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ORIGINAL ARTICLE

Airway quantification using adaptive statistical iterative reconstruction-V on wide-detector low-dose CT: a validation study on lung specimen

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Abstract

Purpose To evaluate the accuracy of airway quantification of adaptive statistical iterative reconstruction (ASIR)-V on low-dose CT using a human lung specimen.

Method A lung specimen was scanned on Revolution CT with low-dose settings (20 mAs, 40 mAs and 60 mAs/100 kV) and standard-dose setting (100 mAs/120 kV). CT images were reconstructed using lung kernel with eleven ASIR-V levels from 0 to 100% with 10% interval. ASIR-V level from 0 to 100% with 10% interval was reconstructed on lung kernel. Wall area percentage (%WA) and wall thickness (WT) were measured.

Results Radiation dose of 20 mAs, 40 mAs and 60 mAs low-dose settings reduced by 87.6%, 75.2% and 62.8% compared to that on standard dose, respectively. Low-dose settings significantly decreased image SNR ($p < 0.05$) and increased noise ($p < 0.001$). ASIR-V level exponentially improved image SNR and linearly decreased image noise (all $p < 0.001$). The mean airway measurement ratios of low-dose to standard-dose were within 2% variation for %WA and within 3% variation for WT. Most %WA and WT values showed no obvious correlation with ASIR-V levels.

Conclusion ASIR-V showed to improve image quality in low radiation dose. However, low-dose settings and ASIR-V strength did not significantly influence airway quantification values, although variation in measurements slightly increased with dose reduction.

Keywords Low dose · Iterative reconstruction · Airway quantification · Phantom · Tomography · x-ray computed

Abbreviations

COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
ASIR	Adaptive statistical iterative reconstruction
ASIR-V	Adaptive statistical iterative reconstruction veo
FBP	Filtered back projection
CTDIvol	volume CT dose index
WT	Wall thickness
%WA	Wall area percentage
SNR	Signal-to-noise ratio
ROI	Region of interest
FEF	Forced expiratory flow
FEV1	Forced expiratory volume in first second
FEV1/FVC	Forced expiratory volume in first second/ forced vital capacity

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Introduction

Airflow limitation defining chronic obstructive pulmonary disease (COPD) is the result of a prolonged time constant for lung emptying, caused by increased resistance of small conducting airways and emphysematous destruction [1]. Accurate quantification of small airways, the sites of airway inflammation and airflow limitation, contributes to separate subtypes and explains physiological changes [2–4]. Visual assessment for airway wall thickening was subjective and only showed fair agreement with quantitative CT [5]. Quantitative CT airway quantification have been validated as an effective approach to evaluate disease severity [6–9]. However, quantitative CT metrics can only be assured if precise and accurate measurements are available [6].

Radiation exposure is challenging for the booming clinical utilization of CT [10]. Although high radiation dose commonly brings images of good quality, the as-low-as-reasonably achievable (ALARA) principle is the direction of CT equipment. Physical and algorithmic approaches have been used to reduce radiation dose, such as fixed tube current technique and automatic tube current modulation [11], peak kilo voltage reduction [12], 3D adaptive raw-data filter [13], and iterative reconstruction techniques [14–18]. The widely used adaptive statistical iterative reconstruction (ASIR) provides clinically acceptable image quality with an estimated dose reduction from 23 to 66% [19]. However, using high strength ASIR reconstruction might be associated with a pixilation texture or a blotchy appearance of images that appearing coarser grained than texture of FBP reconstructed images, which may be undesirable for radiologists and affect lesion observation [17, 20]. ASIR-V is a new generation iterative reconstruction algorithm that contains more advanced noise modeling and object modeling than the previous version ASIR [21–23]. ASIR-V focuses primarily on modeling the system noise statistics, objects, and physics, which are the main contributors to the reduction of noise, improvement of low-contrast detectability, and reduction of artifacts in the reconstructed images [24]. It potentially provides better image quality than the precursor ASIR [22]. These suggest that ASIR-V might be used to quantify small bronchial structure on low-dose CT in clinical setting. But a validation study is necessary to implement ASIR-V on low-dose CT in clinical patients such as COPD.

