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Pulmonary nodule detection in chest CT using a deep learning-based reconstruction algorithm

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Short title

Nodule detection using DL reconstruction

Abstract

This study's aim was to assess whether deep learning image reconstruction (DLIR) techniques are non-inferior to ASIR-V for the clinical task of pulmonary nodule detection in chest CT. Up to 6 (range 3-6, mean 4.2) artificial lung nodules (diameter: 3, 5, 8 mm; density: -800, -630, +100 HU) were inserted at different locations in the Kyoto Kagaku Lungman phantom. In total, 16 configurations (10 abnormal, 6 normal) were scanned at 7.6 mGy, 3 mGy, 1.6 mGy and 0.38 mGy CTDIvol (respectively 0%, 60%, 80% and 95% dose reduction). Images were reconstructed using 50% ASIR-V and a deep learning-based algorithm with low (DL-L), medium (DL-M) and high (DL-H) strength. Four chest radiologists evaluated 256 series by locating and scoring nodules on a five-point scale. No statistically significant difference was found among the reconstruction algorithms ($p=0.987$, average across readers AUC: 0.555, 0.561, 0.557, 0.558 for ASIR-V, DL-L, DL-M, DL-H).

Attributes

Computed Tomography, Cancer, Diagnostic Radiology, Medical, Phantoms, Readers

INTRODUCTION

A pulmonary nodule is a rounded opacity in the lung, well or poorly defined, measuring up to 3 cm in diameter ¹. The differential diagnosis of pulmonary nodules is broad, including benign and malignant etiologies. Identification of these nodules that might present early lung cancers is important since stage at diagnosis is crucial for prognosis ². Size, growth and morphology are key factors in assessing the malignant potential of a nodule ^{3,4}. Subsequent the widespread use of MDCT, small pulmonary nodules are more frequently detected. Furthermore, there is a growing interest in lung cancer screening (LCS) since large randomized controlled trials have shown that lung cancer screening with low-dose CT (LDCT) in high-risk participants can reduce lung cancer-specific mortality. The National Lung Screening Trial (NLST) showed a 20% lung cancer specific mortality reduction in participants who were screened with LDCT, compared to the control group which was screened with chest radiography ⁵. Final data of the randomized Dutch-Belgian NELSON (Nederlands-Leuvens Longkanker Screenings Onderzoek) LCS trial, recently showed a lung cancer mortality reduction of 24% in men and 33% in women at 10-year follow-up ⁶. A 39% reduction of lung cancer mortality after 10 years of screening was found in the Italian MILD (Multicentric Italian Lung Detection) Trial ⁷. The German LUSI (Lung Cancer Screening Intervention) Trial found a non-significant lung cancer-specific mortality reduction of 6% in men, but a significant reduction in lung cancer-specific mortality of 69% in women after an average of 8.8 years of follow-up ⁸. Recently, the European Respiratory Society and European Society of Radiology published a statement paper on LCS, calling to convince policymakers across the European Union to start implementation of high-quality LCS programs ^{9,10}.

In an effective screening program for an asymptomatic population, the potential benefits must outweigh harmful effects. One of the potential harms of LCS is the use of radiation ¹¹. LDCT should allow identification of pulmonary nodules using as low a radiation dose as can reasonably be achieved (ALARA). This is possible using lower tube currents (mA) and lower tube voltages (kVp). The NLST decreased radiation dose through lowering tube current⁵.

Unfortunately, image noise is proportionally increased by decreasing the radiation dose. Iterative reconstruction (IR) techniques have been developed to reduce noise associated with dose reduction and subsequently to improve image quality. When compared to the filtered back projection images however, the look and feel of these iterative reconstruction images is very different^{12,13}. Radiologists experience these IR-images as more 'plastic-looking' and might feel less confident with their diagnosis¹⁴. This might impact the utilization of LDCT protocols.

Recently, deep learning image reconstruction (DLIR) methods have been proposed¹⁵. These new reconstruction techniques open a new era for CT-image reconstruction by addressing challenges of FBP and IR. DLIR features a deep neural network (DNN), which was trained with high quality FBP datasets to learn how to differentiate noise from signals, and to intelligently suppress the noise without impacting anatomical and pathological structures. The purpose of this study was to assess whether detection of pulmonary nodules on low-dose CT with DLIR is non-inferior to detection on low-dose CT with IR techniques, at comparable or even lower dose levels than IR reconstructions.

