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COMPUTED TOMOGRAPHY

# Impact of iterative reconstructions on objective and subjective emphysema assessment with computed tomography: a prospective study

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**Abstract**
*Objectives* To prospectively evaluate the impact of iterative reconstruction (IR) algorithms on pulmonary emphysema assessment as compared to filtered back projection (FBP).
*Methods* One hundred ten unenhanced chest CT examinations were obtained on two different scanners. Image reconstructions from a single acquisition were done with different levels of IR and compared with FBP on the basis of the emphysema index (EI), lung volume and voxel densities. Objective emphysema assessment was performed with 3D software provided by each manufacturer. Subjective assessment of emphysema was performed as a blinded evaluation. Quantitative and subjective values were compared using repeated ANOVA analysis, Bland-Altman analysis and Kendall's coefficient of concordance (W).
*Results* Lung volumes are stable on both units, throughout all IR levels ($P \geq 0.057$). EI significantly decreases on both units with the use of any level of IR ($P < 0.001$). The highest levels of IR are responsible for a decrease of 33-36 % of EI. Significant differences in minimal lung density are found between the different algorithms ($P < 0.003$). Intra- and inter-reader concordance for emphysema characterisation is generally good ($W \geq 0.77$ and $W \geq 0.86$, respectively).
*Conclusions* Both commercially available IR algorithms used in this study significantly changed EI but did not alter visual assessment compared to standard FBP reconstruction at identical radiation exposure.
*Key points*
• *Objective quantification of pulmonary emphysema is sensitive to iterative reconstructions*
• *Subjective evaluation of pulmonary emphysema is not influenced by iterative reconstructions*
• *Consistency in reconstruction algorithms is of paramount importance for pulmonary emphysema monitoring*

**Keywords** Pulmonary emphysema · Multidetector computed tomography · Iterative reconstruction · Quantitative analysis · Visual assessment

**Abbreviations and acronyms**

| | |
|---|---|
| ASiR | Adaptive statistical image reconstruction |
| EI | Emphysema index |
| FBP | Filtered back projection |
| IR | Iterative reconstruction |
| LAV% | Low attenuation value percentage |
| SAFIRE | Sinogram affirmed iterative reconstruction |
| MBIR | Model-based iterative reconstruction |

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## Introduction

The purpose of this prospective study was to evaluate the impact of different IR algorithms on objective and subjective emphysema assessment as compared to FBP and to improve

**Table 1** Discovery CT750 HD means, standard errors of the mean and *P* values

| | Lung volume | | Emphysema index | | Mean lung density | | Minimal lung density | |
|---|---|---|---|---|---|---|---|---|
| | Litres | *P* value | % | *P* value | HU | *P* value | HU | *P* value |
| FBP | 2.474 ± 0.073 | | 3.570 ± 0.53 | | -883.3 ± 3.93 | | -947.8 ± 3.27 | |
| ASiR-20 | 2.476 ± 0.074 | >0.99 | 3.287 ± 0.52 | 0.02 | -883.2 ± 3.92 | >0.99 | -943.5 ± 3.29 | <0.0001 |
| ASiR-40 | 2.476 ± 0.074 | >0.99 | 3.047 ± 0.50 | <0.0001 | -883.1 ± 3.91 | >0.99 | -938.8 ± 3.30 | <0.0001 |
| ASiR-60 | 2.477 ± 0.074 | >0.99 | 2.854 ± 0.50 | <0.0001 | -883.0 ± 3.91 | >0.99 | -934.2 ± 3.33 | <0.0001 |
| ASiR-80 | 2.477 ± 0.073 | >0.99 | 2.683 ± 0.49 | <0.0001 | -883.4 ± 3.84 | >0.99 | -930.2 ± 3.33 | <0.0001 |
| ASiR-100 | 2.476 ± 0.074 | >0.99 | 2.640 ± 0.48 | <0.0001 | -883.9 ± 3.84 | >0.99 | -925.3 ± 3.37 | <0.0001 |
| MBIR | 2.479 ± 0.073 | 0.68 | 2.387 ± 0.48 | <0.0001 | -882.6 ± 3.90 | 0.23 | -925.9 ± 3.60 | <0.0001 |

Summary of lung volume, emphysema index, mean and minimal densities found with different levels of IR on the Discovery CT750 HD unit. Lung volumes were stable, whereas the emphysema index decreased with the use of IR. Mean lung density was not modified by IR, whereas minimal lung density was

*HU* hounsfield units, *FBP* filtered back projection, *ASiR* adaptive statistical iterative reconstruction, *MBIR* model-based iterative reconstruction

our understanding of the differences found in the emphysema index based on voxel densities.