Although low-dose CT has been used for airway evaluation of patients and standard phantom [25, 26], lung specimen study on airway wall quantification was seldom reported. The accuracy of quantification for the effect of radiation dose and ASIR-V strength level has seldom been discussed. The purpose of this study is to investigate the accuracy of airway quantifications using ASIR-V on low-dose CT using a human lung specimen, compared to the quantification using standard-dose CT.

Materials and methods

A human left lung specimen was used for research (Fig. 1). The specimen was from a non-smoker male donor, which had no pulmonary parenchymal disease or interstitial disease and was fixed by formalin but not inflated by air. The specimen was provided by the anatomy department of medical school for research. The lung parenchyma of the specimen was generally collapsed, and the interstitial structure of the bronchial tree was slightly smaller in comparison with air-containing lung tissue. But the small branch lumen structure of sub-segmental bronchus was still present with air in the lumen. Therefore, the CT image of bronchial tree can be reconstructed to study airway wall.

Non-contrast helical thoracic CT was performed using wide-detector 256-slice CT (Revolution, GE healthcare, Milwaukee, USA). The specimen was placed to the left of the center line and scanned in cranio-caudal direction. For low-dose settings, tube voltage was set to 100 kV, and tube current–time product products were 20 mAs, 40 mAs, and 60 mAs. For standard-dose scan, which was considered as reference standard, 120 kV and 100 mAs were selected, which was commonly used and validated in clinical practice according to the previous literatures [2, 3, 6, 8, 14, 27]. Other parameters were constant for low- and standard-dose scans: 256×0.625 mm detector collimation, 0.5s rotation time, 0.625 mm slice thickness and 18 cm field of view (to cover the specimen). The acquisition coverage in z-axis held constant because it may affect the volume CT dose index ($CTDI_{vol}$) values used for calculating effective radiation dose. The scanning protocol containing a standard-dose setting and three low-doses settings was repeated five times, with in between each scanning protocol, a small translocation and rotation of the specimen was made to simulate variability caused by participant movement.

Images of the standard-dose scan and low-dose settings were reconstructed using eleven ASIR-V strength levels from 0 to 100% with 10% interval (hereafter, ASIR-$V_{0–100}$). Images of CT scans were reconstructed using lung kernel (edge enhancement) for airway measurement [9, 28, 29], to facilitate precise segmentation and measurement by software.

A radiologist with fourteen years of experience checked if there is a pixelated appearance for each image after ASIR-V reconstruction and performed bronchial wall quantification using a semi-automated tool (Thoracic VCAR, Advanced workstation 4.6, GE Healthcare),

Fig. 1 Photo of the left lung specimen. **a** The lateral side, **b** the internal side

following the analyzing order from standard-dose to low-dose scans, the data processing time interval of each scan was 15 days in between to avoid reader bias. This software tool followed two steps. First, the software automatically segments the bronchial tree, and showed center line after choosing two points (the left main, and the tail end of the posterior basal segmental bronchus of left lower lobe). If the distal bronchus tree was not fully tracked, manual adding of the bronchial tree was needed to ensure that the lumen of each branch on the path was completely selected. Second, after a mouse-click on a bronchus, the tool automatically outlined the contours of each selected bronchus in the cross section of the selected bronchus perpendicular to the central line of corresponding bronchus, and quantifies airway dimensions. This step was automatically measured by software without manual modification. Seven bronchial generations from the left main to segmental and sub-segmental bronchus (distal lumen average diameter 2.0 ± 0.5 mm) were chosen and named as B1–7 bronchus, with reference to a previous study [30]. The measuring points were placed at the proximal 1/3 section of each B1–7 bronchus, keeping each measured point consistent among different scans by measuring the distances between the measured point and the bifurcation of the bronchus. (Fig. 2). Airway wall thickness (WT) and wall area percentage (%WA) were measured. %WA was defined as: (wall area) / (wall area + lumen area) × 100%. Because it is difficult to determine the physical bronchial wall thickness in the specimen as a standard reference while keeping