MATERIALS AND METHODS

Phantom selection and preparation

The Multipurpose Chest Phantom N1 "LUNGMAN" (Kyoto Kagaku) was used for our experiments. The phantom (Figure 1) is made of polyurethane and is composed of a male chest torso, in which synthetic bones (epoxy resins) are embedded, plus four internal parts: mediastinum (heart, trachea), pulmonary vessels and bronchial branches (right and left) and abdomen (diaphragm). Two 30mm fat slabs were added to the phantom, to represent a torso of an 82kg and 168cm male (body-mass index of 29). A senior chest radiologist, who was not involved in the observer performance experiment, laced up the phantom with simulated lesions having 3 varieties of Hounsfield Unit (HU) number (approx. -800, -630, +100) and available in 3 sizes for each type (diameters 3, 5, 8 mm), shown in Figure 1. These HU cover the spectrum of both solid and ground glass lung nodules: the -800 and -630 HU densities represent nonsolid nodules (type pure ground glass) in clinical practice. The nodule with density of +100 HU represents a solid nodule. Out of these 9 sphere-shaped lesions, 16 different configurations were identified to lace up the phantom: ten consisted of up to 6 (range 3-6) nodules placed in the pulmonary vasculature in a random order, and an additional 6 were without nodules (Table 1).

Image acquisition and reconstructions

The laced-up phantom with the different configurations was imaged using a 256-slice Revolution CT (GE Healthcare) and our clinical chest protocol (120 kVp; 7.6 mGy CTDI_{vol}), with the midline of the phantom positioned at isocenter. Three (3) additional dose levels were acquired: 3 mGy, 1.6 mGy and 0.4 mGy CTDI_{vol}, resulting in 60%, 80% and 95% dose reduction respectively, to possibly represent low-dose chest CT. Other scanning parameters included: rotation time, 350ms; collimation, 40mm and pitch, 0.98.

Consecutive slices of 1.25mm were reconstructed with a STANDARD kernel using iterative reconstruction (ASIR-V) at 50% blending, which is the clinical standard in our hospital. In addition, images were reconstructed using a DL-based algorithm (TrueFidelity) with low (L), medium (M) and high (H) strength¹⁵. L, M, H, are three selectable reconstruction modes that correspond on how the image noise is modeled. While of radiologist preference, for high contrast tissue (e.g. enhanced scans with increased iodine uptake on relatively large areas) a more aggressive noise reduction provided by DL-H has been observed to be of preference, for density difference, (e.g. low contrast detectability) medium to low are generally used in clinical practice. This DLIR algorithm, build upon knowledge of the CT system design, is embedded within a Deep Neural Network (DNN). The DNN is trained by feeding a low-dose sinogram through network and

comparing the output image to a ground truth image – a high dose version of the same data; millions of parameters representing the DNN are fine-tuned through embedded backpropagation based on those differences. The comparison occurs over multiple parameters such as image noise, low contrast resolution, low contrast detectability, noise texture, etc. This process is repeated until the DLIR is able to generate ground truth equivalent high-quality CT images, from an input sinogram that is acquired with low radiation dose. TrueFidelity was first introduced in our department through this study so that no preferred strength existed. In total 256 CT series were generated (16 nodule configurations, 4 dose levels, 4 reconstruction algorithms). The series were randomized and blinded for dose and reconstruction parameters.

Observer performance experiment

The observer performance experiment used the freeresponse paradigm¹⁶. Four radiologists (3 to 12 years of experience in chest imaging), were asked to detect and locate the perceived nodules. The observers were told that each image could contain zero or more nodules. A five points rating scale was used: 1=highly unlikely to be a nodule, 2=unlikely to be a nodule, 3=somewhat confident it is a nodule, 4=moderately confident it is a nodule, and 5=very confident it is a nodule. A clinically reportable lesion would be assigned at a score ≥ 3 . By clicking on the lesion, the location of the cursor (x, y, z) was stored and exported at the end of each reading session. Next, the location was compared with the ground truth coordinates of the nodules in that specific Lungman configuration, as previously defined by an experienced radiologist who did not participate in the reading sessions.

