernel, and HU threshold, in addition to the actual anatomic severity of disease. Thus, the absolute effect of changing the thickness and kernel in any individual subject (the size of the emphysema index difference), and the relative effect among different subjects (linear or polynomial relationship), depended on which thickness-kernel-HU threshold combinations were compared.

The relationship between the effects of these reconstruction parameters and the emphysema index magnitude may be explained, at least in part, through examination of lung CT pixel attenuation histograms (Fig. 5). By definition, the CT emphysema index corresponds to the proportion of the area under the histogram that lies below the selected attenuation threshold. Increasing the section thickness or decreasing the kernel sharpness reduces the amount of noise (random increases and decreases in pixel attenuation values) in the images (26), and causes the attenuation of pixels in any high contrast boundary region to be averaged towards the mean of the region. The result is a narrowing of the width and an increase in the height of the histogram. The difference in a subject's index obtained from any two different combinations of thickness and kernel is determined by the shapes of the two histograms produced, their position on the attenuation scale, and the HU threshold used to define the index. Figure 5 illustrates how kernel-related changes in the emphysema index may vary systematically with the emphysema index magnitude.

Theoretically, when thickness and kernel cannot be held constant, their effects could be controlled for in clinical studies by identifying the combinations of these reconstruction parameters that provide equivalent emphysema index measurements (7,26). Untried approaches that may be worth investigating are the application of correction factors or alteration of the index attenuation threshold to convert the emphysema index values obtained with one technique to those obtained with a reference technique. However, a single equivalent reconstruction technique, correction factor, or HU threshold adjustment may not provide reliable conversion in all subjects. Instead, our findings imply that any attempt to determine if such conversion between two techniques is achievable should consider that the magnitude of the emphysema index may affect the amount of correction needed in a given individual. We did not evaluate the possible additional effects of the distribution of emphysema (homogeneous vs. heterogeneous vs. predominantly bullous) on reconstruction parameter-related shifts in the emphysema index. Thus, whether the same shift would be seen for two individuals with the same emphysema index but different distributions is unknown. While our study illustrates the effects of several subject, technical, and image analysis parameters, the feasibility of actually converting emphysema index values from one technique to another requires further investigation.

As in a previous study (16), the differences in total lung volume we found with the different thickness-kernel combinations were statistically significant but exceedingly small, and not large enough to account for the differences in emphysema index values. Although the maximum differences in cohort mean index values were large, however, certain thickness-kernel-HU threshold combinations produced nearly equivalent cohort mean values (as illustrated in Table 2). Thus, simultaneously varying thickness, kernel, and the HU threshold may provide more options for identifying technically equivalent combinations for emphysema quantification from different scanner sources than varying only one or two of these variables.

Other investigators (11,15,16) have reported that the mean emphysema index of their cohorts increased with thinner CT sections and sharper reconstruction kernels. In examining these effects at different emphysema index thresholds, we additionally found that they diminish as the index threshold is raised. This suggests that any thickness and kernel differences in comparative studies may confound comparisons made at lower index thresholds to a greater degree than those made at higher index thresholds.

Despite its frequent use, controversy has recently arisen over the use of the Lm for quantitative morphometry in emphysema (27–35). Thus, the Lm measurements and quantitative CT-histology correlations presented here should be interpreted with awareness of certain concerns and appropriate caution. One concern is that the Lm is unable to accurately discriminate small gradations of mild emphysema; however, it is likely adequate for distinguishing larger

difference in emphysema severity (28,31). In addition, the Lm measurement depends on the volume of the fixed lung, which was not precisely standardized in our study but likely related to both the volume to which the lungs were inflated during fixation and the amount of formalininduced shrinkage. Thus, there may be an unknown amount of variation between the volumes at which the lungs were fixed and the full inspiratory volume at which the CT scans were performed. However, the correlations we found between the CT emphysema index and Lm agree with the findings of previous studies that used fixation with liquid formalin (11,19,20). Finally, the paraffin-embedding and tissue processing steps may be associated with shrinkage (27), which reduces the measured size of the airspaces. Interestingly, this embedding and processing resulted in only minimal shrinkage in our study, for which we did not correct. While we cannot state with certainty why the shrinkage was less than is typical with liquid formalinfixed lungs, we suspect that the process of fixation by ventilation with concentrated, heated formalin vapor has a substantial dehydrating effect, as lungs fixed by this method are relatively light and dry to moist. Since the major source of shrinkage due to histologic processing of tissues fixed in 10% liquid formalin is dehydration, there may have been little potential for shrinkage of the already-dehydrated tissue fixed by our method during histologic processing. In any case, the Lm values we obtained were similar to or larger than those measured in previous studies that required correction for shrinkage from histologic processing (Lm in these previous studies was approximately 170–475 µm for lung cancer specimens and up to about 750 µm for transplant specimens) (20,24).