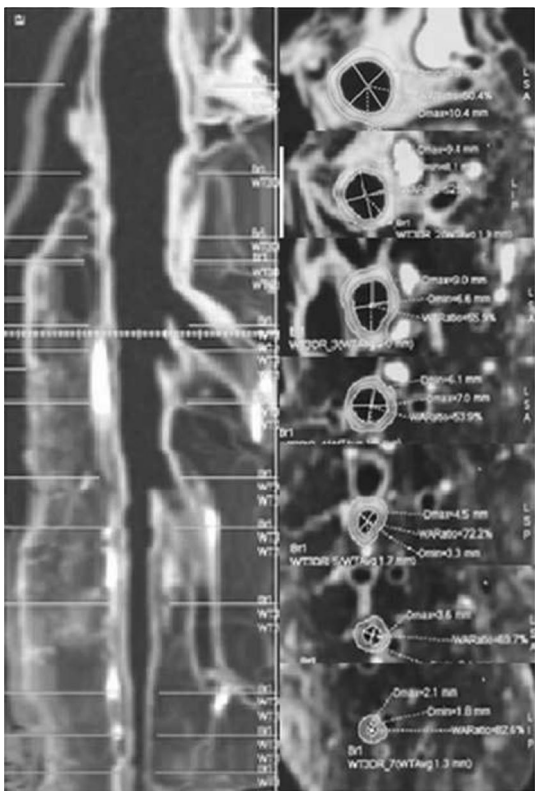

Fig. 2 **a** Curved multi-planar reconstruction image of posterior basal segmental bronchus. **b** Cross-sectional image of the measuring level, where %WA and WT were evaluated and calculated automatically

this specimen intact, the bronchial wall quantification at standard dose was considered as the reference values.

Signal-to-noise ratio (SNR) and noise were measured by placing a circular region of interest (ROI) on the lumen air of left main bronchus [31, 32], size fixed at 20 mm^2. Measurement of the ROI on a solid structure was placed on proximal thicker bronchus (the left lower lobe bronchus), inside the bronchial wall as large as possible, on the same bronchial level among all the images. The SNR value was defined as mean CT value divided by standard deviation in this ROI. Noise was assessed by measuring the standard deviation of Hounsfield values on the ROI.

Statistics

The correlation of dependent variables (SNR, noise, %WA, WT) and independent variables (dose and ASIR-V) was using multivariate correlation. Dose levels were the $CTDI_{vol}$ of 100 kV/60 mAs, 100 kV/40 mAs and 100 kV/20 mAs. ASIR-V levels were 0–100% (10% interval). mAs did not entered the multivariate model as an independent factor since it contributes to the radiation dose. Image SNR and noise among three low-dose settings and the standard-dose setting were compared using multivariate ANOVA. Image SNR, noise and airway quantification values were correlated with ASIR-V levels using Pearson correlation. Difference of quantitative values (%WA and WT) between pairwise comparisons of four dose groups was evaluated using Student–Newman–Keuls test, a stepwise multiple comparison procedure. An agreement of measurement values (%WA and WT) between standard-dose and low-dose settings was evaluated using intra-class correlation coefficient and Bland–Altman analysis. In Bland–Altman analysis, the ratio of measured value of low-dose setting divided by that of standard-dose setting was used, 95% limits of agreement was calculated by mean of ratio $\pm 1.96 \times$ standard deviation of ratio. Bland–Altman analysis was performed using MedCalc statistical software 15.8 (Frank Schoonjans, Mariakerke, Belgium). Statistical analyses were performed using SPSS software (SPSS version 19.0, IBM). A $p < 0.05$ was considered as statistically significant.

