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FULL PAPER

Assessment of chest CT at CTDI_{vol} less than 1 mGy with iterative reconstruction techniques

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Objective: To assess the image quality of chest CT reconstructed with image-based iterative reconstruction (SafeCT; MedicVision®, Tirat Carmel, Israel), adaptive statistical iterative reconstruction (ASIR; GE Healthcare, Waukesha, WI) and model-based iterative reconstruction (MBIR; GE Healthcare, Waukesha, WI) techniques at CT dose index volume (CTDI_{vol}) <1 mGy.

Methods: In an institutional review board-approved study, 25 patients gave written informed consent for acquisition of three reduced dose (0.25-, 0.4- and 0.8-mGy) chest CT after standard of care CT (8 mGy) on a 64-channel multidetector CT (MDCT) and reconstructed with SafeCT, ASIR and MBIR. Two board-certified thoracic radiologists evaluated images from the lowest to the highest dose of the reduced dose CT series and subsequently for standard of care CT.

Results: Out of the 182 detected lesions, the missed lesions were 35 at 0.25, 24 at 0.4 and 9 at 0.8 mGy with

SafeCT, ASIR and MBIR, respectively. The most missed lesions were non-calcified lung nodules (NCLNs) 25/112 (<5 mm) at 0.25, 18/112 (<5 mm) at 0.4 and 3/112 (<4 mm) at 0.8 mGy. There were 78%, 84% and 97% lung nodules detected at 0.25, 0.4 and 0.8 mGy, respectively regardless of iterative reconstruction techniques (IRTs). Most mediastinum structures were not sufficiently seen at 0.25–0.8 mGy.

Conclusion: NCLNs can be missed in chest CT at CTDI_{vol} of <1 mGy (0.25, 0.4 and 0.8 mGy) regardless of IRTs. The most lung nodules (97%) were detected at CTDI_{vol} of 0.8 mGy. The most mediastinum structures were not sufficiently seen at 0.25–0.8 mGy.

Advances in knowledge: NCLNs can be missed regardless of IRTs in chest CT at CTDI_{vol} of <1 mGy. The performance of ASIR, SafeCT and MBIR was similar for lung nodule detection at 0.25, 0.4 and 0.8 mGy.

INTRODUCTION

The reduced dose (RD) CT examinations can be associated with higher image noise which may affect the diagnostic confidence, particularly with filtered back projection (FBP) images.^{1–3} Prior studies have demonstrated improved image quality with iterative reconstruction techniques (IRTs) at RDs.^{4–13} In order to achieve a RD CT, users need to modify the scan parameters and then apply IRTs to improve the image quality. Prior RD studies have assessed CT dose index volume (CTDI_{vol}) of <1 mGy with IRTs to demonstrated uncompromised lung nodule detection.^{7–9}

In this study, we acquired chest CT at CTDI_{vol} of <1 mGy and assessed with three IRTs: adaptive statistical iterative reconstruction (ASIR; GE Healthcare, Waukesha, WI), model-based iterative reconstruction (MBIR or Veo®; GE Healthcare, Waukesha, WI) and SafeCT (MedicVision®, Tirat Carmel, Israel). Two of these techniques require scan projection or sinogram data and are vendor specific (ASIR

and MBIR). The third technique, SafeCT, is a vendor neutral, image-based technique. In our study, standard of care ASIR technique was used as the reference standard. The reference standard in our study was a considerably low ASIR blending with FBP (ASIR 40).

In our study, we evaluated the diagnostic performance of IRTs for chest CT at three different reduced radiation dose levels <1 mGy (CTDI_{vol} of 0.25, 0.4 and 0.8 mGy). Along with lesion detection, we assessed the conspicuity of the lesions at 0.25, 0.4 and 0.8 mGy. The purpose of our study was to assess the image quality of chest CT reconstructed with ASIR, MBIR and SafeCT at CTDI_{vol} of <1 mGy.

METHODS AND MATERIALS

Patients

Health Insurance Portability and Accountability Act-compliant prospective clinical study was approved by the Human Research Committee of our institutional review board.

Patients undergoing either enhanced (17 patients) or unenhanced (6 patients) standard of care chest CT were included in the study. The patients were selected prospectively and non-consecutively regardless of gender, race or clinical indication. The most common clinical indications for standard of care chest CT were neoplasm or cancer follow-up, lung nodule follow-up, shortness of breath and interstitial lung disease. Written informed consent was obtained from 25 patients (18 males and 7 females) for acquisition of an additional three RD chest CT series immediately after acquisition of their standard of care CT. The three RD chest CT image series were acquired at mean CTDI_{vol} of 0.25 ($\text{RD}_{0.25}$), 0.4 ($\text{RD}_{0.4}$) and 0.8 mGy ($\text{RD}_{0.8}$) (total additional dose <1 mSv). Inclusion criteria of our study were hemodynamically stable adult patients (age 18 years or more) who were able to read and speak in English, provide written consent, able to follow simple instructions, hold their breath for at least 10 s and remain still during scanning. Hemodynamically unstable patients, patients undergoing urgent CT or with known contrast allergies, and females who were pregnant or trying to get pregnant were excluded from the study.