That the emphysema index values from all thickness-kernel-HU threshold combinations correlated similarly with quantitative histology is not surprising, since the relative emphysema index values among the different individuals in the cohort were similar with each section thickness and reconstruction kernel (as illustrated by graphs in the first column of Fig. 1 and Fig. 2). As a result, the index measurements obtained with the different thickness-kernel-HU threshold combinations were highly correlated. Our data additionally show similar correlations between CT and quantitative histology for both smooth and sharp reconstruction kernels, a comparison which to our knowledge has not previously been made. This supports the ability to use either smooth or sharp reconstruction kernels for CT emphysema quantification. Because of the tendency for the CT-histology correlations using the smoother CT reconstruction kernels (B20f, B30f, and B40f) to be slightly stronger than those using the sharper kernels (B50f and B60f), use of images reconstructed with a smooth kernel may be preferable when available.

We recognize several limitations of this study. Although different scanner brands offer similar section thickness and reconstruction kernel options, the size of the effects of these technical parameters may differ across the various proprietary scanner hardware and reconstruction software platforms. The size of the effects demonstrated here also may be different using a scanner tube current other than the low radiation dose technique of this study, as the added noise with reduced radiation dose slightly increases emphysema index values (10,26). In addition, the effects of reconstruction parameters on emphysema index values may vary in different lung regions, such as the apex and base which are subject to increased noise (36).

The sample size for quantitative histology was somewhat limited, which may have affected the accuracy of the correlations between the emphysema index and Lm. However, our purpose was to explore the relative correlations with Lm for the different reconstruction parameters, and there was no suggestion that any thickness-kernel-HU threshold combinations may be highly superior or do not correlate at all with quantitative histology. Finally, the maximum Lm measurable on any histologic slide was limited by the microscope field of view, so the Lm may have been underestimated in some subjects.

In summary, this study demonstrates that the effects of section thickness and reconstruction kernel on emphysema quantification vary systematically with the magnitude of the emphysema

index. This relationship may be relevant to assessing whether a reliable algorithm for converting emphysema measurements from one reconstruction protocol to another can be developed. Determining whether such conversion is possible will require further investigation that includes subjects with varying severity and distribution of emphysema. We also found that all combinations of section thickness and reconstruction kernel provided significant correlations with quantitative histology, though limitations to the quantitative histologic methods are noted. This supports the validity of using any one of multiple thickness-kernel combinations to quantify emphysema. It should still be remembered, however, that different thickness-kernel combinations may produce markedly different measurements, and thus these reconstruction parameters should be kept constant in comparative studies. Awareness of the effects of CT section thickness and reconstruction kernel on emphysema quantification may help ensure that reliable measurements are obtained in studies using quantitative CT techniques.

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REFERENCES

- Chatila WM, Hoffman EA, Gaughan J, Robinswood GB, Criner GJ. Advanced emphysema in African-American and white patients: do differences exist? Chest 2006;130:108–118. [PubMed: 16840390]
- 2. Dransfield MT, Washko GR, Foreman MG, Estepar RS, Reilly J, Bailey WC. Gender differences in the severity of CT emphysema in COPD. Chest 2007;132:464–470. [PubMed: 17573503]
- Martinez FJ, Curtis JL, Sciurba F, et al. Sex differences in severe pulmonary emphysema. Am J Respir Crit Care Med 2007;176:243–252. [PubMed: 17431226]
- Demeo DL, Hersh CP, Hoffman EA, et al. Genetic determinants of emphysema distribution in the national emphysema treatment trial. Am J Respir Crit Care Med 2007;176:42–48. [PubMed: 17363767]
- 5. Ogawa E, Nakano Y, Ohara T, et al. Body Mass Index in Male Patients with Chronic Obstructive Pulmonary Disease; Correlation with Low Attenuation Areas on CT. Thorax. 2008
- Dirksen A. Progress of emphysema in severe alpha 1-antitrypsin deficiency as assessed by annual CT. Acta Radiologica 1997;38:826–832. [PubMed: 9332238]
- Roth MD, Connett JE, D'Armiento JM, et al. Feasibility of retinoids for the treatment of emphysema study. Chest 2006;130:1334–1345. [PubMed: 17099008]
- Boschetto P, Quintavalle S, Zeni E, et al. Association between markers of emphysema and more severe chronic obstructive pulmonary disease. Thorax 2006;61:1037–1042. [PubMed: 16769715]
- Patel BD, Coxson HO, Pillai SG, et al. Airway wall thickening and emphysema show independent familial aggregation in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2008;178:500–505. [PubMed: 18565956]
- Gierada DS, Pilgram TK, Whiting BR, et al. Comparison of standard- and low-radiation-dose CT for quantification of emphysema. AJR Am J Roentgenol 2007;188:42–47. [PubMed: 17179344]
- Madani A, De Maertelaer V, Zanen J, Gevenois PA. Pulmonary emphysema: radiation dose and section thickness at multidetector CT quantification--comparison with macroscopic and microscopic morphometry. Radiology 2007;243:250–257. [PubMed: 17392257]
- Coxson HO, Rogers RM. Quantitative computed tomography of chronic obstructive pulmonary disease. Acad Radiol 2005;12:1457–1463. [PubMed: 16253858]
- Friedman PJ. Imaging studies in emphysema. Proc Am Thorac Soc 2008:494–500. [PubMed: 18453361]
- 14. Reilly J. Using computed tomographic scanning to advance understanding of chronic obstructive pulmonary disease. Proc Am Thorac Soc 2006;3:450–455. [PubMed: 16799091]