Results

Radiation dose

$CTDI_{vol}$ of three low-dose settings (100 kV/20 mAs, 100 kV/40 mAs and 100 kV/60 mAs) and standard-dose setting (120 kV/100 mAs) were 0.86 mGy, 1.71 mGy, 2.57 mGy and 6.91 mGy, respectively. Radiation dose on low-dose settings reduced by 87.6%, 75.2% and 62.8% compared to that on standard dose.

Image description and airway wall quantification

No obvious blocky pixelated image appearance was observed at all ASIR-V levels, on all dose protocols. Segmentation of external and internal contours of bronchial wall was clear. Measured by standard-dose settings, mean %WA increased from 39.2% to 68.5% and mean WT decreased from 1.5 mm to 1.0 mm, from proximal to distal bronchus.

Signal-to-noise ratio and image noise

Low-dose settings significantly reduced SNR and deteriorated noise as compared to the standard-dose setting. Significant difference of background SNR was found between each of low-dose settings and standard-dose setting (all $p < 0.05$), but insignificant among three low-dose settings ($p = 0.093$, 0.136, and 0.834 for 20 mAs vs 40 mAs, 20 mAs vs 60 mAs and 40 mAs vs 60 mAs, respectively). Significant difference of background noise was found between each of low-dose settings and standard-dose group (all $p < 0.001$), between three low-dose settings ($p < 0.001$, $p < 0.001$ and $p = 0.001$ for 20 mAs vs 40 mAs, 20 mAs vs 60 mAs and 40 mAs vs 60 mAs, respectively). No significant difference of bronchial wall SNR (noise) in pairwise comparisons of the four dose settings ($p = 0.366$ (0.383), 0.268 (0.237), 0.836 (0.753), 0.108 (0.533), 0.471 (0.955) and 0.607 (0.995) for 20 mAs vs 40 mAs, 20 mAs vs 60 mAs, 40 mAs vs 60 mAs, 20 mAs vs standard dose, 40 mAs vs standard dose and 60 mAs vs standard dose, respectively).

The background image SNR and noise value showed similar trends to those of the bronchial wall ROI. Both background and bronchial wall SNR and noise correlated with dose and ASIR-V levels (all $p < 0.05$) (background ROI results are shown in Figs. 3, 4). SNR of background (bronchial wall) showed exponentially increased correlation

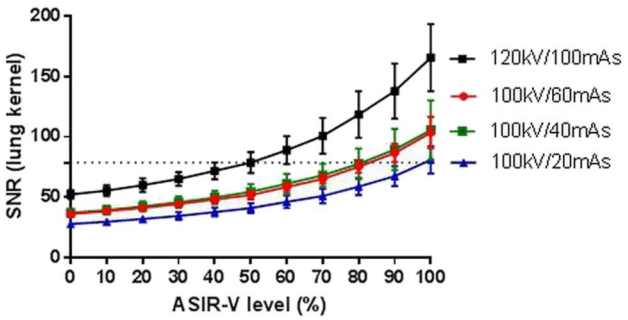

Fig. 3 The correlation between ASIR-V level and SNR is exponential. The SNR of 100 kV/20 mAs ASIR-V100, 100 kV/40 mAs ASIR-V80 or 100 kV/60 mAs ASIR-V80 was comparable to standard-dose ASIR-V50. The SNR of 100 kV/20 mAs ASIR-V70, 100 kV/40 mAs ASIR-V50 or 100 kV/60 mAs ASIR-V50 was comparable to standard-dose ASIR-V0. The SNR with ASIR-V100 was two- to threefold higher compared to ASIR-V0 ($p < 0.001$)

