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FULL PAPER

Low-dose CT screening using hybrid iterative reconstruction: confidence ratings of diagnoses of simulated lesions other than lung cancer

¹N SAKAI, BSc, RT, ¹H YABUUCHI, MD, PhD, ²M KONDO, MSc, RT, ³Y MATSUO, MD, PhD, ³T KAMITANI, MD, ³M NAGAO, MD, PhD, ³M JINNOUCHI, MD, ³M YONEZAWA, MD, ¹T KOJIMA, BSc, RT, ¹Y YANO, MSc, RT and ³H HONDA, MD, PhD

¹Department of Health Sciences, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

²Division of Radiological Technology, Department of Medical Technology, Kyushu University Hospital, Fukuoka, Japan

³Department of Clinical Radiology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Address correspondence to: Dr Hidetake Yabuuchi

E-mail: h-yabu@med.kyushu-u.ac.jp

Objective: To evaluate the confidence ratings of diagnoses of simulated lesions other than lung cancer on low-dose screening CT with hybrid iterative reconstruction (IR).

Methods: Simulated lesions (emphysema, mediastinal masses and interstitial pneumonia) in a chest phantom were scanned by a 320-row area detector CT. The scans were performed by 64-row and 160-row helical scans at various dose levels and were reconstructed by filtered back projection (FBP) and IR. Emphysema, honeycombing and reticular opacity were visually scored on a four-point scale by six thoracic radiologists. The ground-glass opacity as a percentage of total lung volume (%GGO), CT value and contrast-to-noise ratio (CNR) of mediastinal masses were calculated. These scores and values were compared between FBP and IR. Wilcoxon's signed-rank test was used ($p < 0.05$). Interobserver agreements were evaluated by κ statistics.

Results: There were no significant differences in visual assessment. Interobserver agreement was almost perfect. CT values were almost equivalent between FBP and IR, whereas CNR with IR was significantly higher than that with FBP. %GGO significantly increased at low-dose levels with FBP; however, IR suppressed the elevation.

Conclusion: The confidence ratings of diagnoses of simulated lesions other than lung cancer on low-dose CT screening were not degraded with hybrid IR compared with FBP.

Advances in knowledge: Hybrid IR did not degrade the confidence ratings of diagnoses on visual assessment and differential diagnoses based on CT value of mediastinal masses, and it showed the advantage of higher GGO conspicuity at low-dose level. Radiologists can analyse images of hybrid IR alone on low-dose CT screening for lung cancer.

INTRODUCTION

Recently, there have been discussions regarding the efficacy of lung cancer screening using low-dose CT. For example, the National Lung Screening Trial research team's¹ randomized clinical trial comparing the efficacies of chest radiographs and low-dose CT. They found that lung cancer screening using low-dose CT reduces lung cancer-related mortality in groups at high risk of lung cancer. With regard to dose-reduction techniques in CT, a new method of image reconstruction, iterative reconstruction (IR), has been developed and is now widely used for various clinical purposes. This technique has an advantage over the filtered back projection (FBP) method of image reconstruction in that FBP contains quantum noise; IR reduces this quantum noise by repeatedly comparing projection data, including quantum noise or primary reconstruction image data, with ideal anatomical and statistical models.²⁻⁴

Neroladaki et al⁵ recently reported that the rate of pulmonary-nodule detection is maintained when using ultra-low-dose CT combined with IR in the range of exposure dose similar to that when using posterior-to-anterior and lateral chest radiographs (radiation dose, 0.16 ± 0.006 mSv). Hence, IR should be applied to lung cancer screening images obtained using low-dose CT.

