



## Radiation dose reduction techniques for chest CT: Principles and clinical results



Yoshiharu Ohno<sup>a,b,\*,1</sup>, Hisanobu Koyama<sup>c</sup>, Shinichiro Seki<sup>a,b,1</sup>, Yuji Kishida<sup>d</sup>, Takeshi Yoshikawa<sup>a,b,1</sup>

<sup>a</sup> Division of Functional and Diagnostic Imaging Research, Department of Radiology, Kobe University Graduate School of Medicine, Japan

<sup>b</sup> Advanced Biomedical Imaging Research Center, Kobe University Graduate School of Medicine, Japan

<sup>c</sup> Department of Radiology, Osaka Police Hospital, Japan

<sup>d</sup> Division of Radiology, Department of Radiology, Kobe University Graduate School of Medicine, Japan

### ARTICLE INFO

#### Keywords:

CT  
Radiation dose reduction  
Chest  
Iterative reconstruction  
Quantification

### ABSTRACT

Computer tomography plays a major role in the evaluation of thoracic diseases, especially since the advent of the multidetector-row CT (MDCT) technology. However, the increase use of this technique has raised some concerns about the resulting radiation dose. In this review, we will present the various methods allowing limiting the radiation dose exposure resulting from chest CT acquisitions, including the options of image filtering and iterative reconstruction (IR) algorithms. The clinical applications of reduced dose protocols will be reviewed, especially for lung nodule detection and diagnosis of pulmonary thromboembolism. The performance of reduced dose protocols for infiltrative lung disease assessment will also be discussed. Lastly, the influence of using IR algorithms on computer-aided detection and volumetry of lung nodules, as well as on quantitative and functional assessment of chest diseases will be presented and discussed.

### 1. Introduction

The advent of multidetector-row CT (MDCT) technology in the late 1990s has played an important role in many areas of routine clinical practice, including chest imaging. However, the increasing number of CT scans being obtained has also raised some concerns about the resulting radiation exposure, so that currently the issue of radiation dose reduction is drawing widespread attention.

In the last decade, dose reduction strategies have been relying on a variety of techniques for data acquisition, such as tube current or tube voltage reduction, increased helical pitch, scan length optimization, and utilization of automatic exposure control (AEC) [1–3]. Generally speaking, image noise is inversely proportional to the square root of the radiation dose, so that reduced-dose CT images have a higher noise level than standard-dose images, and care must be exercised to ensure that the former remain suitable for diagnosis. To overcome the increase in image noise on reduced-dose CT images, various imaging filters, reconstruction algorithms and kernels have been developed. Among these, imaging filters are software applications designed to improve image quality by removing noise and artifacts. Currently, two types of

imaging filters are in use: spatial domain filters, applied to the reconstructed images, and raw data-based filters, operating before image reconstruction [1–3]. These techniques have been used over the past few decades in conjunction with filtered back projection (FBP).

More recently, enhanced computer performance has made it possible to apply iterative reconstruction (IR) algorithms for image reconstruction in routine clinical practice. Currently, IR algorithms are roughly divided into hybrid-type IR and model-based IR methods, with slight differences in details among vendors. These methods result in less image noise from raw data, although longer reconstruction times are required by some vendors [4]. These algorithms have been reported more useful than FBP for image quality improvements on reduced-dose CT images. They allow acquiring ultra-low-dose CT images, with radiation dose close to that for chest radiographs, for pulmonary nodule detection during lung cancer screening or meta surveillance of oncologic patients [5–10].

With this in mind, we will overview the recent improvements in radiation dose reduction, and discuss 1) image quality improvement methods for reduced-dose CT, 2) influence on computer-aided detection and volumetry of pulmonary nodules and 3) influence on quantitative

\* Corresponding author at: Division of Functional and Diagnostic Imaging Research, Department of Radiology, Kobe University Graduate School of Medicine, 7-5-2 Kusunoki-cho, Chuo-ku, Kobe, 650-0017, Japan.

E-mail addresses: [yosirad@kobe-u.ac.jp](mailto:yosirad@kobe-u.ac.jp), [yosirad@med.kobe-u.ac.jp](mailto:yosirad@med.kobe-u.ac.jp) (Y. Ohno).

<sup>1</sup> Drs. Ohno, Yoshikawa and Seki have received a research grant from Canon Medical Systems Corporation.

and functional assessment of chest diseases.

1.1. Options for image quality improvement: image filtering and iterative reconstruction algorithm

1.1.1. Image filtering

Image data processing is a way to improve image quality without increasing the radiation dose to patients [1–3,11–14]. It allows using CT protocols with reduced radiation doses and attain image quality similar to that obtained with higher dose. Originally, spatial domain-based filters were used after image reconstruction using the FBP algorithm. Since 2008, however, three-dimensional (3D) adaptive raw data filtering has been introduced to be used on raw data before image reconstruction [1–3,13,14]. Raw data can be degraded if an incoming x-ray beam traverses structures with extremely high attenuation, resulting in streak artifacts. The 3D raw data filter removes such streak artifacts by modifying parts of the raw data corrupted by the presence of highly attenuated structures.

The International Multicenter Study for Low-Dose Chest CT Examination and Diagnosis (iLEAD) study group has been reporting on the utility of 3D raw data filters in Japanese [14,15], German [16] and United States (USA) [17] populations. Lung nodule detection and characterization were compared on standard- and reduced-dose CTs with and without using 3D raw data filters [15]. These studies found that 3D raw data filters could markedly decrease streak artifacts and reduce tube current to 50 or 60 mA levels while maintaining image quality and depiction of pulmonary findings without any significant differences in comparison with standard-dose CT [14–17]. In addition, it was demonstrated that lesion characterization on reduced-dose CT images was comparable to that performed using standard-dose CT images [14–17]. However, there was no further radiation dose reduction reported since 2011 using the above-mentioned techniques [18], the reason why iterative reconstruction is currently applied rather than these previous techniques to achieve a larger dose reduction on CT.

1.1.2. Iterative reconstruction algorithms for radiation dose reduction

These last years, most CT vendors have introduced hybrid-type and/or model-based IR algorithms for use in routine clinical practice (Table 1), and many investigators have found them useful for cardiothoracic imaging. As explained in a state-of-the art review of iterative CT reconstruction techniques, hybrid algorithms combine both analytical and iterative methods. The initial image can be generated by means of analytical methods and iterative methods secondarily used to reduce noise in the image domain. However iterative algorithms can also be directly employed in the reconstruction process. The term hybrid IR usually refers to algorithms that mainly reduce image noise through cyclic image processing [4]. In contrast, the term model-based iterative reconstruction usually refers to algorithms that employ models of the acquisition process, image statistics, and system geometry. Moreover, the clinical performance of IR algorithms is not necessarily

related to the complexity of the method. Nevertheless, the reconstruction times of hybrid-type IR algorithms are generally and comparatively faster than those of model-based IR algorithms and more easily applied in routine clinical practice.

Since the first applications of IR algorithms, hybrid-type IR algorithms have been tested more extensively than model-based IR algorithms [5–7,19–22]. Almost all investigators reported that IR algorithms had better potential for greater radiation dose reduction than FBP algorithms for various pulmonary diseases [5–7,19–21].

One study reported that the image quality obtained with tube currents of 100 mA and 50 mA and a FBP algorithm, was significantly lower than that for both protocols using a hybrid-type IR algorithm for image reconstruction [22]. In addition, all inter-method agreements for bronchiectasis, emphysema, ground-glass opacity, honeycomb pattern, interlobar septal thickening, nodules and reticular opacity were moderate, substantial, or almost perfect [22]. Moreover all agreements for the mediastinal and pleural findings among reduced-dose CTs with AIDR 3D algorithms and standard-dose CT with FBP algorithm were almost perfect [22]. The results of this study were supported by those of a multicenter study conducted by the Area-Detector Computed Tomography for the Investigation of Thoracic Diseases (ACTive) study group, evaluating image quality and radiation dose reduction of chest CT using the same hybrid-type IR method, although the multicenter study applied standard-dose CT with a tube current of 240 mA and reduced-dose CTs with tube currents of 120 mA and 60 mA [23].

When considering the use of reduced-dose CT in clinical practice, one of the most important applications is lung cancer screening. The ACTive study group also assessed the utility of the AIDR 3D algorithm for lung nodule detection on reduced-dose CT [24]. No significant differences in solid lung nodule detection was found between reduced-dose CT protocols using tube currents of 120 mA and 20 mA. For the detection of ground glass nodules of at least 8 mm in diameter, the performance of the two protocols was similar [23]. The authors therefore concluded that, for cases with normal body mass index values, lung nodule detection with reduced-dose CT protocol using 20 mA and the AIDR 3D algorithm, at a chest radiograph equivalent dose, was comparable to that obtained with CT protocols using 120 mA and the AIDR 3D algorithm., except for the detection of smaller ground glass nodules of less than 8 mm in diameter [24].

