

# Reconstruction Algorithms Influence the Follow-Up Variability in the Longitudinal CT Emphysema Index Measurements

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**Objective:** We wanted to compare the variability in the longitudinal emphysema index (EI) measurements that were computed with standard and high resolution (HR) reconstruction algorithms (RAs).

**Materials and Methods:** We performed a retrospective review of 475 patients who underwent CT for surveillance of lung nodules. From this cohort, 50 patients (28 male) were included in the study. For these patients, the baseline and follow-up scans were acquired on the same multidetector CT scanner and using the same acquisition protocol. The CT scans were reconstructed with HR and standard RAs. We determined the difference in the EI between CT1 and CT2 for the HR and standard RAs, and we compared the variance of these differences.

**Results:** The mean of the variation of the total lung volume was 0.14 L (standard deviation [SD] = 0.13 L) for the standard RA and 0.16 L (SD = 0.15 L) for the HR RA. These differences were not significant. For the standard RA, the mean variation was 0.13% (SD = 0.44%) for EI -970 and 0.4% (SD = 0.88%) for EI -950; for the HR RA, the mean variation was 1.9% (SD = 2.2%) for EI -970 and 3.6% (SD = 3.7%) for EI -950. These differences were significant.

**Conclusion:** Using an HR RA appears to increase the variability of the CT measurements of the EI.

**Index terms:** Reconstruction algorithm; Emphysema; Computed tomography (CT)

## INTRODUCTION

Emphysema is a major threat to public health. It is currently ranked 12th as a worldwide burden of disease and by 2020 it is projected to rank fifth as a cause of lost

quantity and quality of life (1, 2). Computed tomography (CT) is currently the method of choice for assessing the anatomical changes caused by emphysema. The technique is non-invasive and it has been shown to be well correlated with the histopathology (1-3).

Modern multidetector CT (MDCT) technology allows the entire lung to be scanned in a single acquisition with using high resolution (HR) parameters (< 1 mm slice thickness). The scans can be acquired during a very short time (< 10 s) and the patients can comfortably hold their breath during this time to reduce movement artifact (4). Currently, MDCT scanners are universally available and the majority of them come with standard software that includes tools that are capable of performing volumetric emphysema quantification based on the lung density (4). Although CT imaging is a widely accepted method for measuring emphysema, CT

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pulmonary densitometry is affected by numerous technical variables, including the radiation dose, the slice thickness and the reconstruction algorithms (RAs) (4).

Several studies have demonstrated that RAs, filters and kernels influence the quantification of emphysema (5–7). Nevertheless, some studies have used HR RAs to quantify the emphysema-related anatomical changes, and some of them are longitudinal RAs (8–13). Making an accurate diagnosis and the quantification and assessment of emphysema progression require knowing how technical variables such as the RA affect the measurement consistency. Two kinds of RAs are used in clinical settings: a hard or HR RA is used to increase the image resolution at the expense of an increase in noise. A soft or standard RA decreases the resolution, but there less noise. To date, no studies have evaluated the impact of using different RAs for the follow-up of emphysema quantification. Therefore, the aim of this study was to assess the influence of different RAs on the longitudinal CT emphysema index (EI) measurements with using MDCT.

## MATERIALS AND METHODS

### Patients

This observational and retrospective study was approved by the Institutional Review Board. The need for informed consent was waived. We retrospectively reviewed an initial sample of 475 patients who underwent MDCT between April 2009 and April 2010 for the follow-up of lung nodules. From the initial sample, 50 subjects met the following inclusion criteria: 1) the baseline (CT1) and follow-up (CT2) scans were acquired with the same MDCT scanner, 2) the same acquisition protocols were used at both time points, 3) less than three months passed between baseline and follow-up, 4) MDCT was performed without intravenous contrast medium injection and 5) inclusion of a 512 × 512 matrix of data. Subjects were excluded if consolidation, a ground-glass pattern, atelectasis, pleural effusion, respiratory movement artifacts or other lung abnormalities that could alter the lung density were present on the images.

### CT Acquisition Parameters

The examinations were done with a Philips Brilliance-64 scanner (Philips Medical Systems, Cleveland, OH) and using a 64 × 0.625 mm detector configuration. The parameters were set to 48 mm collimation, a table speed of 67.2 mm per tube rotation (pitch 1.4), 120 kV and 200 mAs. The CT

scanner was periodically calibrated, as recommended by the manufacturer.

