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Accuracy of Emphysema Quantification Performed With Reduced Numbers of CT Sections

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Abstract

Objective—The purpose of this study was to assess the accuracy of emphysema measurements obtained from systematic samples of evenly spaced CT images compared with measurements obtained from the entire scan.

Materials and Methods—Evenly spaced transverse sections from the CT studies of 136 heavy smokers who underwent screening for lung cancer in the National Lung Screening Trial and of 112 subjects who underwent imaging before lung volume reduction surgery were sampled retrospectively. The samples were acquired both by selection of specific numbers of evenly spaced images and by selection of images at specific distance intervals. The percentage of lung pixels with attenuation below specific thresholds was used as an emphysema index. The image sample error was determined as the difference in emphysema index between the image samples and the entire scan.

Results—The largest absolute image sample errors in the National Lung Screening Trial cohort with image sample sizes of five, 10, and 20 were 2.2, 0.8, and 0.5 index percentage points, respectively, at 1-mm section thickness (–960 HU threshold), and 2.6, 1.1, and 0.5 index percentage points at 5-mm section thickness (–930 HU threshold). The largest errors in the lung volume reduction surgery cohort for image sample sizes of five and 10 were 5.6 and 2.3 index percentage points at 8- to 10-mm section thickness (–900 HU threshold). Image sample errors were equivalent for the two sampling methods.

Conclusion—Systematic sampling resulted in very small errors in emphysema quantification and may be useful for decreasing radiation exposure in clinical research studies of emphysema.

Keywords

emphysema; quantitative CT

Quantification of emphysema from CT scans has been increasingly advocated in clinical research for characterizing individuals with chronic obstructive pulmonary disease, monitoring the progression of emphysema, and assessing the response to therapy [1,2]. The CT measurement technique, which is based on the reduced attenuation of lung tissue resulting from air-space enlargement and alveolar destruction, has been used to identify associations between emphysema and sex [3,4], race [5], body mass index [6], and certain genes [7] when applied

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retrospectively to CT scans that had been obtained for other indications. The prospective use of CT specifically for quantifying emphysema in observational studies or treatment trials has the potential to more directly advance knowledge about this disease. However, the cumulative radiation exposure restricts the ability to perform repeated investigational whole-lung CT, particularly on individuals who are younger and have less functional impairment. Use of a low-radiation-dose CT technique can reduce radiation exposure as much as threefold to fourfold [8–10], but the exposure level remains substantial.

Because emphysema typically affects relatively large lung regions diffusely, scanning and analyzing the entire lung may not be necessary to obtain accurate CT measurements, provided the regions involved are adequately sampled. The result can be substantial further reduction in radiation exposure, reducing the risk to subjects in longitudinal studies of emphysema. Although the use of a limited number of CT sections to quantify emphysema is not new, to our knowledge the number of sections required has not been established. We performed this study to assess the accuracy of emphysema measurements obtained from systematic samples of CT images evenly spaced throughout the lung compared with measurements obtained from the entire CT scan.

Materials and Methods

Institutional review board approval was obtained for this retrospective study, which included waiver of informed consent for the use of existing data. Data were managed according to HIPAA guidelines.

Subjects

Two different cohorts at increased risk of emphysema were studied to capture a wide range of emphysema severity and distribution. To capture individuals with minimal emphysema to moderately severe emphysema, we included a cohort of long-term smokers and former smokers participating in the National Lung Screening Trial (<http://www.cancer.gov/nlst>, clinicaltrials.gov identifier NCT00047385) [11] through our institution. This study was not part of the National Lung Screening Trial. From the data on 1,880 participants randomized to the CT screening arm, MDCT raw data from the final screening year (obtained from December 2004 through January 2006) were available for retrospective image reconstruction for 136 participants, whose CT scans were analyzed for this study. The CT raw data were saved when permitted by the daily workflow of the clinical CT service. The 92 men and 44 women (mean age, 63 ± 5 [SD] years) had a smoking history of 61 ± 26 pack-years. No information on pulmonary function was available.