When screening for lung cancer, it is important to be able to detect other chest pathologies, such as emphysema, mediastinal mass and interstitial pneumonia. Identification of emphysema and interstitial pneumonia has particular clinical significance, because these conditions have been shown to be associated with an increased risk of lung cancer.^{6,7} Therefore, chest CT and pulmonary function tests are required in patients with either emphysema or interstitial pneumonia; both to monitor disease severity

and to screen for lung cancer. Mediastinal masses have also been incidentally detected during lung cancer screening by CT.⁸ Contrast-enhanced CT or MRI are usually performed subsequently in order to characterize the mediastinal mass.⁹

Thus far, there have been studies carried out investigating the ability of low-dose CT combined with IR to detect pulmonary diseases such as ground-glass opacity (GGO) nodules,¹⁰ emphysema and interstitial disease.¹¹ The efficacy of the technique with regard to the quantification of emphysema has also been investigated.¹² However, it has been difficult to evaluate detection levels or diagnostic performance using various doses in *in vivo* studies because of the considerable radiation exposure. Moreover, to the authors' knowledge, there have been no studies reporting the accurate evaluation of the CT values of mediastinal masses or the confidence ratings of diagnoses of emphysema, reticular opacity and honeycombing. Thus, the purposes of our study were to assess the quality of images used for the diagnosis of simulated lesions other than lung cancer that were obtained during lung cancer screening using low-dose CT with hybrid IR and to evaluate confidence ratings of diagnoses of these images.

METHODS AND MATERIALS

Phantom and simulated lesions

We used a Chest Phantom N-1TM (Kyoto Kagaku, Kyoto, Japan) to make simulated lesions (emphysema; mediastinal masses with cystic, solid and fat components; and interstitial pneumonia including GGO, reticular opacity and honeycombing).¹³ Figure 1 shows photographs of the simulated lesions, while Figure 2 depicts CT images of the simulated lesions. To simulate emphysematous lesions, we used two balloons fashioned from the finger of a medical glove (maximum diameters: 13 and 18 mm). Mediastinal masses (maximum diameter: 19 mm) were simulated using hollow plastic spheres containing water to represent cysts, water-diluted contrast agent with a CT value of 100 Hounsfield units (HU) to imitate a solid component and oil to simulate fatty component. With regard to interstitial pneumonia, GGO (long axis: 60 mm, short axis: 40 mm, mean CT value: -887 HU) was simulated using a cotton ball that had been made firm using wood glue, while honeycombing (long axis: 43 mm, short axis: 30 mm, mean CT value: -1006 HU) and reticular opacity (long axis: 37 mm, short axis: 30 mm, mean CT value: -930 HU) were simulated using sponges of different coarseness that had been made using wood glue. These simulated interstitial pneumonia lesions were slightly different from those of previous studies, wherein investigators have used silk, gauze or sponges soaked with contrast media or glue.¹⁴⁻¹⁶ Therefore, we had a thoracic radiologist, who did not take any other part in the study, to compare the CT images of our simulated lesions with

those of clinical cases. This radiologist confirmed that the images obtained from each lesion were comparable to clinical findings. Simulated lesions of emphysema, mediastinal masses and interstitial pneumonia were set at the apex of the lung, the anterior mediastinum and the lower lung, respectively. All simulated lesions, with the exception of GGO lesions were set in the left lung of the phantom.

Image acquisition

The simulated lesions were scanned using a 320-detector-row area detector CT (Aquilion ONETM/ViSION Edition; Toshiba Medical Systems Co., Ltd, Tochigi, Japan). We performed 64-detector-row helical scans (13, 9.7, 6.4, 3.2 and 1.1 mGy) and 160-detector-row helical scans (12.9, 9.7, 6.5, 3.2, 1.4 and 0.9 mGy), and reconstructed the images using FBP and hybrid IR (both standard and strong). A commercially available IR system, the Adaptive iterative dose reduction 3DTM (AIDR 3D; Toshiba Medical Systems Co., Ltd) was used for IR. Each scan was repeated six consecutive times. We reconstructed those images that were used to calculate GGO volume as a percentage of total lung volume (%GGO) using sections of 0.5-mm thickness in order to avoid partial volume effects. All other images were reconstructed using 2-mm thickness, because they were used for lung cancer screening. Other scan parameters were as follows: peak tube voltage, 120 kV; gantry speed, 0.5 s/rotation; pitch factor, 0.828 or 0.869; reconstruction interval, 0.5 mm. All data sets were reconstructed using a standard reconstruction algorithm (FC13; Toshiba Medical Systems Co., Ltd).

