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THE ROLE OF IMAGING IN SCREENING SPECIAL FEATURE: FULL PAPER

Screening for lung cancer using sub-millisievert chest CT with iterative reconstruction algorithm: image quality and nodule detectability

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Objective: To investigate the image quality and nodules detectability using ultra-low dose (ULD) protocol with iterative model reconstruction (IMR) algorithm when compared to routine low dose (LD) chest CT in lung cancer screening.

Methods: Chest CT scans were acquired using a 256-slice scanner for 300 subjects. The scan protocol for the ULD group was 120 kVp/17 mAs while for the LD group was 120 kVp/30 mAs. All images were reconstructed with filtered back projection (FBP), hybrid iterative reconstruction (HIR) and IMR algorithms. Effective dose was recorded. Image quality assessments were performed by two radiologists. SD of CT attenuation was measured as objective image noise. The number of non-calcified nodules detected in both groups with different reconstruction algorithms were calculated and compared.

Results: The effective dose of ULD group (0.67 ± 0.08 mSv) was about 44% reduced compared with LD group (1.20 ± 0.08 mSv) ($p < 0.01$). IMR improved image quality and reduced image noise significantly than HIR and FBP in both groups (all, $p < 0.01$). IMR enabled a higher number of nodule detected compared to FBP and HIR in both LD and ULD groups, especially for solid nodules less than 4 mm.

Conclusion: IMR may improve the diagnostic accuracy of ULD CT lung screening with potential nodule detectability improvement.

Advances in knowledge: IMR enables significant reduction of the image noise and improvement of image quality in sub-mSv (66% reduction) chest scans.

INTRODUCTION

Lung cancer is the leading cause of cancer death worldwide. Its 5-year survival rate after diagnosis is merely 15.6%, despite the advances in surgical, medical and radio-therapeutic treatments.¹ In other words, lung cancer has a good prognosis only if detected at a very early tumour stage. Recently, American National Lung Screening Trial (NLST) has suggested that as compared with chest radiography, low-dose CT (LDCT) screening exhibited more sensitivity in early-stage lung cancer detecting and may contribute to a reduction in mortality from lung cancer,^{2,3} which indicates that LDCT has the potential to be widely used in lung cancer screening. However, the LDCT scans performed in NLST involves an approximate dose of 2 mSv, whereas the full-dose chest CT scans, used for nodules follow-up in the major diagnostic, may involve a dose up to 8 mSv, which may present an independent risk of lung cancer and remains a

concern of CT lung screening.⁴ Thus, it is valuable to find an approach that can further reduce radiation dose in CT scans meanwhile maintaining the image quality and diagnostic accuracy.

With the development of CT techniques, iterative reconstruction (IR) algorithms were introduced to help reduce the quantum noise associated with the filtered back projection (FBP) algorithm thus to offer better image quality with less radiation dose,⁵⁻⁷ however, most of the commercially available and widely used IR techniques are hybrid iterative reconstruction (HIR) algorithms which have been reported with certain limits in image noise and artefacts suppression.⁸ In recent years, a new model-based IR algorithm, iterative model reconstruction (IMR), has been reported to enable further dose reduction and image quality improvement in chest CT.⁹ Thus, we assumed that IMR has the potential to help for further dose reduction in

Table 1. Comparisons of patient characteristics and radiation doses between groups

Characteristics	LD group	ULD group	<i>p</i>
Age in years, mean $\pm$ SD	56.4 $\pm$ 6.8	55.4 $\pm$ 7.2	0.462
Males/females, <i>n/n</i>	42/89	42/97	0.196
Body weight in kg, mean $\pm$ SD	67.3 $\pm$ 8.7	66.2 $\pm$ 9.8	0.115
Body mass index in kg m ⁻² , mean $\pm$ SD	24.9 $\pm$ 2.6	24.6 $\pm$ 2.5	0.729
Smokers, <i>n/N</i> (%)	42/130 (32)	45/139 (32)	0.891
Passive smokers, <i>n/N</i> (%)	69/130 (53)	63/139 (45)	0.989
Occupational expose, <i>n/N</i> (%)	13/130 (10)	10/139 (7)	0.549
Effective dose in mSv, mean $\pm$ SD	1.20 $\pm$ 0.08	0.67 $\pm$ 0.08	0.003 ^a

LD, low dose; ULD, ultra-low dose.