All study subjects were given detailed information (study design, methods and risks) about the study before obtaining their written informed consent. They were also informed that additional radiation dose from RD CT would be <1 mSv. They were also informed that there will be no compensation or benefits for participation in the study. Weight, height and demographic information of all patients were recorded, and body mass index (BMI , kg m^{-2}) was also calculated. For all patients, anteroposterior (AP) and lateral (LAT) diameters were measured from axial images. The effective diameter was calculated as the square root of the product of AP and LAT diameters for estimating size-specific dose estimation (SSDE).¹⁴

Image acquisition

All chest CT examinations were performed on a 64-channel single-source multidetector CT scanner (Discovery CT750 HD, GE Healthcare, Waukesha, WI). Patients were isocentered in the gantry and asked to raise their arms above their head. AP and LAT planning radiographs were acquired at 80 kV and 40 mAs. Standard of care chest CT was planned, and three RD CT series were duplicated. The scan length of the RD CT series was kept identical to that of standard of care CT. Standard of care CT was acquired with automatic exposure control technique (AutomA 3D, GE Healthcare, Waukesha, WI). Three RD CT series were acquired at fixed tube current with the following parameters 0.25 (80 and 10), 0.4 (100 and 15) and 0.8 mGy (120 kV and 20 mA). Standard of care chest CT was acquired with or without administration of contrast medium (iopamidol 300 mg%; Bracco Diagnostics, Princeton, NJ). All patients with contrast study received 65–80 cm^3 of intravenous contrast for chest CT based on their weight (<90 kg: 65 cm^3 ; >90 kg: 80 cm^3). For RD CT series, no additional contrast medium was administered. The time delay between the first RD CT series and standard of care CT was 7–10 s. The three RD CT series were randomized and acquired in three separate breath-holds within 30 s of standard of care CT. Other scanning parameters were held constant including gantry rotation time of 0.5 s, 39.37-mm table feed per gantry rotation, helical acquisition mode, 64×0.625 -mm

detector configuration, reconstruction section thickness of 2.5 mm and reconstruction section interval of 2.5 mm. The combined dose-length product of all three RD CT series was <70 mGy cm (<1 mSv).¹⁵ The SSDE was calculated by multiplying CTDI_{vol} with conversion factor for effective diameter obtained from the American Association of Physicists in Medicine Task Group (TG) 204 lookup table.^{14,15}

Image reconstruction

At RDs, FBP images are often associated with greater image noise and artefact. The physical basis of ASIR, MBIR and SafeCT techniques has been described in prior publications.^{4–16} ASIR is a hybrid IRT, which blends with FBP at different percentage levels.⁴ MBIR is a more complex and pure IRT which does not blend with FBP. MBIR takes about 30–60 min for reconstruction of a single CT series.⁵ SafeCT is an image-based technique which uses FBP images for generating images with improved image quality.⁶

Sinogram data of RD chest CT series were reconstructed with FBP, ASIR [two settings: 70% (SS70) and 90% (SS90) blending with FBP] and MBIR (only one setting available at the time of writing manuscript). In contradiction to most prior studies, we used current standard of care, ASIR (at 40% strength), at standard of care radiation dose, as our reference standard. RD FBP images were exported to offline SafeCT server for reconstruction at two settings of SafeCT (CH0 and CH1). The ASIR and FBP images were reconstructed at section thickness of 2.5 mm using detailed kernel. SafeCT images were generated from 2.5-mm FBP images. The MBIR images were generated at section thickness of 0.625 mm (since direct reconstruction of 2.5-mm images was not possible at the time of the study) with standard reconstruction kernel (the only kernel possible with MBIR at the time of the study) and reformatted to 2.5 mm on image processing workstation for comparison. All images were assessed with reconstructed section thickness and a section increment of 2.5 mm as per the clinical standard of care in our department. Patient identifiers were removed from all images. All 368 image series [1 standard of care ASIR (SS40); RD (0.26, 0.4 and 0.8 mGy)—2 ASIR (SS70 and SS90); 2 SafeCT (CH0 and CH1); and 1 MBIR for 23 patients, $n = 23 + (3 \times 5 \times 23) = 368$ series] were assessed for subjective image quality.