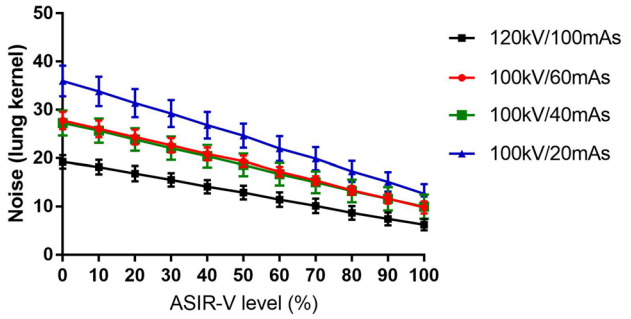

Fig. 4 The correlation between ASIR-V level and image noise is linear. The noise with ASIR-V100 was two- or threefold lower compared to ASIR-V0 ($p < 0.001$)

with ASIR-V level, because logarithmic transformed SNR linearly correlated with ASIR-V level (all $p < 0.001$), the R square was 0.973 (0.982), 0.980 (0.976), 0.977 (0.988), and 0.975 (0.972) for 60 mAs, 40 mAs, 20 mAs and standard-dose settings, respectively. Image noise of background (bronchial wall) showed linear decreased correlation with ASIR-V level (all $p < 0.001$), the R square was 0.999 (0.999), 1.000 (1.000), 1.000 (1.000), and 1.000 (0.999) for 60 mAs, 40 mAs, 20 mAs and standard-dose settings, respectively.

Correlation between airway quantification and ASIR-V level

%WA and WT showed no correlation with dose level (all $p > 0.05$). Most %WA and WT values showed no obvious correlation with ASIR-V levels (all $p > 0.05$) except several values in a few bronchi (see Fig. 5, Online Resource Appendix Fig. 1).

Comparisons of airway quantification values (%WA, WT) in four dose settings

%WA and WT values showed no significant difference between each low-dose setting and standard-dose setting, and between pairwise comparisons in low-dose settings (all $p > 0.05$). The intra-class correlation coefficients between low-dose protocols and standard-dose protocol were within 0.987 and 0.999 for %WA, and within 0.944 and 0.998 for WT. Agreement evaluation of %WA and WT values between each low-dose setting and standard-dose setting with ASIR-V_{0-100} is shown in Table 1.

For %WA, the standard deviations were 0.039, 0.038, 0.035 for 100 kV/20 mAs, 100 kV/40 mAs, 100 kV/60 mAs, respectively. For WT, the standard deviations were 0.067, 0.064, 0.061 for 100 kV/20 mAs, 100 kV/40 mAs, 100 kV/60 mAs, respectively. Bland–Altman plots of consistency between low and standard-dose settings of %WA value are shown in Fig. 6 and Online Resource Appendix Figs. 2, 3, showing visually good agreement in details as summarized in Table 1.

Discussion

The lung specimen phantom used in our airway study is different from the standard chest phantom with real tube values [26], and different from the human air-containing lung in the breathing state [15]. The reason to use this specimen was that it was morphologically closer to human airways, instead of a lung phantom while allowing repetitive CT scanning without considering radiation damage. Similar lung specimen can be found in Yanagawa's CT study [32]. The purpose of this experimental study was to evaluate the influences of different dose levels and ASIR-V strength levels on image quality and airway wall quantification. We selected a long bronchus with more branches, and measured a total of seven measurement points of bronchus from proximal lobar bronchus to distal 6th level branch, including multiple diameters of lobar bronchus, segmental bronchus and sub-segmental bronchus. The measurement of these bronchi would well represent the measurement of pulmonary airway dimensions. Therefore, we expect the simulation was representative and

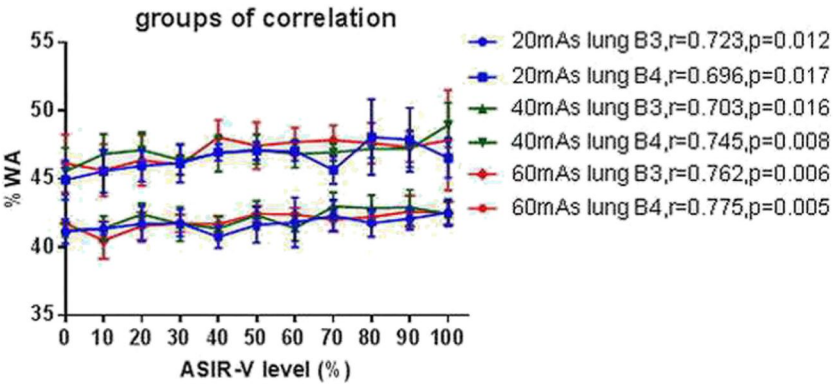

Fig. 5 A line chart of groups of positive correlation between ASIR-V level and %WA value showed small slope linear correlations on lung kernel in B3 and B4 bronchus. The trend lines almost overlapped in low-dose settings