^aSignificant difference between groups.

LDCT scans used for lung cancer screening, and designed this study to investigate the image quality and nodule detectability of the ultra-low dose (ULD)-CT scans with IMR algorithm by comparing with the routine LDCT scans with FBP and HIR algorithms, to determine whether ULD-CT scans with the use of IMR could achieve diagnostic acceptable in lung cancer screening.

METHODS AND MATERIALS

Study design and population

This prospective study received institutional review board approval; prior informed consent was obtained from all patients. We prospectively enrolled 300 consecutive patients who underwent chest CT during a 4-week period in July and August 2013. All had suspected or confirmed risk of lung cancer. The inclusion criteria were (1) at the age of 40 to 74; (2) Smokers with a smoking history of more than 10 pack-years, including those who had quit smoking but not more than 10 years; (3) Passive smokers; (4) Occupationally exposed to asbestos, beryllium, uranium and radon. Exclusion criteria included (1) confirmed histologic diagnosis of lung cancer; (2) had previous surgery or radiotherapy in chest; (3) with current respiratory symptoms; (4) pregnancy or lactation status; (5) severe chronic life-threatening disease with a life expectancy less than 6 months and (6) body mass index (BMI) larger than 30 kg m⁻².

In the first 2 weeks, 150 patients underwent chest CT using routine low dose protocols (LD-group); 20 of them were excluded due

to large BMI and previous surgery in chest and severe chronic disease. In the second 2 weeks, 150 patients underwent CT using a further reduced radiation dose protocol (ULD group) and 11 of them were excluded due to BMI over 30 kg m⁻² and severe chronic disease.

CT acquisition and image reconstruction

All CT examinations were performed on a 256-slice CT scanner (Brilliance iCT; Philips Healthcare, Cleveland, OH). The data acquisition parameters were as follows: detector configuration, 128 $\times$ 0.625 mm; beam pitch, 0.99; rotation time, 0.5 s; field of view, 350 mm; slice thickness, 1.0 mm; slice increment, 0.5 mm, matrix 512 $\times$ 512; tube voltage, 120 kVp; tube current time products, 30 mAs for LD group and 17 mAs for ULD group. Both raw data from LD and ULD groups were reconstructed with FBP, HIR (iDose⁴, Level 4, Philips Healthcare, Cleveland, OH) and IMR algorithms, respectively, using identical parameters of 1.0 mm thickness at 0.5 mm increment, and a sharp reconstruction filter (Y-sharp) for lung structures as well as a standard reconstruction filter (B) for mediastinum structures.

Image quality assessment

All images were reviewed and interpreted on a commercially available workstation (Intellispace portal 5.0, Philips Healthcare, Cleveland, OH). Objective image assessment was performed in lung window as follows: A 200 mm² region of interest was placed within the ascending aorta, the CT value (in Hounsfield units) of the region of interest was recorded and its SD was used as image noise. Measurements were performed three times and expressed as the mean value. On the other hand, two thoracic radiologists who were not aware of any image reconstruction settings with 3 and 7 years of experience were asked to perform subjective image assessment independently. Images were displayed in the lung window setting (window width, 1400 HU; window level, -450 HU) and in the mediastinum window setting (window width, 360 HU; window level, 60 HU) for evaluation. The image quality was evaluated for the following structures: lesion margins, visibility of small structures, noise, artefacts and diagnostic confidence. It was determined using a five-point rating scale to image quality (5 = excellent image quality with very good demarcation of structures, noise free; 4 = good image quality with good demarcation of structures, slight increase in noise or artefact; 3 = moderate image quality with reduction of sharpness, moderate increase in noise or artefact; 2 = poor image quality with blurred demarcation of structures, severe increase in noise or artefact; 1 = unassessable). When they disagreed, a third thoracic radiologist with more than 15 years of experience was asked to adjudicate the differences in order to obtain a consensus score.