The raw data was processed with an edge-enhancing algorithm to create a set of 1 mm thick axial images at 10 mm intervals (this was used only for visual analysis to assess the exclusion criteria). A second set of volumetric images of 0.75 mm continuous slices were created using a standard RA (Convolution Kernel D-Phillips Medical, Best, The Netherlands) and an HR reconstruction algorithm (Convolution Kernel B-Phillips Medical, Best, The Netherlands). All the images were analyzed and processed by a single thoracic radiologist who has more than 15 years of experience in chest CT.

### Emphysema Quantification

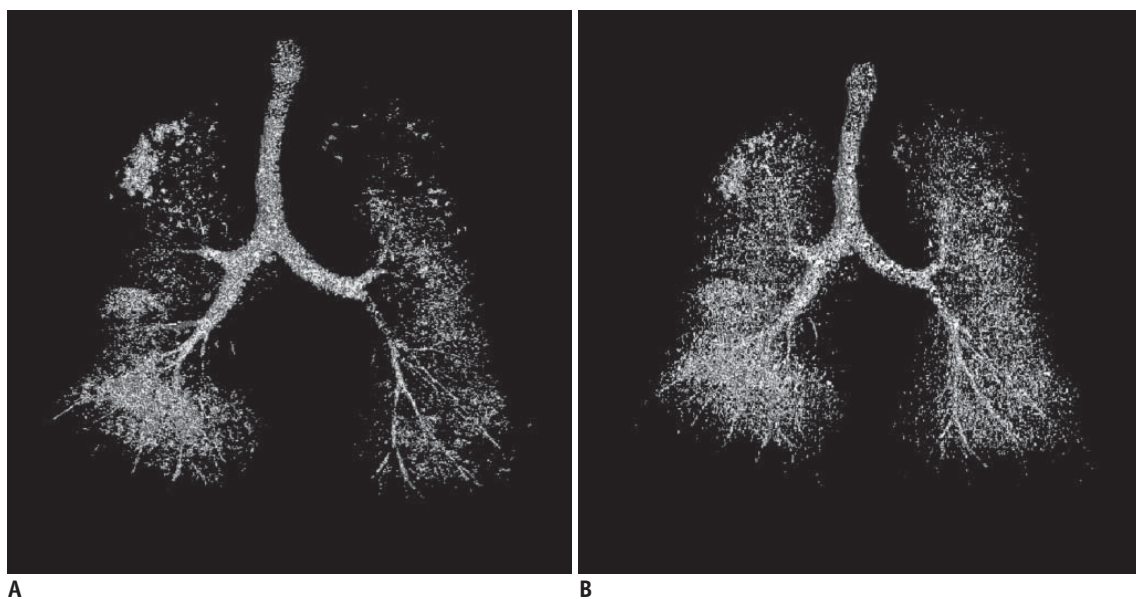
Quantification of the EI in the selected lung was obtained by CT densitovolumetry during the post-processing of the second image set using an Advantage Workstation (GE HealthCare, Milwaukee, WI). The sequence was: 1) segmentation by density band (a threshold between -1024 Hounsfield units [HUs] and -250 HUs), 2) segmentation by object selection (the keep object tool), 3) exclusion of the lung containing nodule by demarcation of the region of interest (ROI), selecting a single lung contralateral to the nodule, as the lesion could affect the results (14), 4) confirmation of the adequacy of the segmentation process by visual analysis of a three-dimensional (3D) model of the remaining data and that was created by volume rendering, 5) measurement of a selected lung volume (TLV) and the mean lung density (MLD) using the histogram tool and 6) measurement of the volume of “emphysema” by threshold band selection, with setting the upper limit at -950 HU (for EI -950) and -970 HU (for EI -970). The histogram tool also provided the percentage of “emphysema” (EI) for each threshold band (15, 16).

The distribution of the emphysematous areas within the lung was analyzed by fusing both the 3D virtual reality images created using volume rendering. The first image contained the entire selected lung with the threshold band set to show all voxels with attenuation values between -1024 HU and -250 HU. The second image showed only the areas of emphysema within that lung with the threshold band set at -1024 HU and -970 HU (for EI -970) or -1024 HU to -950 HU (for EI -950), as shown in Figure 1. This process was performed for baseline and the follow-up sessions.