Subjective image quality evaluation

Subjective image evaluation of all CT series was performed on digital imaging and communications in medicine-complaint workstation (ClearCanvas Inc., Toronto, ON). A 2-megapixel resolution monitor was used to display images for evaluation. Two board-certified thoracic radiologists (RM with 11 years of experience and EF with 7 years of experience) performed image evaluation of all CT series. In one training session, radiologists were trained for image evaluation in CT examinations of two patients out of the total 25 patients collected for the study. These two patients were excluded from study analysis. The final sample size was 23 patients (mean age 63 ± 13 years, mean weight 80 ± 18 kg; 18 males, 5 females). The values of subjective image quality evaluation represent the averaged of score reported by Reader 1 and Reader 2.

Subjective image quality evaluation was performed for each of the CT series independently. Evaluation was performed from the lowest to the highest dose levels of the RD series and subsequently for standard of care chest CT. First, RD_{0.25} CT image series were displayed for evaluation of lesion detection, lesion conspicuity and visibility of normal lung and mediastinal structures. We recorded non-calcified lung nodules (NCLNs) (≥ 2 mm). Small and subtle NCLNs were evaluated if any in all five lobes of the lung. Each IRT (ASIR, SafeCT or MBIR) was evaluated in blinded, randomized and independent manner. The RD ASIR, SafeCT and MBIR images were displayed separately and in random order for lesion detection and image quality evaluation. Then, image evaluation of RD_{0.4} was performed, followed by RD_{0.8} in a similar manner. Finally, standard of care CT images were evaluated to record “true-positive” lesions and findings.

All clinically important lesions and their location (anatomical location, image series and number), number, size and attenuation were assessed both in the lung and mediastinal window. Lesion conspicuity (for at least one lung nodule based on the ease of assessing the lesions relative to standard of care CT examinations) and visibility of normal lung (subsegmental bronchi and lung fissures) and mediastinum structures were assessed on a 3-point scale relative to the standard of care (reference) CT examination (1 = sufficient, 2 = limited and 3 = unacceptable image quality unacceptable for clinical diagnostic performance). Subjective assessment of artefacts was performed on three-point scale (1 = no effect, 2 = limited effect and 3 = significant effect on diagnostic confidence). All chest CT series were displayed at window width (WW) and window level (WL) settings (lungs: 1500 WW, -600 WL; mediastinum: 350 WW, 50 WL). Radiologists were allowed to change the window width and levels as per their preferences.

Objective image noise

CT numbers and objective image noise were measured on the image-processing workstation for standard of care and all RD IRTs. The objective measurements were carried out in thoracic aorta and trachea for patients. A circular region of interest (ROI) was placed on the descending thoracic aorta and tracheal air without touching the wall. The area and location for ROI were kept constant by duplication of the same ROI on different CT image series (ASIR, SafeCT and MBIR).

Statistical analysis

Statistical software (SPSS® v. 21; IBM Corp., New York, NY; formerly SPSS Inc., Chicago, IL) was used to analyze data. A Wilcoxon signed-rank test was used to analyze subjective image quality score of lesion conspicuity and visibility of normal structures. The sensitivity of lesion detection was calculated for all dose levels (0.25, 0.4 and 0.8 mGy). A Fisher's exact test was used to assess the statistical differences among the sensitivity of lesion detection at different dose levels. Paired Student's *t*-tests were performed to compare the CTDI_{vol} among standard of care and RD CT examinations. Analysis of variance tests were performed to compare objective image noise and CT number. The *p*-value of 0.05 with confidence interval of 95% was considered statistically significant. Separate kappa tests were performed to assess the interobserver variability for lesion detection and

subjective image quality. The strength of agreement was categorized based on the kappa values (poor <0.2, fair 0.2–0.4, moderate 0.4–0.6, good 0.6–0.8 and substantial 0.8–1).

RESULTS

Radiation dose

The mean ($\pm$ standard deviation) age, weight, BMI and effective diameter of patients were 63 ± 13 years, 80 ± 18 kg, 27 ± 6 kg m⁻² and 31 ± 4 cm, respectively. There was no significant difference between male and female patients for the above mentioned attributes. The mean CTDI_{vol}, dose-length product, SSDE and estimated effective dose for the three standard of care RD CT series (0.25, 0.4 and 0.8 mGy) are summarized in Table 1.

Objective image quality

Objective image noise (SD) and CT number [Hounsfield unit (HU)] are summarized in Table 2. Regardless of IRTs objective image noise was significantly lower in RD_{0.8} as compared with RD_{0.25} and RD_{0.4} ($p < 0.001$) (Table 2). In addition, objective image noises (in the descending thoracic aorta and tracheal air) were lower for MBIR than for ASIR and SafeCT at RD_{0.25}, RD_{0.4} and RD_{0.8} ($p < 0.001$). Incidentally, we noted significant difference in the measured CT number on RD_{0.25} MBIR images in the descending thoracic aorta (not in tracheal air) as compared with other IRTs ($p = 0.002$). This may have resulted from differential handling of data at extremely reduced radiation dose levels.