Visual assessment

In order to avoid observers stress caused by reading too many samples, we selected the images obtained from the first scan at each dose level (64-helical and 160-helical scans) and using each reconstruction algorithm (FBP and hybrid IR) for visual assessment. The data sets for visual assessments of emphysema, honeycombing and reticular opacity were randomized in order and were independently evaluated by six thoracic radiologists (range of experience in thoracic radiology: 6-23 years, average: 15.2 years). All CT images used for visual assessment were presented to the radiologists as a stack of images and were displayed using the lung (level, -600 HU; width, 1500 HU) window setting. Each observer underwent a training session before the reading session. During the training session, images of each lesion at the highest exposure level (FBP, 13 and 12.9 mGy) and the lowest exposure level (FBP, 1.1 and 0.9 mGy) were presented to each observer, and all observers were told where the abnormal findings existed, as well as what kind of abnormality they represented. Thereby, we ensured that all observers understood the location and type of abnormalities presented. The

Figure 1. Simulated lesions. (a) Emphysema. (b) Mediastinal masses (left, cystic; middle, solid; right, fat component). (c) Interstitial pneumonia (left, ground-glass opacity; middle, reticular opacity; right, honeycombing).

Figure 2. CT findings of simulated lesions. The CT images show simulated emphysema (a); mediastinal masses with solid (b), cystic (c, left) and fat (c, right) components; and interstitial pneumonia including ground-glass opacity (d), reticular opacity (e) and honeycombing (f). Images (b) and (c) are displayed using the mediastinum window setting (window level: 0 HU, window width, 400 HU). All others were displayed using the lung window setting (window level: -600 HU, window width: 1500 HU).

observers were then asked whether the lesion could be diagnosed on the basis of a four-point scale. This was carried out separately for each lesion. The scale was as follows:

- (1) four points: structure of lesion clearly visible with complete diagnosis
- (2) three points: structure of lesion visible with degrading image quality but without restriction for diagnosis
- (3) two points: structure of lesion visible, with degrading image quality and uncertainties about diagnosis
- (4) one point: diagnosis was difficult.

The images obtained at the maximum dose for this study (13 or 12.9 mGy), which had been reconstructed using FBP (to avoid the effects of IR and a shortage of radiation dose), were used as a reference assessment and were given a score of four points. The reason for this was that we predicted the standard of the reference criteria would change during assessment. All images were displayed on a 3-megapixel monochrome liquid-crystal display (RadiForce GS 320TM; EIZO Co. Ltd, Ishikawa, Japan) with a workstation (DxMM; Medasys Japan, Tokyo, Japan). The observer study was performed at a maximum luminance of 450 cd m⁻². The illuminance environment was 30 lux, the same level as in the reading room of our hospital (Kyushu University Hospital).

Quantitative assessment

%GGO

We evaluated the activity of interstitial pneumonia using %GGO.^{17–19} This value was calculated using a three-dimensional image analysis system (SYNAPSE VINCENTTM; Fujifilm, Tokyo, Japan) in order to quantify the GGO. We calculated the mean %GGO of six images obtained from each scan. We did not

use manual adjustment when measuring %GGO, and we measured the value from the right lung only. Thus, other simulated lesions, such as those of reticular opacity or honeycombing, had no effect on the measurements.

CT value and contrast-to-noise ratios

We calculated the CT values and contrast-to-noise ratios (CNRs) of the mediastinal masses. Regions of interest (ROIs) were defined on the simulated mediastinal masses by one author (NS), who located identical ROIs for each measurement by copying and pasting. The CNR was calculated using the following equation:³

$$\text{CNR} = \frac{\text{CT}_m - \text{CT}_b}{\text{SD}_b}$$

CT_m and CT_b were the CT values of the ROIs placed on the simulated mediastinal masses and the normal mediastinum, respectively. SD_b was defined as the mean standard deviation (SD) of the CT values obtained from the six areas of soft tissue. CT_m, CT_b and SD_b were measured at the same axial level. With regard to mediastinal masses with a cystic component, CT_b was defined as the CT value of the ROI placed in the air, because there was no contrast between the mass and the normal mediastinum when using the chest phantom. We calculated the average of the values measured from six images obtained from each scan.