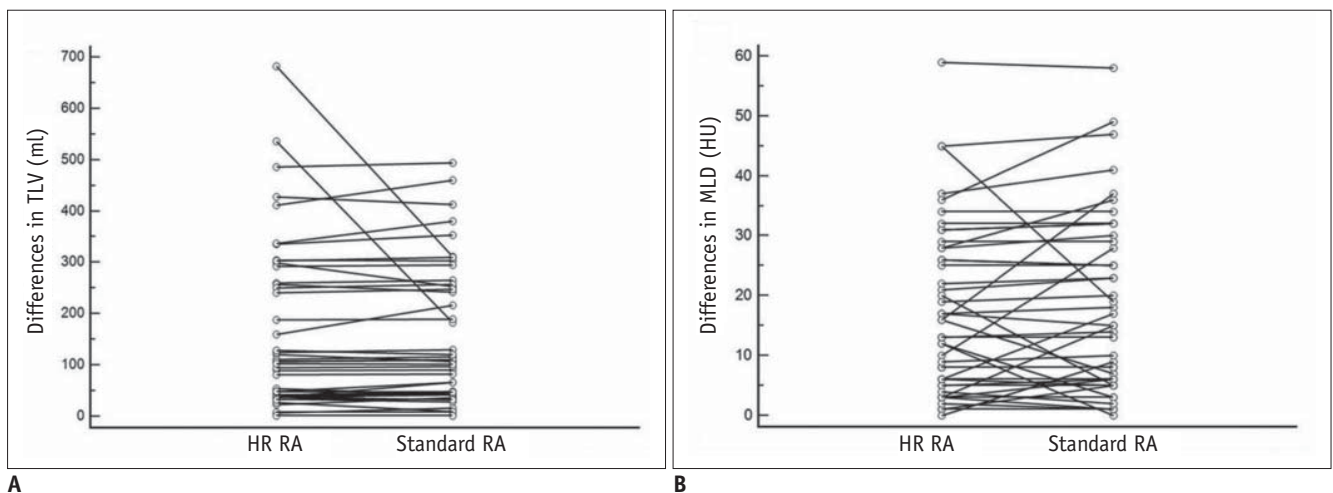
**Statistical Data Analysis**

The quantitative CT results from the CT1 and CT2 sessions were compared for significant differences. The means, standard deviations (SD), *t*-tests and correlation coefficients were calculated with Excel 5.0; (Microsoft, Redmond, WA) and Med-Calculator, version 8.1.1 (MedCalc Software, Mariakerke, Belgium). The normality of the data was tested using a Kolmogorov-Smirnov analysis and the data distributions were created using the “normal plot” tool. We calculate the differences in the EI between CT1 and CT2 for the standard

RA and the HR RA as: Difference standard EI = EI\_CT1 - EI\_CT2; Difference HR EI = EI\_CT1 - EI\_CT2. Subsequently, we calculated and compared the variances between differences in the EI for the one standard RA and the one HR RA. Statistical dispersion (also called statistical variability or variation) is the variability or the spread in a variability or the probability distribution. Common examples of measures of statistical dispersion are variance, standard deviation and the interquartile range. The variance is defined as a measure of the amount of variation within the values of



**Fig. 1. 3D CT volume with emphysema volumes in white.**  
**A.** Reconstruction image with standard algorithm. **B.** Reconstruction image with high resolution algorithm. Note difference in emphysema volumes.



**Fig. 2. Comparison of differences in CT measurements of total lung volume at CT1 and CT2 between reconstruction algorithm.**  
**A.** Comparison of differences in CT measurements of total lung volume (TLV) at CT1 and CT2 between high resolution (HR) reconstruction algorithm (RA) and standard reconstruction algorithm. **B.** Comparison of differences in CT measurements of mean lung density (MLD) at CT1 and CT2 between high resolution reconstruction algorithm and standard reconstruction algorithm.

that variable, with taking account of all possible values and their probabilities or weightings (not just the extremes, which give the range). The F-test was used to compare the variance of the standard and HR RAs. The null hypothesis was rejected if the associated *p* value was less than 0.05, indicating that the two variances are significantly different. The variance ratio was the ratio of the larger variance over the smaller variance.

**RESULTS**

The final cohort of 50 patients (28 males and 22 females) had a mean age of 70 years (standard deviation [SD] = 9.2 years). The mean time between the baseline and follow-up scans was 78 days (range: 68–90 days).