To capture data on individuals with severe emphysema, we included a cohort of patients who had undergone lung volume reduction surgery (LVRS) for severe chronic obstructive pulmonary disease at our institution. Data from previously performed quantitative emphysema analysis of the preoperative CT images (obtained from 1992 to 1996) were available for 112 of these patients and were used for this study. These 62 men and 50 women (mean age, 62 ± 9 years) had a forced expiratory volume in one second of $25\% \pm 7\%$ of the predicted normal value. Six subjects had α -1 antitrypsin deficiency. Quantitative CT data on 45 of these LVRS patients had been published previously [12].

CT

In the National Lung Screening Trial cohort, CT was performed with single breath-hold spiral technique, a 16-MDCT scanner (Sensation 16, Siemens Healthcare), a low radiation dose with 45 mAs at 120 kVp, and a pitch of 1.5 for an effective tube current of 30 mAs. The detector collimation was 0.75 mm. The CT raw data were reconstructed for the current study as

contiguous transverse images at both 1-mm and 5-mm section thicknesses with a medium smooth kernel.

For all 112 patients in the LVRS cohort, contiguous transverse CT images were obtained with incremental technique (different breath-hold for each transverse section) and a tube current of 178–255 mAs at 120 or 137 kVp. For 107 of the patients, CT was performed with a single-detector scanner (Somatom Plus or Somatom Plus S, Siemens Healthcare) at 8-mm ($n = 15$) or 10-mm ($n = 92$) section thickness. The other five patients underwent single-breath-hold helical technique with a 4-MDCT scanner (Volume Zoom, Siemens Healthcare) at 1-mm detector collimation, 8-mm reconstructed section thickness, a pitch of 1.5, and a medium smooth kernel.

CT Image Analysis

One of the authors analyzed the National Lung Screening Trial cohort images using a custom fully automated program (Matlab, Mathworks) based on a previously described segmentation algorithm [13]. The LVRS cohort images were analyzed by a clinical research radiologic technologist using imaging software (Pulmo CT, Siemens Healthcare) [14]. The image analysis results were reviewed visually by an author other than the one who performed the analysis of the National Lung Screening Trial cohort images. Visual review of all images from both cohorts by the same author who visually reviewed the LVRS cohort images revealed no motion blurring other than from occasional minor cardiovascular pulsation. Except for minimal streak artifacts in eight National Lung Screening Trial subjects with metallic hardware from median sternotomy, no other artifacts were seen. No images were excluded from analysis.

Emphysema severity was quantified as an emphysema index, which was calculated as the percentage of lung pixels with an attenuation value lower than a specific threshold. Attenuation thresholds of −960 HU for images of 1-mm section thickness and −900 HU for images 8–10 mm thick were chosen because the same or similar thresholds had been commonly used and validated against tissue specimens [9,15–17]. For the 5-mm-thick images, an intermediate threshold of −930 HU was used. Each image containing lung tissue was analyzed individually, and the results were summed to obtain the emphysema index for the whole lung.

CT Image Sampling

The emphysema index data (number of lung pixels with attenuation below the chosen threshold and total number of lung pixels) from the individual images were used to determine the emphysema index produced by selected combinations of sampled images. One of the authors applied two different methods of systematically sampling the sequential individual slice emphysema index data to draw data from samples of evenly spaced transverse images throughout the lungs. The two methods yielded similar numbers and spacing of images but from different locations. With both methods, we aimed to obtain samples of one, two, five, 10, and 20 images for the 1-mm and 5-mm section thicknesses of the National Lung Screening Trial cohort and one, two, five, and 10 images for the 8- to 10-mm section thicknesses of the LVRS cohort, referred to in this study as the target image sample sizes. A target image sample size of 20 was not drawn from the LVRS cohort because that number was close to the entire number of transverse images in most cases.