- Kemerink GJ, Kruize HH, Lamers RJ, van Engelshoven JM. CT lung densitometry: dependence of CT number histograms on sample volume and consequences for scan protocol comparability. J Comput Assist Tomogr 1997;21:948–954. [PubMed: 9386288]
- Boedeker KL, McNitt-Gray MF, Rogers SR, et al. Emphysema: effect of reconstruction algorithm on CT imaging measures. Radiology 2004;232:295–301. [PubMed: 15220511]
- Bland JM, Altman DG. Comparing methods of measurement: why plotting difference against standard method is misleading. Lancet 1995;346:1085–1087. [PubMed: 7564793]
- Guo, J.; Reinhardt, JM.; Kitaoka, H., et al. Integrated system for CT-based assessment of parenchymal lung disease; IEEE International Symposium on Biomedical Imaging; 2002. p. 871-874.
- Gevenois PA, De Vuyst P, de Maertelaer V, et al. Comparison of computed density and microscopic morphometry in pulmonary emphysema. Am J Respir Crit Care Med 1996;154:187–192. [PubMed: 8680679]
- Madani A, Zanen J, de Maertelaer V, Gevenois PA. Pulmonary emphysema: objective quantification at multi-detector row CT--comparison with macroscopic and microscopic morphometry. Radiology 2006;238:1036–1043. [PubMed: 16424242]
- Muller NL, Staples CA, Miller RR, Abboud RT. "Density mask". An objective method to quantitate emphysema using computed tomography. Chest 1988;94:782–787. [PubMed: 3168574]
- Mittermayer C, Wybitul K, Rau WS, Ostendorf P, Riede UN. Standardized fixation of human lung for radiology and morphometry; Description of a "two chamber"-system with formaldehyde vapor inflation. Pathol Res Pract 1978;162:115–130. [PubMed: 356010]
- Wright BM, Slavin G, Kreel L, Callan K, Sandin B. Postmortem inflation and fixation of human lungs. A technique for pathological and radiological correlations. Thorax 1974;29:189–194. [PubMed: 4598582]
- 24. Woods JC, Choong CK, Yablonskiy DA, et al. Hyperpolarized 3He diffusion MRI and histology in pulmonary emphysema. Magn Reson Med 2006;56:1293–1300. [PubMed: 17058206]
- Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307–310. [PubMed: 2868172]
- Yuan R, Mayo JR, Hogg JC, et al. The effects of radiation dose and CT manufacturer on measurements of lung densitometry. Chest 2007;132:617–623. [PubMed: 17573501]
- Weibel ER, Hsia CC, Ochs M. How much is there really? Why stereology is essential in lung morphometry. J Appl Physiol 2007;102:459–467. [PubMed: 16973815]
- Mitzner W. Use of mean airspace chord length to assess emphysema. J Appl Physiol 2008;105:1980– 1981. [PubMed: 18719230]
- Greaves IA. Commentaries on viewpoint: use of mean airspace chord length to assess emphysema. Mean airspace chord length is useful in assessing emphysema. J Appl Physiol 2008;105:1982. author reply 1986–1987. [PubMed: 19050340]
- Hsia CC, Hyde DM, Ochs M, Weibel ER. Commentaries on viewpoint: use of mean airspace chord length to assess emphysema. To be or not to be-accurate. J Appl Physiol 2008;105:1982–1983. author reply 1986–1987. [PubMed: 19140246]
- Bates JH. Commentaries on viewpoint: use of mean airspace chord length to assess emphysema. Purists versus pragmatists. J Appl Physiol 2008;105:1983. author reply 1986–1987. [PubMed: 19140247]
- 32. Rossiter HB, Breen EC. Commentaries on viewpoint: use of mean airspace chord length to assess emphysema. Assessment of emphysema benefits from quantification of heterogeneity. J Appl Physiol 2008;105:1983–1984. author reply 1986–1987. [PubMed: 19140248]
- 33. Parameswaran H, Majumdar A, Hamakawa H, Suki B. Commentaries on viewpoint: use of mean airspace chord length to assess emphysema. Pattern of parenchymal destruction determines lung function decline. J Appl Physiol 2008;105:1984. author reply 1986–1987. [PubMed: 19140249]
- 34. Fehrenbach H. Commentaries on viewpoint: use of mean airspace chord length to assess emphysema. What does Lm tell us about lung pathology? J Appl Physiol 2008;105:1984–1985. author reply 1986– 1987. [PubMed: 19140250]
- 35. Mata JF. Commentaries on viewpoint: use of mean airspace chord length to assess emphysema. Mean airspace chord length and hyperpolarized gas magnetic-resonance measurements. J Appl Physiol 2008;105:1985. author reply 1986–1987. [PubMed: 19140251]