Statistical analysis

In this study, we could not assume the normal probability distribution for the data obtained. Furthermore, we were using paired data obtained from two groups, because the same chest phantom was scanned. Therefore, the Wilcoxon's signed-rank

test was used for statistical analysis. We had to choose the minimum CT scan times to minimize the effects of the greater heat unit of the X-ray tube that is caused by repeated CT scans. Additionally, the Wilcoxon signed-rank test requires six or more measurements in order to be able to evaluate whether significant differences exist between two groups at the 5% significance level. In the visual assessment, we compared the visual scores of FBP with those of hybrid IR obtained from six observers at each dose level. In the quantitative assessment, the measured values obtained from both FBP and hybrid IR, six repeated CT scans, were compared at each dose level. Differences with a p -value of <0.05 were considered statistically significant. Interobserver agreement in visual assessments was evaluated using weighted κ statistics (slight <0.21 , fair 0.21 – 0.40 , moderate 0.41 – 0.60 , substantial 0.61 – 0.80 , almost perfect 0.81 – 1.00). We calculated the κ values for pairs of readers and an average κ for all possible pairs, because our study used multiple observers.²⁰

RESULTS

Visual assessment

Regarding the reliability of interobserver agreement, the weighted κ values were 0.93, 0.92, 0.91 and 0.93 for emphysema with a 13-mm maximum diameter, emphysema with an 18-mm maximum diameter, reticular opacity and honeycombing, respectively. In order to compare FBP with hybrid IR, we averaged the visual scores of each simulated lesion, assessed by the six observers. The results of visual assessment are shown in Figure 3. There were no significant differences between FBP and

hybrid IR in any of the simulated lesions (emphysema, reticular opacity, honeycombing) at all dose levels. However, hybrid IR tended to degrade the visual score of every simulated lesion. By contrast, visual scores obtained using hybrid IR at our study's minimum-dose level (0.9 mGy) tended to be higher than those obtained using FBP.

%GGO

Figure 4 shows the results of the %GGO evaluation. The %GGO using both FBP and IR significantly increased as dose level decreased ($p < 0.05$). However, at low-dose levels, the elevation of %GGO obtained using hybrid IR was significantly suppressed compared with that obtained using FBP (0.9 and 1.1 mGy).

CT value and contrast-to-noise ratio

Figure 5 shows the CT values of mediastinal masses. At all dose-reduction levels (FBP, both standard and strong), the CT values of the mediastinal masses obtained using FBP were almost equivalent to those obtained using hybrid IR. This held true even at the lowest dose level ($p < 0.01$). Figure 6 shows the CNR distributions of the mediastinal masses. The CNR of the mediastinal masses obtained using IR was significantly higher than that obtained using FBP; on both the 64-helical and the 160-helical scans ($p < 0.05$).

DISCUSSION

Our study showed that hybrid IR tended to degrade visual scores for all simulated lesions when compared with FBP at middle to

Figure 3. Visual assessment of simulated lesions on 160-detector-row helical CT. Graphs showing the results of visual assessment of simulated emphysema (a), reticular opacity (b) and honeycombing (c). There were no significant differences between iterative reconstruction (IR) and filtered back projection (FBP) images with regard to visual scores, but IR tended to degrade the visual score of every simulated lesion. At the lowest dose level (0.9 mGy), visual scores tended to be higher when using IR than when using FBP. CTDI_{vol}, CT dose index volume; STD, iterative reconstruction with standard noise reduction level; STR, iterative reconstruction with strong noise reduction level.

Figure 4. Percentage value of ground-glass opacity relative to total lung (%GGO) by using 160-detector-row helical scan. The %GGO obtained using filtered back projection (FBP) at low-dose levels (0.9 and 1.4 mGy) was significantly higher. However, iterative reconstruction suppressed the elevation ($p < 0.05$). CTDI_{vol}, CT dose index volume; STD, iterative reconstruction with standard noise reduction level; STR, iterative reconstruction with strong noise reduction level.

high dose levels (3.2–12.9 mGy). We think that this tendency was caused by the difference between hybrid IR images and FBP images with regard to the modulation transfer function (MTF).