Another study used model-based and hybrid-type IR reconstruction algorithms from another vendor [25]. In this study, 59 patients gave informed consent to undergo reference-, low-, and ultralow-dose chest CT acquisitions using a 64-row multidetector CT. They used automatic tube current modulation with 2 fixed noise index values (31.5 and 70.44 for reference and low-dose CT images, respectively) reconstructed with 50% adaptive iterative reconstruction (ASiR; GE Healthcare, Waukesha, WI, USA) The ultralow-dose CT was acquired with a fixed tube current-time product of 5 mAs and reconstructed with model-based IR (MBIR). No significant differences were observed between the low-dose ASiR and the ultralow-dose MBIR protocols for

**Table 1**  
Clinically available iterative reconstruction algorithms provided by CT vendors.

	Method	CT vendor
Model-Based Iterative Reconstruction (IR)	Veo	GE Healthcare
	Iterative Model Reconstruction (IMR)	Philips Healthcare
	Forward Projected Model-Based Iterative Reconstruction Solution (FIRST)	Canon Medical Systems (previously Toshiba Medical Systems)
Hybrid-Type Iterative Reconstruction (IR)	Adaptive Statistical Iterative Reconstruction (ASiR)	GE Healthcare
	Iterative Reconstruction in Image Space (IRIS)	Siemens Healthcare
	Sinogram Affirmed Iterative Reconstruction (SAFIRE)	Siemens Healthcare
	Advanced Modeled Iterative Reconstruction (ADMIRE)	Siemens Healthcare
	Adaptive Iterative Dose Reduction using 3D Processing (AIDR 3D)	Canon Medical Systems (previously Toshiba Medical Systems)
	4th-Generation Iterative Reconstruction (iDose [4])	Philips Healthcare
	Intelli Iterative Processing (Intelli IP)	Hitachi



**Fig. 1.** 76-year-old female with ground glass nodule (GGN) in the right lower lobe.

A (L to R: 200 mA, 100 mA, 20 mA and 10 mA): FBP reconstructed CT using Boost 3D (Canon). With a reduction in tube current, GGN in the right lower lobe is visible on each CT image, but streak artifacts increase, especially at tube current of 20 mA and 10 mA. B (L to R: 200 mA, 100 mA, 20 mA and 10 mA): Hybrid type IR (i.e. AIDR 3D, Canon) reconstructed CT. With a reduction in tube current, GGN in the right lower lobe on each CT image reconstructed with the AIDR 3D algorithm is more clearly visible than on that reconstructed with the FBP algorithm. In addition, streak artifacts slightly increased, especially at tube current of 20 mA and 10 mA. C (L to R: 200 mA, 100 mA, 20 mA and 10 mA): Model-based IR (i.e. FIRST, Canon) reconstructed CT. Although the tube current was reduced, GGN in the right lower lobe remains clearly visible and no streak artifacts appear on any CT image.

overall nodule detection, ground-glass, part-solid, or solid nodule detection. They thus concluded that model-based iterative reconstruction enabled nearly 80% radiation dose reduction without affecting nodule detectability [25]. Taking into account these studies, nodule detection in routine clinical practice and during lung cancer screening is probably one of the best applications for CT dose reduction.

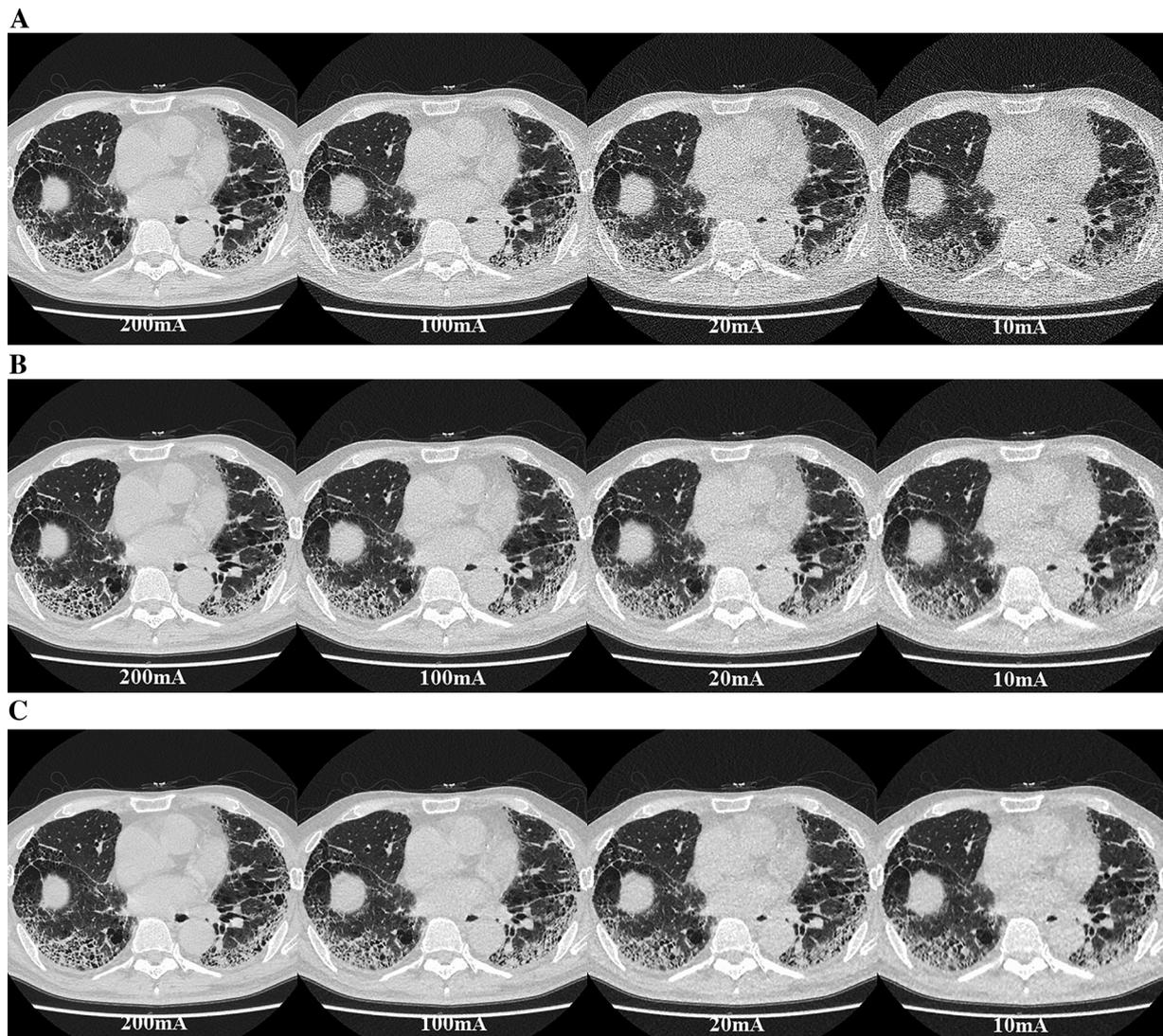
Another important application of radiation dose reduction is pulmonary thromboembolism diagnosis. Pontana et al used IR algorithm and low tube voltage for radiation dose reduction when performing contrast-enhanced CT pulmonary angiography (CTPA) [26]. They compared image quality of low-voltage CTPA acquisitions reconstructed with a hybrid-type IR algorithm (SAFIRE: sonogram-affirmed iterative reconstruction; Siemens Healthcare, Forchheim, Germany), with that of standard-dose, standard-voltage CTPA acquisitions reconstructed with FBP algorithm [26]. The low-voltage CTPA images reconstructed with SAFIRE algorithm showed improved quality at both lung and mediastinal window settings and superior signal-to-noise and contrast-to-noise ratios [26].

Hybrid-type and model-based IR algorithms have also been tested on simulated low-dose CTPA examinations of 16 patients with

pulmonary thromboembolism with dose levels (DL) of 50%, 25%, 12.5%, 6.3% or 3.1% of the original tube current setting [27]. The original and simulated low-dose data sets were reconstructed with three reconstruction algorithms: FBP standard reconstruction algorithm, a hybrid-type IR algorithm (iDose; Philips Healthcare, Cleveland, OH, USA) and a model-based IR algorithm (Iterative Model Reconstruction (IMR), Philips). The authors found that iDose and IMR showed superior capability for detection of pulmonary thromboembolism. With IMR, sensitivity for detection of pulmonary embolism was 100% down to a dose level of 12.5%, and contrast-to-noise ratio was higher than for the 2 other reconstruction algorithms.

Whereas applying dose reduction for lung cancer screening and pulmonary thromboembolism detection seemed validated, there have been some concerns about the diagnostic performance of reduced dose CT for interstitial lung disease (ILD) assessment compared to that standard dose CT. It was therefore important to determine the capability of IR algorithms to maintain diagnostic performance for patients with interstitial lung disease. In 2016, two major studies were published which addressed the above-mentioned concerns [28,29].