Images were presented on a clinical PACS environment using a 30 inch, 4 MP high-contrast color monitor (Barco MDCC-4430) at optimal lighting conditions, according to the AAPM TG18 report¹⁷. A training session (25 images) preceded the evaluation in order to familiarize the radiologists with the user interface and the processing algorithms. The reading sessions were performed according to each user's availability, but each session would not last more than 2h in order to reduce fatigue effects on the results. Within each session, images processed with each of the four algorithms were presented randomly.

Statistical analysis

The primary analysis of the free-response data obtained from this multiple-reader multiple-case (MRMC) study was JAFROC, using version JAFROC1_V1 available from <http://www.devchakraborty.com>. Prior to analysis, each mark had to be classified as a lesion localization (LL) or non-lesion localization (NL), by using the ground truth file generated as described earlier. Specifically, if the observer clicked anywhere within a range of 1.5 times the nodule radius, measured from the center of the nodule, the case was considered a LL, outside this acceptance radius, each case was considered a NL. The size of the acceptance radius was therefore nodule dependent.

Data analysis consists of estimating the JAFROC figure of merit (FoM) and a method for testing the statistical significance of differences in figures of merit between image processing algorithms. The JAFROC FoM is defined as the probability that a lesion is rated higher than all non-lesions on normal images and the significance testing is performed using the ANOVA procedure. The presented analysis treats both readers and cases as random samples, such that results apply to the reader and case populations. Figures of merit, F-statistics, degrees of freedom, p-values, and 95% confidence intervals are reported¹⁶.

RESULTS

The overall results of JAFROC analyses are summarized in Table 2 which lists the F-statistics, the numbers of degrees of freedom (numerator/denominator) and the p-value. A p-value less than 0.05 means that the differences in Figures of Merit (FoMs) between at least two image reconstruction algorithms pairings are statistically significant. JAFROC yielded $F=0.05$, $p=0.987$. No statistically significant difference was found among the four reconstruction algorithms.

Table 3 reports the FoMs for JAFROC for each algorithm; listed are values for each reader and the average of all the readers (last row). The DL algorithms yielded a slightly higher figure of merit than the ASIR-V 50% but the difference was not significant.

Table 4 reports the differences in figures of merit between all modality pairings as well as the 95% confidence intervals for these differences. If a confidence interval does not include zero, the corresponding difference is statistically significant, which was never the case for our data. Corrections for multiple comparisons are automatically considered in the ANOVA analysis.

DISCUSSION

With the increased use of CT and advent of large LCS trials, low-dose imaging of the lungs and implementation of LDCT protocols in clinical practice has gained interest. Dose reduction is especially important in screening, since it is applied to a large number of participants, who are also asymptomatic. Regarding methods to reduce dose, the performance of IR methods in terms of noise and dose reduction has been extensively researched^{14,18,19}. Although dose savings ranging from 30% to 80% are reported in literature^{14,19}, IR methods are often described as having an overly smooth or synthetic noise impression. The low frequency noise texture typically associated with IR techniques has shown to be a clinical limitation for some imaging tasks²⁰. Indeed, it is known in literature that, despite a significant noise reduction compared to FBP methods, a frequency shift in the noise power spectrum (NPS) is present for iterative reconstruction algorithms^{21–23}. Recently, deep learning image reconstruction (DLIR) methods have been proposed¹⁵. These new reconstruction techniques allow reduction of radiation dose, while preserving the image quality of the FBP technique. Several studies reported similar noise texture in DL and FBP reconstructions, based on the comparison of noise power spectra in physical-technical phantoms^{24–26}. Little or no research on the impact of low-dose DL reconstructions on clinical tasks can be found in literature^{27,28}. To our knowledge, our work represents the first pulmonary nodule detection study on DL reconstructed images (TrueFidelity) of low-dose chest CT.

The aim of this study was to assess whether detection of pulmonary nodules of different densities, on low-dose CT with DLIR is non-inferior to detection on low-dose CT with IR techniques, at comparable or even lower dose levels than IR reconstructions.