Emphysema assessment is performed by computed tomography (CT) in order to determine the percentage of low-attenuation volume (LAV%), representing the proportion of voxels under a density threshold of -950 Hounsfield units (HU) in the lung parenchyma [1, 2]. LAV% has been shown to be predictive of chronic obstructive pulmonary disease (COPD) and to correlate well with pathological findings and pulmonary function [3, 4]. Nevertheless quantitative measurement has gained clinical relevance as a predictor of mortality [5] and for therapeutic management of patients with alpha1-antitrypsin deficiency [6, 7].

Emphysema quantification with CT is now commonly performed using an attenuation of -950 HU as the threshold. Gevenois et al. validated this method by using filtered back projection (FBP) as the classical algorithm for image reconstruction [1, 2]. The introduction of iterative reconstruction (IR) algorithms has allowed significantly reducing the radiation dose while maintaining subjective and objective image quality [8]. Some studies seem to indicate that the use of IR can even improve the quantitative consistency between low-dose and standard-dose CT for emphysema assessment [9] whereas other studies suggest that IR renders quantitative imaging less consistent [10]. However, neither the pattern nor the underlying causes of such alterations have been completely determined [11].

## Materials and methods

The local Ethics Committee on research involving humans approved this prospective study (CCER15-048). Oral and written information was given and signed declarations of consent were obtained from all patients prior to examination.

### Patients

Enrolment started on 8 June and finished on 12 August 2015. All consecutive patients undergoing an unenhanced thoracic CT for pulmonary diseases on a Discovery CT750 HD unit (GE Healthcare, Waukesha, WI) or on a SOMATOM Definition Flash unit (Siemens Healthcare, Forchheim, Germany) in our department were included. Seven patients

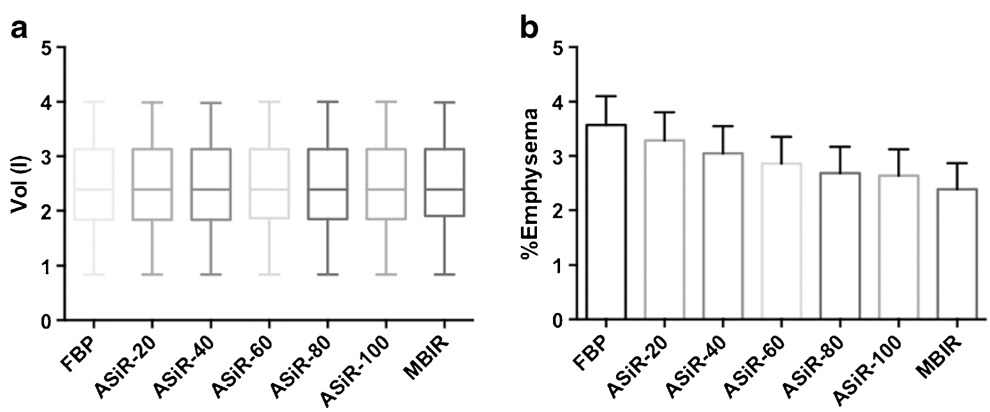


**Fig. 1** *Box-and-whisker plot* summarising lung volumes (**A**) and emphysema index (**B**) with different levels of IR on the Discovery CT750 HD unit. Lung volumes were stable, whereas the emphysema index decreased with the use of IR