Table 2. Objective image quality comparison

	LD group			ULD group		
	FBP	iDose ⁴	IMR	FBP	iDose ⁴	IMR
CT attenuation (HU)	47.6 $\pm$ 7.7	47.9 $\pm$ 7.3	47.4 $\pm$ 7.0	47.6 $\pm$ 7.5	46.8 $\pm$ 7.0	47.4 $\pm$ 7.3
Noise (HU)	62.2 $\pm$ 13.1	37.4 $\pm$ 7.4	12.3 $\pm$ 1.5	82.1 $\pm$ 19.5	46.9 $\pm$ 9.1	14.4 $\pm$ 1.9

FBP, filtered backprojection; HU, Hounsfield units; IMR, iterative model reconstruction; LD, low dose; ULD, ultra-low dose.

Figure 1. Comparison of image noise among LD and ULD groups with different reconstruction algorithms. FBP, filtered backprojection; IMR, iterative model reconstruction; LD, low dose; ULD, ultra-low dose.

Nodule detection

All non-calcified nodules were recorded and classified as solid and ground-glass opacity categories. The solid nodules were further classified by long-axis diameters in axial plane to three groups (less than 4 mm, 4–8 mm and greater than 8 mm), as well as ground-glass opacity nodules to two groups (less than 5 mm and not less than 5 mm).¹⁰ The number of nodules detected in both LD and ULD images with different reconstruction algorithms were recorded and compared.

Radiation dose analysis

Total dose-length product, which represented the total absorbed dose for all the scans, were recorded from CT dose report. Estimated effective dose was calculated from dose-length product using a conversion factor of 0.014.¹¹

Statistical analysis

All continuous values were expressed as mean $\pm$ SD. To compare the invariable relationships of the patients' demographic and pathological characteristics between groups, we used χ^2 test when the predictor was categorical and independent t -test when the predictor was quantitative. The objective image noise were compared with ANOVA analysis; if there was a significant difference, pairwise comparisons would be performed with student-Newman-Keuls (SNK) test. The subjective scores were compared by using the Friedman test; if there was a significant difference, pairwise comparisons would be performed with the Steel–Dwass test. Interobserver agreement for subjective image scores was measured using Kappa test. The number of detected nodules

Figure 2. Image quality score for lung (a) and mediastinum (b) structures in LD and ULD groups. Only IMR images enabled a diagnostic acceptable image quality in both groups for both lung and mediastinum structures (red line, score ≥ 3). FBP, filtered backprojection; IMR, iterative model reconstruction; LD, low dose; ULD, ultra-low dose.

were compared by using χ^2 test. All statistical analyses were performed with commercially available software (SPSS v. 20.0; SPSS Inc, Ill, Excel 2013, Microsoft, Chicago, IL). A value of $p < 0.05$ was considered a statistical significant difference.

RESULTS

Patients demographics and radiation dose

The results of patient demographics and radiation dose are summarized in Table 1. There was no significant difference between the two groups with respect to age, gender, BMI and the clinical characteristics including history of smoking and occupational expose. The effective dose of ULD group was significantly reduced compared to LD group ($1.20 \text{ mSv} \pm 0.08$, $0.67 \text{ mSv} \pm 0.08$, $p = 0.003$).

Table 3. Subjective image quality score

	LD group			ULD group		
	FBP	iDose ⁴	IMR	FBP	iDose ⁴	IMR
Lung	3.91 ± 0.76	4.57 ± 0.52	4.82 ± 0.29	3.42 ± 0.65	4.11 ± 0.47	4.70 ± 0.42
Mediastinum	2.19 ± 0.81	3.51 ± 0.92	4.56 ± 0.58	1.58 ± 0.62	3.03 ± 0.91	4.14 ± 0.69

FBP, filtered backprojection; IMR, iterative model reconstruction; LD, low dose; ULD, ultra-low dose.

Table 4. Number of detected nodules using different algorithms in two dose groups

		SN (<4 mm)	SN (4–8 mm)	SN (>8 mm)	GGN (<5 mm)	GGN (≥5 mm)
LD	FBP	40	39	0	3	11
	iDose ⁴	50	49	0	5	13
	IMR	52 ^a	51	0	6	13
ULD	FBP	37	31	1	12	31
	iDose ⁴	48	38	1	14	31
	IMR	54	36	1	15	32

FBP, filtered backprojection; GGN, ground-glass opacity nodules; IMR, iterative model reconstruction; LD, low dose; SN, solid nodules; ULD, ultra-low dose.

^aSignificant difference in detected nodule numbers compared to FBP using χ^2 test.