Table 1 Bland–Altman analysis for consistency of %WA and WT values was calculated as low-dose setting divided by the standard-dose setting of the same ASIR-V level

ASIR-V level (%)	%WA 20 mAs	%WA 40 mAs	%WA 60 mAs	WT 20 mAs	WT 40 mAs	WT 60 mAs
0	0.99 ± 0.05	0.99 ± 0.06	0.99 ± 0.10	0.98 ± 0.08	0.99 ± 0.09	0.98 ± 0.15
10	0.99 ± 0.08	1.00 ± 0.07	0.99 ± 0.06	0.99 ± 0.11	1.00 ± 0.13	0.99 ± 0.10
20	0.99 ± 0.08	1.01 ± 0.07	1.00 ± 0.06	0.98 ± 0.13	1.01 ± 0.14	1.00 ± 0.10
30	1.00 ± 0.06	1.00 ± 0.06	1.00 ± 0.06	0.99 ± 0.11	1.00 ± 0.09	0.98 ± 0.12
40	1.00 ± 0.07	1.00 ± 0.12	1.01 ± 0.06	0.99 ± 0.12	1.01 ± 0.14	1.01 ± 0.09
50	1.01 ± 0.10	1.01 ± 0.07	1.01 ± 0.07	1.01 ± 0.18	1.00 ± 0.13	1.01 ± 0.12
60	1.01 ± 0.08	1.00 ± 0.08	1.01 ± 0.08	1.00 ± 0.12	0.98 ± 0.16	1.02 ± 0.13
70	1.00 ± 0.07	1.01 ± 0.07	1.01 ± 0.06	0.99 ± 0.17	1.01 ± 0.13	1.02 ± 0.13
80	1.01 ± 0.08	1.01 ± 0.07	1.01 ± 0.06	1.02 ± 0.14	1.02 ± 0.12	1.02 ± 0.12
90	1.01 ± 0.12	1.02 ± 0.08	1.01 ± 0.07	1.02 ± 0.14	1.02 ± 0.13	1.02 ± 0.11
100	1.01 ± 0.06	1.02 ± 0.07	1.01 ± 0.08	1.02 ± 0.15	1.03 ± 0.13	1.01 ± 0.14