In the number method of systematic image sampling, the numbers of images specified by the targets were sampled from each entire set of transverse images. The images for each target sample size were selected so that there was equal distance from the top of the lung to the most superior image sampled, between images sampled, and from the most inferior image sampled to the bottom of the lung.

In the interval method, images were sampled at specified intervals, starting at the top of the lung. The intervals were chosen so that the target image sample sizes would be drawn in most subjects. For 1-mm section thickness (National Lung Screening Trial cohort), samples consisted of every 200th, 100th, 50th, 25th, and 12th image. For 5-mm section thickness (National Lung Screening Trial cohort), samples consisted of every 40th, 20th, 10th, fifth, and third image. For 8- to 10-mm section thickness (LVRS cohort), samples consisted of every 20th, 10th, fifth, and third image. The distance from the top of the lung to the most superior image sampled equaled the distance between images; the distance from the most inferior image sampled to the bottom of the lung varied.

Both sampling methods were also used to evaluate regional emphysema severity in the upper and lower halves of the lung, which may be a clinically relevant means of differentiating emphysema distribution [12,18,19]. The upper and lower halves of the lung were divided according to the number of transverse CT sections containing lung. Image sample size targets for the upper and lower lung evaluations did not include 20 images with either cohort or 10 images with the LVRS cohort because these targets were close to the total number of images in the upper or lower half for the 5-mm and 8- to 10-mm section thicknesses.

Data Analysis

For each subject and section thickness, the emphysema index calculated from the entire scan (or entire upper and lower lung halves) was used as the reference standard and subtracted from the emphysema index calculated from the image samples. This difference was defined as the image sample error and calculated for each subject at each image sample size. The mean, SD, total range, and 95th percentile range (range encompassing 95% of all values, from the 2.5th percentile to the 97.5th percentile) of image sample errors were determined for each cohort, section thickness, and image sample size. Deviation of the mean image sample error from zero was used as an indication of bias due to sampling. A statistical software application (JMP version 6.0, SAS Institute) was used to compare absolute image sample errors among the different image sample size targets by repeated measures analysis of variance (National Lung Screening Trial cohort comparing target sample sizes of five, 10, and 20 images) or two-tailed paired Student's *t* test (LVRS cohort comparing target sample sizes of five and 10 images) and among the two image sampling methods by two-tailed paired Student's *t* test. The emphysema index values for the upper and lower halves of the lungs were compared by use of two-tailed paired Student's *t* tests. Values of $p < 0.05$, or < 0.05 divided by the number of comparisons when multiple comparisons were made, were considered statistically significant. Bland-Altman plots [20] of mean versus difference were generated with a spreadsheet program (Excel 2007, Microsoft) and used to examine the relation between the magnitude of the emphysema index and the image sample error.

Results

Image Sample Sizes

With the number method, the image sample sizes (Table 1) were less than the target sample sizes for some subjects because it is not possible to obtain fractional sections. With the interval method, the image sample sizes (Table 1) were sometimes smaller (in persons with the shortest lungs) and sometimes larger (in persons with the tallest lungs) than the targets. Image sample sizes for the upper and lower lung regions varied depending on the cohort, section thickness, and sampling strategy with a mean of 4.3–5.0 (range, 3–6) for target sample sizes of five images and of 7.9–10.0 (range, 6–13) for target sample sizes of 10 images.

Emphysema Index Values

The emphysema index in the National Lung Screening Trial cohort was low on average, but there was substantial variability (Table 2). In the National Lung Screening Trial cohort, the emphysema index was minimally larger in the upper lungs than in the lower lungs, a difference that was statistically significant for the images with a 1-mm section thickness. In the LVRS cohort, there was a fairly broad range of emphysema index values, but all were high, and the emphysema index was larger in the upper halves of the lungs (Table 2).