36. Trotta BM, Stolin AV, Williams MB, Gay SB, Brody AS, Altes TA. Characterization of the relation between CT technical parameters and accuracy of quantification of lung attenuation on quantitative chest CT. AJR Am J Roentgenol 2007;188:1683–1690. [PubMed: 17515394]

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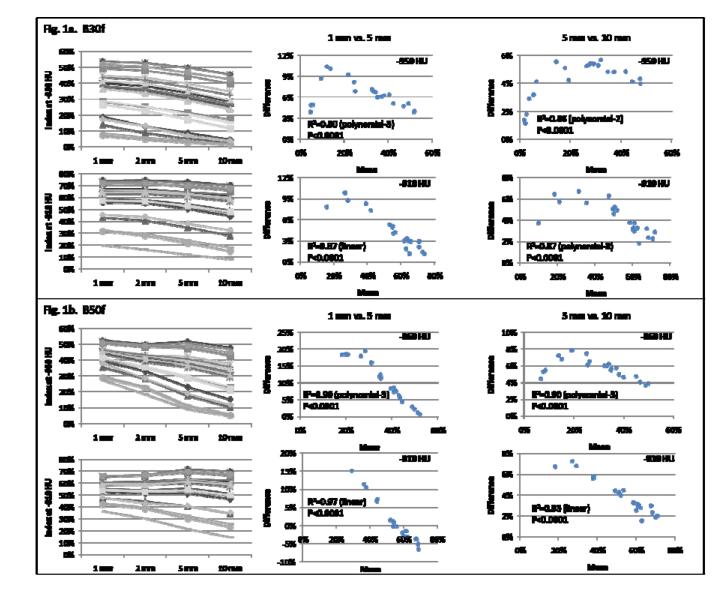


Figure 1.

Relationship of emphysema index magnitude to the effect of section thickness on the emphysema index for representative –950 HU and –910 HU thresholds). First column shows effect of each thickness on individual subjects. Second and third columns show Bland-Altman plots comparing representative 1 mm and 5 mm sections, and 5 mm and 10 mm sections, respectively. (a) Representative smooth (B30f) kernel. (b) Representative sharp (B50f) kernel. Note –Each line in first column graphs, and each point in second and third column graphs, represents an individual subject. Mean – average of the emphysema index obtained with 1 mm and 5 mm section thicknesses in each subject. Difference – difference between the emphysema index obtained with 1 mm and 5 mm section thicknesses, in index percentage points. Linear – best empiric fit was described by linear function. Polynomial-2 – best empiric fit was described by second-order polynomial. Polynomial-3 – best empiric fit was described by third-order polynomial. Same patterns were seen for other kernels, section thickness comparisons, and HU thresholds.