The ratios were expressed as mean ± 1.96 standard deviation

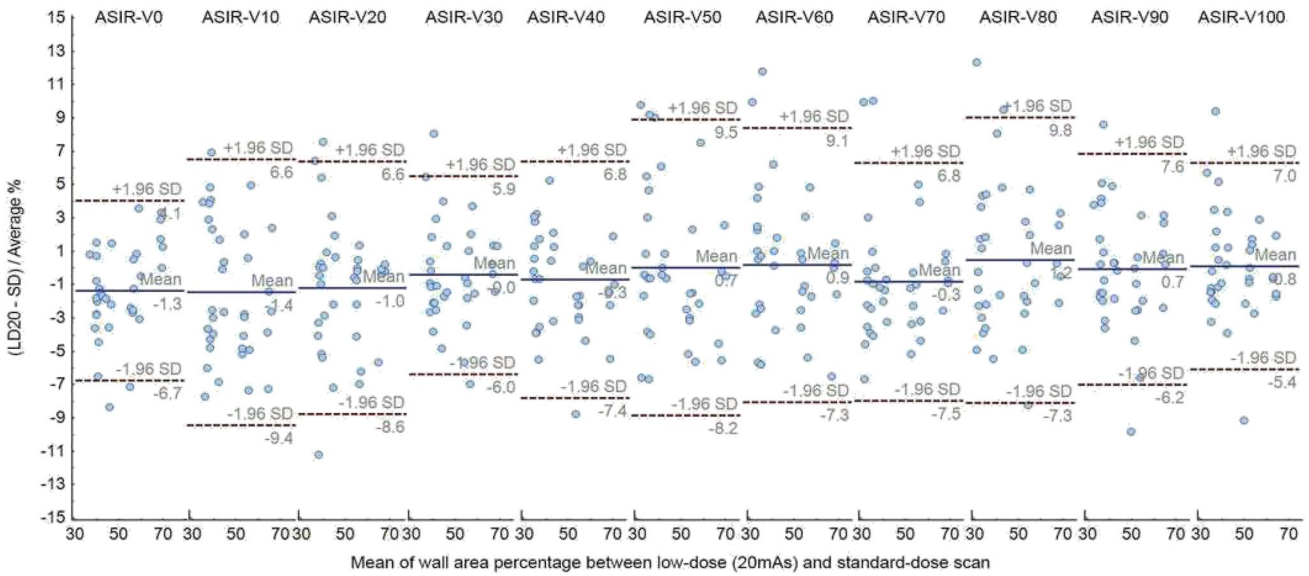

Fig. 6 Inter-scan Bland–Altman plots of %WA value show good consistency between low- (100 kV/20 mAs) and standard-dose setting

effective for the measurable airway walls in vivo by CT quantification.

It is essential to keep patient's radiation dose minimal while provide adequate image quality, so that airway wall can by accurately quantified in clinical practice [6]. It has been a consensus that iterative reconstruction can be applicable to decrease image noise and maintain image quality while reducing radiation dose.[16]. The ability to reduce radiation dose depends on the imaging and noise reduction principle of different iterative reconstructions. Some recent reports have confirmed that advanced version ASIR-V has greater potential to improve image quality [21, 24, 33]. ASIR-V offers the possibility of blending with FBP at various levels, from 0% (i.e., conventional FBP) to 100% (i.e., pure ASIR) [19]. However, previous studies focused a limited range of ASIR-V strength level on image quality. We found that image SNR exponentially increase and noise linearly decrease as ASIR-V level increased from 0 to 100%, which is similar with several previous studies [24, 34, 35] that more contribution of the ASIR or ASIR-V based on the FBP leaded to more noise decrease. We found no obvious blocky pixelated appearance in high ASIR-V proportion images using lung specimen phantom (smaller size and lighter weight), which is different from ASIR studies on patients [15, 17, 20]. In ASIR-reconstructed CT images, the noise is more correlated for higher spatial distance as compared to FBP, with texture of higher ASIR-reconstructed CT images appearing more "coarse grained" than texture of FBP reconstructed images [34]. A phantom study shows that images reconstructed using ASIR-V had

reduced image noise, improved contrast-to-noise ratio, and significantly improved spatial resolution than ASIR [24]. Benz's study using ASIR-V have reported that increasing levels of ASiR-V led to a continuous improvement of image quality in ultralow-dose coronary CT angiography with 100%ASiR-V yield the best image quality, and this is in contrast with previous studies performed with the precursor of ASIR-V (i.e., ASIR) for which degradation of image quality has been observed at levels of 80% and above due to increasing artificial texture perceived as a "plastic" appearance.[36] Our results also observed this interesting phenomenon, and might reach the conclusion that ASIR-V reconstructed with high percentage blending might be more adequate to compensate increased noise at lower radiation doses, at least in lung specimen study. The explanations may be related to the modification of ASIR with more advanced system noise statistics as well as object modeling and added physics modeling—the major contributors to noise reduction and low-contrast resolution improvements. These complex prediction models include modeling of exact geometric features of the cone beam and the absorbing voxels as well as X-ray physics (e.g., scatter, crosstalk).[36] Further studies on high percentage blending on chest and airways of human are needed.