Image Sample Errors

The image sample errors for the whole lung index decreased rapidly with an increase in the number of images (Fig. 1). For an image sample size target of five, the largest absolute error in the National Lung Screening Trial cohort was 1.4 index percentage points at 1-mm section thickness and 2.6 index percentage points at 5-mm section thickness; for 10- and 20-image samples, this value was 1.1 index percentage points (Table 3). In the LVRS cohort, the largest absolute errors with five- and 10-image samples were 5.6 and 2.3 index percentage points, respectively. The largest 95th percentile range of image sample errors with five-image samples was -1.1 to 1.2 index percentage points in the National Lung Screening Trial cohort and -2.8 to 3.4 index percentage points in the LVRS cohort. This range became smaller with image sample sizes of 10 and 20 (Table 3). With image sample size targets of five or more, bias was very small, the mean absolute image sample errors being no greater than 0.5 index percentage points in either cohort. There was no consistent pattern of bias in the mean image sample errors, which were sometimes positive and sometimes negative (Fig. 1, Table 3).

The mean absolute errors for target image sample sizes of five or more decreased as the target image sample size increased ($p < 0.001$) but was extremely small for each sample size (Table 4). After adjustment of the significance criteria because comparisons were made at multiple target image sample sizes, there were no statistically significant differences in the mean absolute errors found with the number and interval methods at any target image sample size (Table 4). In any case, these differences also were extremely small. The image sample errors tended to deviate further from zero as the size of the emphysema index increased (Fig. 2). However, the image sample errors remained very small for emphysema index values of any size.

The image sample errors in the upper and lower lung evaluations were similar to those for the whole lung. In the National Lung Screening Trial cohort, the largest absolute error in the upper or lower lung with image sample sizes of five or 10 was no more than 0.5 index percentage points greater than the largest absolute error in the whole lung with the same sample size for both section thicknesses and sampling methods. In the LVRS cohort, the largest absolute error in the upper or lower lung with an image sample size of five was no more than 1.6 index percentage points greater than the largest absolute error in the whole lung with the same image sample size.

Discussion

Our results indicate that acquiring small numbers of CT sections spaced evenly throughout the lung may be sufficient for quantifying emphysema. The image sample errors were quite small even for the LVRS cohort, in which patients had been selected for surgery because of an exceptional spatial heterogeneity of emphysema. One might expect that image sampling accuracy would be more strongly influenced by the total volume of the lung sampled in addition to the number and location of samples. However, the image sample errors were similarly small for the 1-mm and 5-mm section thicknesses in the National Lung Screening Trial cohort and for the 8- to 10-mm sections in the LVRS cohort at each image sample size. Possible

explanations for this finding include the diffuse distribution of emphysema throughout the lungs, a relatively gradual change in emphysema index over the entire cephalocaudal extent of the lungs in contiguous CT sections, and limited variation in emphysema severity within any one transverse section of the lung up to at least 5 mm in thickness.

With both of the image sampling methods, similar numbers of evenly spaced images were selected but from different locations. Although the image sample sizes deviated from the targets in some individuals, image sample errors were essentially equivalent for the two sampling methods. Although it would have been possible to devise numerous other sampling methods, the methods we used produced very small errors, and no other sampling methods were tested. The interval method, in which the same distance interval between sections would be used for all individuals, may be simpler to apply to prospective scanning than the number method. Both of these image sampling methods are systematic rather than random and therefore may be prone to bias [21]. However, the amount of bias we found empirically was extremely small.

A previous theoretic analysis of CT image sampling [22] concluded that the number of 1-mm sections required to quantify emphysema is greatest if 50% of acini are affected by emphysema and decreases as this percentage either decreases or increases. The percentage of acini typically affected is not known, however, nor is there a means of determining this percentage. Our empirical results show the accuracy of a simple, easily applied sampling approach to imaging of patients with a wide range of emphysema.