True-positive lesions on standard of care chest CT

Out of 182 detected lesions, there were NCLNs ($n = 112$, 2–15 mm), ground-glass opacities (GGOs) ($n = 21$), calcified granulomas ($n = 8$), pleural thickening ($n = 7$), emphysema ($n = 5$), pleural effusions (PIEs) ($n = 5$), consolidations ($n = 6$), thyroid nodules (TNs) ($n = 3$), hiatal hernias ($n = 2$), pericardial effusion ($n = 1$) and 15 other lesions (including interstitial lung diseases, tree-in-bud opacities, mosaic attenuation, lymph nodes, lung mass, lung cysts and chest wall mass). Lesions detected by both readers at this dose level were regarded as the standard of reference for the task of lesion detection.

Lesion detection at CT dose index volume of 0.25 mGy

Missed lesions and pseudolesions are summarized in Table 3. There were 35/182 missed lesions including 25/112 NCLNs (< 5 mm), 4/21 GGOs (< 8 mm), 3/3 TNs (< 3 mm) and 3/5 PIEs (small) (Figure 1) at 0.25 mGy regardless of IRTs (ASIR, SafeCT and MBIR). The average 78% (87/112) of lung nodules were detected at 0.25 mGy regardless of IRTs. At 0.25 mGy, the sensitivity of total (overall) lesion detection and lung nodule detection were 84% and 82%, respectively (Table 4). There were 10 pseudolesions, including NCLNs ($n = 7$) and GGOs ($n = 3$), all measuring < 4 mm on all IRTs.

Subjective image quality at CT dose index volume of 0.25 mGy

The conspicuity of lung nodules and GGOs was sufficient only for 2/18 and 1/10 lesions, respectively, on RD IRT images compared with standard of care CT images ($p < 0.001$). Diagnostic confidence of mediastinal lymph nodes and pericardium was sufficient only for 1/23 and 2/23 patients regardless of IRTs ($p < 0.001$).

Table 1. Mean ($\pm$ standard deviation) CT dose index volume (CTDI_{vol}), dose-length product (DLP), size-specific dose estimation (SSDE), estimated effective dose (EED) of standard of care and three reduced dose (RD) CT series

	CTDI _{vol} , mGy	DLP, mGy cm	SSDE, mGy	EED, mSv
Standard of care CT	8 $\pm$ 3.4	295 $\pm$ 136	9 $\pm$ 3	4.1 $\pm$ 2
RD _{0.25}	0.25 $\pm$ 0.03	10 $\pm$ 1	0.3 $\pm$ 0	0.1 $\pm$ 0
RD _{0.4}	0.4 $\pm$ 0.05	15 $\pm$ 2	0.48 $\pm$ 0.1	0.2 $\pm$ 0
RD _{0.8}	0.8 $\pm$ 0.07	31 $\pm$ 3	0.99 $\pm$ 0.2	0.4 $\pm$ 0
<i>p</i> -value	<0.001	<0.001	<0.001	<0.001

(Figure 2). Visibility of the subsegmental bronchial walls, lung fissures, thyroid, pleura, heart and pericardium was limited for most patients. Artefacts had significant effect on the diagnostic confidence of lung and mediastinal structures on all RD_{0.25} image data sets. There was no significant difference ($p = 0.9$) for lesion detection and subjective image quality among enhanced and unenhanced CT examinations. Interobserver agreement among two radiologists was moderate ($k = 0.46$ – 0.58) for both lesion detection and image quality assessment.

Lesion detection at CT dose index volume of 0.4 mGy

Missed lesions and pseudolesions are summarized in Table 3. There were 24/182 missed lesions including 18/112 NCLNs

(<5 mm), 2/21 GGOs (<4 mm), 2/3 TNs (<3 mm) and 2/5 PLEs (small, Figure 1) on all ASIR, SafeCT and MBIR images at 0.4 mGy (Table 3). The 84% (94/112) lung nodules were detected at 0.4 mGy regardless of IRTs. There were six false-positive (pseudo) lesions which included lung nodules ($n = 4$) and GGOs ($n = 2$) of sizes <4 mm. At 0.4 mGy, the sensitivity of total lesion detection and lung nodule detection were 88% and 86%, respectively (Table 4).