**Table 2** SOMATOM Definition Flash means, standard errors of the mean and *P* values

| | Lung volume | | Emphysema index | | Mean lung density | | Minimal lung density | |
|---|---|---|---|---|---|---|---|---|
| | Litres | *P* value | % | *P* value | HU | *P* value | HU | *P* value |
| FBP | 2.354 ± 0.072 | | 3.13 ± 0.59 | | -883.3 ± 3.93 | | -939.2 ± 3.53 | |
| SAFIRE-1 | 2.355 ± 0.071 | 0.3941 | 2.77 ± 0.58 | 0.0013 | -883.2 ± 3.92 | >0.99 | -934.2 ± 3.46 | 0.0027 |
| SAFIRE-2 | 2.355 ± 0.072 | 0.3417 | 2.48 ± 0.58 | <0.0001 | -883.1 ± 3.91 | >0.99 | -928.4 ± 3.47 | <0.0001 |
| SAFIRE-3 | 2.355 ± 0.072 | 0.2912 | 2.25 ± 0.58 | <0.0001 | -883.0 ± 3.91 | >0.99 | -922.7 ± 3.35 | <0.0001 |
| SAFIRE-4 | 2.357 ± 0.072 | 0.0572 | 2.10 ± 0.58 | <0.0001 | -883.4 ± 3.84 | >0.99 | -917.4 ± 3.58 | <0.0001 |
| SAFIRE-5 | 2.356 ± 0.072 | 0.2224 | 2.00 ± 0.58 | <0.0001 | -883.9 ± 3.84 | >0.99 | -912.0 ± 3.65 | <0.0001 |

Summary of lung volume, emphysema index, mean and minimal densities found with different levels of IR on the SOMATOM Flash Definition unit. Lung volumes were stable, whereas the emphysema index decreased with the use of IR. Mean lung density was not modified by IR, whereas minimal lung density was

*HU* hounsfield units, *FBP* filtered back projection, *SAFIRE* sinogram affirmed iterative reconstruction

refused to participate in the study ($n = 3$ for GE, $n = 4$ for Siemens). The total study sample consisted of 110 CT examinations, 55 on the Discovery CT750 HD unit [male/female 27/28, mean age 63 (range 25-92)] and 55 on the SOMATOM Definition Flash unit [male/female 34/21, mean age 60 (range 18-89)]. In seven examinations ($n = 2$ on the Discovery CT750 HD; $n = 5$ on the SOMATOM Definition Flash) the image quality did not allow automatic segmentation of the lungs. These examinations were excluded from the 3D quantitative analysis database.

The score of the subtypes of emphysema was defined according to the recommendations of the Fleischner Society based on the FBP reconstructions.

## Technical acquisition and reconstruction parameters and radiation dose

Patients underwent a single acquisition that was performed craniocaudally during full inspiration from the lung apex to the base of the lungs. The acquired raw data set of the single acquisition of each patient was then reconstructed multiple times with FBP and multiple levels of IR algorithms from our CT units from two different vendors.

The following acquisition parameters were used on the Discovery CT750 HD unit: collimation 40 × 0.6 mm, pitch 1.375, rotation time 0.6 s, tube voltage 100 kV, tube current 80-500 mAs, 28 noise index and slice thickness interval 0.625-0.625 mm. The raw data were reconstructed with a classical FBP algorithm and with five levels of iterative reconstruction (20 %, 40 %, 60 %, 80 % and 100 %) using Adaptive Statistical Image Reconstruction (ASiR20-100) and a supplementary type of IR using model based iterative reconstruction (MBIR), all with a soft kernel.

The following parameters were used on the SOMATOM Definition Flash unit: collimation 64 × 2 × 0.6 mm, pitch 0.6, rotation time 0.28 s, tube voltage 100 kV (CARE kV), tube current 120 mAs ref. (CARE Dose4D) and slice thickness-interval 1–0.7 mm. The raw data were reconstructed with a classical FBP algorithm and with five levels of IR using sinogram affirmed iterative reconstruction (SAFIRE 1-5).

Dose-length product (DLP) and computed tomography dose index (CTDI) were provided by the manufacturers on the basis of well-calibrated CT with a 32-cm phantom. Size-specific dose estimates (SSDE) were obtained via Bayer's Radimetrics™ Enterprise Platform (Bayer Healthcare, Germany).