In a previous CT morphometric study [23] in which the emphysema index (referred to as the relative area below -950 HU) was determined from 1-mm sections at 10-mm intervals, the investigators concluded that the individual variation with the use of fewer sections was too great to recommend an optimal distance between sections. However, no data on the actual sampling errors were provided that could be compared with our results. In a different study [24], in which 2-mm sections were used, another group of investigators concluded that three sections were sufficient only on the basis of a high correlation between the emphysema index (-960 HU threshold) from three sections and the index from 10 sections. That study also did not show the magnitude of the individual image sample errors, which may be more relevant to the accuracy of image sampling than is the correlation between sampling methods. In the latter study, a scatterplot revealed that despite the high correlation, errors as large as 5–10 index percentage points occurred with use of three sections in multiple subjects, whereas the errors with five sections were closer to the errors found with five sections used in our study. Unlike the standard in these previous studies, the reference standard to which our image samples were compared was the entire lung volume.

The largest absolute image sample error for 1-mm section thickness was 1.0 index percentage point with as few as five evenly spaced images in 95% of subjects. The error was lower with 10 and 20 images. The amount of error that can be considered acceptable depends on the degree of difference or change one wishes to detect, so it can vary depending on the purpose of a clinical research study. The error we found is similar to or less than the interscan variability in the emphysema index [16,25], implying that limited sampling is sufficiently accurate for longitudinal studies. Our results suggest that among the previous prospective studies in which emphysema has been quantified from arbitrary numbers of CT sections, those in which more than five sections were acquired [15,26–31] likely had accurate quantitative CT measurements of emphysema severity in almost all subjects. However, obtaining only two or three CT sections, as in some previous studies [32–35], may not provide accurate CT estimates of emphysema severity in some individuals. Our data on the accuracy of different image sample sizes may provide guidance for future studies in which limited numbers of CT sections are used.

There is growing recognition of the radiation risks posed by CT [36]. Obtaining a limited number of images for emphysema quantification by use of a low-radiation-dose technique would help to greatly reduce radiation exposure in clinical research on emphysema. Low-radiation-dose scanning reduces the effective radiation dose for chest CT from approximately 5 mSv to 1.5 mSv, or to approximately one-half the average annual dose from environmental background radiation in the United States [37]. Use of automatic exposure control, with which dose is modulated on the basis of body habitus and anatomic region [38], may provide an additional approximately 20% decrease for volumetric scanning, although the effect of this scanning technique on emphysema index values is unknown. In contrast, a dramatically greater decrease in radiation exposure might be obtained through acquisition of only five to 10 evenly spaced 1-mm low-dose images (of an average total of 250 images), which would result in scanning of 2–4% of the total lung volume. The effective radiation dose thus would be reduced to the range of 0.03–0.06 mSv, approximating the typical exposure of a chest radiograph.

Whole-lung CT may be necessary or desirable in some clinical research studies of chronic obstructive pulmonary disease, at least at baseline, to allow volumetric quantitative evaluation of the airways or to assess for the presence of other lung diseases. However, restricting subsequent scans to a reduced number of sections may increase the acceptable frequency of serial CT for studying the progression of emphysema. Use of this method may allow more frequent monitoring in observational studies or clinical trials in which the CT emphysema index is used as a short-term or intermediate outcome measure. It also may allow subjects of widespread ages to participate in multiple trials over time without unnecessary radiation risk and is in keeping with the as low as reasonably achievable principle advocated for clinical diagnostic imaging. It would also increase image analysis throughput and reduce image archive space requirements.

One limitation of our study was that the differences in scan technique between the National Lung Screening Trial and imaging of the LVRS subjects prevented direct comparison of the image sample errors in the two cohorts. Although use of the LVRS cohort allowed us to confirm in principle that sampling is effective even in a group consisting only of subjects with severe heterogeneous disease, we were unable to assess sampling with MDCT acquisition and thinner sections in this cohort. However, because each subject's entire scan served as the reference standard for each image sample size target in each subject, the technical differences did not affect the assessment of image sample errors within each cohort and section thickness. If the LVRS scans had all been obtained by volumetric acquisition, minimal respiratory variation would have occurred and the image sample errors might have been even lower. Our results also might have been different with random sampling, which we did not use because it would be impractical in the clinical setting. Finally, our results should not be generalized to patients with lung diseases other than emphysema, in whom different numbers and distributions of lesions occur.