Objective image assessment

There was significant difference for all comparison combinations among the different dose groups with different reconstruction algorithms, except LD-IMR vs ULD IMR ($p = 0.124$). No difference was found in CT attenuation among all six series ($p = 0.883$). IMR images in both groups showed significant noise reduction compared to FBP and iDose⁴. Details are demonstrated in Table 2 and Figure 1.

Subjective image assessment

There was no significant disagreement between the two radiologists ($\kappa = 0.57$ – 0.87), except the ULD-FBP images for lung structures ($\kappa = 0.38$). All the subjective image quality scores for each series were summarized in Table 3 and Figure 2. IMR significantly improved subjective image quality compared to iDose⁴ and FBP, especially for mediastinum structures in ULD

group. There was significant difference in lung structure scores for all comparison combinations among all six series, except for LD-IMR vs ULD IMR images, and LD-iDose⁴ vs ULD-iDose⁴ (both, $p > 0.05$). Significant differences were found in mediastinum structure scores for all comparison combinations among the six series.

Nodule detection

The number of nodules detected in both groups with different reconstruction settings were summarized in Table 4. IMR enabled a higher number of nodules detected in both LD and ULD groups for all kinds of nodules, except for solid nodules between 4 and 8 mm. No difference was found in the number of nodules detected among the three algorithms in both groups for different kinds of nodules, except between IMR and FBP in ULD groups for solid nodules less than 4 mm (54 vs 37 , $p = 0.048$).

Figure 3. Transverse chest CT images of a 52-year-old female (BMI = 18.29 kg m^{-2}) who had two GGOs in the apicoposterior segment of left upper lobe (arrow); the larger one ($32 \times 26 \text{ mm}$) had a solid component. (a) FBP image of LD group; (b) iDose⁴ image of LD group; (c) IMR image of LD group; (d) iDose⁴ image of stand-dose (120 kVp/200 mAs) in 15 days later from the same patient. There was no difference of lesion detection among different algorithms (especially for iMR) in low-dose CT and stand-dose CT. BMI, body mass index; FBP, filtered back projection; GGOs, ground-glass opacities; IMR, iterative model reconstruction; LD, low dose.

Figure 4. Transverse chest CT images of a 54-year-old female (BMI = 21.48 kg m⁻²) who had a nodule with calcification in the left lobe of thyroid gland (arrow) in LD group. Images were obtained with (a) FBP, (b) iDose⁴ and (c) IMR. The diagnostic confidence of IMR image was much higher than iDose⁴ and FBP. The lesion was apparent in IMR image, and available in iDose⁴ image, but missed in FBP image. BMI, body mass index; FBP, filtered back projection; IMR, iterative model reconstruction; LD, low dose.

DISCUSSION

The LDCT scans performed in our study involves a further dose reduction of 40% than the screening CT performed in NLST study (1.2 mSv vs 2 mSv). Diagnostic image quality of both lung and mediastinum structures were achieved in the LDCT scans with the use of iDose⁴ and IMR. IMR offered further objective noise reduction and better subjective image quality scores compared to iDose⁴, while FBP exhibited increased noise and failed in diagnostic image quality of mediastinum structures. Nodule detectability was found not significantly associated with reconstruction algorithms in LDCT scans (Figures 3 and 4). Moreover, ULD-CT scans performed in our study reduced the radiation dose to 0.67 mSv, which was approximately 44% further reduction than LDCT. In ULD-CT scans, only IMR enabled diagnostic image quality of both lung and mediastinum structures, neither FBP nor iDose⁴ enabled diagnostic image quality of mediastinum. In addition, IMR was found superior than FBP in nodule detectability for solid nodules less than 4 mm in ULD group (Figures 5 and 6).

To our knowledge, IMR is an advanced IR algorithm that differs from hybrid IR algorithms for its use of system optics to model the acquisition process as accurately as possible in addition to photon and noise statistics.¹² In theory, IMR enables lower image noise and better low-contrast detectability thus to optimize dose protocol further. Previous study¹³ demonstrated that with the use of IMR, diagnostic image quality can be achieved on sub-mSv (0.9 mSv) chest scans with even better delineation of lesion margins. Our study observed similar results that IMR enabled superior image quality compared to iDose⁴ and FBP, especially for mediastinum structures at ULD scans. Moreover, we observed in ULD scans, iDose⁴ enabled diagnostic acceptable image quality in lung but failed in mediastinum, and similarly, in LD scans, FBP enabled diagnostic image quality in lung but failed in mediastinum.