Figure 5. CT values of mediastinal masses with cystic, solid and fat components by using 64-detector-row helical CT. Graphs showing the results obtained from the images reconstructed by filtered back projection (FBP) (a), iterative reconstruction (IR) with a standard noise reduction level (b) and IR with a strong noise reduction level (c). The CT values of mediastinal masses calculated using FBP were almost equivalent to those calculated using IR. All three types of mediastinal mass were clearly separated by CT value in both image reconstruction types ($p < 0.01$). CTDI_{vol}, CT dose index volume.

The MTF of hybrid IR images has been reported to be lower than that of FBP images owing to the iteration of the smoothing procedure,²¹ and the degradation of MTF that may obscure thin linear structures. Hybrid IR tended to produce higher visual scores than FBP at the minimum-dose level (0.9 mGy) in our study. We speculated that the increase in quantum noise may have a greater adverse effect than decreased MTF at this level.^{22,23}

In our study, %GGO was significantly higher at low-dose levels when using FBP images than when using hybrid IR image ($p < 0.05$). In addition, the CNR of mediastinal masses obtained using hybrid IR images was significantly higher than that obtained using FBP ($p < 0.05$). We think this was a result of the IR-related reduction in quantum noise. The CT values of mediastinal masses obtained using FBP were almost equivalent to those obtained using hybrid IR, even at a minimum-dose level. This indicates that differential diagnosis based on the CT value of mediastinal masses is not affected by image reconstruction method or by radiation dose within the range used in our study (0.9–12.9 mGy). As for the geometry of the multidetector helical CT, both the 64- and 160-helical scans were performed to address the effect of cone angle on visual assessment and quantitative analyses in this study. Images obtained using both 64- and 160-helical scans showed similar results.

Our study has several limitations. Firstly, it was a phantom study. The sizes of the simulated lesions were limited, and this might affect the results of visual assessment. The CT value of the lung parenchyma of the chest phantom we used was

Figure 6. Contrast-to-noise ratio (CNR) of mediastinal masses with cystic, solid and fat components by using 64-detector-row helical CT. Graphs showing the CNRs of mediastinal masses with cystic (a), solid (b) and fat (c) components. The CNR of mediastinal masses was significantly higher when measured using iterative reconstruction than when using filtered back projection (FBP) ($p < 0.05$). CTDI_{vol}, CT dose index volume; STD, iterative reconstruction with standard noise reduction level; STR, iterative reconstruction with strong noise reduction level.

approximately -1000 HU, because it includes only air, whereas the CT value of human lung parenchyma is approximately -800 to -900 HU.²⁴ This implies that we may have overestimated visual assessments in our study, because the contrast between a lesion and air is higher than that between a lesion and normal lung parenchyma. Thus, we might not be able to directly apply our results to low-dose CT screening for lung cancer. Secondly, the visual assessment in our study did not focus on detectability, but rather on the confidence rating of the disease diagnosis. Thirdly, we did not assess images reconstructed using model-based iterative reconstruction (MBIR). Katsura *et al*²⁵ reported that the radiation dose of chest CT images can be reduced by approximately 80% with MBIR, while maintaining acceptable diagnostic standards. On the other hand, Richard *et al*²⁶ showed that the MTF of IR depends on the contrast and noise levels (tube current) in the image. Taken together, it is clear that there is

a need for validation studies investigating the diagnostic performance of low-dose MBIR images obtained using low-to-middle contrast materials. In spite of these limitations, our study is the first to compare the confidence ratings of emphysema, interstitial pneumonia and mediastinal mass diagnoses made using hybrid IR with those of the same diagnoses made using FBP.

In conclusion, hybrid IR is not recommended when using higher dose ranges (≥ 3.2 mGy), but may be recommendable when using lower dose ranges (≤ 1.4 mGy) as there is a higher GGO conspicuity within this range. On the basis of our results, we recommend using the lower dose range (≤ 1.4 mGy) and applying hybrid IR for low-dose CT screening of lung cancer. In this way, thoracic radiologists may become capable of analysing images and making a diagnosis using hybrid IR alone. This may reduce reading times and relieve stress on radiologists.

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