In summary, the accuracy of estimating the CT emphysema index from systematically obtained image samples was high with as few as five sections 1-mm thick in most subjects and with 10 sections in all subjects.

There was no meaningful bias or influence of emphysema severity on the number of sections needed. This or a similar image sampling approach may be a simple and practical means of greatly limiting radiation exposure in clinical research studies on the imaging of patients with emphysema.

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Fig. 1.

Graph shows image sample errors (y-axis) for National Lung Screening Trial (NLST) (1-mm and 5-mm section thicknesses) and lung volume reduction surgery (LVRS) (8- to 10-mm section thickness) cohorts with number and interval sampling methods at each target image sample size (x-axis). Values shown include mean (*diamonds*), SD (*thin horizontal lines*), and range (*thick horizontal lines*). Image sample error is emphysema index calculated from image samples minus index calculated from entire scan. Number method is sampling of specific numbers of images with equal spacing between top of lung and first image sampled, between images sampled, and between last image sampled and bottom of lung. Interval method is sampling of images at constant intervals throughout lung (e.g., every 10th image).

Fig. 2.

Bland-Altman plots show emphysema index mean versus difference for representative target image sample size of 10 images obtained with number method. Mean (x -axis) is mean of index determined from 10 images and index determined from entire scan of each subject. Difference (y -axis) is image sample error (index determined from 10 images minus index determined from entire scan). Number method is sampling of specific numbers of images with equal spacing between top of lung and first image sampled, between images sampled, and between last image sampled and bottom of lung. **A**, National Lung Screening Trial cohort, 1-mm section thickness, -960 HU threshold. **B**, National Lung Screening Trial cohort, 5-mm section thickness, -930

HU threshold. C, Lung volume reduction surgery cohort, 8- to 10-mm section thickness, -900 HU threshold.

TABLE 1
Number of sections in Whole lung and Image samples

Sampling Method	Total No. of Sections in Whole Lung			Target Sample Size ^a				
	Mean	SD	Range	1	2	5	10	20
National Lung Screening Trial (<i>n</i> = 136)								
1-mm section thickness	250	22	190–315					
Number				1 (1–1)	2 (2–2)	5 (5–5)	10 (10–10)	19.6 (19–20)
Interval (every 200th, 100th, 50th, 25th, and 12th image)				1 (0–1)	2 (1–3)	4.6 (3–6)	9.5 (7–12)	20.4 (15–26)
5-mm section thickness	50	4	38–63					
Number				1 (1–1)	2 (2–2)	5 (5–5)	9.5 (8–10)	16.6 (14–20)
Interval (every 40th, 20th, 10th, fifth, and third image)				1 (0–1)	2 (1–3)	4.6 (3–6)	9.6 (7–12)	16.3 (12–21)
Lung volume reduction surgery (<i>n</i> = 112)								
8- to 10-mm section thickness	28	3	23–36					
Number				1 (1–1)	2 (2–2)	5 (4–5)	8.7 (7–10)	
Interval (every 20th, 10th, fifth, and third image)				1 (1–1)	2.3 (2–3)	5.3 (4–7)	9.1 (7–12)	

^aValues are mean number of sections actually sampled with range in parentheses.