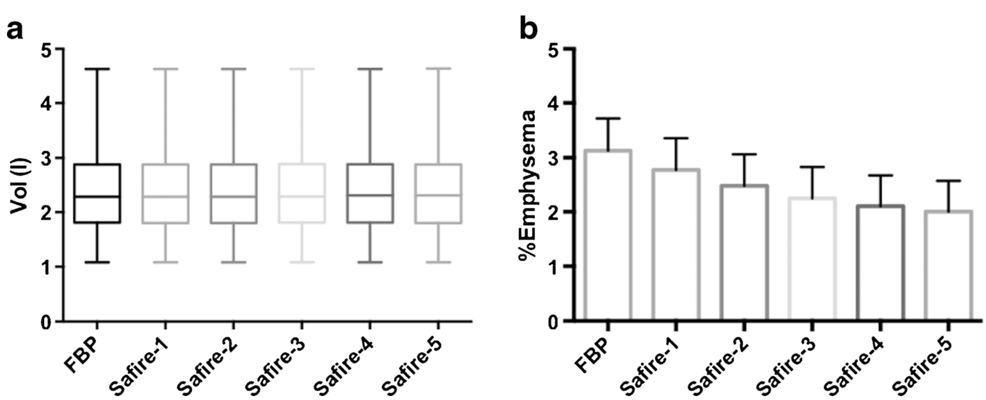


**Fig. 2** *Box-and-whisker plot* summarising lung volumes (**A**) and emphysema index (**B**) with different levels of IR on the SOMATOM Definition Flash unit. Lung volumes were stable, whereas the emphysema index decreased with the use of IR

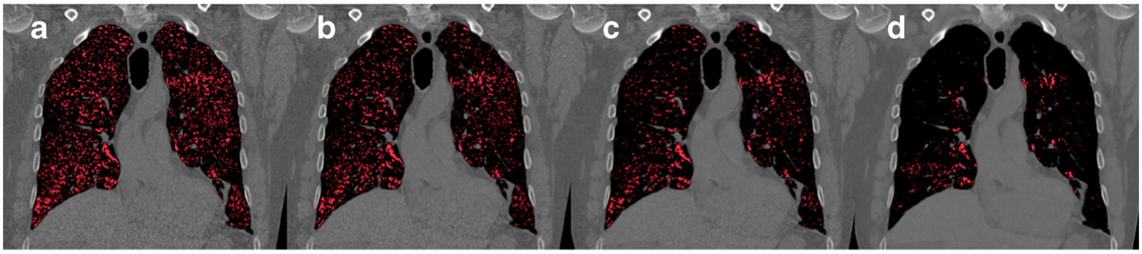


**Fig. 3** Coronal reformatted images of unenhanced chest CT with red-coloured overlays representing emphysematous lesions from FBP (**A**), ASiR-40 (**B**), ASiR-80 (**C**) and MBIR (**D**). A clear reduction of the emphysema index is illustrated

## Image analysis

Quantitative analysis was performed with 3D reading and visualisation software providing an application for automatic pulmonary segmentation of the lungs and emphysema quantification. The low-attenuation density threshold was of -950 HU. In order to be constructor consistent, emphysema assessment was performed with Thoracic VCAR (Advantage Window, GE Healthcare) for the images obtained on the GE Discovery CT750 HD unit and with Pulmo3D (syngo.via VA30, Siemens) for the images obtained on the Siemens SOMATOM Definition Flash scanner. The two applications allowed quantification of lung volume in litres and emphysema index (EI) in percentage. Based on the EI, centrilobular emphysema was subdivided into: (1) trace emphysema (EI < 0.5 %); (2) mild emphysema (0.5–5.0 %); (3) moderate emphysema (EI > 5.0 %) as suggested by the Fleischner Society [12].

Measurements of voxel density (minimal and mean density) in HU were collected by drawing standardised regions of interest (ROI) (~1 $cm^2$) at the level of the carina, one inside the trachea, one in the anterior extracorporeal air and one in the subpleural region of each lung. ROIs were carefully placed to avoid artefacts and clothes around the patients.

Voxel densities were analysed on all slices containing lung parenchyma for all levels of IR. The final result was a three-dimensional histogram containing all the voxel densities.

Subjective analysis was performed as a blinded randomised visual assessment of all the reconstructed data sets by two board-certified radiologists with 7 and 6 years of experience in chest radiology (S.P.M and J.G., respectively), over a period of 2 months, after a consensus reading of ten cases (not included in this study). All images were evaluated on a standard pulmonary windows setting (window width = 1400, window level = -500). Emphysema presence was first assessed on a 5-point Likert scale (1: emphysema certainly not present; 5: emphysema certainly present). When emphysema was present, the readers had to classify the predominant pattern as centrilobular (CLE), panlobular (PLE) or paraseptal (PSE).