One study [28] evaluated the effect of IR algorithms on the



**Fig. 2.** 83-year-old male patient with polymyositis.

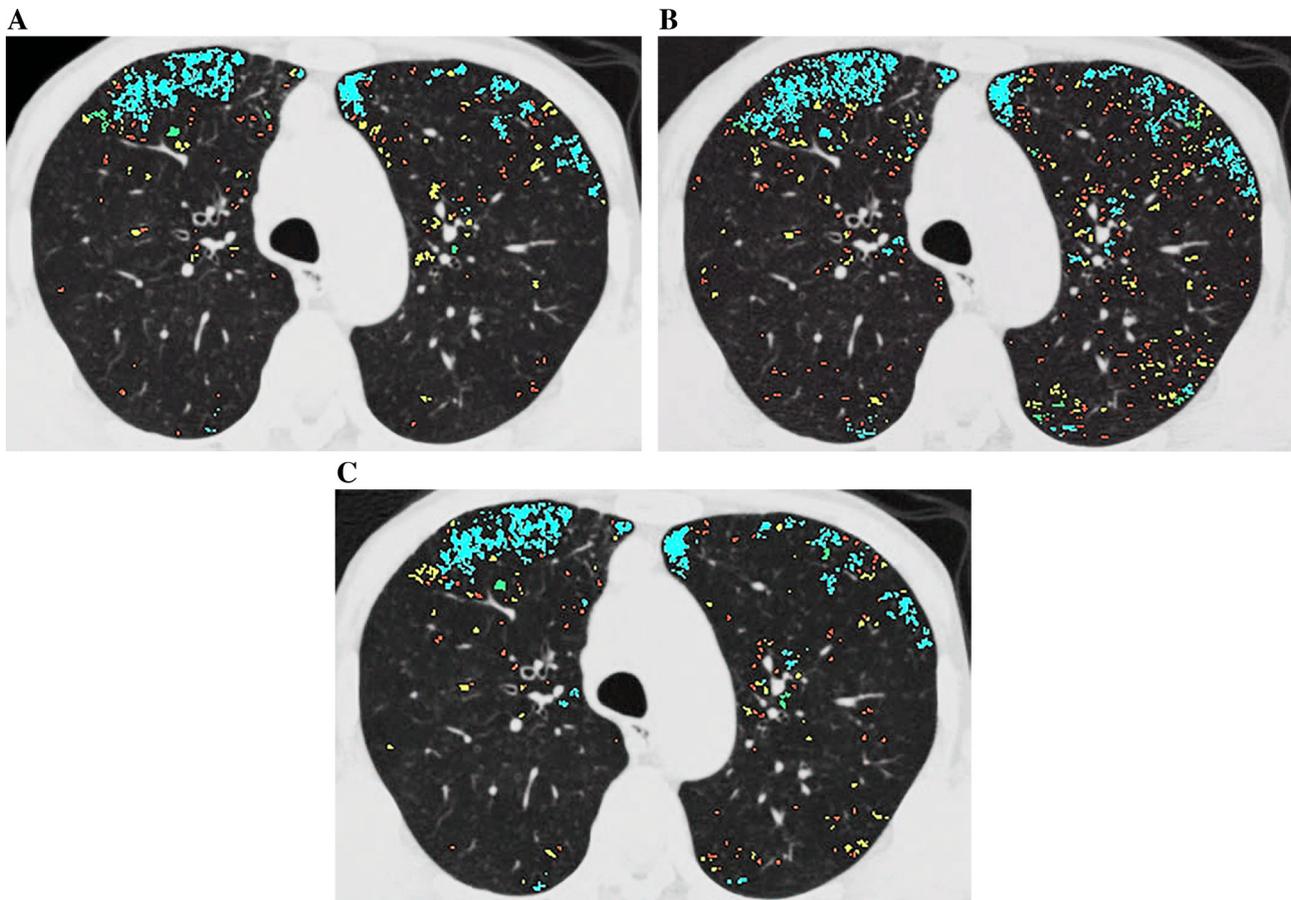
A (L to R: 200 mA, 100 mA, 20 mA and 10 mA): FBP reconstructed CT using Boost 3D. Pulmonary emphysema and reticulation in both lungs, especially the lower lobes, are depicted at tube currents of 200 mA, 100 mA and 20 mA, but are not clearly visible at the tube current of 10 mA. However, image clarity is markedly reduced, and streak artifacts have significantly increased, especially at 20 mA and 10 mA. B (L to R: 200 mA, 100 mA, 20 mA and 10 mA): Hybrid type IR (i.e. AIDR 3D) reconstructed CT. Pulmonary emphysema and reticulation in both lungs, especially the lower lobes, are seen at each tube current. However, image clarity is slightly reduced, and streak artifacts have slightly increased, especially at 10 mA. C (L to R: 200 mA, 100 mA, 20 mA and 10 mA): Model-based IR (i.e. FIRST) reconstructed CT. Pulmonary emphysema and reticulation are equally visible at each tube current. In addition, image clarity remains the same, and no streak artifacts are visible at any tube current.

depiction of systemic sclerosis-related ILD when the radiation dose was reduced by 60%. In this study, 55 patients underwent chest CT examinations using a dual-source CT unit with both tubes set at 120 kVp and the 110 mAs reference milliampere seconds divided into 40% for tube A and 60% for tube B. Two series of images were generated: standard-dose images (group 1), generated from both tubes and reconstructed with FBP algorithm and reduced-dose images (group 2), generated from tube A with 60% dose reduction and reconstructed with SAFIRE algorithm. The authors reported that the mean objective noise level was significantly lower for group 2. The ILD CT features seen in group 1 were always depicted in group 2, with subjective conspicuity scores improved for ground-glass opacity, reticulation, and bronchiectasis. The authors therefore concluded that the hybrid-type IR algorithm allowed for similar detection of systematic sclerosis-related ILD on reduced-dose images, with a CT radiation dose reduced to 60% [28].

Another study evaluated the utility of IR algorithms for the assessment of diffuse ILD on thin-section CT [29]. Chest CT scans were

performed in 23 patients with ILD, using a standard-dose protocol (120 kVp and 142–275 mA with dose modulation) and a reduced-dose protocol (120 kVp and 20 mA). Standard-dose CT images were reconstructed with FBP and reduced-dose CT images were reconstructed with FBP, ASiR, and MBIR algorithms. The disease detection was not significantly different for the various doses. However, in comparison with standard-dose CT images, reduced-dose CT images reconstructed with FBP, ASiR, and MBIR tended to underestimate reticular or honeycombing opacities and overestimate ground glass opacities. The authors therefore concluded that the diagnostic performance of reduced-dose protocols was similar to that of standard-dose but that caution should be exercised when comparing disease extent in follow-up studies using an IR algorithm [29].

The ALARA acronym for "as low as reasonably achievable (i.e. ALARA)" is a fundamental principle for diagnostic radiology. There is no doubt that medical imaging, which has undergone tremendous technological advances in the last decades, is essential for patient care. However, technological advances generally precede the knowledge of



**Fig. 3.** 70-year-old man with mild pulmonary emphysema (permission obtained from reference No. 52).

A: Standard-dose CT reconstructed with FBP algorithm using boost 3D (Canon), B: Reduced-dose CT reconstructed with FBP algorithm using boost 3D (Canon), and C: Reduced-dose CT reconstructed with a hybrid-type IR algorithm (AIDR 3D, Canon). Low-attenuation lung regions shown in images are color coded based on size as follows: class 1, red (2–8 mm [3]); class 2, yellow (8–65 mm [3]); class 3, green (65–120 mm [3]); class 4, cyan (> 120 mm [3]).

end-users concerning the optimal use of imaging equipments, and such knowledge is essential to minimizing potential risks to the patients. It means making all efforts to maintain exposures to ionizing radiation as low as possible. When considering the recently developed IR algorithms, they have made possible to reduce the radiation dose resulting from CT examinations in routine clinical practice, because they can maintain satisfactory diagnostic performance and image conspicuity (Figs. 1 and 2). Moreover, when using IR algorithms, tube current can be reduced at a 50 mA level for the evaluation of most pulmonary diseases and even reduced at a 10 mA level for nodule detection. Model-based IR algorithms might decrease spatial resolution and change the image appearance which can be found disturbing. Therefore, hybrid-type IR algorithms are probably more appropriate to be applied for CT evaluation of pulmonary diseases in routine clinical practice.