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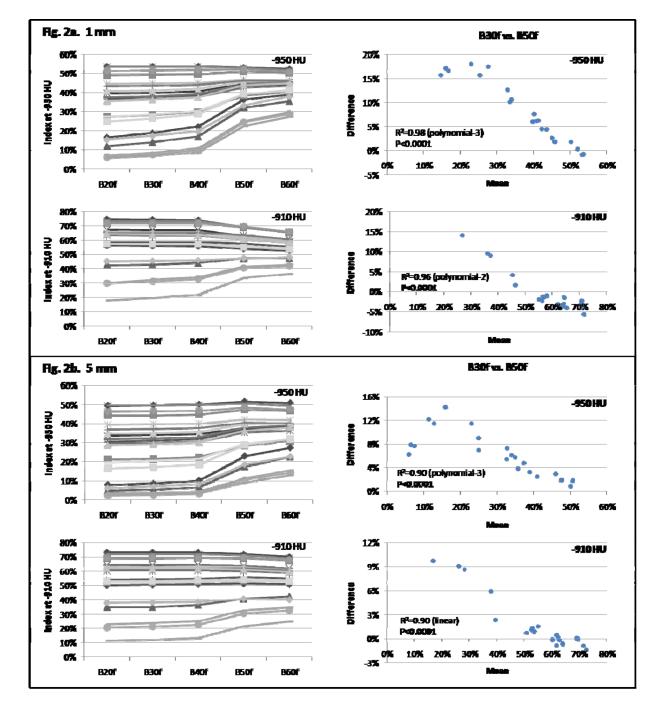
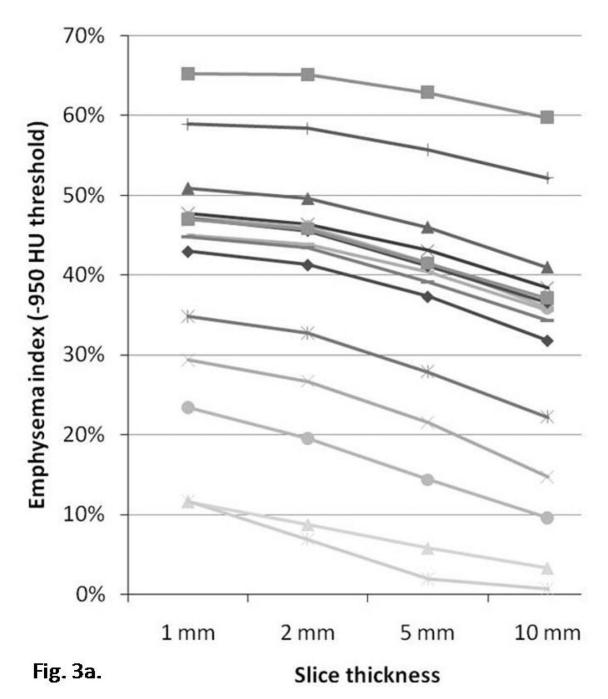


Figure 2.

Relationship of emphysema index magnitude to the effect of reconstruction kernel on the emphysema index for representative –950 HU and –910 HU thresholds. First column shows effect of each kernel on individual subjects. Second column shows Bland-Altman plots comparing representative B30 f and B50f kernels. (a) Representative 1 mm section thickness. (b) Representative 5 mm section thickness. Note –Each line in first column graphs, and each point in second column graphs, represents an individual subject. Mean – average of the emphysema index obtained with B30f and B50f kernels in each subject. Difference – difference between the emphysema index obtained with B30f and B50f kernels, in index percentage points. Linear –best empiric fit was described by linear function. Polynomial-2 – best empiric

fit was described by second-order polynomial. Polynomial-3 – best empiric fit was described by third-order polynomial. Same patterns were seen for other section thicknesses, kernel comparisons, and HU thresholds.



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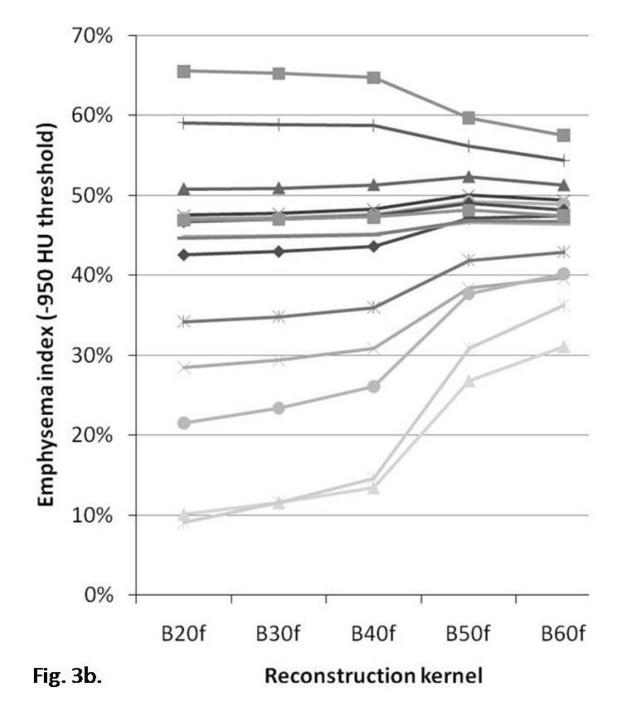


Figure 3.