Subjective image quality at CT dose index volume of 0.4 mGy

The conspicuity of lung nodules and GGOs was sufficient only for 5/18 and 1/12 lesions at RD_{0.4}, respectively, regardless of IRTs ($p < 0.001$). Visibility of mediastinal lymph nodes and

Table 2. Mean Hounsfield unit (HU) values and objective image noise (SD) $\pm$ standard deviation of standard of care and reduced dose CT series (0.25, 0.4 and 0.8 mGy) for iterative reconstruction techniques [SafeCT (MedicVision®, Tirat Carmel, Israel), adaptive statistical iterative reconstruction (ASIR; GE Healthcare, Waukesha, WI) and model-based iterative reconstruction (MBIR; GE Healthcare)]

		ASIR40	ASIR70	ASIR90	SafeCT-CH0	SafeCT-CH1	MBIR	<i>p</i> -value
Descending thoracic aorta								
Standard of care CT	HU	206 $\pm$ 97						
	SD	16 $\pm$ 5						
0.25 mGy	HU		147 $\pm$ 92	146 $\pm$ 91	146 $\pm$ 91	144 $\pm$ 91	55 $\pm$ 101	0.003
	SD		55 $\pm$ 13	49 $\pm$ 13	59 $\pm$ 13	48 $\pm$ 12	40 $\pm$ 15	<0.001
0.4 mGy	HU		148 $\pm$ 58	148 $\pm$ 58	147 $\pm$ 58	147 $\pm$ 57	138 $\pm$ 58	0.9
	SD		40 $\pm$ 10	34 $\pm$ 9	43 $\pm$ 11	34 $\pm$ 9	18 $\pm$ 7	<0.001
0.8 mGy	HU		131 $\pm$ 52	131 $\pm$ 52	131 $\pm$ 52	130 $\pm$ 52	130 $\pm$ 53	0.9
	SD		27 $\pm$ 9	22 $\pm$ 8	29 $\pm$ 10	21 $\pm$ 8	16 $\pm$ 4	<0.001
Tracheal air								
Standard of care CT	HU	−938 $\pm$ 21						
	SD	25 $\pm$ 13						
0.25 mGy	HU		−814 $\pm$ 123	−814 $\pm$ 124	−815 $\pm$ 125	−814 $\pm$ 131	−757 $\pm$ 146	0.5
	SD		67 $\pm$ 22	66 $\pm$ 21	65 $\pm$ 21	60 $\pm$ 22	28 $\pm$ 12	<0.001
0.4 mGy	HU		−933 $\pm$ 36	−933 $\pm$ 36	−934 $\pm$ 36	−935 $\pm$ 37	−916 $\pm$ 42	0.4
	SD		52 $\pm$ 18	51 $\pm$ 17	47 $\pm$ 17	40 $\pm$ 18	23 $\pm$ 12	<0.001
0.8 mGy	HU		−947 $\pm$ 22	−947 $\pm$ 22	−946 $\pm$ 23	−947 $\pm$ 22	−941 $\pm$ 23	0.8
	SD		37 $\pm$ 12	36 $\pm$ 12	33 $\pm$ 15	27 $\pm$ 13	18 $\pm$ 12	<0.001

CH0 and CH1 are two settings of SafeCT.

Table 3. Missed lesions and false-positive lesions at 0.25, 0.4 and 0.8 mGy with SafeCT (MedicVision®, Tirat Carmel, Israel), adaptive statistical iterative reconstruction (GE Healthcare, Waukesha, WI) and model-based iterative reconstruction (GE Healthcare)

	0.25 mGy	0.4 mGy	0.8 mGy
Missed lesions			
Non-calcified lung nodules	25 (<5 mm)/112	18 (<5 mm)/112	3 (<4 mm)/112
GGOs	4 (<8 mm)/21	2 (<4 mm)/21	2 (<4 mm)/21
Thyroid nodules	3 (<3 mm)/3	2 (<3 mm)/3	2 (<3 mm)/3
Pleural effusions	3 (small)/5	2 (small)/5	2 (small)/5
False-positive lesions			
Non-calcified lung nodules	7 (<4 mm)	4 (<4 mm)	none
GGOs	3 (<4 mm)	2 (<4 mm)	none

GGOs, ground-glass opacities.

pericardium was sufficient for 4/23 patients on ASIR, 5/23 patients on SafeCT and 7/23 patients on MBIR images at RD_{0.4} ($p < 0.001$) (Figure 2). The subsegmental bronchial walls, lung fissures, thyroid, pleura, heart and pericardium were limited for diagnostic confidence on RD IRTs. Artefacts had minimal effect on diagnostic confidence of lung structures and significant effect on the mediastinal structures. Lesion detection and subjective image quality among patients with enhanced and unenhanced CT examinations were not significantly different ($p = 0.9$). Interobserver agreement between two readers was good (0.65–0.78) for lesion detection and was fair to moderate ($k = 0.35$ –0.56) for image quality assessment.