## 1.2. Influence of iterative reconstruction for computer-aided detection and volumetry of lung nodules

### 1.2.1. Computer-aided detection of lung nodules

A Computer-Aided Detection and Diagnosis (CAD) system is a class of computer systems designed to assist in the detection and/or diagnosis of diseases through a “second opinion” [30]. The main purpose of CAD systems is to improve the accuracy of radiologists by reducing the time needed for the interpretation of images and /or limiting the detection errors. CAD systems are classified into two groups: computer-aided detection (CADe) systems and computer-aided diagnosis (CADx) systems.

Several studies have reported improvements in radiologists’

detection of lung nodules when using CADe. A wide range of sensitivities, from 54% to 95%, with false positive rates of 0.55–8.3 per examination, has been reported when CADe is employed alone [31]. It has also been suggested that image quality is an important factor, with a decline in CADe performance when it is used on reduced-dose CT acquisitions reconstructed with FBP algorithm [32–34].

One study evaluated CADe performance for the detection of artificial pulmonary nodules [32]. In this study, seven porcine lung explants were inflated in a dedicated *ex vivo* phantom shell and supplied with 162 artificial nodules, after which CT was performed with different combinations of 120 and 80 kV with 120, 60, 30 and 12mAs. CT images were reconstructed with an FBP algorithm and the SAFIRE hybrid-type IR algorithm. Subsequently, 16 data sets per lung were analyzed using a dedicated CADe software (Syngo Via VA20 A, Siemens), and the rates of true-positive, false-negative and false-positive CADe marks were determined for each reconstruction. It was found that the rates of true-positive findings were not significantly different for most exposure settings except for the combination of 80 kV and 12mAs. The authors therefore concluded that the CADe results were robust over a wide range of exposure settings. In addition, noise reduction by SAFIRE was not detrimental, and had the potential to be used to improve image quality of reduced-dose CT acquisitions performed for lung cancer screening [32].

The results of two *in vivo* studies were recently reported [33,34]. Ohno et al. evaluated the proprietary CADe software developed by Canon Medical Systems Corporation (previously Toshiba Medical Systems Corporation) and Kobe University, using standard-, reduced- and ultra-low-dose CT acquisitions reconstructed by means of FBP and IR

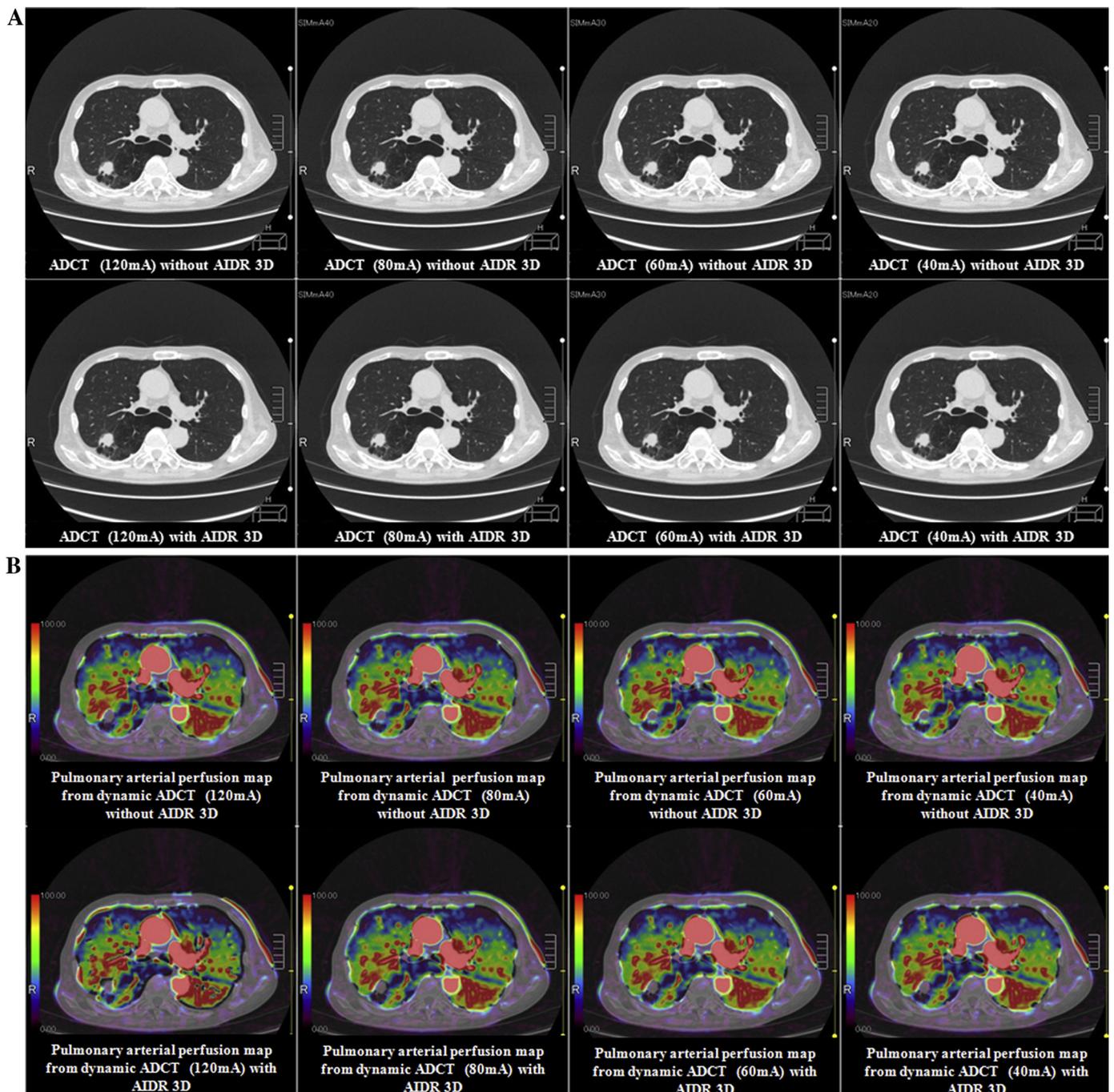


Fig. 4. 72-year-old male patient with invasive adenocarcinoma in the right lower lobe (permission obtained from reference No. 60).

(A: standard-dose perfusion ADCT at 120 mA, reduced-dose ADCT at 80 mA, that at 60 mA and that ADCT at 40 mA reconstructed with and without AIDR 3D (Canon); B: pulmonary arterial perfusion maps derived from all ADCT data obtained with and without AIDR 3D; C: systemic arterial perfusion maps derived from all ADCT data obtained with and without AIDR 3D; D: total perfusion maps derived from all ADCT data obtained with and without AIDR 3D; E: perfusion maps derived from all ADCT data obtained with and without AIDR 3D; F: extraction fraction maps derived from all ADCT data obtained with and without AIDR 3D; G: blood volume maps derived from all ADCT data obtained with and without AIDR 3D. Although image noise slightly increased on all reduced-dose ADCTs obtained with and without AIDR 3D, all perfusion maps except for the blood volume map showed only minor differences among all simulated dose data, for both lung parenchyma and nodules evaluation. Regional blood volumes within lung parenchyma and nodules derived from data obtained without AIDR 3D changed more than those obtained from data reconstructed with AIDR 3D.

algorithms. Doses of 250 mA, 50 mA and 10 mA, were respectively used for standard-, reduced- and ultra-low-dose chest CTs, reconstructed by FBP and hybrid-type IR algorithm (AIDR 3D, Canon) in 40 patients who had both solid and subsolid nodules to be automatically detected. Volume CT dose indexes (CTDIvol) obtained with ultra-low-dose CT, reduced-dose CT and standard-dose CT were 0.5 mGy, 2.5 mGy and 12.6 mGy, respectively. The sensitivity of CADE for nodule detection on

ultra-low-dose CT reconstructed by means of an FBP algorithm was significantly reduced compared to what was observed for standard- and reduced-dose CTs and ultra-low-dose CT reconstructed with the AIDR 3D algorithm. Thus, the authors concluded that the hybrid-type IR algorithm had a positive effect on nodule detection capability of the CADE system when the radiation dose was reduced [33]. In addition, there were no significant difference of sensitivity and false-positive rate