Re-sizing, level windowing, multi-planar and minimal intensity projection (MinIP) reformatting were allowed.

## Statistical analysis

Lung volume in litres, emphysema index in percentage and density in HU were compared using a repeated ANOVA analysis with a $P$ value < 0.05 considered statistically significant.

The mean differences and the limits of agreement of EI were studied with a Bland-Altman analysis.

The results of the subjective analysis were compared using Kendall's coefficient of concordance to determine the intra- and the inter-observer correlation upon diagnosis of presence of emphysema and to determine the preponderant type of emphysema among our study population depending on the level of IR.

The necessary sample size was calculated for LAV% as the primary outcome. If the hypothesis was truly no difference between FBP and IR emphysema quantification, 55 patients had to be included in order to be 80 % sure that the limits of a

**Table 3** Bias and 95 % confidence interval of the emphysema index related to FBP according to Bland-Altman analysis

| Discovery CT750 HD | ASiR-20 | ASiR-40 | ASiR-60 | ASiR-80 | ASiR-100 | MBIR |
|---|---|---|---|---|---|---|
| BIAS | 0.28 | 0.52 | 0.72 | 0.89 | 0.93 | 1.18 |
| 95 % CI | -0.45–1.02 | -0.88–1.93 | -1.24–2.67 | -1.81–3.59 | -1.86–3.72 | -2.55–4.92 |
| SOMATOM Definition Flash | | SAFIRE-1 | SAFIRE-2 | SAFIRE-3 | SAFIRE-4 | SAFIRE-5 |
| BIAS | | 0.36 | 0.65 | 0.88 | 1.03 | 1.13 |
| 95 % CI | | -0.42–1.13 | -0.81–2.10 | -1.13–2.89 | -1.43–3.48 | -1.61–3.86 |

The Bland-Altman analysis showed an increase of the bias (ranging from 0.28 to 1.18) and a widening of the 95 % confidence interval (ranging from 1.47 to 7.47) with any levels of IR compared to FBP

*FBP* filtered back projection, *ASiR* adaptative statistical iterative reconstruction, *MBIR* model-based iterative reconstruction, *SAFIRE* sinogram affirmed iterative reconstruction, *CI* confidence interval

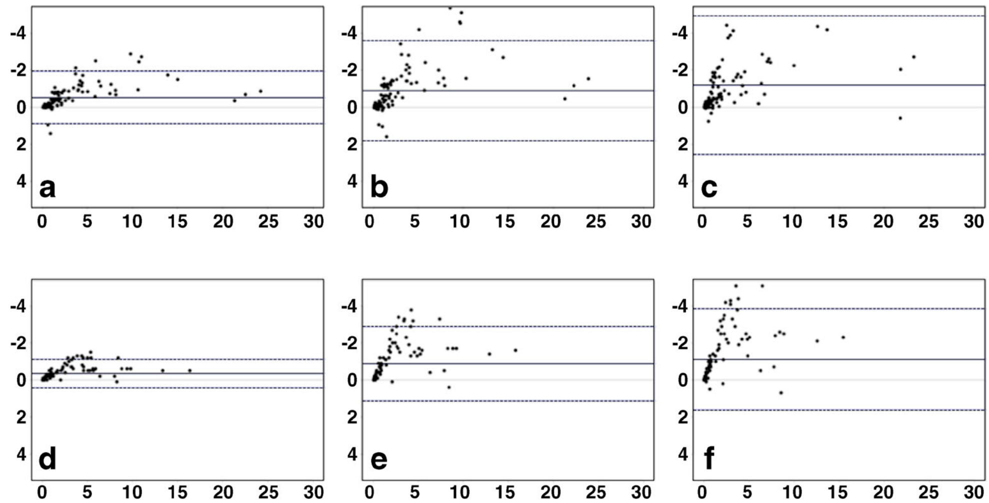


**Fig. 4** Bland-Altman plots of the emphysema index between iterative reconstructions and FBP. X-axis: mean of FBP and IR; Y-axis: difference between FBP and IR. *Outer lines* correspond to the 95 % confidence interval (CI); *inner line* corresponds to the bias. (**A**) FBP~ASiR-40; (**B**) FBP~ASiR-80; (**C**) FBP~MBIR; (**D**) FBP~SAFIRE-1; (**E**) FBP~SAFIRE-3; (**F**) FBP~SAFIRE-5

two-sided 90 % confidence interval will exclude a difference of 5 % in LAV%.