Lesion detection at CT dose index volume of 0.8 mGy

Missed lesions and pseudolesions are summarized in Table 3. Subjective image quality scores for RD_{0.8} are summarized in Table 5. There were 9/182 missed lesions including 3/112 NCLNs (<4 mm) (Figure 3), 2/21 GGOs (<4 mm), 2/3 TNs (<3 mm) and 2/5 PLEs (small) (Figure 2) regardless of IRTs (Table 3). The 97% (109/112) lung nodules were detected at 0.8 mGy regardless of IRTs. There were no false-positive lesions at this dose level. At 0.8 mGy, the sensitivity of total lesion detection and lung nodule detection were 95% and 97%, respectively. The lesion detection was

Figure 1. Transverse chest CT images of a 71-year-old male (body mass index of 34 kg m^{-2}) acquired at standard of care (SOC) and reduced doses (RDs) and reconstructed with different iterative reconstruction techniques. Small left pleural effusion (arrows) was depicted optimally on SD but was missed on RD CT [adaptive statistical iterative reconstruction (ASIR; GE Healthcare, Waukesha, WI)] at 0.25, 0.4 and 0.8 mGy. CTDI, CT dose index.

Table 4. Sensitivity of total lesion detection and lung nodule detection at 0.25, 0.4 and 0.8 mGy with iterative reconstruction techniques [adaptive statistical iterative reconstruction (GE Healthcare, Waukesha, WI), model-based iterative reconstruction (GE Healthcare) and SafeCT (MedicVision®, Tirat Carmel, Israel)]

	Total lesion detection (total 182 lesions) (95% CI)	Fisher's exact test	Lung nodule detection (total 112 nodules) (95% CI)	Fisher's exact test
0.25 mGy	84% (78–89%)	0.25 vs 0.4 mGy, $p = 0.2$	82% (74–88%)	0.25 vs 0.4 mGy, $p = 0.4$
0.4 mGy	88% (83–92%)	0.4 vs 0.8 mGy, $p = 0.017$	86% (79–92%)	0.4 vs 0.8 mGy, $p = 0.002$
0.8 mGy	95% (91–98%)	0.8 vs 0.25 mGy, $p < 0.001$	97% (93–99%)	0.8 vs 0.25 mGy, $p < 0.001$
	<5 mm (total 149 lesions)		<5 mm (total 101 nodules)	
0.25 mGy	84% (78–89%)	0.25 vs 0.4 mGy, $p = 0.4$	80% (72–87%)	0.25 vs 0.4 mGy, $p = 0.4$
0.4 mGy	87% (83–92%)	0.4 vs 0.8 mGy, $p = 0.01$	85% (77–91%)	0.4 vs 0.8 mGy, $p = 0.002$
0.8 mGy	95% (91–98%)	0.8 vs 0.25 mGy, $p < 0.001$	97% (21–99%)	0.8 vs 0.25 mGy, $p < 0.001$

CI, confidence interval.

significantly greater at 0.8 mGy than at 0.4 and 0.25 mGy ($p = 0.002$) (Table 4).

Subjective image quality at CT dose index volume of 0.8 mGy

Diagnostic confidence of lung nodules was sufficient for 13/18 patients with ASIR and SafeCT and for 11/18 patients with

MBIR (Figure 4). There was no significant difference in the BMI of patients with sufficient diagnostic confidence of lung nodules compared with limited diagnostic confidence ($p = 0.8$). Diagnostic confidence of GGOs was sufficient only for 2/15 patients with ASIR, SafeCT and MBIR images ($p < 0.001$). Subsegmental bronchial walls were sufficiently seen in 22/23 patients ($p = 0.3$). Mediastinal lymph

Figure 2. Transverse chest CT images of a 65-year-old male (body mass index of 30.5 kg m^{-2}) acquired at standard of care (SOC) and RD doses and reconstructed with different iterative reconstruction techniques. Mediastinal lymph nodes (arrows) were depicted optimally on SD and RD CT [adaptive statistical iterative reconstruction (ASIR; GE Healthcare, Waukesha, WI)] at 0.8 mGy. The lymph node delineation was limited at 0.4 mGy. At 0.25 mGy, none of the readers detected these lymph nodes. CTDI, CT dose index; MBIR, model-based iterative reconstruction.

Table 5. Summary of subjective image quality score of different iterative reconstruction techniques [adaptive statistical iterative reconstruction (ASIR; GE Healthcare, Waukesha, WI), SafeCT (MedicVision®, Tirat Carmel, Israel) and model-based iterative reconstruction (MBIR; GE Healthcare)] at 0.8mGy