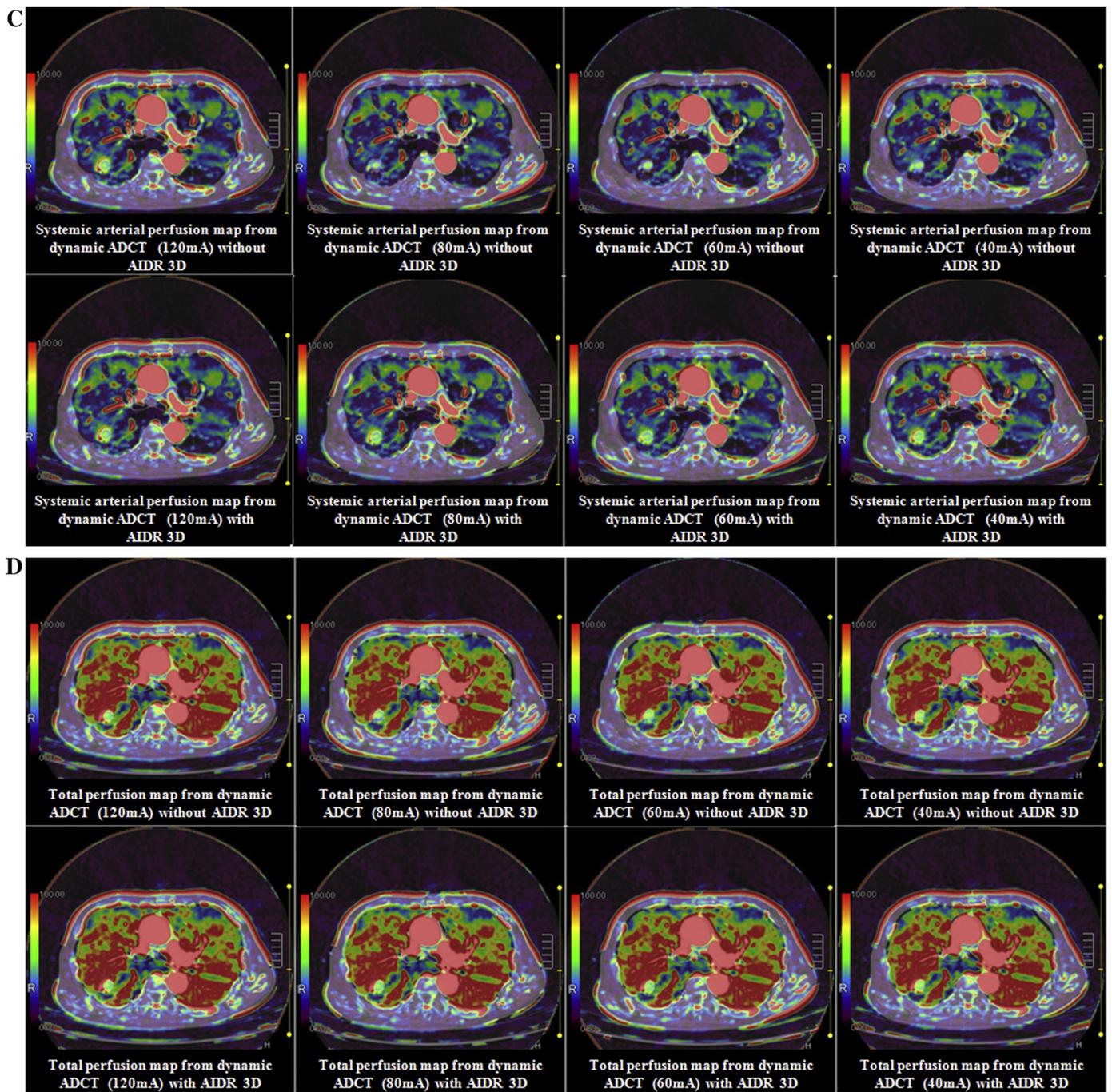


Fig. 4. (continued)

between standard-dose and reduced and ultra-low-dose CT acquisitions when reconstructed with AIDR 3D.

Similar results were obtained in another study by Nomura et al., which used the same FBP and hybrid-type IR algorithms, and in addition a model-based IR algorithm (Forward projected model-based Iterative Reconstruction SoluTion (FIRST); Canon, previously Toshiba) [34]. A reduced-dose CT protocol with a CTDI value of 3.02 mGy and an ultra-low-dose CT protocol with a CTDI of 0.3 mGy were used for 85 subjects enrolled in a lung cancer screening program. The reduced-dose CT images were reconstructed with the FBP algorithm, and the ultra-low-dose CT images with the FBP, AIDR 3D and FIRST algorithms. Each image dataset was evaluated by using the authors' proprietary CADE software. The sensitivity of CADE on the ultra-low-dose CT datasets reconstructed both IR algorithms was significantly higher than that on

the ultra-low-dose dataset reconstructed with the FBP algorithm [34]. These studies [32–34] demonstrate that IR algorithms are capable of maintaining the CADE performance as high as that observed on standard-dose CT images, despite the radiation dose reduction. In addition, as compared with previously applied FBP algorithm, both IR algorithms can achieve further radiation dose reduction in this setting.

### 1.2.2. Computer-aided volumetry of pulmonary nodules

Since the demonstration by the National Lung Screening Trial (NLST) that lung cancer screening reduces the lung cancer-related mortality [35], several other trials have been performed worldwide [36,37]. Some investigators, especially The Dutch-Belgian Randomized Lung Cancer Screening Trial (Dutch acronym: NELSON study) group, have suggested that volume measurements and/or doubling time of

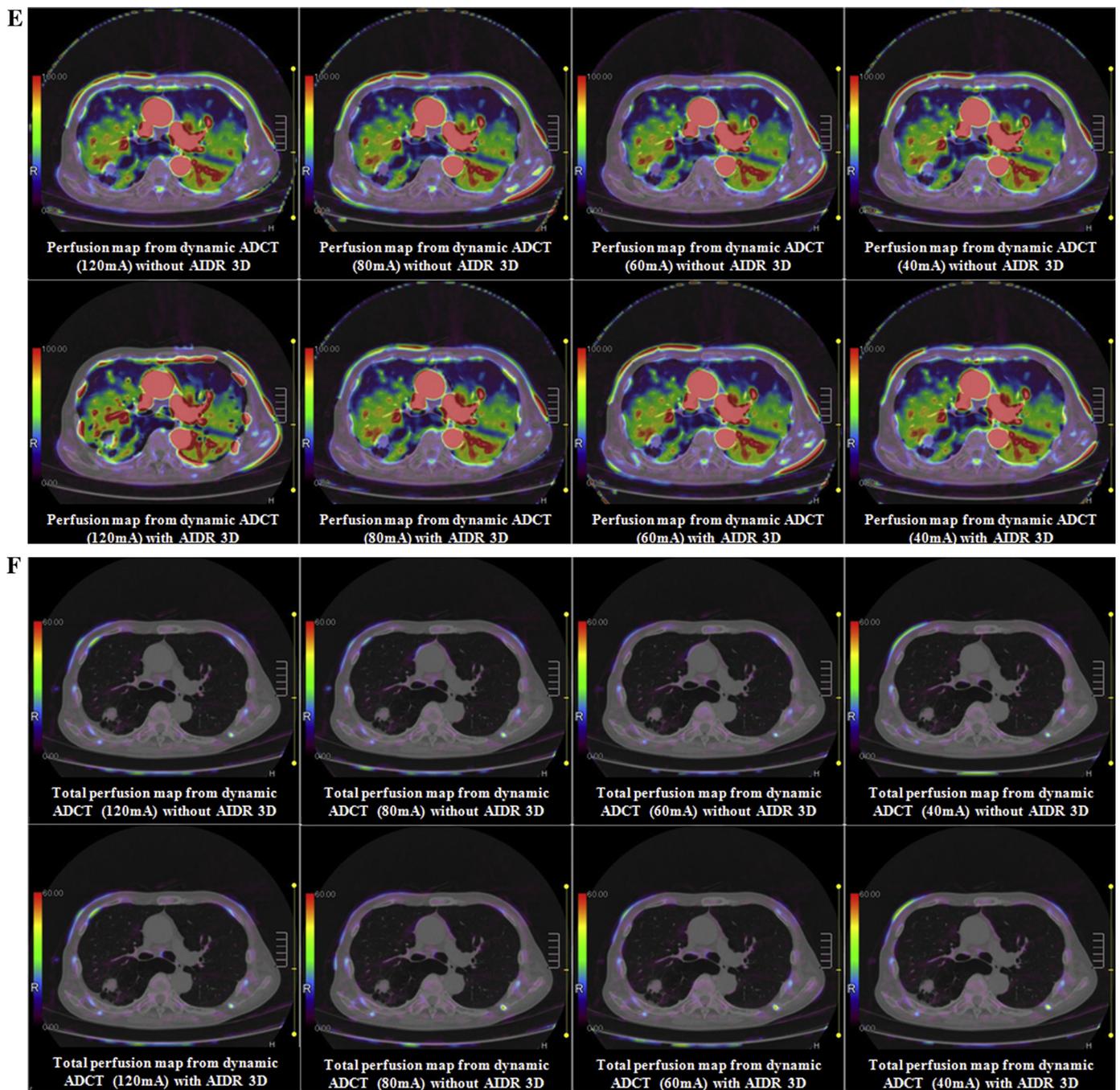


Fig. 4. (continued)

assessment by computer-aided volumetry (CADv) software should be used for the evaluation of indeterminate screen-detected lung nodules [38–41]. The Quantitative Imaging Biomarkers Alliance (QIBA), established by the Radiological Society of North America, has evaluated the measurement accuracy of CADv software from many vendors on a QIBA recommended phantom study [40].