All results are given as means and standard errors of the mean.

## Results

### Radiation dose

The dose delivered by the Discovery CT750 HD unit was: DLP 256 ± 20 mGy.cm; CTDI 6.35 ± 0.46 mGy; SSDE = 8.59 ± 0.58 mGy.

The dose delivered by the SOMATOM Definition Flash unit was: DLP 226 ± 19 mGy.cm; CTDI was 6.05 ± 0.5 mGy; SSDE was 8.23 ± 0.51 mGy.

### Quantitative and objective analysis

Lung volume, emphysema index, mean and minimal densities obtained from FBP and different levels of IR are summarised in Table 1 and in Fig. 1 for the Discovery CT750 HD unit and in Table 2 and in Fig. 2 for the SOMATOM Flash Definition.

Proper automatic segmentation of the lungs was confirmed as lung volume revealed no statistical differences between any reconstructions ($P$ ranging from 0.057 to > 0.99).

Even the lowest level of IR showed statistically significant differences in the emphysema index (all $P \leq 0.02$) (Tables 1, 2, Figs. 1, 2 and 3). The Bland-Altman analysis showed an increase of the bias (ranging from 0.28 to 1.18) and a widening of the 95 % confidence interval (ranging from 1.47 to 7.47) with any levels of IR compared to FBP (Table 3, Fig. 4).

Objective analysis of lung densities showed no statistical differences in mean density between FBP and all IR algorithms (all $P \geq 0.23$), whereas minimal densities showed significant differences (all $P \leq 0.003$).

Overall, 33 patients had trace emphysema (Discovery CT750 HD $n = 14$; SOMATOM Definition Flash $n = 19$), 51 had mild emphysema (Discovery CT750 HD $n = 29$; SOMATOM Definition Flash $n = 22$) and 19 had more than 5 % EI (Discovery CT750 HD $n = 10$; SOMATOM Definition Flash $n = 9$).

### Repartition of voxel densities

The histogram of voxels in the lung parenchyma showed a decrease of the number of voxels below -950 HU (Fig. 5) when comparing IR with FBP.

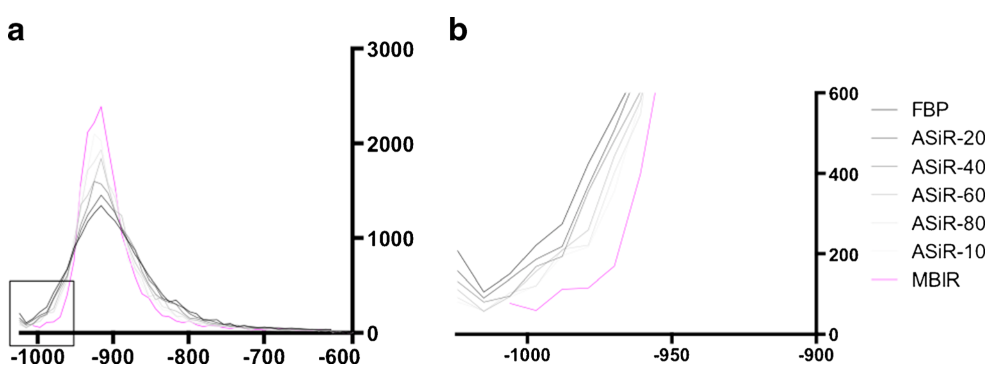


**Fig. 5** Histograms of low-density pixels from one patient of the study population are shown in (**A**) and (**B**). (**B**) corresponds to a zoom of the *black square* in (**A**). Histograms show a reduction of pixels bellows -950 HU