	ASIR 70/90			SafeCT CH0/CH1			MBIR		
	Sufficient	Limited and unacceptable	p-value	Sufficient	Limited and unacceptable	p-value	Sufficient	Limited and unacceptable	p-value
Reader 1									
Subsegmental bronchi	20/23	3/23	0.083	23/23		0.9	22/23	1/23	0.3
GGO	2/15	13/15	0.001	2/15	13/15	0.001		15/15	<0.001
Non-calcified lung nodules	12/18	6/18	0.001	12/18	6/18	0.001	9/18	9/18	0.005
Mediastinal lymph nodes	10/23	13/23	<0.001	11/23	12/23	0.001	18/23	5/23	0.025
Pericardium	2/23	21/23	<0.001	2/23	21/23	<0.001	3/23	20/23	<0.001
Reader 2									
Subsegmental bronchi	21/23	2/23	0.16	23/23		0.9	21/23	2/23	0.16
GGOs	5/7	2/7	0.16	5/7	2/7	0.16	6/7	1/7	0.3
Non-calcified lung nodules	14/15	1/15	0.3	14/15	1/15	0.3	13/15	2/15	0.16
Mediastinal lymph nodes	18/23	5/23	0.025	19/23	4/23	0.046	22/23	1/23	0.3
Pericardium	18/23	5/23	0.025	19/23	4/23	0.046	21/23	2/23	0.16

GGOs, ground-glass opacities.

ASIR columns represent the average score of ASIR70 and ASIR90. SafeCT columns represent the average scores of two settings of SafeCT, CH0 and CH1. Empty boxes represent no data for that point [score of sufficient/limited and unacceptable (seen by number of lesions or patients/total number of lesions or patients) for diagnostic confidence].

Figure 3. Transverse chest CT images of a 56-year-old male (body mass index of 32 kg m^{-2}) acquired at standard of care (SOC) (a) and reduced doses (RDs), and reconstructed with different iterative reconstruction techniques (IRTs). Non-calcified lung nodules ($<4 \text{ mm}$) (arrows) were depicted optimally on standard dose (SD) and missed on RD CT regardless of IRTs [adaptive statistical iterative reconstruction (ASIR; GE Healthcare, Waukesha, WI), SafeCT (MedicVision®, Tirat Carmel, Israel) and model-based iterative reconstruction (MBIR; GE Healthcare)] at 0.25 mGy (b), 0.4 mGy (c) and 0.8 mGy (d). CTDI, CT dose index.

nodes were optimally seen in 14/23 patients with ASIR, 15/23 patients with SafeCT and 20/23 patients with MBIR (Figure 2). Visibility of the thyroid, heart, pericardium, and oesophagus was limited on IRTs. Interobserver agreement among two radiologists was excellent (0.89) for lesion detection and was fair to good ($k = 0.35\text{--}0.75$) for image quality assessment.

DISCUSSION

Our study revealed differences in evaluability of different lung and mediastinum findings at CTDI_{vol} of $<1 \text{ mGy}$ with different IRTs. In our study, missed lesions and pseudolesions were noted at 0.25, 0.4 and 0.8 mGy with IRTs. Most missed lesions ($<5 \text{ mm}$) and pseudolesions (4–5 mm) were NCLNs at radiation doses of 0.25 and 0.4 mGy, regardless of the IRTs (ASIR,

Figure 4. Transverse chest CT images of a 71-year-old male (body mass index of 34 kg m^{-2}) acquired at standard of care (SOC) and reduced doses (RDs) and reconstructed with different iterative reconstruction techniques. Non-calcified lung nodules (5–6 mm, arrows) were depicted optimally on standard of care and RD CT [adaptive statistical iterative reconstruction (ASIR; GE Healthcare, Waukesha, WI), SafeCT (MedicVision®, Tirat Carmel, Israel) and model-based iterative reconstruction (MBIR; GE Healthcare)] at 0.25 mGy. CTDI, CT dose index.

SafeCT or MBIR). Pseudolesions were not noticed on 0.8 mGy. Most NCLNs (109/112) (≥ 2) were detected and sufficient for diagnostic confidence at 0.8 mGy with IR. There were 78%, 84% and 97% NCLNs detected at 0.25, 0.4 and 0.8 mGy regardless of IRTs, respectively. Also, the sensitivity lung nodule detection was significantly greater at 0.8 mGy (97%) than at 0.4 mGy (86%) and 0.25 mGy (82%). At 0.8 mGy, three missed lung nodules were all < 4 mm in size. A visibility of GGOs was also suboptimal at RD CT with IRTs. From evaluation of airway perspective, subsegmental bronchi could only be seen optimally at 0.8 mGy ($p = 0.9$) but not at 0.25 and 0.4 mGy ($p < 0.001$). Most mediastinum structures were not sufficiently seen at 0.25–0.8 mGy. Also, we could not find significant differences for the lesion detection and subjective image quality for lung parenchymal and non-vascular mediastinal lesions among enhanced and unenhanced CT examinations on RD CT examinations ($p = 0.9$).