TABLE 2
CT Emphysema Index Values for all lung CT sections (Whole lung Index), superior half of all lung CT sections (upper lung Index), and Inferior half of all lung CT sections (lower lung Index)

Section Thickness and Attenuation Threshold	Whole Lung Index			Upper Lung Index			Lower Lung Index			<i>p</i> ^a
	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range	
National Lung Screening Trial (<i>n</i> = 136)										
1 mm, -960 HU	6.8	5.5	0.4–43.5	7.2	7.1	0.2–58.0	6.4	4.5	0.4–28.9	0.03
5 mm, -930 HU	9.2	9.1	0.3–60.2	9.5	11.0	0.1–72.8	8.8	8.1	0.1–46.4	0.21
Lung volume reduction surgery (<i>n</i> = 112)										
8–10 mm, -900 HU	60.9	7.7	41.5–79.5	71.8	12.1	31.7–92.1	51.3	13.1	19.8–82.9	< 0.0001

^aUpper versus lower lung, two-tailed paired Student's *t* test

TABLE 3
Sample Error Values (Index Percentage Points)

Value	Target Sample Size		
	5	10	20
National Lung Screening Trial ($n = 136$)			
1-mm section thickness, -960 HU threshold			
Number method			
Mean	-0.2	-0.1	-0.0
95th percentile range	-1.0 to 0.7	-0.5 to 0.4	-0.3 to 0.3
Total range	-1.4 to 0.9	-0.8 to 0.7	-0.4 to 0.5
Interval method			
Mean	-0.1	-0.0	-0.0
95th percentile range	-0.9 to 0.7	-0.4 to 0.5	-0.2 to 0.2
Total range	-2.2 to 1.0	-0.8 to 0.7	-0.3 to 0.3
5-mm section thickness, -930 HU threshold			
Number method			
Mean	-0.0	-0.0	-0.0
95th percentile range	-1.0 to 1.2	-0.6 to 0.8	-0.4 to 0.3
Total range	-1.5 to 1.7	-0.8 to 0.9	-0.5 to 0.5
Interval method			
Mean	0.0	0.0	-0.0
95th percentile range	-1.1 to 1.2	-0.6 to 0.9	-0.4 to 0.3
Total range	-1.8 to 2.6	-0.8 to 1.1	-0.5 to 0.5
Lung volume reduction surgery ($n = 112$)			
10-mm section thickness, -900 HU threshold			
Number method			
Mean	0.5	0.2	—
95th percentile range	-2.8 to 3.4	-1.4 to 1.7	—
Total range	-4.8 to 3.7	-1.9 to 2.3	—
Interval method			
Mean	0.5	0.2	—
95th percentile range	-2.7 to 3.4	-1.3 to 1.7	—
Total range	-4.8 to 5.6	-1.9 to 2.3	—

Note—Dash [—] indicates not applicable.

TABLE 4
Mean Absolute Error in Index Percentage Points for Image sample size Targets of 5, 10, and 20

Sampling Method	Mean Absolute Error at Each Image Sample Size Target ^a			<i>p</i> ^b
	5	10	20	
National Lung Screening Trial				
1-mm section thickness				
Number	0.36 (0.27)	0.18 (0.14)	0.11 (0.09)	< 0.001
Interval	0.32 (0.29)	0.17 (0.14)	0.09 (0.07)	< 0.001
<i>p</i> ^c	0.202	0.477	0.027	
5-mm section thickness				
Number	0.41 (0.35)	0.25 (0.20)	0.13 (0.11)	< 0.001
Interval	0.44 (0.40)	0.25 (0.21)	0.13 (0.11)	< 0.001
<i>p</i> ^c	0.379	0.626	0.687	
Lung volume reduction surgery				
8- to 10-mm section thickness				
Number	1.34 (0.92)	0.62 (0.48)		< 0.001
Interval	1.24 (0.99)	0.57 (0.48)		< 0.001
<i>p</i> ^c	0.085	0.092		

Note—Values in parentheses are SD.

^aTarget (5, 10, 20) is number of images intended for sampling via either image sampling method.

^bComparison of mean absolute errors in the three image sample size targets (repeated measures analysis of variance for National Lung Screening Trial cohort, two-tailed paired Student's *t* test for lung volume reduction surgery cohort).

^cComparison of mean absolute errors between number and interval image sampling methods (two-tailed paired Student's *t* test; *p* < 0.017 considered statistically significant in comparison of three sample size targets at each section thickness).