Emphysema index values at representative –950 HU threshold in 4 lobes (four lowest indexes) and 11 lungs of 11 subjects in whom quantitative histology was performed. (a) Effect of section thickness with representative smooth B30f reconstruction kernel. (b) Effect of reconstruction kernel with representative 1 mm section thickness. Note – Each line represents an individual lung or lobe.

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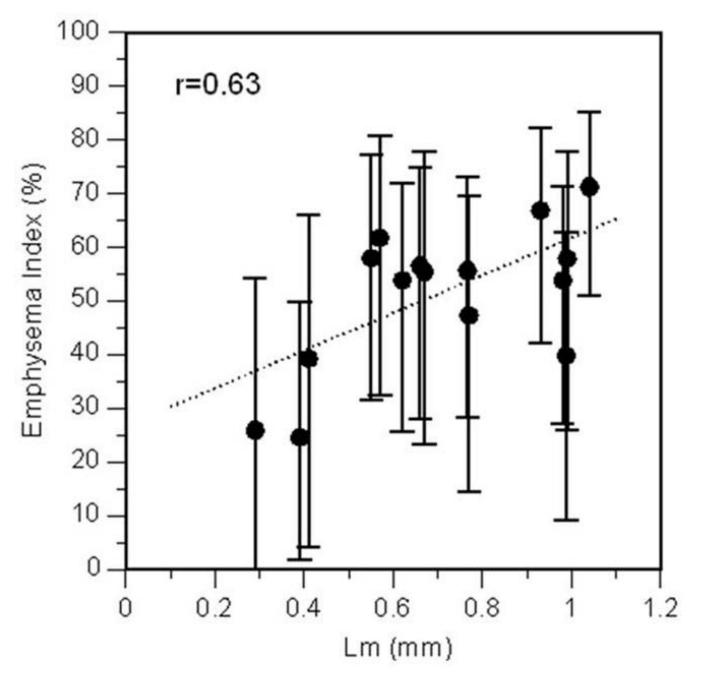


Figure 4.

Scatter plot with regression line shows mean linear intercept (Lm) for each of 11 lungs and 4 lobes (x-axis) versus mean (solid circles) and range (horizontal bars) of all emphysema index values obtained with all section thickness-reconstruction kernel combinations at all HU thresholds.

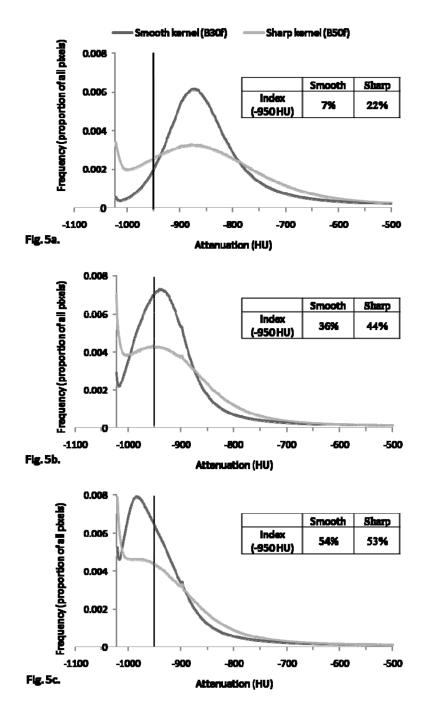


Figure 5.

CT attenuation histograms in 3 subjects (a–c) demonstrating progressively greater emphysema severity by lung attenuation values, shown for representative smooth (B30f; black curves) and representative sharp (B50f; gray curves) kernels at representative 1 mm section thickness. Emphysema index for each histogram corresponds to the proportion of the entire area under each curve that lies to the left of the chosen HU threshold (–950 HU in this example). As histograms become shifted toward more negative HU values in (b) and (c), area below the smooth kernel curve to the left of the threshold increases more than area under the sharp kernel curve. Note – pixel attenuation values are truncated at -1024 HU by the scanner software; frequency of pixels at -1024 to -1023 HU shown for sharp kernel is smaller than actual

frequency to avoid compressing the frequency scale (actual frequency at -1024 to -1023 HU is 0.05 in (a), 0.13 in (b), and 0.17 in (c).