**Table 4** Emphysema index by emphysema subtypes

| | None | CLE | PSE | PLE |
|---|---|---|---|---|
| Reader 1 | | | | |
| Discovery CT750 HD unit | 0.35 ± 0.07 | 4.92 ± 1.00 | 1.77 ± 0.80 | NA |
| SOMATOM Definition Flash unit | 0.40 ± 0.12 | 6.76 ± 1.73 | 1.97 ± 1.57 | 37.1 |
| Reader 2 | | | | |
| Discovery CT750 HD unit | 0.28 ± 0.05 | 5.45 ± 1.15 | 1.73 ± 0.50 | NA |
| SOMATOM Definition Flash unit | 0.21 ± 0.07 | 5.74 ± 1.43 | 2.30 ± 1.33 | 37.1 |

Emphysema index corresponding to emphysema classification by each reader. Please note that both readers were unable to detect emphysema below 0.5 %

CLE: centrilobular emphysema; PSE: paraseptal emphysema; PLE: panlobular emphysema; NA: not available

### Subjective analysis

Intra-observer (between different levels of IR) and inter-observer agreements were good according to Kendall's coefficient of concordance (W ≥ 0.77 and ≥ 0.86, respectively). The type of emphysema detected by each reader is given in Table 4. Both readers were unable to detect an emphysema index below 0.5 % (i.e. trace emphysema).

## Discussion

Dose reduction is a major concern in healthcare management. IR is a promising technology to lower the radiation dose of CT while maintaining image quality [13] and diagnostic accuracy [14].

Quantitative imaging is another trend gaining many clinical applications, among them, emphysema monitoring [7]. Previous studies confirmed the impact of IR on emphysema quantification with various outcomes. Nishio et al. suggested an improved consistency between low-dose and standard-dose CT with the use of adaptive iterative dose reduction using 3D processing (AIDR 3D) from Toshiba Medical Systems (Otawara, Japan) [9]. Mets et al. showed significant alterations in quantitative CT measures with the use of iDose$^4$ level 6 from Philips Healthcare (Best, The Netherlands) [10]. Yung Choo et al. demonstrated a decrease in the emphysema index with the use of ASiR and MBIR from GE Healthcare (Waukesha, WI) [11]. Our multi-level IR and multi-vendor approach illustrates the impact of the different IR algorithms on the quantitative analysis of CT images in pulmonary emphysema. The lowest levels of IR (ASiR-20 and SAFIRE-1) showed a significant alteration in LAV% (Tables 1 and 2, Figs. 1, 2 and 3). The increase of the bias and the widening of the confidence interval of EI with IR related to FBP mean that emphysema quantification was less accurate (Table 3, Fig. 4). Since the technical details of the IR algorithms are mathematically complex and only partly revealed by the vendors it is difficult to define the exact reasons for the alterations observed with each algorithm [13]. There is however little doubt that the change in the distribution of the voxel densities is an important underlying factor. The histograms of the lung parenchyma ROI (Fig. 5, Tables 1, 2) show identical values for the peak of the curve, and the mean lung density values do not differ ($P > 0.99$). These observations confirm previous studies that have indicated that FBP and IR provide similar image quality based on mean attenuation values for calculating the signal-to-noise ratio [15, 16]. The histograms also clearly demonstrate the decrease of the area under the curve for extreme values, reflecting the decline in the number of voxels under the -950 HU threshold and corresponding to the decrease in the emphysema index, illustrated by the red-coloured overlay as a relative area under -950 HU (Fig. 3) [4]. This observation also correlates with the significant difference of minimal lung density values (Tables 1, 2).

The human eye is able to detect emphysema lesions, but not to quantify their attenuation. This may explain why the presence or absence of IR had no influence on subjective emphysema analysis as demonstrated by a good intra-observer correlation. It is not surprising therefore that both readers were unable to visually detect areas of the low emphysema index (<0.5 %) accurately scored on the FBP reconstructions. Only automatic quantifications were able to detect such lesions, correlating well with the new classification of emphysema, where trace emphysema is defined as LAV% <0.5 % [12].

Our study has some limitations. First, our study population had mostly mild emphysema. The impact of IR on confluent or advanced destructive emphysema could somehow be different and would need further studies. Second, the equipment of the two different vendors used different software for quantitative analysis, which renders comparative interpretation of the numerical values difficult.

In conclusion, even the lowest levels of iterative reconstructions have a significant impact on quantitative imaging with a low-density threshold but do not alter visual assessment compared to standard FBP reconstruction at identical radiation exposure.

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