Prior studies have reported improved lung nodule detection on IRTs at RDs.^{16–18} Yamada et al¹⁶ assessed the diagnostic confidence of MBIR and FBP images for lung nodule detection at 0.3 mGy with FBP images as reference standard at 4 mGy. The results of the study showed that MBIR improves the detectability of NCLNs compared with FBP images at 0.3 mGy. In addition, patients in this study were smaller with mean BMI of 22 kg m^{-2} . In another study, Katsura et al¹⁷ used ASIR as a reference standard (1.8 mGy) for comparison with RD MBIR images (0.4 mGy) for lung nodule detection (≥ 4 mm). The authors reported that lung nodule detectability was not affected on RD MBIR images compared with ASIR images at 1.8 mGy. However,

the reference CTDI_{vol} (1.8 mGy) was lower than the CTDI_{vol} (8 mGy) used in our study for the standard of reference. Patients in this study were also smaller (mean weight 59 kg) than in our study (80 kg). Neroladaki et al¹⁸ assessed the diagnostic image quality of RD MBIR images (0.16 mSv) to the higher dose FBP images (2.7 mSv). The authors concluded that RD MBIR showed similar sensitivity for detection of non-calcified pulmonary nodules compared with FBP images at higher dose. On the other hand, more micronodules (≤ 3 mm) were detected on MBIR images at RD than on FBP images at 2.7 mGy.

We do not have definitive explanation for false-positive lesions or pseudolesions seen in RD CT performed at 0.25 and 0.4 mGy in our study. However, it is possible that the radiologists may have been biased by the presence of increased noise or artefacts at such RDs. Similar to previous studies, we noted a dramatic improvement in image noise with MBIR compared with other IRTs at all dose levels. However, improved noise with MBIR did not translate into improved lung nodule detectability or lower number of pseudolesions on these images compared with other IRTs. Although, evaluation of mediastinal structures such as lymph nodes was better on MBIR-RD CT images, the difference was not statistically significant. Also, we conclude that current IRTs (ASIR, SafeCT and MBIR) cannot provide sufficient diagnostic confidence for assessing most mediastinal abnormalities at CTDI_{vol} of ≤ 0.8 mGy ($p < 0.001$). The lack of improvement in chest findings even with improvement in image noise with different IRTs suggest that image noise is not a very relevant objective image quality predictor in chest CT.

MBIR images at 80 kV had significantly lower HU (55 ± 101) than at 100 kV (138 ± 58) and 120 kV (130 ± 53) ($p < 0.01$) in the descending thoracic aorta. This may be related to excessive denoising of the images associated with MBIR-based image reconstruction algorithm. Future studies should thoroughly assess the cause and effect of this finding prior to the use of MBIR-based HU numbers at such reduced radiation doses.

Implication of our study is that few NCLNs (<4 mm) can be missed at CTDI_{vol} of 0.8 mGy. However, lung nodules missed were small in size (<4 mm) and their clinical significance is not similar to larger lung nodules (>5 mm). The Fleischner Society recommends no follow-up for low-risk patients (≥ 35 years of age) for lung nodules ≤ 4 mm. For high-risk patients (history of smoking or other known risk factors), the Fleischner Society recommends CT scan at 12 months, following which the stable lung nodules do not require further follow-up.¹⁹ The British Thoracic Society does not recommend nodule follow-up for lung nodules <5 mm (or 80 mm^3).²⁰ In our study, the performance of ASIR, SafeCT and MBIR images were similar for nodule detection at 0.25, 0.4 and 0.8 mGy. In our study, the tested IRTs (ASIR, MBIR and SafeCT) had lesser effect on diagnosis than in scanning patients with variable sizes using a fixed CT dose, variable kVp and reconstruction kernels.

There are few limitations in our study that must be considered. First, the study population was small comprising 23 patients.

Second, owing to difference in the time of acquisition between standard of care and RD image series, there were differences in the contrast enhancement between standard of care and RD images which could have resulted into suboptimal image quality for some vascular lesions with IRTs. RD CT series were acquired at fixed tube current as opposed to the most commonly used AEC technique. The use of fixed kV and fixed mA to achieve targeted low-dose CT may have resulted in inadvertently lower image quality in some larger patients, which likely contributed to limited or suboptimal performance of IRTs in some patients. Different reconstruction kernels were applied to generate MBIR (standard kernel) and ASIR and SafeCT (detail kernel) images. This could have affected subjective image quality evaluation of these images, although at the time of the study, only standard reconstruction kernel could be applied to MBIR images. Although, standard of care and RD CT were performed over identical scan range (the start and end positions), the lack of control over identical X-ray tube angular position can lead to some misalignment. Blinding of images was difficult due to distinct appearance of MBIR images as compared with other IRTs.

In conclusion, NCLNs can be missed on chest CT at CTDI_{vol} of <1 mGy (0.25, 0.4 and 0.8 mGy) regardless of IRTs. The most lung nodules (97%) were detected at CTDI_{vol} of 0.8 mGy. The most mediastinum structures were not sufficiently seen at 0.25–0.8 mGy.

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