Ohno et al. performed a phantom study in accordance with QIBA recommendations using standard-, reduced- and ultra-low-dose CT acquisitions. Images were reconstructed by means of FBP and hybrid-type and model-based IR algorithms (AIDR 3D and FIRST) provided by Canon Medical Systems Corporation, and analyzed using a commercially available 3D CADv software (CT Lung Nodule Analysis; Vital Images Inc., Minnetonka, MN) [41]. In this study, an anthropomorphic thoracic phantom with 30 simulated nodules of three density types (100, -630, and -800 HU) and five different diameters was scanned

with an area-detector CT at tube currents of 270, 200, 120, 80, 40, 20, and 10 mA. Each dataset was reconstructed as a thin-section CT with the three algorithms (FBP, AIDR 3D and FIRST) and all simulated nodules were measured with CADv software. The percentages of absolute measurement errors for all three reconstruction methods were then statistically compared among all data sets. Statistical analyses determined that the mean absolute measurement errors for both IR algorithms for each nodule type were significantly lower than those observed for the FBP algorithm used on 20 mA and 10 mA CT acquisitions. Moreover, there were no significant differences of absolute measurement errors between standard-dose CT with all reconstruction methods and reduced- and ultra-low-dose CTs with both IR algorithms. Both IR algorithms were thus shown to be more effective than the FBP algorithm for radiation dose reduction, while CADv yielded more accurate measurements [41].

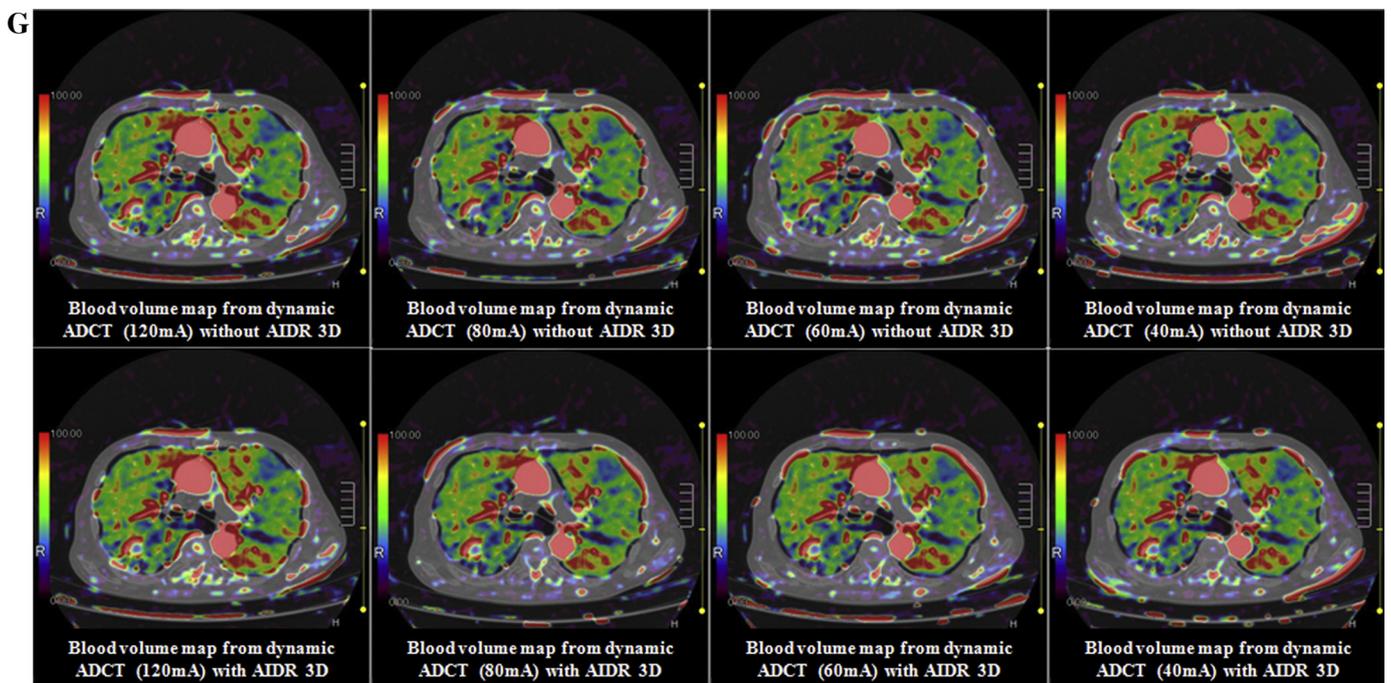


Fig. 4. (continued)

### 1.3. Quantitative and functional evaluation of chest diseases

#### 1.3.1. Quantitative assessment of chronic obstructive pulmonary disease

CT can be used to evaluate morphologic and functional changes related to chronic obstructive pulmonary disease (COPD) [42–46]. A large number of commercially available and proprietary software as well as various visual scoring systems have been used for CT-based assessment of pulmonary emphysema [42,43]. Two major approaches have been reported for quantitative CT assessment of COPD [42,43,46–48]. One is the determination of the percentage of low attenuation area (%LAA) in the lung, which reflects emphysema changes and the other is the determination of the wall area ratio (WA%) of the bronchi, which reflects bronchial lumen narrowing and bronchial wall thickening [48]. In addition, three-dimensional (3D) airway luminal volumetry has been introduced as another quantitative method for airway evaluation in COPD patients [49–51]. Taking these quantitative CT assessments of COPD and the current situation regarding radiation dose reduction strategies into consideration [45–53], the application of IR algorithms is viewed as an important issue for an accurate quantitative CT evaluation of COPD.

The %LAA was evaluated in 26 patients who had undergone standard-dose and reduced-dose CT acquisitions with tube currents of 300 mA and 50 mA [52]. Standard-dose CT images were reconstructed with the FBP algorithm whereas reduced-dose CT images were reconstructed with both the FBP and the AIDR 3D algorithm. Agreement for %LAA between standard-dose and reduced-dose CTs tended to improve when using the AIDR 3D algorithm [52] (Fig. 3). The ACTIVE study group applied the same hybrid-type IR algorithm and obtained similar results for standard-dose CT at 240 mA and reduced-dose CTs at 120 mA and 60 mA [53]. Thus, the use of a hybrid-type IR algorithm resulted in a greater consistency of emphysema quantification on reduced-dose and ultra-low-dose CTs as compared with the quantification performed on standard-dose CT images.

Although %LAA and WA% have been advocated as the two main quantitative parameters for COPD assessment, [42,43,48–51], 3D airway luminal volumetry has also been proposed as another method for quantitative evaluation of airflow limitation in COPD [50,49–51]. Koyama et al. evaluated the utility of a hybrid-type IR algorithm for quantitative bronchial assessment on reduced-dose CT in patients with

and without COPD [51]. Fifty patients underwent standard-dose CT acquisition at a tube current of 300 mA, with image reconstruction using FBP and reduced-dose CT acquisition at 50 mA, with image reconstruction using the AIDR 3D algorithm. For quantitative bronchial assessment, WA% of the sub-segmental bronchi and the airway luminal volume percentage (LV%) from the main bronchus to the peripheral bronchi were assessed for each dataset. A significant correlation of WA% and LV% were found between the standard and reduced-dose CT images. The LV% agreement between standard-dose CT and reduced-dose CT reconstructed with AIDR 3D was moderate, while the other agreements proved to be poor.

#### 1.3.2. Quantitative assessment of lung parenchyma and tumors perfusion using dynamic contrast-enhanced first-pass perfusion on area-detector CT

Reports published during these last years have suggested that dynamic contrast-enhanced (CE-) first-pass perfusion area-detector CT (ADCT) could be used for quantitative evaluation of perfusion within the lung as well as for tumor assessment, characterization of pulmonary nodules or prediction of therapeutic response in non-small cell lung carcinomas [54–60]. One drawback for clinical application of dynamic CE-first-pass perfusion ADCT examination is the resulting higher radiation dose. Consequently, radiation dose reduction when performing dynamic CE-first-pass perfusion ADCT is considered a key issue for fostering the acceptance of this technique in routine clinical practice.

To address radiation dose reduction for dynamic CE-first-pass perfusion ADCT examinations, a simulation study was published in 2016 [60]. In this study, 36 lung cancer patients underwent dynamic CE-first-pass perfusion ADCT at 120 mA, and the original ADCT data were computationally simulated at 80 mA, 60 mA and 40 mA tube current values. Each dataset was then reconstructed with and without the AIDR 3D algorithm (Fig. 4). At every tube current level, the image quality of CE-perfusion ADCT reconstructed with the AIDR 3D algorithm was significantly higher than of that observed for datasets reconstructed with the FBP algorithm. Significant correlations were found for each lung or tumor perfusion matrix between the standard-dose and the reduced-dose methods using AIDR 3D. Therefore, the AIDR 3D algorithm allowed dose reduction for dynamic CE-first-pass perfusion ADCT, while maintaining image quality and reducing measurement errors.