The TLV and MLD were normally distributed, but the EI -950 and EI -970 measurements were not. The baseline

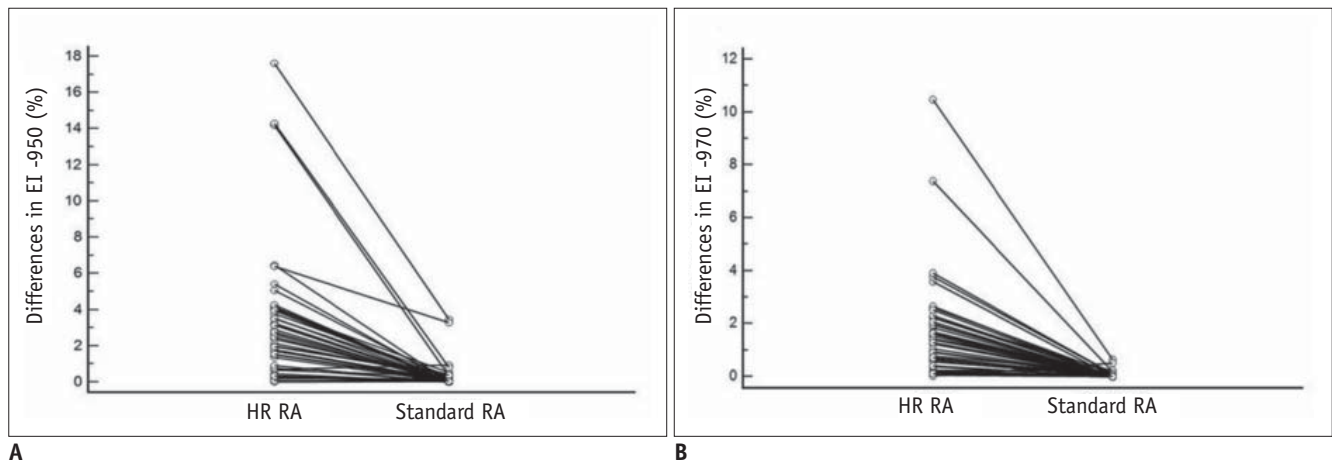
values for the TLV (standard CT1 TLV = 2578 mL ± 584 mL; HR CT1 TLV = 2546 mL ± 578 mL) were not statistically different from those at follow-up (standard CT2 TLV = 2518 mL ± 591 mL; HR CT2 TLV = 2525 mL ± 612 mL) (*p* > 0.05) (Fig. 2). The baseline MLD values (standard CT1 MLD = -795 HU ± 30; HR CT1 MLD = -839 HU ± 30) were not significantly different from those at follow-up (standard CT2 MLD = -789 HU ± 36; HR CT2 MLD = -832 HU ± 34) (*p* > 0.05) (Fig. 2).

The differences in the EI -950 for the CT1 and CT2 measured by the standard and HR RAs were significantly different (*p* < 0.001) (Fig. 3). The differences between the EI -970 at CT1 and CT2 as measured with the standard and HR RAs were also statistically different (*p* < 0.0001) (Fig. 3). The differences between the measurements are shown in Table 1.

**Table 1. Differences in Measurements between CT1 and CT2 on Images Reconstructed with Standard Algorithm**

|        | Dif TLV<br>Soft | Dif MLD<br>Soft | Dif EI -970<br>Soft | Dif EI -950<br>Soft | Dif TLV<br>Hard | Dif MLD<br>Hard | Dif EI -970<br>Hard | Dif EI -950<br>Hard |
|--------|-----------------|-----------------|---------------------|---------------------|-----------------|-----------------|---------------------|---------------------|
| Min    | 1               | 0               | 0.00%               | 0.00%               | 1               | 0               | 0.02%               | 0.01%               |
| Max    | 494             | 58              | 304%                | 3.94%               | 683             | 59              | 10.48%              | 17.62%              |
| Mean   | 148.28          | 17.86           | 0.13%               | 0.39%               | 159.22          | 17.32           | 1.93%               | 3.58%               |
| SD     | 129             | 14              | 0.44%               | 0.88%               | 155             | 13              | 2.18%               | 3.72%               |
| Median | 104.5           | 14.5            | 0.02%               | 0.05%               | 107             | 13              | 1.42%               | 2.75%               |

**Note.**— Dif EI -950 = differences in emphysema indexes, as measured with threshold of -950 HU, between CT1 and CT2, Dif EI -970 = differences in emphysema indexes, as measured with threshold of -970 HU, between CT1 and CT2, Dif MLD = differences in mean lung density between CT1 and CT2, Dif TLV = differences in total lung volumes, as measured with threshold of -950 HU, between CT1 and CT2 at standard reconstruction algorithm, SD = standard deviation



**Fig. 3. Comparison of differences in CT measurements of EI -950 at CT1 and CT2 between reconstruction algorithm.**

**A.** Comparison of differences in CT measurements of EI -950 at CT1 and CT2 between high resolution (HR) reconstruction algorithm (RA) and standard reconstruction algorithm. **B.** Comparison of differences in CT measurements of EI -970 at CT1 and CT2 between high resolution reconstruction algorithm and standard reconstruction algorithm.