Table 1

Subject characteristics

	Transplant (n=12)	Lobectomy (n=9)	All (n=21)
Female:Male	5:7	5:4	10:11
Age, years	58±5	65±5	61±6
(range)	(46–64)	(58–74)	(46–74)
Smoking history, pack years (range)	58±19	60±39	59±29
	35–90	13–135	(13–135)
FEV ₁ , % of predicted (range)	20±7	78±29	43±34
	(13–37)	(45–128)	(13–128)
FVC, % of predicted (range)	52±16	99±25	71±30
	(36–90)	(61–140)	(36–140)
FEV ₁ /FVC	0.32±0.12	0.63±0.14	0.44±0.20
(range)	(0.19–0.67)	(0.37–0.81)	(0.19–0.81)
TLC, % of predicted (range)	139±19	130±24	135±20
	(109–171)	(111–180)	(109–180)
RV, % of predicted (range)	295±64	177±72	249±88
	(146–395)	(111–320)	(111–395)
DLCO, % of predicted (range)	31±11	81±17	52±29
	(15–47)	(53–102)	(15–102)

Values are mean±std. dev.

Note-The following data were not available: FEV1 in one lobectomy patient, FVC in one lobectomy patient, TLC and RV in one transplant and two lobectomy patients, and DLCO in two transplant and two lobectomy patients

Table 2

Mean CT emphysema index values shown at four representative attenuation thresholds (-950, -930, -910, and -890 HU) for each combination of section thickness (1 mm, 2 mm, 5 mm, and 10 mm) and reconstruction kernel (B20f, B30f, B40f, B50f, and B60f)

	B20f	B30f	B40f	B50f	B60f
-950 HU					
1 mm	32 ± 16	33 ± 15	34 ± 15	41 ± 9	42 ± 7
2 mm	29 ± 17	30 ± 16	31 ± 16	37 ± 11	6 ∓ <i>L</i> £
5 mm	26 ± 16	26 ± 16	27 ± 16	32 ± 13	34 ± 11
10 mm	22 ± 15	22 ± 15	22 ± 15	27 ± 14	28 ± 13
-930 HU					
1 mm	45 ± 17	45 ± 16	46 ± 15	49 ± 10	49 ± 8
2 mm	43 ± 18	44 ± 17	44 ± 17	47 ± 12	46 ± 10
5 mm	39 ± 18	40 ± 18	40 ± 18	44 ± 15	44 ± 13
10 mm	35 ± 19	35 ± 19	36 ± 18	39 ± 16	40 ± 14
-910 HU					
1 mm	57 ± 16	57 ± 15	58 ± 14	57 ± 10	56 ± 8
2 mm	56 ± 16	56 ± 16	57 ± 15	57 ± 12	55 ± 10
5 mm	53 ± 18	53 ± 17	53 ± 17	55 ± 14	54 ± 13
10 mm	49 ± 19	49 ± 18	49 ± 18	51 ± 16	51 ± 15
UH 068-					
1 mm	68 ± 13	67 ± 13	67 ± 12	64 ± 10	62 ± 10
2 mm	67 ± 14	67 ± 13	67 ± 13	65 ± 11	62 ± 10
5 mm	64 ± 15	65 ± 15	65 ± 14	64 ± 13	63 ± 12
10 mm	61 ± 16	61 ± 16	61 ± 16	61 ± 14	60 ± 14

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Index values are mean index in % ± SD. Differences were statistically significant (P<0.001) for section thickness at all attenuation thresholds (including those not shown in table), and for reconstruction kernel at all attenuation thresholds (including those not shown in table) except -910 HU.