To the best of our knowledge, accuracy evaluation of iterative reconstruction strength level on airway quantification is seldomly reported. Choo's phantom study [26] showed that wall thickness was thicker on FBP algorithms than on ASIR. Inconformity to previous study, we found no obvious variation of %WA or WT values from ASIR-V_0 to ASIR-V_{100} in all small bronchi and some large and medium bronchi, and slight increase of %WA or WT quantification values from ASIR-V_0 to ASIR-V_{100} in some large and medium bronchi, on lung reconstruction kernel. We speculate that the reason why ASIR-V has no obvious influence on measurement results is due to the natural good contrast between the airway wall and air-containing lung tissue, and also due to our recently introduced reconstruction algorithm. Some exceptions in the proximal airway may be measurement error due to air insufficiency of our lung specimen, a lack of contrast between proximal airway wall and adjacent atelectasis lung tissue. Therefore, we could come to the conclusion on ASIR-V that the higher ASIR-V strength associates with higher image signal-to-noise ratio and lower image background noise. For the measurement results of airway wall, ASIR-V strength had no significant influence on the airway measurement values. In clinical practice, a thoracic CT scan is used for visual diagnosis and quantitative evaluation in many domains, in which variable ASIR-V strength level may be used. Our study indicates that the accuracy of airway measurement is not influenced by ASIR-V strength, thereafter airway measurement can be applied, without special attention on the ASIR-V level.

CT evaluation of the medium and small airways is helpful in COPD, as it provides an index for airway inflammation and remodeling that correlates with exacerbation and other symptoms [6, 7, 37]. In mild emphysema, quantitative CT measurements of airway correlate better with the physiological indices, sub-segmental WA% and segmental WA% had the strongest correlation with forced expiratory flow (FEF) $_{25–75\%}$ and specific airway conductance [8]. Ratios of peripheral-to-central airway %WA show improved correlation with COPD severity [28]. WT correlated with the extent of small airway disease [7]. However, visual assessment agreement for airway wall thickening was just fair, and the number of lobes with thickened bronchial walls correlated with forced expiratory volume in first second (FEV1) and FEV1/ forced vital capacity (FVC) ratio [5]. In our study, acceptable consistency can be found in small airway branches (luminal diameter 2.6 mm and wall thickness 1.0 mm) between standard and low-dose settings, according to Bland–Altman analysis. Dose reduction effect can be found that both %WA and WT values showed a slightly increased variation as radiation dose reduced. Similar results of dose reduction effect can be found in Hammond's study [29].

There are some limitations in this study. First, the human lung specimen is a more optimal representation of human airway than artificial phantoms. However, evaluations of the influence of absorption and scattering in the human thorax on image quality were lacking, similar cadaveric human lungs for structure CT study can be found in Yanagawa's study [32], and further in vivo study would be necessary to validate phantom results. Second, although the alveoli of the specimen have collapsed and the bronchial interstitial structure is slightly atrophic compared to air-containing lung, the lung tissue has no large area of consolidation and has good contrast with airway wall. However, indicators of emphysema cannot be measured in the lung specimen. The results need to be combined with the impacts on emphysema measurements before used in COPD studies in the future. Third, although the lung specimen is not a standard lung phantom and cannot be disassembled to measure the true value of the bronchial wall, the measurement under the standard-dose scanning is used as the reference standard value, and the feasibility of low-dose scan compared to standard-dose scan is also in line with human studies. Fourth, although our study showed better image quality when using higher ASIR-V blending, the subjective image appearance observed in our lung specimen phantom does not reflect clinical diagnostic acceptance because of the blotchy appearance of the highly blended image.

Conclusion

ASIR-V improves image SNR and reduces noise when iterative reconstruction strength increases in low-dose settings, but not significantly influence airway wall quantification. Although measurement variability slightly increased, low-dose settings show acceptable agreement of %WA and WT compared to standard-dose setting. Therefore, low-dose CT settings are possible to be applied in airway wall quantification if in vivo studies confirm the finding.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest. Publication is approved by all authors and by the responsible authorities where the work was carried out.

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