Our results show an excellent interobserver agreement in nodule detection in terms of JAFROC figure of merit between all four radiologists (Table 3). DL algorithms yielded a slightly higher figure of merit than ASIR-V 50%, yet differences were not significant. A possible explanation could be the considered clinical task of searching for several artificial nodules which are not fully representative of the typical clinical scenario. The absolute difference in HU between the lesions and the background (air: -1000 HU) was 200, 370 and 1100 HU, for the low, medium and high density nodules respectively. Therefore, detection of pulmonary nodules is considered a high-contrast task. It is shown in literature that DL algorithms generally maintain intermediate- and high-contrast spatial resolution performances compared with FBP and ASIR-V 50% at all doses levels^{24,26}. Greffier et al reported higher 50% task-based transfer function values (TTF_{50%}) with DL than with IR from 15 to 2.5 mGy and the opposite from 1 to 0.5 mGy²⁵. Our research shows no significant difference in pulmonary nodule detection between DL and IR reconstruction techniques.

This study has some limitations. (1) Our research was conducted on a phantom with simulated nodules. These nodules are too uniform and spherical. Furthermore, our phantom study included nodules with different densities simulating solid and ground glass morphology, but it did not include subsolid nodules with part-solid morphology. Part of the phantom is composed by pulmonary vasculature and bronchial branching to simulate normal lung architecture, but the low density of the surrounding air is still different from that of normal lung tissue. (2) We focused on the impact of DLIR on visual detection of pulmonary nodules by radiologists. Regardless of the impact of dose, this task is prone to errors related to search, recognition and decision. We aimed to overcome this by including four independent readers. It is without doubt that AI-algorithms will play an important role in lung cancer screening, including computer-aided detection. The impact of DLIR on computer-aided detection needs to be unraveled. (3) This study investigated only the first step in the diagnostic algorithm of pulmonary nodules in chest CT, being detection of lung nodules. The impact of DLIR on nodule characterization, volumetric assessment and nodule morphology still needs to be investigated.

CONCLUSIONS

In conclusion, current study shows that TrueFidelity is non-inferior to ASIR-V for the clinical task of nodule detection in chest CT, even at very low dose levels.

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FIGURE LEGENDS

Figure 1. (left) internal structure of Kyoto Kagaku Lungman phantom showing the pulmonary vessels and (right) a selection of 9 round, solid nodules used to mimic pulmonary lesions.

Table 1. Different configurations (16) of nodule placement in Lungman phantom.

Configuration	Number of lesions	Lesions*						
A	4	M 8mm	H 8mm	H 5mm	M 5mm			
B	5	L 3mm	H 8mm	M 3mm	H 3mm	M 8mm		
C	3	L 5mm	H 8mm	H 3mm				
D	3	H 5mm	L 8mm	L 5mm				
E	6	L 8mm	L 5mm	L 3mm	H 3mm	H 5mm	M 8mm	
F	3	M 3mm	L 5mm	H 5mm				
G	4	M 3mm	L 5mm	H 8mm	L 3mm			
H	6	M 5mm	L 8mm	H 3mm	L 5mm	L 3mm	H 5mm	
I	5	H 3mm	L 8mm	M 3mm	M 8mm	H 8mm		
J	3	M 8mm	L 5mm	M 5mm				
K-P	0							

*L (low density, -800 HU); M (medium density, -630 HU); H (high density, +100 HU)

Table 2. F-statistics (numerator, denominator, degrees of freedom) and p-values calculated for JAFROC statistical analysis.

Statistical Analysis	F-statistics (degrees of freedom, numerator/denominator)	p-value
JAFROC	0.05 (3/61.9)	0.987

Table 3. JAFROC figures of merit (FoMs) for the detection of lung nodules on chest images processed with each of the investigated image reconstruction algorithms. The FoMs are reported for individual readers and for the average across readers.

Observer	Reconstruction algorithm			
	ASIR-V 50%	DL-L	DL-M	DL-H
1	0.557	0.560	0.560	0.558
2	0.548	0.558	0.557	0.557
3	0.568	0.576	0.562	0.570
4	0.550	0.553	0.552	0.547
Average	0.556	0.561	0.558	0.558

Table 4. Difference in figure of merit between all modality pairings with 95% confidence intervals.

Reconstruction algorithms	Difference in mean FoM	95% CI of the difference in FoM
ASIR-V vs DL-L	-0.00535	[-0.03417, 0.02348]
ASIR-V vs DL-M	-0.00205	[-0.03088, 0.02678]
ASIR-V vs DL-H	-0.00219	[-0.03088, 0.02678]
DL-L vs DL-M	0.00330	[-0.02553, 0.03213]
DL-L vs DL-H	0.00315	[-0.02567, 0.03198]
DL-M vs DL-H	-0.00015	[-0.02897, 0.02868]