Table 3

Correlation coefficients comparing CT emphysema index and Lm values for each combination of section thickness, reconstruction kernel, and emphysema index HU threshold

иш т	B20f	B30f	B40f	B50f	B60f
∩H 096−	.67	.67	.66	.63	.60
-950 HU	.67	.67	.66	.62	.59
-940 HU	.67	.67	.66	.61	.59
-930 HU	.66	.66	.65	09.	.58
-920 HU	.65	.64	.64	65.	.57
-910 HU	.63	.63	.62	65.	.57
∩H 006−	.60	.60	.60	.58	.56
UH 068-	.57	.57	.58	.57	.56

2 mm	B20f	B30f	B40f	B50f	B60f
-060 HU	.67	.67	.67	.64	.63
-950 HU	.68	.68	.67	.64	.62
-940 HU	.68	.67	.67	.63	.61
-930 HU	.67	.67	.66	.62	.60
-920 HU	.65	.65	.65	.61	.60
-910 HU	.63	.63	.63	.59	59.
UH 006-	.60	.60	.60	.58	.58
-890 HU	.57	.57	.57	.58	.57

um 2	B20f	B30f	B40f	B50f	B60f
-060 HU	.64	.65	.66	.61	.64
-950 HU	.66	.67	.67	.60	.64
-940 HU	.66	.67	.67	.60	.63
-930 HU	.66	.67	.66	.60	.62
-920 HU	.64	.65	.65	.59	.61
-910 HU	.63	.64	.63	.58	.60
-900 HU	.60	.61	.61	.57	.59

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UH 068-5 mm

I0 mm B20f B30f B40f B50f B40f B50f B60f -960 HU .61 .62 .63 .63 .63 -950 HU .61 .62 .63 .63 .63 -950 HU .64 .64 .63 .63 .63 -940 HU .65 .65 .65 .63 .61 -930 HU .65 .65 .65 .63 .61 -930 HU .64 .64 .63 .61 .61 -920 HU .64 .64 .62 .61 .61 -920 HU .64 .64 .63 .61 .61 -920 HU .64 .64 .63 .61 .61 -920 HU .60 .59 .56 .56 .56 .56 .56 -920 HU .64 .64 .64 .63 .56 .56 -910 HU .50 .59 .56 .58 .58	UH 068-	IJ	.56	.58	.58	.55	.58
B20f B30f B40f B50f U .61 .62 .63 .63 U .61 .62 .63 .63 U .64 .64 .63 .63 U .65 .65 .65 .63 U .64 .64 .64 .63 U .64 .64 .64 .63 U .62 .63 .63 .63 U .60 .59 .50 .60 U .60 .59 .58 .60 U .56 .56 .56 .58 U .50 .59 .58 .58 U .56 .56 .58 .58 U .56 .59 .58 .58<							
.61 .62 .63 .63 .64 .64 .64 .63 .65 .65 .65 .63 .65 .65 .65 .63 .65 .65 .65 .63 .65 .65 .65 .63 .64 .64 .64 .63 .65 .65 .63 .63 .64 .64 .64 .63 .62 .63 .63 .63 .64 .64 .64 .60 .63 .65 .62 .60 .60 .60 .60 .59 .59 .58 .58 .50 .56 .56 .56 .56 .56 .56 .56 .56 .56	10 mm		B20f	B30f	B40f	B50f	B60f
.64 .64 .63 .63 .65 .65 .65 .63 .63 .65 .65 .65 .63 .63 .65 .65 .65 .63 .63 .64 .64 .64 .63 .63 .62 .65 .65 .63 .63 .64 .64 .64 .64 .63 .62 .63 .63 .63 .63 .64 .64 .64 .64 .64 .64 .64 .65 .62 .60 .60 .60 .59 .59 .58 .56 .56 .56 .56	960 F	IU	.61	.62	.62	.63	.63
.65 .65 .65 .63 .65 .65 .63 .63 .64 .64 .64 .62 .62 .63 .63 .63 .63 .64 .64 .64 .64 .64 .64 .63 .63 .63 .63 .63 .64 .64 .64 .64 .65 .62 .60 .60 .59 .58 .56 .56 .56 .56 .56 .56	-950 H	IU	.64	.64	.64	.63	.63
.65 .65 .65 .63 .64 .64 .64 .62 .62 .62 .60 .60 .60 .59 .59 .58 .56 .56 .56 .56	940 F	IU	.65	.65	.65	.63	.62
.64 .64 .64 .62 .62 .62 .60 .60 .59 .58 .56 .56 .58	-930 F	IJ	.65	.65	.65	.63	.61
.62 .62 .62 .60 .60 .59 .59 .58 .56 .56 .56 .56	-920 H	IU	.64	.64	.64	.62	.61
.60 .59 .59 .58 .56 .56 .56 .56	-910 F	IU	.62	.62	.62	.60	.59
.56 .56 .56 .56	H 006–	IU	.60	.59	.59	.58	.58
	-890 F	IU	.56	.56	.56	.56	.56

p<0.05 for all r values

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Section thickness in italics. Reconstruction kernels ordered from smoothest (B20f) to sharpest (B60f).