**Table 2. Emphysema Index Measurements at CT1 and CT2**

|         | CT1 Std EI<br>-970 (%) | CT2 Std EI<br>-970 (%) | CT1 Std EI<br>-950 (%) | CT2 Std EI<br>-950 (%) | CT1 HR EI<br>-970 (%) | CT2 HR EI<br>-970 (%) | CT1 HR EI<br>-950 (%) | CT2 HR EI<br>-950 (%) |
|---------|------------------------|------------------------|------------------------|------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Average | 0.11                   | 0.13                   | 0.53                   | 0.71                   | 0.78                  | 0.32                  | 10.54                 | 10.19                 |
| SD      | 0.17                   | 0.22                   | 0.77                   | 1.19                   | 1.23                  | 0.72                  | 7.84                  | 6.03                  |
| Perc50  | 0.04                   | 0.03                   | 0.15                   | 0.19                   | 0.21                  | 0.04                  | 8.90                  | 9.51                  |
| Perc95  | 0.46                   | 0.56                   | 2.44                   | 2.28                   | 2.72                  | 0.93                  | 25.77                 | 21.45                 |

**Note.**— EI -950 = emphysema indexes, as measured with threshold of -950 HU, between CT1 and CT2, EI -970 = emphysema indexes, as measured with threshold of -970 HU, between CT1 and CT2, HR = high resolution reconstruction algorithm, Perc50 = 50th percentile, Perc95 = 95th percentile, SD = standard deviation, Std = standard reconstruction algorithm

### Emphysema Indexes Variances

For EI -970, the variance ratio for the means of the differences between the standard and HR RAs in CT1 and CT2 was 218.3 ( $p < 0.001$ ). For EI -950, this ratio was 27.3 ( $p < 0.001$ ) (Table 2).

### Total Lung Volumes and the Mean Lung Densities Variances

The variance ratio for the means of the differences between the standard and HR RAs for the TLV in CT1 and CT2 was 1.4 ( $p = 0.2$ ). For MLD, the variance ratio was 1.1 ( $p = 0.7$ ).

## DISCUSSION

The patient's size and lung volume, as well as the technical parameters such as the slice thickness and radiation dose, can affect the comparability of quantitative CT emphysema measurements (6, 17). In addition, when the CT scan data is reconstructed with different algorithms, the mean HU value of a region is expected to stay the same, but the distribution of the attenuation values and subsequent measures derived from this distribution might change (7). HR or edge-enhancing RAs modify the HU values of the voxels at the interface between structures with significantly different attenuation coefficients (6). For example, vessels and air, the chest wall and lungs or emphysema and the preserved lung tissue have substantially different attenuation coefficients, and detection of these interfaces may be dramatically affected by the algorithm used for reconstruction. The HR RAs (e.g., bone, sharp, B60 and FC50) were developed to facilitate the identification of margins (or edges) of structures by changing the original HUs of the interface zones and assigning new values that are similar to the ones of the adjacent structure. This image processing is very helpful for the visual analysis of

emphysema; however, analysis of emphysema by computer software does not require additional artificial processing of the original raw data. Computers can measure the attenuation value of each individual pixel from the raw data. When the HR RA is applied, the computer will measure the new artificial value at each interface zone, but the mean HU value of a region remains constant (6). Because of this alteration in the distribution of attenuation values, the measures from some voxels will change (6). This explains why the variation in the TLV and the MLD were stable and the EI changed in our sample.