## 2. Conclusion

Many efforts have been deployed by institutions and companies for radiation dose reduction during CT examinations. IR algorithms have been developed and clinically tested for various clinical applications and evaluation of chest diseases. These applications include lung nodule detection especially during lung cancer CT screening, pulmonary thromboembolism diagnosis and assessment of infiltrative lung diseases. Iterative reconstruction algorithms may be supportive for maintaining accuracy of CAde and CADv especially for reduced and ultra-low-dose CT protocols. New algorithms and techniques are continually being developed for further reduction of radiation dose resulting from chest CT examinations. Clinicians as well as academics should therefore follow closely any progress made with regard to these issues, and, where appropriate, clinically apply these improvements for optimizing the morphological and functional evaluation of pulmonary diseases in routine clinical practice.

## References

- [1] T. Kubo, P.J. Lin, W. Stiller, et al., Radiation dose reduction in chest CT: a review, *AJR Am. J. Roentgenol.* 190 (2) (2008) 335–343.
- [2] T. Kubo, Y. Ohno, H.U. Kauczor, H. Hatabu, Radiation dose reduction in chest CT-review of available options, *Eur. J. Radiol.* 83 (10) (2014) 1953–1961.
- [3] T. Kubo, Y. Ohno, J.B. Seo, et al., Securing safe and informative thoracic CT examinations-progress of radiation dose reduction techniques, *Eur. J. Radiol.* 86 (2017) 313–319.
- [4] L.L. Geyer, U.J. Schoepf, F.G. Meinel, et al., State of the art: iterative CT reconstruction techniques, *Radiology* 276 (2) (2015) 339–357.
- [5] A. Neroladaki, D. Botsikas, S. Boudabbous, C.D. Becker, X. Montet, Computed tomography of the chest with model-based iterative reconstruction using a radiation exposure similar to chest X-ray examination: preliminary observations, *Eur. Radiol.* 23 (2) (2013) 360–366.
- [6] J.W. Siegelman, M.P. Supanich, M.A. Gavrielides, Pulmonary nodules with ground-glass opacity can be reliably measured with low-dose techniques regardless of iterative reconstruction: results of a phantom study, *AJR Am. J. Roentgenol.* 204 (6) (2015) 1242–1247.
- [7] S. Seki, H. Koyama, Y. Ohno, et al., Adaptive iterative dose reduction 3D (AIDR 3D) vs. Filtered back projection: radiation dose reduction capabilities of wide volume and helical scanning techniques on area-detector CT in a chest phantom study, *Acta Radiol.* 57 (6) (2016) 684–690.
- [8] A. Huber, J. Landau, L. Ebner, et al., Performance of ultralow-dose CT with iterative reconstruction in lung cancer screening: limiting radiation exposure to the equivalent of conventional chest X-ray imaging, *Eur. Radiol.* 26 (10) (2016) 3643–3652.
- [9] V. Vardhanabhuti, C.L. Pang, S. Tenant, J. Taylor, C. Hyde, C. Roobottom, Prospective intra-individual comparison of standard dose versus reduced-dose thoracic CT using hybrid and pure iterative reconstruction in a follow-up cohort of pulmonary nodules-Effect of detectability of pulmonary nodules with lowering dose based on nodule size, type and body mass index, *Eur. J. Radiol.* 91 (2017) 130–141.
- [10] A. Ahmed, N. Verma, I. Barreto, T.L. Mohammed, Low-dose lung Cancer screening at an academic medical center: initial experience and dose reduction strategies, *Acad. Radiol.* 25 (8) (2018) 1025–1030.
- [11] M. Kachelriess, O. Watzke, W.A. Kalender, Generalized multi-dimensional adaptive filtering for conventional and spiral single-slice, multi-slice, and cone-beam CT, *Med. Phys.* 28 (4) (2001) 475–490.
- [12] M.K. Kalra, C. Wittram, M.M. Maher, et al., Can noise reduction filters improve low-radiation-dose chest CT images? Pilot study, *Radiology* 228 (1) (2003) 257–264.
- [13] T. Kubo, M. Nishino, A. Kino, et al., 3-dimensional adaptive raw-data filter: evaluation in low dose chest multidetector-row computed tomography, *J. Comput. Assist. Tomogr.* 30 (6) (2006) 933–938.
- [14] T. Kubo, Y. Ohno, S. Gautam, P.J. Lin, H.U. Kauczor, H. Hatabu, iLEAD Study Group, Use of 3D adaptive raw-data filter in CT of the lung: effect on radiation dose reduction, *AJR Am. J. Roentgenol.* 191 (4) (2008) 1071.
- [15] T. Kubo, Y. Ohno, D. Takenaka, iLEAD Study Group, et al., Standard-dose vs. low-dose CT protocols in the evaluation of localized lung lesions: capability for lesion characterization-iLEAD study, *Eur. J. Radiol. Open* 3 (2016) 67–73.
- [16] J. Ley-Zaporozhan, S. Ley, F. Krummenauer, Y. Ohno, H. Hatabu, H.U. Kauczor, Low dose multi-detector CT of the chest (iLEAD Study): visual ranking of different simulated mAs levels, *Eur. J. Radiol.* 73 (2) (2010) 428–433.
- [17] T. Kubo, Y. Ohno, M. Nishino, iLEAD Study Group, et al., Low dose chest CT protocol (50 mAs) as a routine protocol for comprehensive assessment of intrathoracic abnormality, *Eur. J. Radiol. Open* 3 (2016) 86–94.
- [18] K. Matsumoto, Y. Ohno, H. Koyama, et al., 3D automatic exposure control for 64-detector row CT: radiation dose reduction in chest phantom study, *Eur. J. Radiol.* 77 (3) (2011) 522–527.
- [19] M. Yanagawa, O. Honda, S. Yoshida, et al., Adaptive statistical iterative reconstruction technique for pulmonary CT: image quality of the cadaveric lung on standard- and reduced-dose CT, *Acad. Radiol.* 17 (10) (2010) 1259–1266.
- [20] F. Pontana, J. Pagniez, T. Flohr, et al., Chest computed tomography using iterative reconstruction vs filtered back projection (Part 1): evaluation of image noise reduction in 32 patients, *Eur. Radiol.* 21 (3) (2011) 627–635.
- [21] F. Pontana, A. Duhamel, J. Pagniez, et al., Chest computed tomography using iterative reconstruction vs filtered back projection (Part 2): image quality of low-dose CT examinations in 80 patients, *Eur. Radiol.* 21 (3) (2011) 636–643.
- [22] Y. Ohno, D. Takenaka, T. Kanda, et al., Adaptive iterative dose reduction using 3D processing for reduced- and low-dose pulmonary CT: comparison with standard-dose CT for image noise reduction and radiological findings, *AJR Am. J. Roentgenol.* 199 (4) (2012) W477–W485.
- [23] T. Yamashiro, T. Miyara, O. Honda, Investigators of Active Study Group, et al., Adaptive iterative dose reduction using three dimensional processing (AIDR3D) improves chest CT image quality and reduces radiation exposure, *PLoS One* 9 (8) (2014) e105735.
- [24] Y. Nagatani, M. Takahashi, K. Murata, investigators of Active Study Group, et al., Lung nodule detection performance in five observers on computed tomography (CT) with adaptive iterative dose reduction using three-dimensional processing (AIDR 3D) in a Japanese multicenter study: comparison between ultra-low-dose CT and low-dose CT by receiver-operating characteristic analysis, *Eur. J. Radiol.* 84 (7) (2015) 1401–1412.
- [25] M. Katsura, I. Matsuda, M. Akahane, et al., Model-based iterative reconstruction technique for ultralow-dose chest CT: comparison of pulmonary nodule detectability with the adaptive statistical iterative reconstruction technique, *Invest. Radiol.* 48 (4) (2013) 206–212.
- [26] F. Pontana, J. Pagniez, A. Duhamel, et al., Reduced-dose low-voltage chest CT angiography with Sinogram-affirmed iterative reconstruction versus standard-dose filtered back projection, *Radiology* 267 (2) (2013) 609–618.
- [27] A. Sauter, T. Koehler, A.A. Fingerle, et al., Ultra low dose CT pulmonary angiography with iterative reconstruction, *PLoS One* 11 (9) (2016) e0162716.
- [28] F. Pontana, A.S. Billard, A. Duhamel, et al., Effect of iterative reconstruction on the detection of systemic sclerosis-related interstitial lung disease: clinical experience in 55 patients, *Radiology* 279 (1) (2016) 297–305.
- [29] H.J. Lim, M.J. Chung, K.E. Shin, H.S. Hwang, K.S. Lee, The impact of iterative reconstruction in low-dose computed tomography on the evaluation of diffuse interstitial lung disease, *Korean J. Radiol.* 17 (6) (2016) 950–960.
- [30] K. Suzuki, A review of computer-aided diagnosis in thoracic and colonic imaging, *Quant. Imaging Med. Surg.* 2 (3) (2012) 163–176.
- [31] J.M. Goo, A computer-aided diagnosis for evaluating lung nodules on chest CT: the current status and perspective, *Korean J. Radiol.* 12 (2) (2011) 145–155.
- [32] M.O. Wielpütz, J. Wroblewski, M. Lederlin, et al., Computer-aided detection of artificial pulmonary nodules using an ex vivo lung phantom: influence of exposure parameters and iterative reconstruction, *Eur. J. Radiol.* 84 (5) (2015) 1005–1011.
- [33] Y. Ohno, K. Aoyagi, Q. Chen, et al., Comparison of computer-aided detection (CAde) capability for pulmonary nodules among standard-, reduced- and ultra-low-dose CTs with and without hybrid type iterative reconstruction technique, *Eur. J. Radiol.* 100 (2018) 49–57.
- [34] Y. Nomura, T. Higaki, M. Fujita, et al., Effects of iterative reconstruction algorithms on computer-assisted detection (CAD) software for lung nodules in ultra-low-dose CT for lung Cancer screening, *Acad. Radiol.* 24 (2) (2017) 124–130.
- [35] National Lung Screening Trial Research Team, D.R. Aberle, A.M. Adams, C.D. Berg, et al., Reduced lung-cancer mortality with low-dose computed tomographic screening, *N. Engl. J. Med.* 365 (5) (2011) 395–409.
- [36] Z. Saghir, A. Dirksen, H. Ashraf, et al., CT screening for lung cancer brings forward early disease. The randomised Danish lung cancer screening trial: status after five annual screening rounds with low-dose CT, *Thorax* 67 (4) (2012) 296–301.
- [37] N. Horeweg, E.T. Scholten, P.A. de Jong, et al., Detection of lung cancer through low-dose CT screening (NELSON): a prespecified analysis of screening test performance and interval cancers, *Lancet Oncol.* 15 (12) (2014) 1342–1350.
- [38] D.M. Xu, H. Gietema, H. de Koning, et al., Nodule management protocol of the NELSON randomised lung cancer screening trial, *Lung Cancer* 54 (2) (2006) 177–184.
- [39] C.I. Henschke, D.F. Yankelevitz, R. Yip, et al., Writing Committee for the I-ELCAP Investigators. Lung cancers diagnosed at annual CT screening: volume doubling times, *Radiology* 263 (2) (2012) 578–583.
- [40] Q. Li, M.A. Gavrielides, B. Sahiner, K.J. Myers, R. Zeng, N. Petrick, Statistical analysis of lung nodule volume measurements with CT in a large-scale phantom study, *Med. Phys.* 42 (7) (2015) 3932.
- [41] Y. Ohno, A. Yaguchi, T. Okazaki, et al., Comparative evaluation of newly developed model-based and commercially available hybrid-type iterative reconstruction methods and filter back projection method in terms of accuracy of computer-aided volumetry (CADv) for low-dose CT protocols in phantom study, *Eur. J. Radiol.* 85 (8) (2016) 1375–1382.
- [42] H.O. Coxson, J. Mayo, S. Lam, G. Santyr, G. Parraga, D.D. Sin, New and current clinical imaging techniques to study chronic obstructive pulmonary disease, *Am. J. Respir. Crit. Care Med.* 180 (2009) 588–597.
- [43] E.A. Hoffman, D.A. Lynch, R.G. Barr, E.J. van Beek, G. Parraga, IWPF Investigators. Pulmonary CT and MRI phenotypes that help explain chronic pulmonary obstruction disease pathophysiology and outcomes, *J. Magn. Reson. Imaging* 43 (2016) 544–557.
- [44] E.A. Park, J.M. Goo, S.J. Park, et al., Chronic obstructive pulmonary disease: quantitative and visual ventilation pattern analysis at xenon ventilation CT performed by using a dual-energy technique, *Radiology* 256 (3) (2010) 985–997.
- [45] M. Remy-Jardin, J.B. Faivre, F. Pontana, F. Molinari, N. Tacelli, J. Remy, Thoracic applications of dual energy, *Semin. Respir. Crit. Care Med.* 35 (2014) 64–73.
- [46] Y. Ohno, T. Yoshikawa, D. Takenaka, et al., Xenon-enhanced CT using subtraction CT: basic and preliminary clinical studies for comparison of its efficacy with that of dual-energy CT and ventilation SPECT/CT to assess regional ventilation and