This indicates that it is more difficult for LD scans to achieve diagnostic image quality in mediastinum compared to in lung and further noise reduction is needed for diagnostic image

Figure 5. Transverse chest CT images of a 55-year-old female (BMI = 20.43 kg m⁻²) who had a GGO (3 × 3 mm) in the apicoposterior segment of left upper lobe (arrow) in the ULD group. (a) FBP image; (b) iDose⁴ image; (c) IMR image from the same patient. This lesion was visible on IMR and iDose⁴ image, but missed on FBP image in this study. As compared with images a and b image c shows reduced artefacts and higher diagnosis confidence. BMI, body mass index; FBP, filtered back projection; GGO, ground-glass opacity; IMR, iterative model reconstruction; ULD, ultra-low dose.

Figure 6. Transverse chest CT through the ascending aorta in a 61-year-old female (BMI = 26.37 kg m⁻²) with mediastinum lymph node enlargement (arrow). Images were obtained with FBP (a), iDose⁴ (b) and IMR (c) in ULD group. Note the excellent depiction of mediastinum lymph node on the IMR image (score 5), compared with FBP (score 3) and iDose⁴ (score 4). SNR on IMR image is 3.32 dB, showing higher than those on FBP (0.55 dB) and iDose⁴ (0.89 dB) in this patient. BMI, body mass index; FBP, filtered back projection; IMR, iterative model reconstruction; SNR, signal-noise ratio; ULD, ultra-low dose.

quality of mediastinum images. The main reason could be that it is easier for image quality of mediastinum to be deteriorated by substantial increased image noise at LD conditions, considering there is relatively lower contrast between different tissues in mediastinum as compared to lung.¹⁴

However, to find suspicious nodules by observing lung structures plays the main role in lung screening chest scans, which indicates that ULD scans with iDose⁴ may enable the key demands of lung screening scans by providing diagnostic image quality of lung structures, despite it failed in diagnostic image quality of mediastinum structures. As to the lung nodule detection, we found that there was no significant difference in the number of nodules detected between IMR and iDose⁴ in both LD and ULD scans for each kind of nodule, while FBP detected lower number of solid nodules with a diameter less than 4 mm in ULD scans. We attribute this to inadequate image quality of FBP for both lung and mediastinum structures in ULD scans. Moreover, diagnostic information acquired by observation of mediastinum structures such as lymph node and pleural is necessary and in favour of evaluating other complications in lung screening chest scans.^{15,16} Hence, it is of practical importance because sub-mSv chest CT with IMR are able to help reduce the risk of radiation exposure without any compromising of diagnostic information including both lung and mediastinum information for patients who undergo lung screening scans.

In addition, it is worth to note that the LDCT protocol combined with iDose⁴ was practiced as reference standard instead of full-dose protocol with FBP reconstruction in our study, considering iDose⁴, the hybrid IR, has already been used routinely with

robust reconstruction speed, as well as the hybrid IRs such as iDose⁴, sinogram-affirmed iterative reconstruction, and adaptive statistical iterative reconstruction were observed yielding diagnostic image quality in LD chest CT with similar dose setting at around 1 mSv.^{13,17,18}

Our study has several limitations. First, a relatively small number of positive cases were reviewed in the study. Second, the pathological results have not come out for the positive cases. There was no gold standard to verify lesion detection accuracy of all the algorithms. Third, protocols with fixed tube current products were used in our study for stable scan dose; automatic tube current modulation techniques can be used in further study to maintain the image noise at consistent for patients with different sizes. Fourth, the overweight subjects (BMI ≥30 kg m⁻²) were excluded; further studies will need to investigate the effect of IMR in chest CT on obese patients.

CONCLUSION

In conclusion, both IMR and iDose⁴ enables diagnostic image quality in 40% reduction LD chest scans; meanwhile, IMR enables significant reduction of the image noise and improvement of image quality in sub-mSv (66% reduction) chest scans. IMR with significant better image quality may emphasize its potential to better nodule detectability in ULD scans and help the sub-mSv protocols become the clinical routine in lung cancer screening.

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