Different kernels, filters or RAs can greatly influence the extent of the emphysema-related changes in lung anatomy when measured using a threshold cutoff value (5-7). All the previous studies have shown an increment of the EI using HR RAs, but none compared this influence on a longitudinal assessment of emphysema. HR RAs produce noisy images, and the density of the emphysematous lung is affected by this noise, which can be random and variable. Therefore, a follow-up image using the same reconstruction method will have a different amount or degree of noise than the initial image. This effect can occur for any interval between the CT scans. Our results suggest that longitudinal assessments of the EI can be affected when the RA is changed between the standard and HR RAs. This is the first study to report the influence of filters in the longitudinal assessment of EI. The large variance ratios can be explained by the change in the surface of lung high density structures (vessels and bronchi) that are affected by RAs. The HR RA alters densities in the interfaces of high and low density tissues. For two different CT scans of the same patient, modifying the level of inspiration can alter the distribution of high density vessels and bronchi, and this can change the influence of RAs. This change is not the same between different RAs. Based on our results, HR RAs may not provide valid results for the longitudinal assessments of EI, even under ideal conditions

in which the patient is able to hold his or her breath during the scan. Our results demonstrate that HR RAs must not be used for the computerized evaluation of emphysema.

Gevenois et al. (15) were the first group to report on the correlation of the EI with using thin-slice CT (1 mm). Using an HR RA, they reported that the best threshold correlation with the histopathology was -950 HUs. Following this methodological report, the influence of RAs on the EI was reported on by other authors (5-7). In a more recent paper, Madani et al. (16) reported the correlations between standard RA MDCT and the pathology, demonstrating that the thresholds of -950 HU and -970 HUs were most closely correlated with the histopathology. Despite this report, some studies (8-13) have used HR filters for the measurement and follow-up of emphysema. Those studies were based on the hypothesis that constant RA parameters will not influence the results (18). However, we found a variance ratio of 218 between the standard and HR RAs for the mean differences of EI -970 in the CT1 and CT2, and a variance ratio of 27 for the mean differences of EI -950 in the CT1 and CT2 ( $p < 0.01$ ). We also report significant differences between the variations in the longitudinal measurement of EIs when only the RA was changed. This data shows that RAs alter the variability between the baseline and follow-up emphysema measurements. Based on this data, longitudinal studies that used an HR RA should be interpreted with caution.

Several thresholds have been published to differentiate normal lung tissue from emphysematous lung tissue (15, 16, 19, 20). In a recent paper using MDCT and a standard RA, Madani et al. (16) reported the strongest correlation between the CT and pathology with thresholds of -950 HU and -970 HU. Despite using an MDCT scanner, Madani et al. (16) performed the evaluation with axial reconstructions of 1 mm and they did not include a volumetric analysis. Therefore, no threshold has been established for the volumetric analysis of emphysema using MDCT scanners. We chose to use thresholds of -950 HU and -970 HU because of a lack of consensus in the literature.

Low-dose protocols have been applied in numerous trials of emphysema because radiation has an intrinsic risk of inducing a neoplasm (21-23). In the early stages of emphysema, the contrast between emphysema and the normal lung parenchyma is low. In this situation the increased image noise associated with low dose CT leads to an increase in the EIs, and it may also affect the variability of measurements. This effect can be reduced,

but not excluded, with the application of a noise reduction RA (24). The standard dose was used in this study because we intended to assess the variability of EI during routine clinical scans. The retrospective analysis excluded some biases, including technician commands attention.

The influence of the inspiration level on the EI has been described (8). In a recent paper, Stoel et al. (25) reported the importance of volume corrections in the emphysema measurements; however they used this correction only for variations over 200 mL. We did not perform this adjustment because our focus was on the variation induced by the RA. Because both RAs were applied to the same volumes, this did not affect the results. In addition, more than 75% of the patients in our sample had TLV variations below 200 mL.

Our paper has some limitations. First, we compared two convolution kernels of a specific scanner, and these kernels may not be usable in other scanners from different manufacturers. However, the magnitude of the differences found in the data suggests that all post-processing tools influence the evaluation of emphysema. Our timeline for the assessment of variability was only three months. However even though the variability may be low, it exists and it is probably because of technique (25). The section thickness influences the image noise (26), so this noise may have been increased by our section thickness of 0.75 mm. However, variation of the section thickness does not substantially influence the strength of the correlations between the histopathologic indexes and the relative areas of emphysema, so this influence in our results should be low. In our cohort, we studied patients with a low EI, but when comparing these findings with other cohorts of heavy smokers, the EIs were similar (25). We also did not describe the clinical characteristics or lung function tests, but this would not have any influence on our evaluation.

In conclusion, a significant increase in variability of the longitudinal CT EI measurements was observed when using an HR RA compared to using a standard RA. The variance ratio for the standard and HR RAs was 218 for mean differences of for the EI -970 and 27 for the EI -950 on the CT1 and CT2. Longitudinal analysis of the progression of emphysema must consider these variations when using an HR RA. As demonstrated here, HR RAs should not be used for automatic assessment of the EI.

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