- pulmonary functional loss in smokers, *Eur. J. Radiol.* 86 (2017) 41–51.
- [47] M. Mishima, Y. Oku, K. Kawakami, et al., Quantitative assessment of the spatial distribution of low attenuation areas on X-ray CT using texture analysis in patients with chronic pulmonary emphysema, *Front. Med. Biol. Eng.* 8 (1) (1997) 19–34.
- [48] Y. Nakano, N.L. Müller, G.G. King, et al., Quantitative assessment of airway remodeling using high-resolution CT, *Chest* 122 (6 Suppl) (2002) 271S–275S.
- [49] M. Hasegawa, Y. Nasuhara, Y. Onodera, et al., Airflow limitation and airway dimensions in chronic obstructive pulmonary disease, *Am. J. Respir. Crit. Care Med.* 173 (12) (2006) 1309–1315.
- [50] H. Koyama, Y. Ohno, Y. Yamazaki, et al., Quantitative bronchial luminal volumetric assessment of pulmonary function loss by thin-section MDCT in pulmonary emphysema patients, *Eur. J. Radiol.* 81 (2) (2012) 384–388.
- [51] H. Koyama, Y. Ohno, M. Nishio, et al., Iterative reconstruction technique vs filter back projection: utility for quantitative bronchial assessment on low-dose thin-section MDCT in patients with/without chronic obstructive pulmonary disease, *Eur. Radiol.* 24 (8) (2014) 1860–1867.
- [52] M. Nishio, S. Matsumoto, Y. Ohno, et al., Emphysema quantification by low-dose CT: potential impact of adaptive iterative dose reduction using 3D processing, *AJR Am. J. Roentgenol.* 199 (3) (2012) 595–601.
- [53] T. Yamashiro, T. Miyara, O. Honda, et al., Iterative reconstruction for quantitative computed tomography analysis of emphysema: consistent results using different tube currents, *Int. J. Chron. Obstruct. Pulmon. Dis.* 10 (2015) 321–327.
- [54] Y. Ohno, H. Koyama, K. Matsumoto, et al., Differentiation of malignant and benign pulmonary nodules with quantitative first-pass 320-detector row perfusion CT versus FDG PET/CT, *Radiology* 258 (2) (2011) 599–609.
- [55] Y. Ohno, M. Nishio, H. Koyama, et al., Comparison of quantitatively analyzed dynamic area-detector CT using various mathematic methods with FDG PET/CT in management of solitary pulmonary nodules, *AJR Am. J. Roentgenol.* 200 (6) (2013) W593–W602.
- [56] Y. Ohno, M. Nishio, H. Koyama, et al., Solitary pulmonary nodules: comparison of dynamic first-pass contrast-enhanced perfusion area-detector CT, dynamic first-pass contrast-enhanced MR imaging, and FDG PET/CT, *Radiology* 274 (2) (2015) 563–575.
- [57] Y. Ohno, H. Koyama, Y. Fujisawa, et al., Dynamic contrast-enhanced perfusion area detector CT for non-small cell lung cancer patients: influence of mathematical models on early prediction capabilities for treatment response and recurrence after chemoradiotherapy, *Eur. J. Radiol.* 85 (1) (2016) 176–186.
- [58] Y. Ohno, Y. Fujisawa, H. Koyama, et al., Dynamic contrast-enhanced perfusion area-detector CT assessed with various mathematical models: its capability for therapeutic outcome prediction for non-small cell lung cancer patients with chemoradiotherapy as compared with that of FDG-PET/CT, *Eur. J. Radiol.* 86 (2017) 83–91.
- [59] Y. Ohno, Y. Fujisawa, N. Sugihara, et al., Dynamic contrast-enhanced perfusion area-detector CT: preliminary comparison of diagnostic performance for N stage assessment with FDG PET/CT in non-small cell lung Cancer, *AJR Am. J. Roentgenol.* 209 (5) (2017) W253–W262.
- [60] Y. Ohno, H. Koyama, Y. Fujisawa, et al., Hybrid Type iterative reconstruction method vs. filter back projection method: Capability for radiation dose reduction and perfusion assessment on dynamic first-pass contrast-enhanced perfusion chest area-detector CT, *Eur. J. Radiol.* 85 (1) (2016) 164–175.